IMMUNO-MEDIATED DISEASES OF THE GI TRACT: WHERE DO WE STAND?

November, 8-9, 2024

Symposium 238

FLORENCE, ITALY



12 CME CREDITS

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12 CME CREDITS

12 credit hours (CME) have been awarded by the European Union of Medical Specialists (UEMS).

PREFACE

Dear colleagues and friends,

it is our privilege and honor to welcome you cordially to the Symposium "Immuno-Mediated Diseases of the GI Tract: Where Do We Stand?" in Florence (Italy).

While the prevalence of immuno-mediated diseases of the gastrointestinal tract increases, relevant progress in the field of celiac disease, eosinophilic esophagitis, inflammatory bowel disease and microscopic colitis has been observed. In order to learn from each other, to discuss the novel insights in gastrointestinal immunopathology, as well as diagnosis and therapeutic approaches while fostering interaction, we designed this cross-diseases symposium.

The program aims to mix lectures and knowledge in an attempt to learn from outstanding experts in the field of immuno-mediated diseases of the gastrointestinal tract. We will discuss novel pathways in pathophysiology, the role of the microbiome and exposome, current management algorithms, and new treatment options that might be relevant for clinical practice not only for a specific condition. Moreover, we will discuss current dietary approaches for these disorders, given the primary role of diet in today's practice.

We look forward to meeting you in the wonderful city of Florence for this exciting symposium, with the opportunity to learn, but also to meet with friends and colleagues from Europe and all over the world.

Flavio Caprioli, Nicola de Bortoli, Axel Dignass, Iris Dotan,
Edoardo V. Savarino

IMMUNO-MEDIATED DISEASES OF THE GI TRACT: WHERE DO WE STAND?

November 8-9, 2024

Scientific Organization:
Flavio Caprioli, Milan
Nicola de Bortoli, Pisa
Axel Dignass, Frankfurt
Iris Dotan, Petah Tikva
Edoardo V. Savarino, Padua

Congress Venue:
Palazzo dei Congressi
Piazza Adua 1
50123 Florence
Italy

For admission to scientific events your name badge should be clearly visible. Accompanying persons are not permitted during the conference at any time.

Start of Registration:
Thursday, November 7, 2024
16:00-20:00 h
at the congress office

Friday, November 8, 2024

9:00 Welcome and opening remarks
Edoardo V. Savarino, Padua

9:10 **State of the Art Lecture:** Examining complex biological systems: Holistic vs reductionistic approaches. Benefits and drawbacks
Matthieu Allez, Paris

SESSION I

Epidemiology of chronic gastrointestinal disorders: Road to 2030

Chairs: *Nicola de Bortoli, Pisa; Tine Jess, Copenhagen*

9:30 Epidemiologic burden and projections for eosinophilic esophagitis
Christopher Ma, Calgary

9:50 Celiac disease epidemiology: Population screening or case finding strategy
David S. Sanders, Sheffield

10:10 Update on the molecular epidemiology of IBD
Tine Jess, Copenhagen

10:30 Microscopic colitis: New results of the prospective European MC registry
Andreas Münch, Linköping

10:50 **Coffee break with poster session**

SESSION II

Pathophysiology of immune mediated gastrointestinal disorders – lessons for clinicians

Chairs: *Federica Facciotti, Milan; Federica Ungaro, Milan*

11:20 Mechanisms of Type 2 immunity in eosinophilic esophagitis
Marc E. Rothenberg, Cincinnati

Friday, November 8, 2024

11:40	Interaction between gluten and immune system in celiac disease *Detlef Schuppan, Mainz*
12:00	Interplay between epithelium and the mucosal immune system in inflammatory bowel diseases *Britta Siegmund, Berlin*
12:20	Microscopic colitis: Immunological insights *Celia Escudero-Hernández, Kiel*
12:40	**Lunch with poster session**

SESSION III

Current therapeutic and monitoring algorithms: Practical guidelines for clinicians

Chairs: *Flavio Caprioli, Milan, Axel Dignass, Frankfurt*

14:00	Monitoring patients with eosinophilic esophagitis in routine clinical practice *Glenn Furuta, Aurora*
14:20	Monitoring celiac disease activity and gluten free diet adherence *Luca Elli, Milan*
14:40	TANDEM: Inflammatory bowel disease: PROs, biomarkers, endoscopy, ultrasonography or all? *Alessandro Armuzzi, Milan; Hagar Banai-Eran, Petah Tikva*
15:10	Microscopic colitis: Impact of cohort studies on monitoring and therapeutic algorithms *Hamed Khalili, Danvers*
15:30	**Coffee break with poster session**

Friday, November 8, 2024

SESSION IV

Current therapeutic strategies in different settings of IBD

Chairs: *Axel Dignass, Frankfurt; Jürgen Schölmerich, Hofheim*

16:00	Inflammatory bowel disease and primary sclerosing cholangitis: One disease or two? *Nora Cazzagon, Padua*
16:20	Ulcerative proctitis – just UC or a different to treat entity? *Ferdinando D'Amico, Milan*
16:40	TANDEM: Management of stricturing Crohn's disease *Willem A. Bemelman, Amsterdam; Charlotte Hedin, Solna*
17:10	Cutaneous manifestations in IBD: How to manage *Pascal Juillerat, Bern/Fribourg*

Saturday, November 9, 2024

8:30 Welcome
Edoardo V. Savarino, Padua

SESSION V

Future therapeutic strategies in immune mediated gastrointestinal disorders

Chairs: *Iris Dotan, Petah Tikva; Edoardo V. Savarino, Padua*

8:40 TANDEM: Eosinophilic esophagitis therapy: Topical steroids or biologics?
Luc Biedermann, Zurich; Arjan Bredenoord, Amsterdam

9:10 Drug based therapies for celiac disease
Michael Schumann, Berlin

9:30 IBD treatments: what is new and in your clinic next years?
Silvio Danese, Milan

9:50 Treatment of MC patients with budesonide-failure
Andreas Münch, Linköping

10:10 **Coffee break with poster session**

SESSION VI

Disease-specific nutrition, current algorithm and future trends

Chairs: *Paolo Lionetti, Florence; Ulrike von Arnim, Magdeburg*

10:40 TANDEM Eosinophilic esophagitis: To diet or not to diet, that's the question?
Nirmala Gonsalves, Chicago; Alfredo Lucendo, Tomelloso

11:10 Qualitative aspects of a mediterranean gluten free diet in celiac disease
Nick Trott, Sheffield

Saturday, November 9, 2024

11:30	TANDEM: Do diets provide a feasible and effective personalized treatment approach in IBD? *Rotem Sigall-Boneh, Tel Aviv; Julie van der Stappen, Leuven*
12:00	Presentation of poster awards *Flavio Caprioli, Milan; Nicola de Bortoli, Pisa*
12:20	**Lunch with poster session**

SESSION VII

Managing chronic gastrointestinal inflammation in special populations

Chairs: *Carolina Ciacci, Baronissi; Tamás Molnar, Szeged*

13:20	TANDEM: Eosinophilic esophagitis with other type 2 disorders: What clinicians should know for improving management and treatment *Seema S. Aceves, San Diego; Alain Schoepfer, Lausanne*
13:50	Diagnosing and monitoring celiac disease in elderly patients *Fabiana Zingone, Padua*
14:10	Chronic pouchitis and refractory pouchitis: How to deal with them? *Paolo Gionchetti, Bologna*
14:30	Acute severe colitis: New possibilities *David Laharie, Bordeaux*
14:50	**Coffee break with poster session**

Saturday, November 9, 2024

SESSION VIII

What have we learned from patients?

Chairs: *Hagar Banai-Eran, Petah Tikva; Massimo C. Fantini, Monserrato*

15:20	Celiac disease: What do the patients want? *Carolina Ciacci, Baronissi*
15:40	Eosinophilic esophagitis: Are patients' needs satisfied? *Evan S. Dellon, Chapel Hill*
16:00	TANDEM: Discrepancy between treatment goals of physicians and patients in IBD *Fernando J. Magro, Porto; Ciara Drohan, Brussels*
16:30	Microscopic colitis: Creating the European MC activity index (PROM) - what have we learned from patients? *Katarina Pihl-Lesnovska, Linköping*
16:50	Closing words *Edoardo V. Savarino, Padua*

LIST OF SPEAKERS, MODERATORS AND SCIENTIFIC ORGANIZERS

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REGISTRATION

You can register for the event via our homepage:
www.falkfoundation.org
Registration is only possible online.

CONGRESS FEES

Scientific Program of Symposium 238	EUR 300
Students (copy of student ID required)	EUR 150

The congress fees include:

- Pre-Opening and Welcome on Thursday, November 7, 2024
- Refreshments during coffee breaks
- Lunch on Friday and Saturday, November 8-9, 2024
- A copy of the final program

CONGRESS OFFICE AND REGISTRATION

Opening Hours:

Thursday, November 7, 2024	16:00 – 20:00 h
Friday, November 8, 2024	08:00 – 17:30 h
Saturday, November 9, 2024	08:00 – 17:00 h

The Falk Foundation will take pictures during the meeting. Additionally, parts of the meeting might be recorded. By participating all attendees consent and agree with the recording and the photo shoots.

ARRIVAL

Palazzo dei Congressi
Piazza Adua 1
50123 Florence
Italy

By plane

The International Airport (FLR) is only 4 km away from the Florence city centre, and Line T2 of the tramway connects it to the main Santa Maria Novella railway station in 20 minutes.

The Galileo Galilei International Airport in Pisa (PSA) is only one hour away from the Florence city centre and is connected to the Tuscan capital with trains departing every hour.

By train

The Palazzo dei Congressi is located just a few steps away from the main Santa Maria Novella railway station.

By Tram

Line T1 and Line T2 of the tramway are connected to the main Santa Maria Novella railway station which is next to Palazzo dei Congressi.

By car

Via the A1 motorway it only takes 20 minutes to reach the Palazzo dei Congressi, taking either the Firenze Nord or Firenze Sud exit.

You can also leave your car right next to the motorway at the Villa Constanza parking lot and take the streetcar (Drive & Tramway) to the Palazzo dei Congressi.“

CONFLICTS OF INTEREST

The members of the scientific committe declare the following potential conflicts of interest:

Flavio Caprioli: Giuliani, Sofar, MSD, Takeda, Abbvie, Celltrion, Pfizer, Jannsen, Roche, Celgene, Bristol-Meyer Squibb, Galapgos, Gllead, Munidpharma, Eli-Lilly, Biogen, Ferring, Nestlè, Lionhealth, Allergy Therapeutics, Sandoz, Tillotts Pharma

Nicola de Bortoli: Dr Falk Pharma, Sanofi-Genzyme, Malesci, PharmaLine, AlfaSigma, Rechitt-Benckiser, Sofar

Axel Dignass: Materia Prima, Galapagos, BMS, Takeda, Janssen, Amgen, Sandoz, Celltrion, Streamed-Up, MedToday, Biogen, Thieme, Fresenius Kabi, Pharmacosmos, Novartis, Gilead, Arena, Lilly, Abivax, Abbvie, Vifor, High5MD, Pfizer, Tillotts, Roche/Genentech, Dr. Falk Pharma

Iris Dotan: Altman, BMS, Helmsley Charitable Trust, Abbott, Abbvie, Arena, Cambridge Healthcare, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Roche/Genentech, Integra Holdings, Iterative Scopes, Janssen, Materia Prima, Pfizer, Prometheus, Sangamo Sublimity, Takeda, Dr. Falk Pharma

Edoardo V. Savarino: Bonollo, Difass, Pfizer, Reckitt Benckiser, SILA, Sofar, Unifarco, Zeta Farmaceutici, Abbvie, Abivax, Agave, AGPharma, Alfasigma, CaDiGroup, Dr. Falk Pharma, EG Stada Group, Fenix Pharma, Galapagos, Johnson&Johnson, JB Pharmaceuticals, Innovamedica/ Adacyte, Eli-Lilly, Maesci, Mayoly Biohealth, Omega Pharma, Pfizer, Sandoz, Takeda, Tillots, Unifarco

POSTER ABSTRACTS

1. Development of an algorithm to identify the best donor-recipient match for FMT in IBD patients based on immune system/microbiota interactions
   C. Amoroso, F. Strati, B. Caridi, F. Perillo, D. Noviello, M. Vecchi, F. Caprioli, F. Facciotti (Milan, IT)
2. Cancer development and recurrence in IBD patient receiving biologic therapy
   D. Arna, A. Theodoropoulou, A. Psistakis, I. Psaroudakis, K. Karmiris, G. Paspatis (Heraklion, GR)
3. Active inflammatory bowel disease and its impact on the quality of life
   C. Aulinei, C. Ciobanu, A. Barna, O. Nedelciuc, M. Dranga, C. Cijevschi-Prelipcean (Iasi, RO)
4. Long-term maintenance therapy for eosinophilic esophagitis: A systematic review and meta-analysis of observational studies and randomized controlled trials
   A. Barchi, L. Massimino, F. Mandarino, M. Yacoub, L. Albarello, E. Savarino, F. Ungaro, S. Danese, S. Passaretti, E. Vespa (Milan, Padua, IT)
5. Colectomy in microscopic colitis: A rare indication
   D. Bergman, A. Forss, J. Sun, F. Ebrahimi, J. Ludvigsson (Solna, SE)
6. Evaluation of acute terminal ileitis in hospitalized patients: Development of a predictive model to distinguish Crohn's disease from other etiologies
   A. Bermont, R. Aminov, D. Cohen, H. Shirin (Beer Yaakov, IL)
7. Efficacy of orodispersible budesonide in eosinophilic esophagitis: A comprehensive analysis of clinical, endoscopic, and histological outcomes
   L. Bertin, D. Maniero, T. Rigoni, F. Zingone, B. Barberio, E. Savarino (Padua, IT)
8. The impact of inflammation activity and therapy on mucosal mature CD83+ dendritic cell in ulcerative colitis
   A. Bratanic, B. Rosic Despalatovic, M. Babic, A. Tonkic, Z. Ardalic (Split, HR)
9. Persistent dysphagia in stricture-free eosinophilic esophagitis in histological remission: Effectiveness of empirical esophageal dilation
   L. Cini, B. Marinoni, G. Aldinio, N. Siragusa, M. Vecchi, M. Coletta, R. Penagini (Milan, IT)
10. The prevalence of cardiovascular and hepatic risk in eosinophilic esophagitis patients
    C. Deliu, O. Chirea, V. Popescu, A. Genunche, D. Neagoe (Bals, Craiova, RO)
11. The ADEII project: A microlearning programme for patients with inflammatory bowel disease increased adherence and improved understanding of disease
    L. De Castro Parga, L. Sanroman Alvarez, V. Hernandez Ramirez, J. Martinez Cadilla, I. Rodriguez Prada (Vigo, ES)
12. Prevalence of clinical characteristics and eosinophilic esophagitis in elderly patients
    C. Deliu, V. Popescu, O. Chirea, D. Neagoe, A. Genunche (Bals, Craiova, RO)
13. Selective deficiency of memory marginal zone B lymphocytes in patients with uncomplicated celiac disease
    L. Douda, I. Tacheci, D. Vokurkova (Hradec Kralove, CZ)
14. Liver transplantation for primary sclerosing cholangitis, association with IBD – Analysis of the Slovak transplant registry
    S. Drazilova, J. Gazda, S. Adamcova-Selcanova, L. Skladany (Kosice, Banska Bystrica, SK)

15. First-in-human trial of IMU-856, an orally available regulator of barrier function and regeneration for the treatment of celiac disease
S. Elhag, M. Wirth, F. Burianek, J. Mihajlovic, D. Proebst, E. Peelen, J. Fonseca, I. Kehler, A. Schreieck, D. Vitt, H. Kohlhof, A. Muehle (Gräfelfing, DE)

16. Particularities of inflammatory bowel diseases in elderly patients
H. Elloumi, I. Cheikh (Bizerte, TN)

17. Oral immunotherapy-associated eosinophilic esophagitis
N. Epstein-Rigbi, A. Elizur, M. Levy, L. Nachshon, Y. Koren, T. Shalem, E. Broide (Beer Yaakov, IL)

18. Diabetes mellitus in patients with autoimmune hepatitis (AIH): An independent adverse prognostic factor
S. Flatley, A. Dube, B. Hoeroldt, L. Harrison, S. Dixon, D. Gleeson (Sheffield, GB)

19. Exploring the novel calcineurin inhibitor voclosporin in a colitis model: Is this a novel therapy for IBD?
M. Gabel (Erlangen, DE)

20. Ensemble bioinformatics approach for ustekinumab therapeutic response prediction models in ulcerative colitis
M. Gazouli, K. Koustenis, N. Dovrolis, N. Viazis, A. Ioannou, G. Bamias, G. Karamanolis (Athens, GR)

21. Biodegradable stents at ERCP – A pilot study
B. George (Maidstone, GB)

22. Analysis of the functional role of mast cells: Bridging the gap between the development of colitis and colitis-associated cancer (CAC)
K. Gerlach, B. Weigmann (Erlangen, DE)

23. The effects of gluten-free diet on body mass indexes in adults with celiac disease: A systematic review and meta-analysis of observational studies
R. Gingold-Belfer, Y. Niv, N. Peleg (Petah Tikva, Tel Aviv, IL)

24. Safety of LMWH for the prevention of venous thromboembolism in patients with severe ulcerative colitis
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1. Development of an algorithm to identify the best donor-recipient match for FMT in IBD patients based on immune system/microbiota interactions

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Introduction: IBD are characterized by uncontrolled immune responses, in genetically predisposed individuals, to the dysbiotic microbiota. Its modulation has thus emerged as a potential therapeutic strategy. Fecal microbiota transplantation (FMT) showed encouraging results for the treatment of mild-to-moderate ulcerative colitis (UC) patients. However, currently the success rate of FMT in UC patients is around 30%, and there are no criteria to predict it.

We hypothesized that the immune system-microbiota interaction can dictate which graft will be accepted or rejected.

Thus, we generated an algorithm to identify the best donor-recipient match for FMT treatment in IBD patients based on the functional interaction of recipient's immune system with possible donors' microbiota.

Methods: Mucosal and circulating immune cells isolated from 16 active IBD patients, potentially eligible for FMT, were exposed to the microbiota of a panel of 8 potential healthy FM donors collected in the FM biobank of the Policlinico Hospital, Milan. The functional profile of recipients' immune cells before and after the in vitro exposure to the possible donors' microbiota was assessed by cytokine production, gene expression profiling and activatory or inhibitory surface molecules modulation on T cells. Sequencing of the microbiota of each individual FM donor was performed by 16S and shotgun metagenomics. These functional data were used to develop an algorithm to identify the best donor-recipient match based on the capability of individual donors' microbial ecologies to simultaneously reduce the inflammatory functional profile and increase the tolerogenic functional profile of the recipient's immune cells.

Results: We demonstrated that mucosal immune cells from IBD recipients exhibited a variety of responses upon exposure to the microbiota from distinct healthy donors, which clusters in two different enterotypes. Each recipient exhibited specific preferences for one or more FM donor in the reduction of the inflammatory profile of immune cells and concomitantly enhancement of anti-inflammatory cytokines. On the basis of these data we generated an algorithm capable of predicting the most successful functional interaction between donors and recipients.

Discussion/Conclusion: Our study suggests that specific functional characteristics of both the donor microbiota and the recipient's immune system should be considered when selecting an optimal donor-recipient match for FMT. This study contributes to the development of a screening tool for donor selection in FMT, enabling personalized and effective therapeutic interventions for IBD patients.

2. Cancer development and recurrence in IBD patient receiving biologic therapy

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Introduction: Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), often requires biologic therapy for effective management. Nevertheless, concerns have been raised regarding an increased risk of cancer related to their use. The purpose of this study was to record IBD patients who developed cancer while on biological therapy.

Methods: A retrospective study was conducted at Venizeleio Hospital of Heraklion, covering data from 2005–2023. We collected information on patient demographics, disease characteristics, treatment, and cancer details.

Results: Among 563 IBD patients on biologics, 29 (5.6%) developed cancer. Of these, 71% had CD, 32% were male, 56% were smokers, with a mean age of 39 (3 12.6) years and disease duration of 16.5 (3 8.8) years. Patients were treated with anti-TNF (24), anti-integrin (4), anti-interleukin 12/23 (1), and combination therapy (7).

Cancer types included hematologic (3), gastrointestinal (6), gynecologic (4), breast (2), prostate (2), thyroid (6), laryngeal (1), pancreatic (2), kidney (1), lung (1), and skin (1). Cancer was diagnosed in 12 patients before and 17 after initiating biologics, with 15 discontinuing therapy. The mean duration of biologics before cancer was 5.13 years. Seven patients restarted biologics. In total, biologics were resumed in 19 patients after cancer diagnosis with a mean lag time of 2.25 (3 1.6) years. The mean follow-up period after cancer diagnosis for 21 patients who resumed or continued biological therapy was 11.29 years (range, 2–31 years). Cancer recurrence was observed in one patient.

Discussion/Conclusion: 5.6% of IBD patients on biologics developed cancer, with three-quarters continuing therapy. Cancer recurrence was observed in a minority of 7% of patients who were closely followed up for a long time, although the number of cases is too small to draw reliable conclusions.

3. Active inflammatory bowel disease and its impact on the quality of life

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Introduction: Inflammatory bowel disease (IBD) it is characterized by the chronic inflammation of the gastrointestinal gut caused by the dysregulated immune response to a dysbiosis in host intestinal microflora, among genetic factors and permeability defects. IBD is divided in Crohn's disease (CD) and ulcerative colitis (UC). The most common symptoms related to IBD are diffuse abdominal pain, diarrhea, fecal urgencies, rectal bleeding, anemia, weight loss, and fatigue. All these symptoms have an important morbidity and considerable impact on the quality of life.

Methods: We conducted a study over a period of 1year assessing 75 IBD patients having mild to moderate disease, being in clinical remission at the baseline. We questioned them every 3 months in respect of the abdominal pain, diarrhea, nocturnal stool, fecal urgencies and the impact of these symptoms on sleep schedule, anxiety, fatigue, personal relationship or work schedule. We compared the answers of those reporting these symptoms and the impact on their quality of life at the moment of the questionnaire with those not having the same symp-

toms at that time. From the 75 IBD patients, 31 were women, 41.33%, mean age 39.47 (ages between 19–63 years), 14 with CD (45.16%) and 17 with CU (54.83%) and 44 were men, 58.66%, mean age 42.95 (ages 21–70 years), 18 with CD (40.90%) and 26 with UC (59.09%).

Results: Among the group of 75 patients, 16 (21.33%) reported the symptoms in question at baseline and 33 (44%) reported the symptoms at one or more time points. Among the 16 patients with symptoms at baseline, symptoms had fluctuated in 3 (18.75%), resolved in 2 (12.5%) and were persistent at all points in 5 (31.25%).

Among the 26 remaining patients that have not reported symptoms at the baseline, 11 (42.33%) have not reported symptoms at any point, 2 (7.69%) have reported symptoms at 1 point, 4 (15.38%) have reported symptoms at 2 points, 3 (11.53%) have reported symptoms at 3 points, 6 (23.07%) have reported symptoms at 4 points.

Every time patients reported symptoms (abdominal pain, fecal urgencies, diarrhea or nocturnal stool), they were also related an impairment in the quality of life manifested by persistent fatigue with interruption in their sleep schedule, increased anxiety, and social isolation.

Also, we conducted a thorough anamnesis and we discovered that 50 among the 75 patients (66.66%) declared that the anxiety, tachycardia, and the impairment of their interpersonal relationship begun approximately 5 years before the diagnosis of the IBD.

Discussion/Conclusion: IBD is a disease that affects the patients on a multilevel aspect of their lives, firstly well-being with fluctuant abdominal pain, fecal urgencies and interruption the sleep schedule, leading to impairment of interpersonal relationships, social isolation, and depression. These implications reinforce the need for interventions aimed at improving the quality of life of IBD patients. There is a need to closely survey the patients who present in consultation complaining of abdominal pain and anxiety related symptoms, meaning that these may be the early symptoms of a silent IBD.

4. Long-term maintenance therapy for eosinophilic esophagitis: A systematic review and meta-analysis of observational studies and randomized controlled trials

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Introduction: The aim of this study was to evaluate long-term efficacy and safety of maintenance treatments for EoE.

Methods: PubMed-Medline, Embase and Cochrane databases were searched until October 2023. Studies reporting histologic success of therapies > 48 weeks, following induction of 8–12 weeks, were included. Primary outcomes were histologic success (defined as < 15 eosinophils/HPF) and histological relapse risk versus placebo (PBO) (for RCTs) and versus induction (for both RCTs and observational studies). Random effects and I2 statistic for heterogeneity evaluation were used.

Results: From 3916 articles, 23 papers (17 observational and 6 RCTs) comprising 1923 patients (M 70.1%, mean age 29.8 3 12.6 years) were included. Mean follow-up of 78.4 weeks. Budesonide was administered in 7 studies, PPI in 6 (4 pediatric), Fluticasone in 5, biologics in 3. Long-term histologic success was 83% (95% CI: 77–89%; I2 73.1%) for RCTs, and 53% (95% CI: 42–65%; I2 93.5%) for observational studies. Maintenance therapy showed a risk difference (RD) of histologic relapse of -0.71 (95% CI: -0.92–0.50; p < 0.01; I2 88.9%) versus

PBO and of -0.06 (95% CI: -0.11–0.01; p < 0.016; I2 23.1%) versus induction in RCT, while a non-significant (p = 0.38) odds ratio (OR) of 1.37 in observational studies. Clinical success was 61% (95% CI: 51–75%; I2 71.3%) and 60% (95% CI: 42–77%; I2 97.3%] in RCTs and observational studies. Biologics ranked first (histologic success 79% (95% CI: 71–87%; I2 54.9%), followed by PPIs with 64% (95% CI: 50–78%; I2 88.7%). Most common adverse event (AE) was candidiasis infection with 6% (95% CI: 2–10%; I2 61.9%) and 5% (95% CI: 2–7%; I2 66.7%) in RCTs and observational studies

Discussion/Conclusion: This meta-analysis showed all long-term treatments reduce histologic relapse without clear disadvantage in de-escalating therapy during maintenance in real-word data. Biological therapies resulted most effective in RCTs, while PPIs in real-world data. Safety analysis showed long-term treatment is well tolerated

5. Colectomy in microscopic colitis: A rare indication

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Introduction: Little is known about the colectomy risk in microscopic colitis (MC). With current incidence rates of MC rivalling those of ulcerative colitis and Crohn´s disease, knowledge on the risk of colectomy in patients with MC is warranted.

Methods: Leveraging the nationwide Swedish ESPRESSO histopathology cohort, we estimated the risk of colectomy in patients with biopsy-verified MC (diagnosed 1990–2017) compared to matched reference individuals from the general population (matched by age, sex, county of residence and calendar year). Colectomy was defined as having a surgical procedure code recorded in the National Patient Register indicating total colectomy.

Results: From 1990 to 2017, 13,038 patients with a first-time diagnosis of MC (32% collagenous colitis and 68% lymphocytic colitis) met the eligibility criteria. These patients were matched to 62,183 general population reference individuals. The median age at MC diagnosis was 63.1 years and 72% were women. During a median follow-up of 9.5 years, 16 individuals (0.12%) with MC underwent colectomy, compared with 20 (0.03%) matched individuals from the general population. This corresponds to an incidence rate of colectomy of 12.3 (95% CI: 7.5–20.0) per 100,000 person-years for patients with MC and 2.9 (95% CI: 1.8–4.5) per 100,000 person-years for reference individuals. After adjustment for the matching variables and educational attainment, the adjusted hazard ratio of colectomy was 4.35 (95% CI: 2.23–8.46) in patients with MC compared to reference individuals. Notably, in contrast to the distribution of subtypes and sex in our cohort, about two-thirds of patients with MC who underwent colectomy had collagenous colitis (n = 10) and approximately 90% were women.

Discussion/Conclusion: In conclusion, we report a four-fold increased relative risk of colectomy in MC patients compared to the general population. The risk was substantially higher for women and patients with collagenous colitis. Physicians should be aware of these risks and aim for early and sustained clinical remission to prevent colectomy.

6. Evaluation of acute terminal ileitis in hospitalized patients: Development of a predictive model to distinguish Crohn's disease from other etiologies

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Introduction: Terminal ileitis (TI) is often identified on CT scans in emergency room setting. Diagnosing Crohn's disease (CD) as a cause of TI is crucial due to its significant long-term implications. This study aims to investigate the causes and outcomes of patients presenting to with acute TI, as diagnosed on a CT scan, as a marker of an initial presentation of CD and develop a predictive model for CD diagnosis.

Methods: A retrospective case-control study was conducted at Shamir Medical Center including adults diagnosed with acute TI from January 2012 to December 2020. Patients with a history of inflammatory bowel disease or prior intestinal surgery were excluded. Patients were categorized into CD and non-CD groups. Follow-up data was available for a mean of 5.7 3 2.5 years. A logistic regression model was developed and subsequently validated with additional patients hospitalized between 2021 and 2023.

Results: Among 135 patients, 37 (27.4%) were diagnosed with CD. CD patients were younger (median age 27 vs. 39 years, $p = 0.003$), predominantly male (83.8% vs. 51%, $p = 0.001$), and had higher rates of chronic abdominal pain, diarrhea, anemia, and weight loss prior to hospitalization. Significant laboratory differences included higher platelet counts ($p = 0.006$) and lower mean corpuscular volume (MCV) ($p = 0.001$) in CD patients. Radiologic signs of complicated disease were more common in CD (35.1% vs. 4.1%, $p < 0.001$). The predictive model incorporating gender, abdominal pain history, and MCV showed an area under the curve (AUC) of 0.87, with sensitivity of 100% and specificity of 63.6% in the validation group of 18 patients.

Discussion/Conclusion: This study identified key predictors of CD in patients presenting with acute TI and developed a predictive model with substantial diagnostic capability. Use of this model for early identification and treatment of CD may potentially improve patient outcomes. Further prospective validation of this model is warranted.

7. Efficacy of orodispersible budesonide in eosinophilic esophagitis: A comprehensive analysis of clinical, endoscopic, and histological outcomes

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease characterized by esophageal eosinophilic infiltration, leading to symptoms such as dysphagia and food impaction. This study evaluates the clinical, endoscopic, and histological characteristics of an EoE population undergoing treatment with orodispersible budesonide (Jorveza®).

Methods: We included 85 EoE patients (21.2% female, 22.8% smokers) with a median age of 27 years (IQR, 13–36) at diagnosis. The primary symptoms were dysphagia (71.8%) and food impaction (65.9%). At therapy initiation, patients' median age was 30 years (IQR, 22–50), with a BMI of 22.2 (IQR, 20.1–23.8). Prior treatments included proton pump inhibitors (PPIs, 83.5%) and Flixotide® (52.9%).

Results: At baseline, 71.8% had dysphagia, 29.4% experienced heartburn, and 65.9% had food impaction. Endoscopically, 49.4% had absent exudates, 47.2% had absent rings, and 75.3% had no edema. Histologically, the proximal esophagus had a median of 21 eos/hpf (IQR, 16–41). The ISEE score median was 7 (IQR, 6–8). After 12 weeks of budesonide treatment, dysphagia decreased significantly to 6.0% ($p < 0.001$), with marked improvements in other symptoms and endoscopic findings. EREFS scores improved from a median of 3 (IQR, 2–4) to 1 (IQR, 0–2) ($p < 0.001$). Histologically, the median eosinophil count in the proximal esophagus decreased to 0 eos/hpf (IQR, 0–0) ($p < 0.001$). At 52 weeks, all symptoms were

resolved in 100% of patients. Endoscopic examination showed significant reductions in exudates, rings, and strictures. The EREFS score further decreased to a median of 1 (IQR, 0–2) ($p < 0.001$). Histologically, the proximal eosinophil count remained low at 0 eos/hpf (IQR, 0–0) ($p < 0.001$). The ISEE score also improved significantly, with a median of 2 (IQR, 1–3) ($p < 0.001$). The logistic regression analysis revealed significant predictors for clinical remission at 52 weeks. The factors included initial ISEE score (OR = 1.5, 95% CI: 1.1–2.1, $p = 0.003$), baseline EREFS score (OR = 2.3, 95% CI: 1.4–3.8, $p < 0.001$), and eosinophil count reduction after 12 weeks (OR = 3.8, 95% CI: 2.2–6.7, $p < 0.001$). This indicates that higher baseline ISEE and EREFS scores, as well as significant reduction in eosinophil counts early in the treatment, are strong predictors of achieving clinical remission. Adverse events were reported in 19.0% of patients, with 8.3% experiencing oral candidiasis, 5.9% dyspepsia, and 3.6% cough. Therapy discontinuation due to adverse events occurred in 1.2% of cases.

Discussion/Conclusion: Orodispersible budesonide significantly improves clinical, endoscopic, and histological parameters in EoE patients, with a favorable safety profile. This study supports the efficacy of budesonide as a primary treatment for EoE. Further research is recommended to validate these findings over longer follow-up periods.

8. The impact of inflammation activity and therapy on mucosal mature CD83+ dendritic cell in ulcerative colitis

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Introduction: Mechanism of regulation of chronic inflammation in ulcerative colitis (UC) partly is controlled by intestinal dendritic cell (DC). DC is the main population of antigen-presenting cells in lamina propria. This cell controls, “feels “and catches an intraluminal antigen, and transports it to the lymphatic tissue. Therefore, its role is balancing of the response to the luminal antigen. In this study we observed a mature CD83+DC in colonic bioptic samples, and its correlation with inflammation activity and therapy.

Methods: The study included 175 subjects: 100 with UC and 75 healthy subjects. Colonic biopsy specimens were incubated with primary antibody anti-CD83. Presence of CD83+DC was analysed according histopathologic inflammation activity and Mayo endoscopic score (MES) and applied therapy.

Results: A multivariate logistic regression confirmed the combined effect of MES and histopathologic results on CD83+DC presence. The odds for CD83+DC presence were 5 times higher in group with MES 0,1 and with no/chronic inflammation than in group with MES 2.3 and with acute inflammation (OR = 5;95% CI: 1.4–17.5; $p = 0.012$), adjusted for therapy. Number of subjects without CD83+DC in group with no therapy was 2 times higher than in control group, 3.5 times higher than in group on azathioprine, and 2.6 times higher than in group on anti- TNF.

Discussion/Conclusion: Presence of CD83+DC could be used as a possible parameter as predictor of Inflammation activity in histopathology and endoscopically findings and treatment outcome.

9. Persistent dysphagia in stricture-free eosinophilic esophagitis in histological remission: Effectiveness of empirical esophageal dilation

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Introduction: Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder characterized by symptoms of esophageal dysfunction. Despite achieving clinico-histological remission through medical and dietary interventions, some patients continue to experience dysphagia and food impaction, even when eosinophils count have normalized and no overt strictures are observed on endoscopy. This persistent symptomatology may be attributed to reduced esophageal compliance. Empirical esophageal dilation could potentially alleviate these symptoms, but data on its efficacy are currently lacking. This study aims to evaluate the role of empirical endoscopic dilation in achieving clinical remission in symptomatic EoE patients with histological remission but persistent dysphagia.

Methods: We conducted a retrospective analysis of prospectively collected data from EoE patients without stenotic features on endoscopy (i.e., no R3/S1 according to the EREFS classification), who achieved histological remission through pharmacological and/or dietary treatment at a single referral center between July 2018 and December 2023. Patients who did not achieve concurrent remission of dysphagia and/or bolus impaction were subjected to empirical endoscopic dilation. Inclusion required at least six months of follow-up post-remission. Demographic, clinical, and endoscopic data were compared between patients who required dilation and those who did not.

Results: The study included 33 patients, with male prevalence (23) and a median age of 40 years (IQR, 30–51). 76% of patients were treated with proton pump inhibitors (PPIs). 19 patients (Group 1) achieved both clinico-histological remission, while 14 patients (Group 2) attained only histological remission and subsequently underwent empirical dilation to 15–17 mm, with no complications reported. Clinical remission was achieved in 13 out of 14 patients following dilation, with two patients requiring a second dilation at 25 and 31 months to maintain remission. The EREFS score at the time of histological remission, but not at diagnosis, was significantly higher in Group 2 compared to Group 1 ($p = 0.02$), along with a higher prevalence of R1 or R2 rings (78% vs. 37%, $p = 0.04$). A lower percentage of Group 2 patients received topical steroids (7% vs. 26%, p = n.s.).

Discussion/Conclusion: In this cohort of EoE patients with histological remission and without overt esophageal strictures, over 40% experienced residual obstructive symptoms that were effectively managed with empirical esophageal dilation, indicating the significance of reduced esophageal compliance. Further prospective multicenter studies utilizing FLIP technology are necessary to evaluate whether topical steroids may more effectively reverse esophageal remodeling and prevent the need for dilation compared to PPIs.

10. The prevalence of cardiovascular and hepatic risk in eosinophilic esophagitis patients

Cristina Deliu (Bals, RO), Oana Chirea (Craiova, RO), Veronica Popescu (Bals, RO), Amelia Genunche (Craiova, RO), Daniela Neagoe (Craiova, RO)

Introduction: Eosinophilic esophagitis is an allergic disease of the esophagus characterized by esophageal eosinophilia and symptoms of esophageal dysfunction. Inflammatory diseases have been associated with an increased cardiovascular and hepatic risk. The aim of this study was to explore systematically the prevalence and risk factors for NAFLD and incident major adverse cardiovascular events at patients with eosinophilic esophagitis.

Methods: We included observational study, which included 43 patients diagnosed with eosinophilic esophagitis. Diagnosis of NAFLD could be based on abdominal ultrasound, FibroScan, and hepatic steatosis index. Multivariable-adjusted hazard ratios (aHRs) for incident major adverse cardiovascular events (ischemic heart disease, congestive heart failure, stroke and cardiovascular mortality) were calculated using Cox proportional hazards models.

Results: A total of 43 patients were enrolled in the study. NAFLD was detected by abdominal ultrasound in 19 (44.1%) patients. The mean age was 24 3 5.0 years, and mean BMI was 22.6 3 3.9 kg/m2. Comparison between patients with and without NAFLD showed no significant differences in terms of eosinophilic esophagitis severity, disease duration, use of eosinophilic esophagitis - related medications. NAFLD was significantly associated with the presence of metabolic syndrome [MetS; odds ratio (OR) = 4.12, p = 0.001]. No significant difference was observed in the odds ratio of NAFLD among masculine patients disease compared with feminine patients. During a median follow-up of 5.0 years, we observed 7 incident major adverse cardiovascular events in patients with eosinophilic esophagitis. Eosinophilic esophagitis was not associated with a higher risk of major adverse cardiovascular events (aHR = 1.14, 95% CI: 0.86–1.51) or any of its components. No differences between age, sex and follow-up time were observed.

Discussion/Conclusion: The results of the study confirms the patients with eosinophilic esophagitis had no increased risk of major adverse cardiovascular events compared to reference individuals, but they have relatively high prevalence of NAFLD.

11. The ADEII project: A microlearning programme for patients with inflammatory bowel disease increased adherence and improved understanding of disease

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Introduction: Information and communication technologies (ICTs) represent a novel approach to chronic disease management. However, their use in Inflammatory bowel disease (IBD) is scarce as no specific tools are available. We developed a microlearning programme for IBD patients and evaluate its outcomes regarding adherence and disease perception.

Methods: Prospective cohort study in adult IBD patients (18–70 years) who underwent a microlearning programme over 2 months, through 4-minute videos organised into individualised video pathways that were sent via mobile phone using a Telegram bot. All patients received a main pack of 4 videos, consisting of 2 videos with information about their disease (ulcerative colitis or Crohn's disease), 1 video on adherence and 1 video on corticosteroid treatment. We then add a video for each medication used by the patient in the management of IBD. The IBD unit staff recorded the videos, which included short questions of its content. At the beginning of the programme and 6 months later, patients completed the BMQ (Beliefs Medicines Questionnaire), HADS (Hospital Anxiety and Depression Scale) and BIPQ (Brief Illness Perception Questionnaire). We checked their medication possession rate (MPR) at these same intervals, considering a MPR ≥ 80% as adequate adherence. A QR code links to an explanatory video of the ADEII Project https://adeii.iisgaliciasur.es

Results: Between June and October 2022, 1226 videos were sent to 200 IBD patients: 51.5% female (103), UC 52.5% (105), median age 46.1 (13.2) years (Table 1). The median of videos per patient was 6 (6–7). Attendance to the ADEII programme ranged from 78% to 90%. Baseline non-adherence was 29.8% (59 patients), decreasing significantly to 18.1% (36) after the programme (p = 0.02). Likewise, in the BMQ scale, we found significant decreases in the median and IQR of the BMQ scores: Medication Abuse: 8 (7–9) vs. 8 (6–9) (p = 0.001), BMQ-Medication Harm 10 (8–12) vs. 9.5 (7–11) (p = 0.002) and BMQ-Treatment Concern 13.5 (11–16) vs. 13 (10–16) (p = 0.001), with no change in BMQ-Treatment Need. Regarding illness perception, on the post-intervention BIPQ scale there were significant decreases in P8 Negative Emotions 6 (3–8) vs. 5 (3–7) (p = 0.003) and P5 Identity 6 (4–8) vs. 5 (3–7) (p = 0.003), as well as a significant increase in P7 Understanding of illness 7 (5–9) vs. 8 (7–9) (p = 0.003).

We found significant differences between the pre-intervention versus post-intervention medians and IQR in anxiety score 8 (5–11) vs. 7 (4–11) (p = 0.008) but no in depression.

Discussion/Conclusion: The ICT-based ADEII educational programme was widely accepted by patients, demonstrating an increase in medication adherence along with a decrease in negative beliefs about medications, anxiety, negative emotions and representations, in addition to improving the understanding of the disease.

12. Prevalence of clinical characteristics and eosinophilic esophagitis in elderly patients

Cristina Deliu (Bals, RO), Veronica Popescu (Bals, RO), Oana Chirea (Craiova, RO), Daniela Neagoe (Craiova, RO), Amelia Genunche (Craiova, RO)

Introduction: Eosinophilic gastrointestinal disorders including eosinophilic esophagitis are a group of gastrointestinal tract characterized by pathologic eosinophilic infiltration and clinical symptoms.

Methods: We included an observational study which included 61 patients diagnosed with eosinophilic gastrointestinal disorders between two years. We compared younger adults (18–50) with elderly adults (> 55) in terms of clinical characteristics (gender, age, presenting symptoms, comorbidities, histological activity, treatment modality and response to treatment. 54 patients who underwent endoscopy and esophageal biopsy and were found to have ≥ 15 eosinophils/HPF were defined as having eosinophilic esophagitis and were included for study.

Results: 54 cases of eosinophilic esophagitis were recorded, mean age 41.3, range (19–71 years), of which 14 patients were aged 55 years and over. Compared to younger patients, those aged ≥ 55 had more medical comorbidities (9 [64.2%] vs. 19 [35.1%], p = 0.002), and instead a non-significant trend toward less fibrosis (0.25 vs. 0.46, p = 0.117). Although rate of cases required topical steroid therapy was similar, none received repeated or maintenance therapy topical steroid therapy in elderly.

Discussion/Conclusion: In our study the clinical characteristics of eosinophilic esophagitis in the older age group were similar to the younger patients. Only 14 patients (29.6%) were aged 55 years or older, suggesting that eosinophilic esophagitis is less common in the elderly.

13. Selective deficiency of memory marginal zone B lymphocytes in patients with uncomplicated celiac disease

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Introduction: Celiac disease (CD) is a chronic, multi-organ, immune-mediated disease associated with gluten intake in genetically susceptible individuals. It is noted that there is an increasing trend in its prevalence, with about 1% of the global population being affected. CD can be associated with splenic dysfunction, known as hyposplenism. In complicated and more severe forms of CD, the prevalence of functional hyposplenism is reported to be as high as 80% and may be associated with serious clinical consequences, particularly severe bacterial infections. However, there is limited information available about hyposplenism in patients with uncomplicated CD.

Methods: The aim of our study was to verify the presence of hyposplenism by determining the abundance of memory marginal zone B lymphocytes in peripheral venous blood in cohort-treated patients with asymptomatic uncomplicated celiac disease. The results in CD

patients were compared to healthy individuals. We analyzed B lymphocyte subpopulations in peripheral venous blood using flow cytometry, focusing specifically on marginal zone B lymphocytes, which have previously been shown to be potential markers of hyposplenism in patients with complicated forms of CD. Our study included 100 CD patients (30 men, average age 52 3 16 years; 70 women, average age 45 3 14 years) and 35 healthy participants without CD as confirmed serologically (10 men, average age 51 3 14 years; 25 women, average age 46 3 12 years). We gathered essential clinical and laboratory data, such as age, weight, duration of the disease, BMI, body surface area, and complete blood count. Additionally, we collected serological profiles for CD, including anti-tissue transglutaminase IgA (in the subgroup of patients) and anti-tissue transglutaminase IgG, anti-endomysial IgA and IgG, anti-deamidated gliadin peptide IgA and IgG, and anti-reticulin IgA and IgG (in the subgroup of healthy controls).

Results: In the analysis of B lymphocyte subpopulations, we found a statistically significant difference between the group of patients with celiac disease and the group of healthy controls in the marginal zone B lymphocyte subpopulation. The relative values of marginal zone B lymphocytes were on average 0.91 3 0.74% in the celiac patients and 1.63 3 1.09% in the healthy controls group ($p < 0.0001$). The absolute values of marginal B lymphocytes were on average 17.37 3 14.55 x 109/l in the celiac patients and 31.77 3 22.65 x 109/l in the healthy control group ($p = 0.0002$). Basic white blood cell parameters (leukocytes, total lymphocytes, B lymphocytes) were normal in both groups, with no statistically significant differences between them.

Discussion/Conclusion: Determining the levels of marginal zone B lymphocytes in peripheral blood could be valuable for assessing the severity of hyposplenism in patients with uncomplicated celiac disease. Comprehensive studies that delve deeper into B cell subpopulations in patients with celiac disease are necessary to draw conclusive findings.

14. Liver transplantation for primary sclerosing cholangitis, association with IBD – Analysis of the Slovak transplant registry

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Introduction: Patients with IBD, especially with UC, are at increased risk of PSC, which worsens their prognosis. The natural course of PSC is variable and difficult to predict and is not only determined by the well-known fibrosis-cirrhosis-portal hypertension-hepatocellular carcinoma cascade, but also by the co-occurrence of IBD, acute cholangitis, and a higher risk of cholangiocellular and colorectal carcinoma. Liver transplantation is the only treatment modality for patients with PSC, which has its own specificities. A risk in the post-transplant course is PSC recurrence, which affects the prognosis of patients.

Methods: Retrospective analysis of Slovak liver transplant registry data.

Results: In the period from 2008 to 2024, 412 patients underwent liver transplantation in Slovakia, 51 of them for primary sclerosing cholangitis, which represents 12.3% of all transplanted patients. The median age at the time of transplantation was 39 (13) years, 73% of patients transplanted for PSC were male, 18% of patients had PSC/AIH overlap. 84% of patients suffered from IBD, only 12% of them were treated with biologics. 22% of patients had recurrence of IBD after transplantation. 24% of patients developed recurrent PSC in the post-transplant course, median time to recurrence was 39 (4.1) months. 14% of patients underwent liver retransplantation. IBD relapse after transplantation (OR = 3.70, 95% CI: 0.63–19.8, p: 0.12), 5-ASA use (OR = 4,25, 95% CI: 0,95–30,2, p: 0,086) and cyclosporine use (OR = 3.20, 95% CI: 0.65–16.0, p: 0.14) trended toward statistical significance in predicting recurrence.

Discussion/Conclusion: PSC is classified as a rare disease, yet it is a relatively common indication for liver transplantation. Proper timing of transplantation and identification of risk factors for disease recurrence after transplantation, including concomitant IBD, remain a medical challenge. Transnational registries are needed to obtain relevant data.

15. First-in-human trial of IMU-856, an orally available regulator of barrier function and regeneration for the treatment of celiac disease

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Introduction: IMU-856 is an orally available and systemically acting small molecule modulator targeting Sirtuin 6, a transcriptional regulator of intestinal barrier function and regeneration of bowel epithelium. In preclinical studies, IMU-856 has been shown to avoid suppression of immune cells. IMU-856´s mechanism of action could therefore present a new approach to treating celiac disease and other intestinal barrier function associated diseases without the serious consequences associated with immunosuppressive therapies.

Methods: This was a three-part phase I/Ib, double-blind, randomized, placebo-controlled first-in-human trial of IMU-856 in healthy subjects and patients with celiac disease. Healthy subjects received single and multiple ascending doses of IMU-856 or placebo to assess safety, tolerability, and pharmacokinetics. Moreover, two doses of IMU-856 were tested versus placebo in patients with well-controlled celiac disease during periods of gluten-free diet and a 15-day gluten challenge with 6 g gluten daily to measure histology, symptoms, nutrient uptake and non-invasive biomarkers.

Results: IMU-856 was safe and well-tolerated with a benign adverse event profile and pharmacokinetics that allow once-daily dosing. Treatment with IMU-856 showed positive effects in four main dimensions of clinical outcome in celiac disease: protecting gut architecture, reducing symptom severity, enhancing nutrient absorption, and improving biomarker levels reflecting enterocyte functional mass.

Discussion/Conclusion: IMU-856 was safe and well-tolerated. The Phase Ib portion provided proof-of-concept data for IMU-856 in patients with celiac disease, underlining its positioning as a potential first-in-class oral celiac disease therapy. IMU-856 may also offer extensive potential beyond celiac disease in other diseases with compromised intestinal barrier function.

16. Particularities of inflammatory bowel diseases in elderly patients

Hanen Elloumi (Bizerte, TN), Imed Cheikh (Bizerte, TN)

Introduction: The global incidence of inflammatory bowel diseases (IBD) is increasing, with a growing trend of late-onset cases in the elderly. Managing IBD in the elderly is complex. This study aims to determine the clinical, therapeutic, and evolutionary characteristics of IBD in individuals aged ≥ 60 years.

Methods: A retrospective, observational study conducted from 2009 to 2019 included all patients treated for IBD at the Gastroenterology Department of Bizerte. The aim of the study is to compare the clinical, therapeutic, and evolutionary features of IBD between elderly patients and those under 60 years.

Results: Among our 255 patients, 18.6% of those with Crohn's disease (CD) and 29% with ulcerative colitis (UC) were ≥ 60 years at diagnosis. Comorbidities and polymedication were significantly more common in the elderly. For CD, diarrhea was more frequent in elderly patients (p = 0.015). Colonic and ileocolonic localization, inflammatory phenotype, and moderate severity of flares were predominated in both groups. Therapeutic modalities were similar between two groups. For UC, older patients had less diarrhea (p = 0.023) and more rectal bleeding (p = 0.015). Left-sided localization and moderate severity were predominant in both groups. For therapeutic modalities, there was less use of 5-aminosalicylates (5-ASA) (p = 0.001) and steroids (p = 0.04) in elderly patients. There was no significant difference in the use of azathioprine, anti-tumor necrosis factor, and surgical resection between the two groups.

Discussion/Conclusion: The results of our study showed that patients with IBD diagnosed at an advanced age had a moderate disease profile and a relatively benign prognosis, with a lower prevalence of complications and infections. Thiopurines and 5-ASA were often effective and safe, sparing elderly individuals from the need for corticosteroids and surgery.

17. Oral immunotherapy-associated eosinophilic esophagitis

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Introduction: Oral immunotherapy (OIT) for food allergy may cause a spectrum of gastrointestinal adverse effects, representing different etiologies, among them Eosinophilic Esophagitis (EoE). These adverse effects can impede the success of treatment. The current study, utilizing a large cohort of patients that completed OIT, aimed to describe the management and treatment outcomes with OIT-associated eosinophilic esophagitis.

Methods: Patients (n = 1994) treated with OIT for milk, egg, peanut, sesame and tree nut allergy between April 2010 to May 2021 were reviewed. Among these patients, those who developed EoE were retrospectively recruited. Demographic, clinical and histological data were investigated and analyzed.

Results: Thirteen patients (0.7%), ages 7–27 years (median 13), developed EoE. The median interval between the start of treatment and symptom appearance was 25 months (7–84). 77% of patients were male, and 69% were treated for milk allergy. 69% had macroscopic findings suggestive of EoE, and upon histology the median eosinophil count per high power field was 50 (range, 25–100). 85% (11/13) were initially treated with high dose proton-pump inhibitor (PPI), leading to complete clinical resolution in all patients, and either complete (n = 5, 45%) or partial (n = 6, 55%) histologic resolution. Among those with incomplete histologic resolution, two added swallowed topical corticosteroids, two continued low dose PPI and two stopped OIT. In terms of OIT treatment, 77% (10/13) continued allergen dose consumption.

Discussion/Conclusion: OIT-associated EoE occurs in late stages of treatment and can be managed pharmacologically with high dose PPI without discontinuing allergen consumption.

18. Diabetes mellitus in patients with autoimmune hepatitis (AIH): An independent adverse prognostic factor

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Introduction: Autoimmune hepatitis (AIH) is an inflammatory liver disease that has strong associations with other autoimmune diseases. Standard treatment of AIH comprises corticosteroids and a "steroid-sparing agent", usually azathioprine. Corticosteroids are known to increase blood glucose levels and increase insulin resistance. However, the prognostic implications of diabetes mellitus (DM) in patients with AIH are unclear. We aimed to assess the association of DM with mortality in patients with AIH.

Methods: Retrospective/prospective single-centre audit of 505 patients with AIH (1999 IAIHG Criteria) presenting 1971–2023 and followed to death, liver transplant, loss to follow up, or to 31/12/2023. Diabetes was defined by WHO criteria or by starting antidiabetic drug treatment.

Results: DM was present in 48 patients (10%) at AIH diagnosis and developed later in a further 63 (15%). The cumulative incidence rate of new-onset DM was 11 3 2% and 19 3 3% after 10- and 20-years follow-up respectively. Multivariate analysis showed that new-onset DM was associated with older age, initial prednisolone dose > 40 mg/day, Black/Asian ethnicity, higher BMI at diagnosis and weight gain after 2 years of follow-up. Death/transplantation rates after 10 and 20 years respectively were 27 3 2% and 59 3 4% (all-cause), and 7 3 1% and 15 3 3% (liver-related). DM at diagnosis showed associations with all-cause and liver-related death/transplantation rate on univariate but not multivariate analysis. New-onset DM was associated with all-cause death/transplantation rate on both univariate and multivariate analysis.

Discussion/Conclusion: Overall prevalence of DM was 22%, with new-onset DM occurring in 15% of patients. Risk factors for new-onset DM were older age, initial prednisolone dose, Black/Asian ethnicity, higher BMI at diagnosis and weight gain. We report a novel association between diabetes and all-cause death/transplantation rate in AIH, that is independent of baseline prognostic variables.

19. Exploring the novel calcineurin inhibitor voclosporin in a colitis model: Is this a novel therapy for IBD?

Michael Gabel (Erlangen, DE)

Introduction: The treatment of inflammatory bowel disease (IBD) is still challenging. A promising new calcineurin inhibitor is voclosporin, which emerged recently to medicate lupus nephritis. Preliminary studies also discovered voclosporin as a promising treatment option for IBD. In this work, we want to explore the therapeutic benefits of voclosporin in experimental colitis models and decipher the intracellular signalling. Due to the related structure of cyclosporine A and voclosporin and the fact that cyclosporine A has been used previously to treat patients with IBD, we aimed to further elucidate the efficiency, benefits and molecular mechanism of action of voclosporin in the context of IBD.

Methods: We used in vivo analysis to evaluate hapten induced oxazolon colitis accessing mini-endoscopy, histology, multiphoton endomicroscopy measurements (MPEM), flow cytometry and immunofluorescence stainings. In a second approach, we examined the in vitro effect of voclosporin on ITK activation at the molecular level in human PBMCs.

Results: Treatment with voclosporin suppressed established colitis in mice and was able to diminish the activation of the IL2-inducible tyrosine kinase ITK, which in previous studies has been shown to be a driver of inflammation in IBD. Further in vitro stimulation of human PBMCs resulted in alleviated protein expression of the kinases ITK, LCK and ZAP70 when applying voclosporin as well as cyclosporine A. However, Voclosporin showed better effects in reducing the activity of T cells than cyclosporine A. Therefore, we further endorse voclosporin to be an attractive novel approach for the treatment of acute intestinal inflammation.

Discussion/Conclusion: Voclosporin as a further development of cyclosporine A demonstrates a protective effect in oxazolone induced colitis and exhibits a mechanism of action comparable to cyclosporine A. Given the impressive results and optimised tolerability of voclosporin in other diseases like lupus nephritis, repurposing this drug for conditions such as inflammatory bowel disease seems very promising.

20. Ensemble bioinformatics approach for ustekinumab therapeutic response prediction models in ulcerative colitis

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Introduction: The optimization of treatment with biological agents is an ideal goal for patients with ulcerative colitis (UC). Recent data suggest that mucosal inflammation patterns and cytokine profiles differ between patients who respond and those who do not. Ustekinumab, has shown promise, but predicting treatment response remains a challenge. Our aim is to identify prognostic markers of response to Ustekinumab, in patients with active UC, based on their mucosal transcriptome profile.

Methods: We performed a prospective observational study on 36 UC patients initiating treatment with Ustekinumab. Colonic mucosal biopsies were obtained before treatment initiation for gene expression analysis using a microarray panel. Differential gene expression analysis (DGEA), correlation analysis, and co-expression network analysis were performed. Additionally, machine learning (ML) models were employed to predict treatment response based on gene expression data

Results: Seven genes, including BCL6, CXCL5, and FASLG, were significantly upregulated, while IL23A and IL23R were downregulated in non-responders compared to responders. Co-expression analysis revealed distinct patterns between responders and non-responders, with key genes like BCL6 and CRP highlighted in responders and CCL11 and CCL22 in non-responders. ML algorithms demonstrated high predictive power, highlighting the significance of IL23R, IL23A, and BCL6 genes

Discussion/Conclusion: Our findings indicated potential biomarkers associated with Ustekinumab response in UC patients, shedding light on underlying mechanisms and variability in treatment outcomes. Integrating transcriptomic approaches, including gene expression analysis and ML, offers valuable insights for personalized treatment strategies

21. Biodegradable stents at ERCP – A pilot study

George Bird (Maidstone, GB)

Introduction: Biodegradable stents are now available for biliary and pancreatic stenting at ERCP. One of their potential advantages is the possibility to avoid the need for temporary plastic stents, which have to be removed and which usually require a second procedure, involving extra patient risk, discomfort and expense. This study aimed to explore the potential for biodegradable stent use in a centre with a single operator providing an unselected and urgent ERCP service.

Methods: All urgent ERCP cases presenting over a 12-month period were considered for stents if clinically justified along the usual criteria. Patients were fitted with biodegradable stents (Archimedes, amg International) if

a – protection of pancreatic duct during difficult biliary cannulation (fast degrading stent)

b – after bile duct stone removal cholecystectomy planned within 3 months (slow degrading) Cases were treated with plastic stents if

c – biliary stricture waiting definitive diagnosis

d – cholangitis secondary to CBD gallstones and incomplete / uncertain stone extraction We assessed post ERCP complication rate and outcome after 6 months.

Results: Of a total 145 ERCPs there were a-2, b-4, c-2 and d-4

In a-d there were no post-ERCP complications.

In group b, one patient had recurrent CBD stones due to a delay in cholecystectomy

In groups c and d repeat ERCP was necessary in 3 cases due to recurrent cholangitis at 3-5 months.

Discussion/Conclusion: Plastic stents have a risk of dysfunction and it is overoptimistic to expect a stent lifespan of more than 2 months, as stated in some guidelines. Biodegradable biliary stents (slow degrading have a life of minimum 11 weeks) are therefore non-inferior and increase the likelihood of avoiding repeat procedures. There were no complications seen with the use of biodegradable stents.

22. Analysis of the functional role of mast cells: Bridging the gap between the development of colitis and colitis-associated cancer (CAC)

Katharina Gerlach (Erlangen, DE), Benno Weigmann (Erlangen, DE)

Introduction: In the gut, mast cells (MCs) are underestimated and play a crucial role in the regulation of numerous physiological and pathological processes, including the orchestration of local inflammatory responses. They are observed in a tumor microenvironment, suggests their contribution in the transition from chronic inflammation to cancer. As the functions of MCs in the cancer milieu is unclear, this study aims to decipher their contribution to the development of colitis-associated cancer (CAC).

Methods: Patient samples from colorectal cancer (CRC) and CAC tissue were analysed for specific mast cell markers by quantitative PCR. Immunofluorescence staining from CAC tissue of patients was analysed for the distribution of mast cells and T cells. Additionally, mice were treated with AOM/DSS and were analysed by quantitative PCR and immunofluorescence staining to evaluate mast cell and T cell presence. Furthermore, mast cell deficient mice and control mice were investigated in the AOM/DSS model.

Results: We observed significant upregulation of mast cell markers in CAC tumors of patients compared to CRC tumors and healthy controls. Functional analysis of wildtype (WT) mice in an experimental model of CAC (AOM/DSS) made evident that the FceR1 and CD117 (c-kit) is highly expressed in the adjacent tumor tissue but not within the tumor. Mast cell expression significantly increased during the remission phases of DSS colitis, whereas T cell presence was more available during periods of severe inflammation. In the AOM/DSS model we found a higher inflammation score in the initial cycle of DSS when mast cells were absent. Conversely, during the third cycle of DSS mast cell deficient mice were significantly lower inflamed compared to the WT mice. The tumor score and the number of tumors was significantly lower in the absence of mast cells.

Discussion/Conclusion: Previously neglected MCs show increasing evidence for their role in tumour prognosis and therapeutic efficacy. Our results indicate that they are mediators in CAC and can act as novel targets for the prevention and future treatment of CAC.

23. The effects of gluten-free diet on body mass indexes in adults with celiac disease: A systematic review and meta-analysis of observational studies

Rachel Gingold-Belfer (Petah Tikva, IL), Yaron Niv (Tel Aviv, IL), Noam Peleg (Petah Tikva, IL)

Introduction: While a gluten free diet (GFD) is the cornerstone of treatment in patients with Celiac disease (CD), this diet is associated with consumption of simple carbohydrates, low fiber intake and higher intake of sugars and saturated fat. Previous longitudinal and observational studies have investigated the effect of GFD on body mass index (BMI) in adults with CD. However, since their conclusions were contradictive, the effect of a GFD on BMI is still a controversial issue. Thus, we conducted a systematic review and meta-analysis examining the effect of GFD on BMI in patients with CD.

Methods: Through systematic research of the literature conducted in January 2022 using Medline, Scopus and Embase, we identified 1565 potential studies/abstracts. Only studies of patients with CD under a GFD with recorded BMI before and after dietary intervention were included. Subgroup analyses based on study design and BMI categories were performed. We calculated the pooled odds ratios (ORs) and 95% confidence intervals (CIs) for the number of patients in each BMI group according to the World Health Organization (WHO) definitions after GFD using fixed and random effect meta-analysis.

Results: The analysis included 10 studies and 38 sub-studies, which encompassed 2450 patients from 5 countries. We found non-significant odds for changing the BMI group (pooled OR = 0.972, 95% CI: 0.858–1.101, p = 0.65) after GFD. However, looking specifically on BMI subgroups, we found higher odds for BMI category change after GFD in underweight patients (OR = 0.588, 95% CI: 0.479–0.723, p < 0.001), and overweight patients, 25 < BMI < 30 (OR = 1.332, 95% CI: 1.167–1.521, p < 0.001). No publication bias was demonstrated, and the amount of heterogeneity between studies was moderate (I2 = 54.13).

Discussion/Conclusion: Although crucial in patients with CD, GFD is associated with increased BMI in some CD patient's populations. Accordingly, special considerations and follow-up should be maintained in overweight patients with CD.

24. Safety of LMWH for the prevention of venous thromboembolism in patients with severe ulcerative colitis

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Introduction: Active ulcerative colitis (UC) is associated with an increased risk of venous thrombosis that occurs prevalently as deep vein thrombosis and pulmonary embolism. The prevention of venous thromboembolic events (VTE) in UC patients includes the use of low molecular weight heparin (LMWH), particularly in hospitalized patients with severe disease. However, data on the safety and efficacy of LMWH for the prevention of VTE in patients with UC are limited, so we decided to perform a prospective open study to address these objectives.

Methods: All consecutive patients with severe UC admitted to the Institute of Gastroenterology and Hepatology from January 2010 to December 2015 were included in this study. Enoxaparin (ENX), at a dose of 100 IU per kg subcutaneously once a day, was added to standard therapy for all the time period considered at risk for VTE. In case of clinical suspi-

cion or laboratory findings suggestive of VTE the diagnostic tests required for the diagnosis of VTE were performed. The occurrence of new cases of VTE and side effects attributable to ENX, in particular an increase of rectal bleeding, was recorded. The obtained data were compared with those of a historical cohort of hospitalized UC patients with severe disease but not treated with ENX.

Results: Thirty patients were enrolled in the study, 15 in the group treated with ENX (group A) and 15 in the control group (group B). The average duration of treatment with ENX was 14 3 7 days. No patient in group A presented VTE during treatment, while four patients in group B developed thrombosis (p = 0.04). In group A two patients presented an increase of rectal bleeding compared to three patients in the control group (p = 0.5).

Discussion/Conclusion: The results of the present study show that in a population of hospitalized UC patients with severe disease the use of ENX for the prevention of VTE is effective and safe. However, further studies on larger populations of patients are needed to confirm these findings.

25. MicroRNAs in plasma-derived extracellular vesicles as non-invasive biomarkers for eosinophilic esophagitis

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Introduction: The lack of non-invasive biomarkers imposes the dependence of endoscopy with biopsies for the diagnosis and monitoring of eosinophilic esophagitis (EoE), a prevalent chronic inflammation of the esophagus mediated by a type 2 immune response. We aimedto identify potential non-invasive biomarkers using microRNAs (miRNAs) in plasma-derived extracellular vesicle (pEVs).

Methods: This is a prospective single-center observational study including a discovery cohort of EoE patients (n = 26) with active disease (EoE.Basal) and after anti-inflammatory treatment (EoE.Post.tx), and control subjects (n = 16). Small-RNA-seq of RNA-pEVs was performed to identify differentially regulated small-RNAs (sRNAs) in EoE.Basal vs. controls and EoE.Basal vs. EoE.Post.tx comparisons. Candidate miRNAs were validated in an independent cohort (EoE patients, n = 33; controls, n = 14), and the diagnostic potential of miRNA-pairs was assesed.

Results: The pEVs-sRNA cargo differed among controls, EoE.Basal and EoE.Post.tx conditions. Compared with controls, Ser_Comb_22, Comb_5, miR-10b-5p and miR-125a-5p were upregulated in EoE.Basal, and miR-224-5p, miR-221-3p, let-7d-5p and miR-191-5p were downregulated. Combination of miR-221-3p and miR-10b-5p showed the best diagnostic performance in discovery (AUC = 0.87) and validation (AUC = 0.70) cohorts. Comparing EoE.Basal and EoE.Post.tx paired samples, miR-374-5p and miR-30a-3p were upregulated in EoE.Basal, while miR-15a-5p and let-7d-5p were downregulated. Here, combination of miR-30a-3p and miR-15a-5p showed AUC values of 0.90 and 0.71 in discovery and validation cohorts respectively. MiR-30a-3p remained highly upregulated in EoE.Basal when compared to EoE.Post.tx in the validation cohort (p = 0.001).

Discussion/Conclusion: The sRNA cargo of pEVs is related to the inflammatory activity in EoE. This study pioneers the use of pEVs as a non-invasive biomarker for EoE.

26. Food bulus and subsequently eosinophilic oesophagitis management, a two years audit

Lucianno Guimaraes Carneiro (Doncaster, GB)

Introduction: Food bolus is the most commun presentation of eosinophilic oesophagitis and the most commun GI emergency after GI bleed. This research was conducted to analyse the management of food bolus and afterwards the management of eosinophilic oesophagitis related to it in Doncaster Royal Infirmary.

Methods: We collected data from patient who presented to our emergency endoscopy list with food bolus impaction from November 2021 to November 2023.

Data collected for:

- Oesophageal biopsies at index endoscopy.
- Number of biopsies.
- Number of patients with histoplogical diagnosis of EoE.
- Started on topical sterodis (Jorveza®).

Results: 100 patients have been collected from November 2021 to November 2023. Biopsies were taken in 55 patients. 14 out of 45 patients there was enough biopsies taken were suffient to rule out EoE (14 patient 6 biopsies were taken, 1 patient 5 biopsies were taken, in 5 patients 4 biopsies were taken, 2 patients 3 biopsies were taken, in 13 patients 2 biopsies were taken, 3 patients 1 biopsy was taken). In total 17 patients were diagnosed with EoE.

Discussion/Conclusion: Oesophageal biopsies should be taken at index endoscopy in patients with food bolus, as If biopsies are not taken they are likely to get lost to secondary care follow-up, missing the opportunity to diagnose EoE. Sufficient biopsies should be taken to reliably exclude EoE.

27. EMpowering endoscopy trainees in PATHology recognition and management (EmPath): Trainee-led pathology teaching in endoscopy

Eleanor Ruth Hackney (South Shields, GB), Fraser Brown (Stockton-on-Tees, GB)

Introduction: The Northern Endoscopy Training Academy (NETA) was launched to provide quality endoscopy training across the region. As part of this, trainees undertake an immersion block lasting 2–4 weeks receiving high intensity endoscopy training in a designated regional training hub, supported by regular training lists in their base hospital. The aim is to accelerate endoscopy training, particularly relevant following the implementation of the 2022 Gastroenterology curriculum which shortened higher specialty training.

Anecdotally, trainees expressed that pathology recognition was an area in which they felt less confident. As senior gastroenterology trainees, we experienced this in our own training and the feasibility of reaching competency in endoscopy without seeing a significant spread of pathology. The delivery of pathology teaching can be opportunistic and trainer dependent.

Methods: A series of study days was developed named EmPath (EMpowering endoscopy trainees in PATHology recognition and management). These were designed by senior gastroenterology trainees with input from surgical trainees in content delivery. In addition, consultant involvement took the form of talks on specific pathologies. The study days were advertised to surgical, gastroenterology and clinical endoscopists who had recently undertaken an immersion block as part of NETA.

The structure of the day included a quiz based upon questions from the European Speciality Examination in Gastroenterology and Hepatology. Case based discussions focused around pathology recognition with emphasis on interaction and sharing of personal experiences. A simulation session was conducted with participants performing an upper GI endoscopy on a manikin using a pathology video. The participant was expected to assess the findings, write the report and then communicate this to the 'patient' who was a role player. The days also include workshops around subjects such as report writing, room management, and managing complications. Feedback was collected via an online survey after the study day.

Results: At point of submission, the first two study days focusing on oesophageal and gastric pathology had been delivered. All participants rating the days as 'very useful' and 'very relevant'. The feedback was overwhelmingly positive with comments for improvement centred around providing more sessions. A mean increase in quiz scores was seen across both days (day 1: 10%; day 2: 15%). Participants were open to, and appreciative of, the multidisciplinary nature of the day.

Discussion/Conclusion: The EmPath programme provides an opportunity to explore common pathology to support trainees as they gain technical competence. The near peer nature of teaching was appreciated by trainees. A mix of participant backgrounds enriched discussion by utilising different perspectives, whilst helping to develop a community of practice. The development of the EmPath programme is iterative and can be tailored to the needs of trainees. It provides a valuable resource in helping trainees to develop their pathology recognition skills in order to improve endoscopy quality.

28. Eosinophilic esophagitis: Our experience with the emerging disease at a single center in Northern Israel

Jawad Hindy (Haifa, IL)

Introduction: Data on Eosinophilic esophagitis (EoE) in Israel is sparse. We appraised the clinical, endoscopic, and histological characteristics of 50 Israeli adults with EoE.

Methods: We reviewed the medical records of 50 adult patients with a diagnosis of EoE who were referred to our center at Bnai Zion Medical Center, Haifa, Israel from 2020 until 2024.

Results: 50 patients with EoE were included; the mean age at diagnosis was 34 years 3 9.5 years. The sex ratio of males to females was approximately 2:1 with 34 males (68%) and 16 females (32%). 22 of the 50 patients had a history of allergic diseases. Symptoms at diagnosis were as follows: Dysphagia was the primary presenting symptom observed (n = 25, 50%), followed by food impaction (n = 17, 34%) and GERD-like symptoms (n = 14, 28%). Less frequent symptoms included vomiting, nausea, and chest pain. The most common endoscopic findings were normal mucosa (n = 21, 42%) followed by trachealization (n = 17, 34%), esophagitis (n = 7, 14%), and exudates (n = 5, 10%). 66% of the subjects were initially treated with proton-pump inhibitors (PPIs). 9 patients (18%) were asymptomatic without any treatment. The remaining 8 patients (16%) were given topical steroids. Clinical and histological resolution was detected in 50% of the patients who underwent a second EGD after 6 weeks-8 weeks of PPI.

Discussion/Conclusion: Our current study describes the clinical features of adult patients with EoE in north Israel. This is the first demographic study in Israel that defines the clinical, endoscopic, and histological manifestations of EoE in the adult population.

29. Interplay of cytokines, genes and gap junction intercellular proteins in IBD

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Introduction: IBD is characterized by the functional impairment of intestinal epithelial cells concomitant with the infiltration of the lamina propria by inflammatory cells. Gap junction proteins (connexins) are high-resistance pathways that mediate intercellular coupling, allowing passive spread of ions and large molecules in the GI tract. Gap junction intercellular mechanism plays an important role in multiple normal and pathophysiological processes such as acute pancreatitis, cholestasis, diabetes, and nephritis. However, little is known about its role in the intestinal inflammation and some reports have suggested that some pro-inflammatory mediators are involved in its regulation, too. The close proximity of immunocompetent cells to the epithelium advocate a cross-talk between these cell types, which may realize directly via gap junctional channels or via mediators and exosomes. Taking into account known significance of several cytokines in IBD pathogenesis and their possible proximity to gap junction mechanism, we hypothesized that C-590T polymorphism of IL-4 gene and 35delG polymorphism of Gap junction β-2 protein/connexin (GJB2) gene may have pathogenetic significance in IBD.

Methods: One hundred and two IBD patients participated in the study. Diagnosis and management provided according to ECCO Guidelines. Female – 31 (30.4%), male – 71 (69.6%), control group was formed by 40 practically healthy individuals (female – 17 (42.5%), $\chi 2 = 1.88$, $p > 0.05$, male – 23 (57.5%), $\chi 2 = 1.38$, $p > 0.05$). Levels of pro- and anti-inflammatory (not only IL-4) cytokines' production (by ELISA) statistically calculated compared to control group quartiles. 'Low' (LQ) was L-1β < 23 pg/ml (lower quartile of control), TNF-α ≤ 15 pg/ml, IL-4 ≤ 4.95 pg/ml, IL-10 & IL-13 ≤ 15 pg/ml & ≤ 28 pg/ml, respectively. 'High' (HQ) was TNF-α > 32 pg/ml (upper quartile), IL-1β ≥ 60 pg/ml, IL-4 ≥ 45 pg/ml, IL-10 & IL-13 ≥ 25.96 pg/ml & ≥ 38 pg/ml, respectively. Allelic and genotypes distributions of GJB2 (rs80338939) and IL-4 (rs2243250) mutations analysed in PCR.

Results: All observed polymorphisms fully adhered to the Hardy-Weinberg equilibrium in both the IBD and control. Homozygous GJB2 gene mutation (35delG) in control has frequency of 5.0%, whereas among IBD patients in every second person, by 20.58% more often in male, $\chi 2 = 38.32$, $p < 0.001$. The distribution of IL-4 (C-590T) genotypes between groups including gender stratification was similar. The presence of GJB2 mutation in haplotype, regardless of IL-4 (C-590T) genotypes, increases the likelihood of IBD (UC, CD) 7.5 and 15.0 fold (OR = 9.67, 95% CI: 2.13–43.9, $p < 0.001$ and OR = 19.67, 95% CI: 2.53–102.9, $p < 0.001$, respectively). Number of patients with LQ of TNF-α and IL-4 gene's CC/CT genotypes dominate over TT-genotype: 22.06%/26.47% vs. 4.41% ($\chi 2 = 34.0$, $p < 0.001$). The same trend registered for IL-1β. Lower IL-1β production found in 35delG genotype of CJB2 gene, compared to non-del-carriers by 30.35%: 63.16% vs. 32.81% $\chi 2 = 8.91$, $p = 0.003$).

Discussion/Conclusion: It was found that IL-4 gene's C-allele (CC/CT) associates with lower TNF-α; high or normal IL-4, IL-10, IL-13 in 36delG-genotype of CJB2 gene. IL-4 hyperproduction in TT-genotype of IL-4 gene create predisposition for chronic intestinal inflammation. 35delG mutation of GJB2 gene is characterized by increased production of TNF-α, without significant growth of IL-1β and hyperproduction of IL-4 backed by activity of IL-10, IL-13. The obtained results may be used for prognostic as well as treatment customization purposes, including anti-cytokine therapies. More data must be collected and further wider studies are needed for clinical implementations.

30. Antibiotic treatment efficacy in Crohn's disease patients with small intestinal bacterial overgrowth

David Janelidze (Kyiv, UA), Igor Lopukh (Kyiv, UA), Mykhailo Aryskin (Kyiv, UA)

Introduction: Small intestinal bacterial overgrowth (SIBO) sometimes deteriorates the clinical manifestation of Crohn's disease (CD). Our aim was to evaluate the prevalence of SIBO in patients with CD and to assess the efficacy and compliance of rifaximin and metronidazole treatment in cases with SIBO by using a lactulose hydrogen breath test (LHBT).

Methods: 46 adult unselected patients (22 females, 24 males; mean age 36.1 years) with CD and 15 healthy subjects (7 females, 8 males; mean age 34.2 years) consented to participate in the study. After an oral dose of 10 g lactulose, breath hydrogen concentrations were recorded every 15 min for 120 min. Patients with positive LHBT were treated with rifaximin (200 mg t.i.d.) and metronidazole (500 mg t.i.d.) for 10 days and the test was performed repeatedly.

Results: In comparison to controls, CD patients had significantly ($p < 0.05$) higher basal breathed hydrogen (15.54 3 1.04 ppm; range, 5–52 vs. 4.61 3 0.87 ppm; range, 3–13). From 46 CD patients, SIBO was documented in 16 (34.8%) but in none of the controls ($p < 0.05$). The mean basal breathed hydrogen in CD patients with evidence of SIBO (39.15 3 1.72 ppm) was significantly reduced (9.54 3 1.42 ppm) after antibiotic treatment. SIBO eradication was achieved in all of the patients. No adverse effects were observed.

Discussion/Conclusion: SIBO is a frequent condition in CD. Short-term administration of rifaximin and metronidazole was well-tolerated and effective treatment for these patients. The LBHT is a simple, noninvasive, inexpensive and repeatable method for diagnosis and monitoring of SIBO in CD patients.

31. Pioneering hope: Harnessing TIM1 and TIM3 surface proteins and their intricate signaling cascades for potential therapeutic approaches

Annkathrin Knauss (Erlangen, DE)

Introduction: Inflammatory bowel disease (IBD) manifests as a persistent inflammatory condition within the gastrointestinal tract, driven by aberrant T cell activity and cytokine secretion. Our research group has identified the Tec kinase Itk as a pivotal player in perpetuating inflammation in IBD patients, hindering resolution. Nevertheless, Itk signaling along with the proteins modulating its activity in conjunction with the T cell receptor, remains incompletely elucidated. T cell immunoglobulin and mucin domain surface receptors TIM1 and TIM3, which exhibit divergent co-stimulatory or co-inhibitory effects on T cells and thereby influence inflammation, necessitate thorough examination in the context of Itk signaling and IBD.

Methods: Both human and murine tissues were analyzed for gene and protein expression of TIM molecules. Additionally, the effects of both stimulatory and inhibitory agents targeting TIM were examined using in vitro and in vivo models. In vivo experiments further utilized mice with functional knockouts to elucidate the impact of TIM1 and TIM3 on induced colitis.

Results: Both TIM1 and TIM3 receptors on T cells increased during inflammation or after TCR stimulation. Blocking TIM1 in vitro and in vivo showed beneficial effects regarding inflammation. A TIM3 deficiency resulted in exacerbated colitis development and course in vivo and led to elevated levels of pITK. However, stimulating TIM3 with its ligand Galectin-9 not only decreased levels of pro-inflammatory cytokines and increased T cell death but could also significantly reduce the activation of ITK in T cells.

Discussion/Conclusion: In summary, TIM proteins exert a modulatory influence on human and murine cells and on experimentally induced colitis. Continued exploration and analysis of TIM proteins in the context of IBD are imperative, given their promise as targets for future therapeutic interventions.

32. The experience of using ustekinumab in bio-naive patients with Crohn's disease with unfavorable prognosis factors: Real clinical practice

Oleg Knyazev (Moscow, RU)

Introduction: The purpose of this study was to study the effectiveness of ustekinumab (UST) depending on the dosage regimen (90 mg subcutaneously once every 8 or 12 weeks) in patients with Crohn's disease (CD) who have unfavorable prognosis factors.

Methods: To assess the effectiveness of the drug, we included in the study 38 patients with CD who had unfavorable prognosis factors, who were randomized into two groups of patients who received the drug in a 90 mg subcutaneous regimen once every 12 weeks (1-st group, n = 20) and 90 mg subcutaneously once every 8 weeks (2-nd group, n = 18). The gender and age of the patient were analyzed, including at the time of diagnosis, the severity and prevalence of CD; the presence of intestinal complications; the presence and localization of extraintestinal manifestations; previous treatment was analyzed.

Results: Clinical response and clinical remission were achieved in 19 (95.0%) patients of the first group and 18 (100.0%) patients of the second group ($p > 0.05$). Clinical remission was maintained (without the need for optimization of therapy) by the 52 week of follow-up in 18 (90.0%) patients, in the second group – 18 (100.0%) patients ($p = 0.516$). In the 1-st group 10 (50.0%) patients achieved and maintained endoscopic remission by the 52 week of follow-up, in the 2-nd group – 16 (88.9%) patients ($p = 0.01492$). During one year of follow-up, 10 (50.0%) patients of the 1-st group maintained clinical and endoscopic remission of CD, 8 (40.0%) patients maintained clinical response and clinical remission (a decrease of ≥ 100 points from the initial CDAI), 16 (88.9%) patients in the 2-nd group maintained clinical and endoscopic remission of CD. Clinical response and clinical remission were maintained in 2 (11.1%) patients. Clinical and endoscopic remission in patients with CD receiving the drug was achieved in the 2-nd group ($p = 0.01492$). Without steroidal remission in patients in 1-st group was 65.0%, and in in 2-nd group about 95% ($p = 0.04502$).

Discussion/Conclusion: This clinical observation demonstrated statistically significantly higher therapeutic efficacy (clinicoendoscopic, without steroidal remission) in CD patients with adverse prognosis factors receiving UST 90 mg subcutaneously every 8 weeks.

33. IBD treatment and adverse events in dependence on the age of patients

Michal Konecny (Olomouc, CZ)

Introduction: Inflammatory bowel diseases (IBD) are a chronic inflammatory disease that usually manifest at a younger age. However, the age of patients at the time of diagnosis is variable; the incidence of the first detection of IBD shows a bimodal age distribution in the third and sixth decades of the patient's life.

Methods: In the period 2015–2023, the 2nd Internal Clinics admitted 86 patients (with a mean age of 28.5 years) with recent incidence of IBD. The patients were divided into groups according to their age when IBD was diagnosed and we monitored different types of drug therapy (aminosalicylates, corticosteroids, immunosuppressives, biological therapy) and se-

rious adverse effects of therapy in patients in the following age groups: 18–29 years (group A), 30–49 years (B), older than 50 years (C). The data obtained was subjected to statistical analysis using standard descriptive methods for continuous data.

Results: For the use of aminosalicylates (87.2%, 90.7%, and 90.4% respectively), and corticosteroids (72.3%, 71.1%, and 59.4% respectively), no statistically significant difference ($p = 0.13$, $p = 0.8$, respectively) was found for the above age categories. On the other hand, a statistically significant difference ($p < 0.001$) was found between group A and C (62.7% and 38.1%, respectively) in the use of immunosuppressive drugs and between groups A, B, and C (39.2%, 28.0%, and 11.3% respectively) in the use of biological therapy. The incidence of serious adverse effects of IBD treatment did not exceed 2% in any age group and the difference was statistically insignificant ($p = 0.3$ and $p = 0.6$, respectively).

Discussion/Conclusion: The drug treatment of IBD is relatively safe for all age groups; the incidence of adverse effects is below 2%. Immunosuppressives and biological therapy are used primarily in younger patients when the course of the disease is more severe with frequent relapses.

34. Long-term health outcomes in offspring of women with inflammatory bowel disease: A nationwide population-based study

Ja Seol Koo (Ansan, KR), Dongwoo Kim (Ansan, KR), Geum Joon Cho (Seoul, KR), Young Mi Jung (Seoul, KR)

Introduction: Long-term health outcomes of children of mother with inflammatory bowel disease (IBD) are poorly understood. Therefore, this study aimed to evaluate the long-term impact of maternal IBD on disease in children, including IBD.

Methods: This nationwide retrospective study included women who delivered a singleton baby after 37 weeks between 2003 and 2004 in South Korea. Women gave birth to low-birth weight babies were excluded from the study. We compared risk of diseases in offspring according to maternal IBD. Multivariate analysis was performed to estimate the hazard ratios (HRs) for the future disease risk.

Results: Among a total 542,780 woman who gave birth during study periods, 1096 women with IBD and 541,684 non-IBD control were identified. In multivariate analysis, the offspring of IBD women frequently had lower respiratory infections (HR = 1.124 [95% CI: 1.018–1.242]), asthma (HR = 1.209 [1.065–1.372]), atopic dermatitis (HR = 1.217 [1.112–1.332]), allergic urticaria (HR = 1.276 [1.129–1.443]), and allergic rhinitis (HR = 1.151 [1.084–1.222]) than those of women without IBD. And the offspring of IBD mother had a higher risk of developing ulcerative colitis (UC) (HR = 6.334 [4.391–9.136]) and Crohn's disease (CD) (HR = 2.325 [1.463–3.694]) than others. Offspring of CD women were significantly associated with asthma (HR = 1.244 [1.048–1.476]), allergic rhinitis (HR = 1.132 [1.043–1.229]), and CD (HR = 3.44 [2.035–5.813]). The offspring of UC women had higher rates of pneumonia (HR = 1.332 [1.052–1.687]), gastroenteritis (HR = 1.469 [1.152–1.873]), juvenile arthritis (HR = 2.872 [1.194–6.909]), atopic dermatitis (HR = 1.330 [1.174–1.507]), allergic urticaria (HR = 1.391 [1.174–1.647]), allergic rhinitis (HR = 1.158 [1.063–1.261]), and UC (HR = 11.776 [8.002–17.340]).

Discussion/Conclusion: Our results show that the offspring of IBD women have higher risk of developing allergic and autoimmune disorders including UC and CD.

35. Intestinal ultrasound for assessment of disease severity in hospitalized patients with acute severe colitis

Maya Kornowski Cohen (Petah Tikva, IL)

Introduction: Intestinal ultrasound (IUS) has been shown to reliably detect disease activity in patients with ulcerative colitis (UC). The aim of this study was to evaluate IUS features of patients admitted with acute severe UC (ASUC).

Methods: A retrospective review was conducted on 19 patients admitted to our center with ASUC requiring salvage therapy (infliximab or cyclosporine) who underwent IUS and sigmoidoscopy. We characterized patients' ultrasonographic features during the severe flare (bowel wall thickness [BWT] and hyperemia assessed by color Doppler). We used the Milan Ultrasound Criteria (MUC) score to assess disease activity and collected data on endoscopic features (MAYO score) and laboratory markers.

Results: Patients in our cohort were severely ill: The median albumin, hemoglobin, CRP and calprotectin was 2.5 g/dl, 8.9 g/dl, 9.3 g/dl and 4510 ug/l, respectively. Most (76%) had an endoscopic Mayo score of 3. Five patients (26%) underwent colectomy within a year of admission. In the MAYO score 2 group, mean BWT was 4.38 with a mean MUC score of 7.732, while in the MAYO score 3 group mean BWT was 5.36 with a mean MUC score of 9.2. Among patients requiring a colectomy within 1 year, mean MUC was 9.7 compared with 8.5 in patients not requiring surgical treatment.

Discussion/Conclusion: In patients hospitalized with ASUC, IUS is reflective of disease severity and shows more severe findings among patients with higher endoscopic Mayo scores. In our small cohort patients with the most severe IUS findings underwent colectomy at higher rates. Larger studies should be performed to assess its predictive value among outcomes of interest in this patient population.

36. In vitro development of a colon epithelial monolayer system for studying barrier damage in inflammatory bowel disease

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Introduction: Inflammatory bowel diseases (IBDs), including Crohn's disease and ulcerative colitis, are chronic inflammatory disorders of the gastrointestinal tract, which are distinguished by the disruption and inflammation of the intestinal layer. The occurrence of IBD has been increasing over the last few decades due to various factors including immune modulation and microbes. In vitro epithelial models have emerged as a powerful tool to study the morphology, as well as the interaction between pathogens and intestinal epithelial cells (IECs). In this work, we present the development of a fully differentiated colon epithelial monolayer system that was subjected to various stimulation factors, including pro-inflammatory cytokines. This monolayer was then integrated into a co-culture setting with Citrobacter rodentium (C. rodentium) to investigate bacteria-induced barrier damage. Additionally, we investigated the ability of C. rodentium to infect and translocate through the monolayer following barrier disruption.

Methods: Murine colon crypts were isolated and digested into single cells and were grown onto a transwell system. Once fully differentiated, they were stimulated with pro-inflammatory cytokines and also infected with luminescent strain of C. rodentium. They were further characterised with fluorescence staining and permeability assays.

Results: The model displayed the expression of markers representative of various epithelial cell types, including EpCAM for epithelial cells, mucin 2 for goblet cells, and chromogranin A for enteroendocrine cells. Additionally, the epithelial monolayer formed tight junctions, as demonstrated by transepithelial electrical resistance (TEER) measurements and the presence of tight junction proteins mainly claudin-1, claudin-2, claudin-3, occludin, and ZO-1. To assess barrier disruption, the system was stimulated with IFN-γ, which led to a significant increase in cell death and permeability. Similarly, infection with C. rodentium caused a notable decrease in TEER and an increased level of cell death compared to the control. Furthermore, 3D imaging revealed that C. rodentium translocates from the apical to the basolateral side of the monolayer while inducing epithelial cell death, indicating greater damage to the barrier. To better mimic IBD pathophysiology, monolayers were first pre-stimulated with IFN-γ and TNF-α, followed by infection with C. rodentium. Interestingly, IFN-γ treatment alone or in combination with TNF-α resulted in a higher level of cell death compared to the control and enhanced bacterial translocation from the apical to the basolateral side.

Discussion/Conclusion: Overall, our data demonstrate that our monolayer model can be used efficiently to study colon barrier damage as well as bacterial infections and in vitro host-pathogen interactions in the context of IBD.

37.Investigation of the role of p53 in CD4+ T cells during the anti-tumor immune response against colorectal cancer

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Introduction: Colorectal cancer (CRC) is one of the leading causes of cancer-related deaths worldwide, and the host immune system plays a key role in modulating it. In particular, tumor infiltrating CD4+ T cells contribute to a positive outcome by activating other immune cells and directly killing tumor cells. Cellular senescence, a permanent state of cell cycle arrest, regulated by the p53/p21 or p16pRB pathways, is also involved in the initiation and progression of CRC, and can regulate the immune response. Tp53 is a key regulator of cellular senescence, but its role in the antitumor immune response of CD4+ T cells in CRC remains unclear. This work aims to elucidate the regulatory pathway of Tp53 in CD4+ T cells associated with CRC, using a murine model of sporadic colorectal cancer model as well as in vitro co-culture models.

Methods: In order to study the functional role of Tp53 in CD4+ T cells in the pathogenesis of CRC, CD4+ T cells were isolated from a conditional knock out mouse model with deletion of Tp53 (Exons 2-10) in CD4+ T cells, and injected in Rag-/- mice to reconstitute their immune system. Orthotopic injection of genetically engineered APTAK tumor organoids (ApcΔ/Δ, Trp53Δ/Δ, Tgfbr2Δ/Δ, myristoylated human Akt, KrasG12D) was performed and the tumor microenvironment was further characterized by flow cytometry, ELISA, IHC and H&E staining. Besides, in vitro T cell polarization and bulk RNA sequencing of CD4+T cells were performed, and important markers were additionally investigated.

Results: Deletion of Tp53 in CD4+ T cells resulted in a significantly increased tumor growth in conditional knock out mice compared to control mice. Moreover, loss of Tp53 resulted in reduced levels of IFNγ and TNFα in the tumor microenvironment. In a co-culture of Th1 polarized CD4+ T cells with APTAK tumor monolayers, Tp53-deficiency in Th1 cells resulted in decreased levels of cell death and increased proliferation of tumor cell monolayers in comparison to control Th cells. Interestingly, bulk RNA sequencing data from conditional knockout CD4+ T cells revealed a significant downregulation of the T cell receptor (TCR) signaling pathway, including the key regulator genes ZAP70 and LCK. Notably, our findings demon-

strate that p53 is upregulated in CD4+ T cells only upon TCR stimulation with both anti-CD3 and anti-CD28. This p53 upregulation leads to the phosphorylation of ZAP70 and LCK, which in turn results in the expression of IFNγ. This highlights the pivotal role of p53 in the TCR signaling pathway and its crucial function in the immunomodulation of CD4+ T cells.

Discussion/Conclusion: Collectively, our findings suggest that Tp53 has an important role in the antitumor response of CD4+ T cells against colorectal cancer. However, more work needs to be done in order to fully understand the mechanisms that regulate Tp53 activity in CD4+ T cells, which could potentially result in the development of novel immunotherapeutic strategies against CRC.

38. Evaluating the management of eosinophilic oesophagitis in a specialist clinic of Cardiff & Vale: A real-world audit and proposed new management algorithm

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Introduction: Eosinophilic oesophagitis (EoE) is a clinicopathologic disease characterised by eosophageal dysfunction symptoms, such as dysphagia and food bolus obstruction, alongside a peak eosinophil count (EOS) of ≥ 15/0.3 mm2 in oesophageal biopsies. Emerging as the predominant cause of FBO in emergency departments, EoE instills a pervasive fear of eating and drinking, leading to a deterioration of patients' quality of life.

Methods: We undertook a retrospective observational study evaluating the medical records of patients diagnosed with EoE and treated at a specialist clinic within a tertiary hospital. We analysed demographic data, diagnostic approaches, initial presentations, treatment modalities and management plans, including remission surveillance strategies.

Results: We identified 93-patients with a full dataset for analysis, 90 of whom presented with dysphagia. Our findings indicate a male predominance in EoE, with a strong association with atopic conditions. Treatment modalities included oral dispersible budesonide (ODB, Jorveza®), n = 41; proton-pump inhibitors (PPI), n = 36; food elimination diet (FED), n = 4; and other treatments (including combination treatments), n = 12. Histological remission outcomes were significantly better in patients treated with ODB than other treatments (p = 0.019). However, the true rate of remission of each treatment was limited by a low 12-week post-treatment endoscopy rate and histological assessment of 58.1%, reflecting a significant drop-off in patient concordance.

Discussion/Conclusion: Achieving adherence to BSG guidelines, which recommend a repeat endoscopy within 8–12 weeks, is challenging due to low compliance, patient tolerability of the procedure and the extensive waiting list in the NHS. Many patients refuse follow-up endoscopies due to the lack of perceived clinical benefit and potential adverse events. This study reviews the implications of current management guidelines and proposes a new management algorithm for EoE, eliminating the need for endoscopy in patients treated with ODB. This approach underscores the importance of balancing clinical and histological remission outcomes with cost and patient concordance challenges.

39. Efficacy and safety of biotherapies in inflammatory bowel disease

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Introduction: Anti-TNF alpha drugs have revolutionized the management of patients suffer-

ing from chronic inflammatory bowel disease (IBD). However, there are many reasons for discontinuing anti-TNFs: primary failure, secondary failure or intolerance. The aim of this study was to investigate the efficacy and tolerability of anti-TNF alpha in patients undergoing follow-up for IBD.

Methods: Retrospective study extended over 12 years, including 53 patients followed at the gastroenterology department of Mohamed Taher Maamouri Hospital in Nabeul, for IBD of the Crohn's disease (CD) or ulcerative colitis (UC) type and treated with anti-TNF alpha. Clinical, biological and evolutionary data were collected from patient records. The significance level was set at 0.5

Results: Fifty-three patients on anti-TNF alpha were enrolled, with a mean age of 36 years [16–68]. The sex ratio (M/F) was 1.3. Forty-eight had CD (92.3%), 5 had UC (5.7%). The 3 main indications for anti-TNF alpha were: the presence of complex anoperineal fistulas (n = 16), postoperative recurrence (n = 15), failure or intolerance to azathioprine (n = 8).

The first-line biologics used were infliximab (94.3%) and adalimumab (5.6%). Switching between these 2 types of biotherapy was noted in 10 patients (18.8%). In 48 patients, anti-TNF alpha was combined with azathioprine (90.5%). Mean follow-up was 42 months [12–168]. Loss of primary or secondary response was noted in 18 patients (33.9%). Complications due to biotherapies were noted in 13 patients (24.5%): 3 had an allergic reaction authenticated by a pharmacovigilance survey and resolved by reducing the infusion rate, and 10 patients had an infectious complication. Five patients had pneumopathy that was controlled by oral antibiotic therapy, with a favorable outcome. Three patients had skin abscesses that had been resolved by flattening and antibiotic therapy. One patient had a medically treated renal abscess, and a single case of pulmonary tuberculosis treated with anti-tuberculosis drugs, with resumption of biotherapy after 6 months.

In univariate analysis, the presence of anoperineal manifestations (p = 0.01), colonic involvement (p = 0.002) and previous resection > 50 cm (p = 0.01) were significantly associated with loss of response. Risk factors for complications were fistulizing phenotype (p = 0.02) and association with azathioprine (p = 0.03).

Discussion/Conclusion: Biotherapies represent a major advance in the treatment of IBD, with good tolerability. The main complications in our series were allergic reactions and non-severe infectious complications.

40. Oral manifestations and salivary lactoferrin concentration in inflammatory bowel disease patients based on therapy type

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Introduction: The objectives of the study were to determine the prevalence of oral manifestations and the concentration of salivary lactoferrin in patients with inflammatory bowel disease (IBD) based on therapy type.

Methods: A total of 71 IBD subjects (27 in the anti-TNFα, 22 in the anti-integrin α4β7 and 22 in the conventional group – 15 with aminosalicylates in therapy and 7 without pharmacological treatment) and 71 healthy control subjects participated in the study. In the salivary lactoferrin concentration analysis, 21 subjects in the anti-TNFα group, 10 subjects in the anti-integrin α4β7 group, 15 subjects in the conventional group and 20 control subjects were included.

Oral examination, oral mucosa swab test and non-stimulated salivary flow test were conducted. An enzyme-linked immunosorbent assay was used to analyse the lactoferrin concentration in the saliva samples.

Results: Higher prevalence of atrophic glossitis and denture palatitis were found in the anti-TNFα ($p < 0.05$ and $p < 0,01$, respectively) and anti-integrin α4β7 group ($p < 0.001$ and $p < 0.05$, respectively) compared to controls. The coated tongue was more frequent in the conventional group compared to the anti-TNFα ($p < 0.05$) and control group ($p < 0.001$). Prevalence of hyposalivation was higher in the anti-TNFα ($p < 0.05$), anti-integrin α4β7 ($p < 0.001$) and conventional group ($p < 0.001$) compared to controls, and in the anti-integrin α4β7 ($p < 0.05$) compared to the anti-TNFα group. Candidiasis was more frequent in the anti-TNFα ($p < 0.01$) and anti-integrin α4β7 group ($p < 0.05$) compared to controls. Salivary lactoferrin concentration (mean 3 standard deviation) was 12505.5 3 7923.63 ng/ml in the anti-TNFα, 18363.4 3 14645.05 ng/ml in the anti-integrin α4β7, 13791.8 3 9964.74 ng/ml in the conventional and 6657.9 3 4268.23 ng/ml in the control group. Anti-integrin α4β7 group had a significantly higher salivary lactoferrin concentration than the control group ($p < 0.01$).

Discussion/Conclusion: IBD patients have a higher prevalence of oral manifestation, especially those receiving biologic therapy. Salivary lactoferrin concentration is elevated in the IBD patients, suggesting its value as a potential biomarker for the IBD.

41. Predictive factors of confocal laser endomicroscopy evaluation for histologic activity in inflammatory bowel disease

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Introduction: Inflammatory bowel diseases (IBD) represent heterogeneous and relapsing intestinal conditions, with a severe impact on the quality of life. Advances in treatment have targeted new therapeutic goals, with histological healing emerging as a potential target. However, histological assessment requires multiple biopsies and prolonged procedures. Confocal laser endomicroscopy (CLE) offers a promising alternative, allowing for real-time, in vivo assessment of mucosal healing and inflammation. This study aims to determine if parameters obtained through CLE correlate with histopathological inflammation Robarts Histopathology Index (RHI) and whether persistent histological inflammation predicts relapse within twelve months.

Methods: The study included 63 patients in clinical remission: 41 with ulcerative colitis (UC) and 22 with Crohn's disease (CD). Clinical characteristics, laboratory parameters, endoscopic scores were documented. CLE parameters, such as increased crypt distance, vessel diameter > 20 Qm, dilated crypt lumen, and fluorescein leakage were assessed during colonoscopy before taking biopsies while the histopathological inflammation was defined as RHI > 3.

Results: Half of UC, respectively 72% of CD patients had a RHI > 3. Among CLE findings, three parameters correlated with histopathological inflammatory activity: increased crypt distance (OR = 3,22, 95% CI: 1.56–5.90, $p = 0.002$), vessel diameter > 20 Qm (OR = 4.31, 95% CI: 2.24–6.15, $p = 0.006$), and fluorescein leakage (OR = 6.17, 95% CI: 3.26–15.79 $p = 0.001$) while fecal calprotectin did not correlate with RHI in the studied group. At 12-month surveillance, histological inflammatory activity is a significant predictor of disease relapse, with patients showing such activity having a threefold increased risk of relapse (OR = 3.17, 95% CI: 1.50–6.00, $p < 0.01$).

Discussion/Conclusion: CLE represents a valuable tool in assessing histological inflammation in IBD patients in remission. The presence of RHI > 3 correlates with specific CLE findings and serves as a predictor of disease relapse. These results support the use of CLE for

real-time, non-invasive evaluation in clinical practice, potentially guiding more precise therapeutic interventions.

42. Vascular leakage as an early diagnostic marker for inflammation in IBD: Insights from a multiphoton endomicroscopy study in mice

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Introduction: The diagnostic landscape for Inflammatory bowel disease (IBD) faces challenges due to the complex nature of the disease, necessitating reliable and cost-effective markers. The gut vascular barrier (GVB) plays a critical role in immune cell recruitment and infiltration into intestinal tissue, contributing to inflammation. Increased vascular permeability in both IBD patients and DSS-treated mice correlates with disease activity, yet it remains unclear whether this increase occurs at early or late stages of inflammation.

Methods: We introduced a novel marker-based multiphoton endomicroscopy (MPEM) for repetitive vascular permeability measurements in preclinical models (DSS-induced colitis, T-cell transfer-induced colitis, intrarectal ethanol treatment). Mucosal inflammation was monitored using mini-endoscopy, with H&E staining used for histopathological assessment and flow cytometry for immune cell detection.

Results: MPEM-based measurements during DSS-induced colitis revealed that vascular permeability increases significantly earlier than traditional disease indices, including endoscopic score, body weight change, colon shortening, histopathological scoring, and immune cell infiltration. Early onset was confirmed in T-cell transfer-induced colitis. Ethanol treatment validated MPEM sensitivity by detecting vascular leakage even after a single transient mild exposure of the colonic mucosa. The technique high penetration depth enabled 3D visualization of colonic mucosal vessels, showing early vascular leakage near the colon lumen as initial responders to DSS-induced colitis. As inflammation progressed, deeper vessel permeability increased, with epithelial barrier breaches at upper crypts while crypt bases remained intact. This led to significant serum tracer leakage pooling in crypts, forming dye foci in each crypt's lumen, indicating extensive endothelial and epithelial barrier disruption.

Discussion/Conclusion: Our findings support monitoring vascular permeability as an early, sensitive marker for colonic inflammation. Integrating this technique with clinical assessments could enhance diagnostic accuracy and provide a reliable method to monitor therapy responses, predict flares, and improve therapeutic strategy based on treatment outcomes.

43. Patient preferences regarding medical treatment options in eosinophilic esophagitis

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Introduction: Until a few years ago, only off-label medical treatment options for eosinophilic esophagitis (EoE) existed. Historically, proton-pump inhibitors (PPI) or swallowed topical corticosteroids (STC) with various formulations and ingredients were used with promising

but varying clinical results. The approval and promising clinical results of a budesonide orodispersible tablet (BOT) in Europe was the start of a continuing development of new therapeutic agents. Just recently the first biological agent (dupilumab) as well as another budesonide oral suspension (EOHILIA) was introduced and approved in the USA. Currently, several phase 3 trials with different drugs are running, resulting in various future treatment options. However, data about patients' perspectives are lacking. We therefore aimed to assess patients' awareness, beliefs, fears, wishes and restrictions to medical treatment options in EoE.

Methods: We developed a web-based survey using SurveyMonkey and sent a questionnaire comprised of 47 questions about patients' preferences regarding medical treatment options to patients with established EoE in Switzerland, Austria and Germany.

Results: A total of 127 patients (64% male, 19% with other atopic diseases) from Switzerland (66%), Austria (17%) and Germany (17%) answered the questionnaire. A swallowed topical therapy was ranked first (56% of patients) in terms of patient's preference followed by a subcutaneous therapy every 4 weeks (21%) and by an oral therapy with systemic effect (19%). Although 41% of the patients do not have reservations against long-term medical therapy, half of patients are skeptical about long-term treatment and 65% are afraid of adverse events. However, more than half (55%) of patients are not aware that STC are locally effective medications with nearly no systemic effect. Furthermore, 48% of patients believe that physicians underemphasize adverse events of medication. All patients understand the importance of not only treating symptoms but also inflammation.

Discussion/Conclusion: Patients with EoE prefer topical agents over other available routes of administration. Patient education should be carried out to address reservations about long-term treatment.

44. Assessment of knowledge about pregnancy and conception possibilities in women of reproductive age with ulcerative colitis using the CCPknow score

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Introduction: Inflammatory bowel diseases are systemic diseases that include Crohn's disease and ulcerative colitis. The onset of the first symptoms of ulcerative colitis often aligns with the reproductive period of life. Deficient knowledge among ulcerative colitis patients regarding the prospects of conception and pregnancy could lead to avoiding parenthood or irregularly managing the disease during pregnancy.

Methods: A cross-sectional study was conducted using the CCPknow questionnaire to assess the knowledge of planning and course of pregnancy in patients with ulcerative colitis. Patients completed the CCPknow questionnaire from 2020 through 2022. A total of 119 patients were included in the analysis of demographic data, duration and disease phenotype, current therapy, employment and educational level of women with ulcerative colitis. According to the questionnaire results, the patients were divided into 4 categories: a-unsatisfactory knowledge; b-adequate knowledge; c-good knowledge; and d-very good knowledge.

Results: Out of 119 patients, the majority belonged to the b category (n = 60).). The median duration of disease from Category C was the longest (42 months), while the shortest was among patients from Category D (12 months). A higher number of married women was

shown in the category with the highest points compared to the expected number (7.56% compared to 6.8% of the total number of patients). A total of 91.84% of women with lower education belonged to categories with lower CCPknow scores.

Discussion/Conclusion: The level of awareness about the impact of ulcerative colitis on pregnancy among women was the highest in cases of shorter duration of the disease, and better than statistically expected among married women. It has been shown that a higher level of education is a good predictive factor for better knowledge about fertility and pregnancy.

45. Short-term exposure to environmental air pollution and inflammatory bowel disease flares: A time-stratified case cross-over study

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Introduction: Some epidemiological studies suggest that long-term exposure to environmental air pollutants, such as particulate matter (PM), could have a role in inflammatory bowel disease (IBD) incidence and pathogenesis. However, less is known about the potential effect of short-term air pollution exposure. The aim of this study is to investigate whether short-term exposure to environmental air pollution is associated with the occurrence of IBD flares.

Methods: Anonymized hospital discharge records (HDR) with ICD-9-CM codes 555 (Crohn's disease) and 556 (ulcerative colitis) for years 2002–2009 from all hospitals of the Lombardy region were collected. All HDR of adult patients (18–75 years) resident in Milan were included, except for recurrent hospitalizations within 6 months. Each record was assigned daily PM ≤ 10 Qm (PM10) concentrations at municipality level by averaging PM10 levels of the day of admission with the levels of the day before (lag01) and of each preceding day up to six days before (lag06). To evaluate the association between PM10 and IBD-related hospitalizations, a time-stratified case-crossover study design was applied. Conditional logistic regression models, calculating odds ratios (OR) and 95% confidence intervals (95% CI) per increments of 10 Qg/m3 of PM10, were performed.

Results: Overall, 2176 hospital admissions (males = 1137, Crohn's disease = 1264, ulcerative colitis = 912) were included. In the entire population no clear association between PM10 and IBD-related hospitalization was identified, notwithstanding a small risk increase for males (OR = 1.03; 95% CI: 0.99–1.08 at lag04). When further stratifying for ICD code, an increased risk of hospitalization for "left-sided ulcerative colitis" (ICD code: 556.5) was found in males only, for exposures in all days preceding hospitalization up to lag04 (1.28; 1.05–1.28; 59 cases, 207 controls) (Figure 1). In females, the association was weaker, although positive (1.14; 0.91–1.42; 49 cases, 164 controls). No relevant findings emerged when looking at other ICD codes.

Discussion/Conclusion: We observed an increased risk of IBD-related hospitalization in male patients with left-sided ulcerative colitis per increasing levels of air pollution in the days preceding hospital admission. Although preliminary, our findings suggest the possible role of sex as an effect modifier of the influence that air pollution might exert on IBD flares. Further studies are needed to better comprehend the complex framework characterizing the interplay between environmental and individual factors contributing to IBD.

46. Can patients with ulcerative colitis in remission have IBS or are we missing inflammation?

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Introduction: Patients with ulcerative colitis (UC) often report symptoms consistent with irritable bowel syndrome (IBS). Since both diseases are characterized by abdominal pain, bloating and disturbed defecation, sometimes it is hard to differentiate between them. Previous studies that estimated prevalence of IBS in patients with UC did not include histological markers of remission, but rather only clinical, biological and/or endoscopic criteria, which leaves the possibility that these symptoms are due to "hidden" inflammation rather than coexisting IBS. The aim of this study was to determine prevalence of IBS in patients with UC, who are treated with biologics and have reached clinical, biological, endoscopic and histological remission.

Methods: This single-center cross-sectional study included 53 patients with UC who are treated with biologics and have reached clinical, biological, endoscopic and histological remission. We defined clinical remission as Mayo partial score ≤ 1, biological remission was defined as fecal calprotectin (FCP) < 250 ug/g, endoscopic remission as Mayo subscore ≤ 1, and histological remission was defined as Nancy index ≤ 1. Presence of IBS was defined by Rome IV criteria.

Results: We selected all patients with UC from our referral center that were treated with biologics, and have reached clinical, biological and endoscopic remission. Among 68 patients, 53 (78%) UC patients reached histological ("deep") remission as well. Total of 9/68 (13.2%) patients with clinical, biological and endoscopic remission reported symptoms consistent with IBS, as opposed to 8/53 (15%) in the group of patients with "deep" remission.

Discussion/Conclusion: Prevalence of IBS in patients with UC varies according to how remission is defined; when clinical, biological, endoscopic and histological criteria are included, one in 7 patients presents with IBS. Including histological parameters does not affect the prevalence; however, further research and meta-analysis is necessary, due to a small sample in our study.

47. Neutrophil infiltration combined with necrosis in the primary tumor is a useful prognostic indicator for three-year disease-free survival time in patients with colorectal cancer

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Introduction: Histopathological evaluation plays a key role in the diagnosis of colorectal cancer (CRC). Tumour-related local inflammation is regarded as a novel prognostic parameter whereby neutrophils constitute one of the main inflammatory cells. The aim of the present study was to evaluate the prognostic value of intratumoural tumour-associated neutrophils (intraTANs), stromal TANs (stromaTANs) and necrosis, as well as their combined parametric value in formalin-fixed paraffin-embedded tissue sections from patients with CRC.

Methods: A retrospective study of 160 patients with CRC who underwent surgery was conducted. The association of intraTANs, stromaTANs, necrosis and their combined parametric value with the clinicopathological features of patients with CRC was examined. The Kaplan-

Meier method and the logrank test were used to compare survival curves. To identify independent prognostic factors, uni- and multivariate Cox proportional hazards regression models were used.

Results: StromaTANs were associated with lymph node metastasis (p = 0.049) and tumour deposits (p = 0.041). In addition, necrosis was found to be associated with hematogenous (p = 0.003), lymphatic (p = 0.007), perineural (p = 0.015) invasion, and lymph node metastasis (p = 0.033), as well as the number of invaded lymph nodes (p = 0.012), and lymph node pouch invasion (p = 0.043). Furthermore, necrosis was found to be associated with white blood cell count (p = 0.030), neutrophil count (p = 0.011), combined neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (NLR-PLR) (p = 0.038), and the combined platelet and NLR (PLT-NLR status) (p = 0.030), as well as serum carcinoembryonic antigen (CEA) levels following surgery (p = 0.011) and monocyte-to-lymphocyte ratio (p = 0.023). The combined parametric value was found to be associated with pT stage (p = 0.049), hematogenous (p = 0.034) and lymphatic (p = 0.026) invasion, and with serum CEA levels prior to surgery (p = 0.029). The analysis of the 3-year disease-free survival (DFS) time revealed that tumour growth (hazard ratio [HR] = 2.070; 95% CI: 1.837–3.808; p = 0.003] and the combined parametric value (intraTANs, stromaTANs and necrosis, HR = 1.577; 95% CI: 1.372–3.032; p = 0.028) were independent factors for patients with CRC.

Discussion/Conclusion: The findings of this current study demonstrated that the combined value of neutrophils and necrosis examined in the cancerous tissue may be used as a prognostic factor for the 3-year DFS time in patients with CRC.

48. Maintenance of clinical, biochemical and transmural remission in IBD patients switching from intravenous to subcutaneous infliximab

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Introduction: Subcutaneous (SC) infliximab (IFX) effectively maintains biochemical, clinical and endoscopic remission in inflammatory bowel disease (IBD). Especially in Crohn's disease (CD), transmural healing is considered a desirable treatment endpoint. The effectiveness of switching from IV to SC-IFX in maintaining transmural remission in IBD is unknown.

Methods: This is a prospective cohort study on IBD patients in clinical and endoscopic remission switched from IV to SC-IFX. Biochemical markers (fecal calprotectin and C-reactive protein), infliximab levels and anti-drug antibodies (ADAs) were dosed at baseline, week 12, 24 and 52. Intestinal ultrasound was performed at baseline, week 24, and 52, with a full colonoscopy at week 52 for disease assessment. Remission rates and safety profile beyond 48 weeks were recorded. T-Test and ANOVA for mean comparisons and Kaplan Meier estimates were used for survival curves.

Results: 45 IBD patients (71% males, 55% CD) were enrolled. During a median follow-up of 77 weeks (range, 16–88) clinical remission rate was 90%. Biochemical parameters remained stable (p > 0.05). Median baseline infliximab level was 9.42 ug/m (range, 0.1–41.8), undetectable infliximab levels (< 1 ug/ml) and positive ADAs were found in 7 and 16 patients, respectively; at week 12, a significant increase in infliximab levels (mean increase 27.4 ng/ml; 12.6 SD; p < 0.001) and a decrease of ADAs titer were observed (mean decrease 10.87 ng/ml; 27.8 SD; p = 0.01). No significant changes were found at follow-up ultrasound. 3 out 41 patients showed mild endoscopic activity. Safety profile was good with 14 mild infections, 2 injection

site reaction, one ocular, one mild neurologic, and one non-IBD related hospitalization. One cutaneous adverse event required switching back to IV-IFX.

Discussion/Conclusion: Switching from IV to SC infliximab in selected IBD patients is safe and effective in maintaining clinical, biochemical, and transmural remission. IUS is a useful and non-invasive tool for periodic disease assessment in this subset of patients.

49. Younger age but not atopic disease, sex, previous food impaction or general anaesthesia is associated with obtaining biopsies in case of esophageal food impaction

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Introduction: Esophageal food impaction (EFI) is a common first presentation in patients with an undiagnosed eosinophilic esophagitis (EoE). Obtaining biopsies at index endoscopy is recommended by many guidelines to diagnose the cause of EFI. However, real-world data suggest that only the minority of endoscopists take biopsies in case of EFI. The aim of this study was to investigate which factors affect the decision for obtaining biopsies.

Methods: This was a retrospective multicentre study collecting the data from four major gastroenterology centres in Switzerland of patients presenting with EFI. Patients with known reflux strictures or esophageal cancer were excluded. Data on demographics, type of endoscopy performed, biopsy results were obtained from the electronic health records. The associations of clinical factors on the decision of taking biopsies were tested via logistic regression.

Results: Between January 2015 and December 2020, 198 EFI (median age 50 years of age (IQR, 27.8), 22% female, 28% with previous EFI) were recorded. 94% (n = 186) of patients required an endoscopy for bolus removal. The median time from ER presentation to endoscopy was 150 minutes (IQR, 120 minutes). Esophageal biopsies were taken in more than a half of the individuals (n = 97, 53.8%), of whom 71 patients had a previous diagnosis of EoE. Although no procedural complications were recorded, 18% of patients needed inpatient admission. The only factor associated with obtaining biopsies in the multivariate regression analysis was younger age (OR = 0.96; 95% CI: 0.95–0.98; $p < 0.001$). Sex, atopic disease, previous EFI or general anaesthesia were not associated with obtaining biopsies.

Discussion/Conclusion: Although EoE is one of the most common causes of EFI, only few patients with risk factors are biopsied. To shorten diagnostic delay in patients with EoE, endoscopists should be encouraged to obtain biopsies in case of EFI.

50. What is the role of measuring urinary gluten immunogenic peptides in clinical practice in patients with coeliac disease?

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Introduction: In coeliac disease, the clinical role of urinary gluten immunogenic peptides is unclear. One possible role is to help identify patients with ongoing villous atrophy. We pres-

ent the largest clinical data in patients with coeliac disease to establish the diagnostic accuracy of the urinary gluten immunogenic peptide in identifying villous atrophy.

Methods: Patients providing urinary gluten immunogenic peptide were identified between September 2018 and August 2023 at the National Health Service (NHS) England National Centre for Non-Responsive and Refractory CD (Sheffield Teaching Hospitals NHS Foundation Trust, UK). In our retrospective study, the results of the urinary gluten immunogenic peptide test, self-reported adherence to a gluten free diet, serology and histology collected around the same time were compared in individuals with coeliac disease either not on or on immunosuppression (group 1 and 2 respectively).

Results: Group 1 had 158 patients (70.3% female, median age 48 years) and group 2 had 46 (63% female, median age 57 years) providing in total, 641 urine samples. In group 1, the sensitivity, specificity, positive predictive value and negative predictive value for detecting villous atrophy of a urinary gluten immunogenic peptide taken within 1 week of their gastroscopy was 37.1%, 80.3%, 45.6% and 74.1% respectively. Where the urinary gluten immunogenic peptide was positive, a total of 79.2% of patients reported adherence to a gluten free diet and of these, 52.6% had no villous atrophy. When the IgA-tTG was negative, 19.4% of cases had a positive urinary gluten immunogenic peptide.

More patients in group 2 had a positive urinary gluten immunogenic peptide (43.3% vs. 24.1%, $p < 0.001$).

Discussion/Conclusion: The urinary gluten immunogenic peptide may have a role in identifying gluten ingestion but not identifying villous atrophy. Therefore, to assess for villous atrophy an upper gastrointestinal endoscopy is still required.

51. The effect of milk-derived extracellular vesicles (MDEs) on the epithelial cells of IBD patients and heathy control

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Introduction: The pathogenesis of inflammatory bowel diseases (IBD) is considered to be multifactorial, comprising factors such as immune dysregulation, environmental influences, microbial dysbiosis, and genetic predispositions of the host. In this regard, the contribution of factors associated with intestinal epithelial cells (IECs) has been less studied.

Milk-derived exosomes (MDEs) are nanovesicles that transport microRNA (miRNA). We demonstrated that MDEs are internalized by IECs and impart a therapeutic and anti-inflammatory effect in a murine model of colitis. This study aimed to determine the impact of MDEs on human IECs

Methods: We have employed organoids derived from human intestinal biopsies from IBD patients and heathy controls. Gene and miRNA expression were analyzed by qRT-PCR. Proliferation was analyzed by immunofluorescent staining Ki67.

Results: We demonstrated that milk-derived exosomes (MDEs) were internalized by the organoids, altering their miRNA profile. The expression of miRNA that are abundant in MDEs, such as miR-148, was higher in organoids treated with MDEs compared to untreated ones (10.44 3 0.17 vs. 4.06 3 0.76, respectively). DNMT1, a target gene of miR-148, was downregulated in MDE-treated organoids (from 0,49 8 3 0.037 to 0.064 3 0.011). Additionally, other MDE-associated miRNAs showed increased levels in treated organoids: Let-7a (2.05 3 0.06 vs. 1.37 3 0.025) and miR-30 (7.85 3 0.51 vs. 5.44 3 0.9, respectively). Incubation with MDEs in the culture medium of intestinal organoids induced enhanced epithelial cell proliferation, as evidenced by significantly increased Ki67 staining. Moreover, the expression of β-catenin, which is involved for intestinal epithelium integrity and barrier function, was upregulated in organoids treated with MDEs in comparison to untreated controls.

Discussion/Conclusion: Results from this study offer preliminary new preclinical tool to analyze the role of MDEs on human ICEs and intestinal homeostasis and to understand the clinical applications of MDE. A deeper understanding of the mechanistic effect of MDEs on the IECs can help to target and potentiate the therapeutic effect of this non-toxic natural nutraceutical component, adding MDEs to our armamentarium to fight inflammatory bowel diseases.

52. Influence of pharmacogenetics on response to proton-pump inhibitors in eosinophilic esophagitis: Results from a large retrospective cohort from four Spanish hospitals

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Introduction: Proton-pump inhibitors (PPIs) are the most prescribed first-line treatment for eosinophilic esophagitis (EoE). However, only around half of patients respond histologically to a double dosage of PPI. Pharmacogenetics of PPIs is largely known to depend on CYP2C19 haplotypes. Previous studies in EoE have shown promising results to predict PPI response by analyzing genetic variations in CYP2C19 and STAT6 genes, while other single nucleotide variations (SNPs) could play also a role.

Methods: The study aims to analyze the effect of 60 previously described SNPs associated with the response to PPIs in EoE or other diseases, or related to EoE genetics. Those SNPs were genotyped using an Open Array platform on DNA obtained from peripheral blood. Inclusion criteria were patients diagnosed with EoE according to clinical guidelines and treated with PPIs. Exclusion criteria were: response not evaluated under double or higher PPI doses, lack of histopathologic response assessment or unresponsiveness to PPIs before 8 weeks of treatment length. Patients were recruited in 4 Spanish referral hospitals and demographical and clinical data were obtained retrospectively. Patients were classified as non-responders (peak of eosinophils ≥ 15 per high power field, hpf) or responders (< 15 eos/hpf). Chi-square or Fisher's exact test were used for statistical comparisons. Statistical significance was established for $p < 0.05$.

Results: Overall, 505 patients (75% male and 15% < 18 years old at PPI onset, mean age 34.5 3 14.9 years) were included; 48% responded to double o higher PPI doses. Omeprazole was the most common PPI (57%). Seventeen percent of patients presented mixed or stricturing EoE phenotypes. Regarding clinical variables, sex and age did not influence PPI effectiveness. In concordance with previous studies, a lower response rate was found in patients with mixed/structuring compared with inflammatory phenotypes (27% vs. 52%, $p < 0.001$). Treatments length over 10 weeks achieved higher effectiveness ($p = 0.028$). Using omeprazole and rabeprazole trended to produce higher effectiveness ($p = 0.067$). Two SNPs were found to be associated with response to double or higher PPI doses: CYP3A5 rs776746 ($p = 0.013$, intermediate phenotype associating to a lower response rate of 35% and being present in 14% of patients) and KCNJ2 rs312691 (recessive model, $p = 0.006$, this variant increasing response up to 69%, and being present in 8% of patients). Since phenotype had a great influence in response to PPIs, patients' genotypes were analyzed according to this variable. The 2 aforementioned variants had no effect on mixed/stricturing phenotypes, while statistical significance was kept for CYP3A5 rs776746 and KCN J2 rs312691 in patients with inflamma-

tory phenotypes (p = 0.007 and p = 0.005, respectively). For patients with mixed/stricturing phenotypes, the presence of variants in chr14 rs7144958 (dominant model), STAT6 rs3024974 (recessive model) or being a CYP2C19 rapid/ultrarapid metabolizer (frequency of 18%, 19% and 28% in this type of patients, respectively) produced a trend to unresponsiveness to PPI (93%, p = 0.097; 92% p = 0.100; and 86%, p = 0.094, respectively). On the other hand, when sub-groups were created according to PPI drug, the use of esomeprazole in patients carrying the CYP3A5 rs776746 variant further reduced the response rate to only 19% (p = 0.072).

Discussion/Conclusion: We have identified two SNPs affecting the response to double or higher doses of PPI in EoE patients with inflammatory phenotype and three SNPs that may decrease PPI effectiveness in patients with mixed or stricturing phenotypes.

53. High prevalence of steatotic liver disease in IBD patients

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Introduction: The connection between Inflammatory bowel disease (IBD) and the recently introduced term steatotic liver disease (SLD), with its wide spectrum, is clearly indicated by emerging data. While there has been an increase in the occurrence of obesity in IBD patients, individuals with IBD and MASLD frequently tend to be categorized as lean, with a body mass index (BMI) ≤ 25 kg/m2. The aim of this study was to evaluate the prevalence and risk factors of SLD in lean IBD patients.

Methods: This monocentric retrospective study included patients with IBD who underwent vibration-controlled transient elastography with controlled attenuation parameter (CAP) evaluation. Patients with infectious or suspected alcoholic liver disease or recent history of steroids consumption were excluded. Demographic characteristics, disease activity and medications were analyzed as potential risk factors.

Results: A total of 142 patients with IBD were included, mostly male (61.3%), with a mean age of 47.1 3 12.8 years. The most common IBD type was Crohn's disease (59.8%, 85 patients). SLD was more frequently diagnosed in patients with ulcerative colitis (UC) (37%, 21 vs. 26%, 22, p = 0.032). Metabolic dysfunction-associated steatotic liver disease (MASLD) was observed in 32 (23.1%) patients, while cryptogenic SLD was present in 11 (7.7%) subjects. Patients with SLD presented a higher BMI (p < 0.001), had a higher disease duration (p = 0.013), a higher fasting plasma glucose (p = 0.029) and a more important inflammatory status (p = 0.041). Moreover, disease activity and history of bowel resection were IBD-related factors associated with the presence of SLD.

Discussion/Conclusion: SLD exhibits a higher prevalence in lean IBD cohorts compared to the general population, representing a much-neglected group that is frequently linked with a negative outcome. As such, this is an important study that contributes to the growing body of evidence supporting IBD as an independent risk factor for SLD.

54. Unusual ocular manifestations in Crohn's disease

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Introduction: Extra-intestinal manifestations in Crohn's disease (CD) are frequent. Ocular disorders are polymorphic and generally under diagnosed as they are challenging diagnosis.

Episcleritis is the most common ocular manifestation. However, posterior ocular involvement is more unusual. We report a series of 6 patients followed up for CD and presenting with posterior uveitis and retinal vasculitis.

Methods: We analyzed retrospectively the records of 6 patients (8 eyes) followed up for CD and presenting with posterior ocular disorders. Each patient underwent a complete ophthalmologic examination and a retinal fluorescence angiography.

Results: The average age was 32 years. The M/F gender ratio was 2. The average interval between the diagnosis of CD and the onset of ocular involvement was of 16.3 months (range, 6–32 months). Ocular manifestations included: hypopyon in 2 eyes, panuveitis in 4 eyes, retinal periphlebitis in 2 eyes, isolated posterior segment inflammation in 2 eyes and a serous retinal detachment in one patient. Systemic steroids associated to immunosuppressants therapy were prescribed to all cases. Complications were observed in 3 eyes (pupillary seclusion 1 eye, retinal neovascularization 1 eye and macular hole 1 eye).

Discussion/Conclusion: Ocular manifestations during Crohn's disease are rare. They require regular monitoring and a collaborative clinical care team for appropriate management in order to improve the prognosis and to prevent recurrence.

55. Loss of response to off-label swallowed topical corticosteroids can be overcome by a switch to an esophageal-targeted budesonide formulation

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Introduction: Swallowed topical corticosteroids (STC) are effective in inducing and maintaining remission in patients with eosinophilic esophagitis (EoE). However, real-world data about loss of response to STC are limited and whether patients with off-label STC (olSTC) failure may achieve histologic remission after switch to budesonide orodispersible tablets (BOT), is unknown.

Methods: We analyzed prospectively collected data between 2015 to 2023 from the Swiss Eosinophilic Esophagitis Cohort Study (SEECS). We compared EoE patients with prior histologic olSTC-failure (≥ 15 eos/hpf), histologic remission after olSTC (< 15 eos/hpf) and STC-naïve patients before BOT treatment. Furthermore, we evaluated the course of olSTC-failure patients after a switch to BOT and used logistic regression to explore associations between patients with olSTC-failure and clinical factors.

Results: A total of 340 patients (76% male, median 43 years of age) were analyzed of whom 26% (n = 89) had a prior olSTC non-response, 16% were in remission with prior olSTC and 58% were STC-naïve before BOT. The groups differed significantly in age, disease duration, quality of life, endoscopic and histologic activity and number of bolus impactions. In the multivariable logistic regression, olSTC treatment duration in years (OR = 1.30 [95% CI: 1.11–1.52], p = 0.001), low STC adherence (OR = 3.20 [95% CI: 1.11–9.24], p = 0.03) and age less than 30 years (OR = 6.78 [95% CI: 1.37–33.58], p = 0.02) were independently associated with histologic non-response to olSTC. After switch from olSTC to BOT (n = 66) the peak eosinophils decreased from a median of 70/hpf (29–120) to 9/hpf (1–59) in patients with prior non-response to olSTC. There was a numerically higher histologic response to BOT in patients that responded to olSTC before (n = 44) compared to patients non-responded to olSTC (n = 66) (77.3% vs. 62.1%, p = 0.095).

Discussion/Conclusion: Most patients non-responding to olSTC are not true corticosteroid-refractory but respond to an esophageal-targeted budesonide formulation. Age below 30 years, longer treatment duration and low adherence are associated with olSTC-failure.

56. Exploring the impact of an inflammatory bowel disease biologics nurse on the management of a biologics service

Glyn Scott (Margate, GB)

Introduction: Biologics nurses play a critical role in the management of patients receiving treatment for Inflammatory bowel disease (IBD). Their impact spans various facets of patient care and service management. Prior to December 2021 all patients who required biological therapy were reviewed by any member of the IBD nursing team. This review would entail a comprehensive history taken, screening bloods ordered and explained and a thorough explanation of the risks and benefits of the medication including a detailed explanation of the use of the drug. The nurses were also responsible for the preparation of biologic prescriptions and checking of bloods. With a number of nurses undertaking this can lead to duplication of work or patients not receiving medication timely.

Methods: A business case was written to secure funding for extra nurses and was unsuccessful. At the time of the Covid pandemic workload escalated to an extent that the current IBD Helpline and nurse led clinics could not continue in their present form. Resulting in a suspension of nurse clinics which led to a backlog of reviewing patients who required biological therapy, thus delaying their treatment. A meeting was convened with the senior management team and staffing numbers were increased resulting in the development of a biologics nurse.

Results: A band 6 biologics nurse was employed who completely transformed the biologics service. One person completing a role independently assumes total responsibility for all of the tasks annexed to the role. This involved patient education and support, monitoring and assessment of patients, coordination and communication with patients and relevant departments. quality improvement, patient advocacy, emotional support to patients and patient empowerment. One person responsible for this role has now led to a reduction in complaints, more timely treatment, less missed treatment appointments and a single point of contact for patients and departments. Our biologics nurse has not only achieved all of these roles but has been fundamental in the biologic switch to more cost effective biological therapies.

Discussion/Conclusion: The impact of a dedicated biologics nurse in an IBD service is significant. They enhance the overall quality of care, improve patient outcomes, and contribute to the efficient functioning of the service by ensuring proper management, patient education, and support throughout the treatment journey. The team have had an increased number of praise and favourable comments from patients, families and departments that interact with our service such as the Medical Day Unit. The introduction of this role has been invaluable to our service has increased to such an amount that the team could do with a second nurse in post. Patient satisfaction surveys and patient testimonials are available.

57. Utilising an inflammatory bowel disease dashboard to record the workload of the IBD team enabling them to build a fully resourced service

Glyn Scott (Margate, GB)

Introduction: An inflammatory bowel disease (IBD) dashboard can be incredibly valuable in managing and optimizing the workload of an IBD team. It allows for the centralized collec-

tion and visualization of key metrics and data points, which can aid in resource allocation and improving the efficiency of the service. The IBD Dashboard Data System was developed to account for the activity of the team and could be used for future business planning and ensuring the delivery of a safer IDB service. This project ensured that the senior management team were aware of the increased activity of the team, ensuring that no nurses were redeployed during the Covid 19 pandemic or since.

Methods: This was developed over the last 5 years and we were able to test the data collected over this period to provide the data required to increase staffing numbers. Key performance indicators were set for nurses to collect weekly. This included number of patients with Crohn's disease, ulcerative colitis, other patients seen, DNA rates, numbers of staff taught, patients prepared for biologics or immuno-modulator therapy, number of helpline calls and time taken over the call, ward patients seen and number of prescriptions prepared and signed by the Consultant Nurse. Key metrics and data points have been initiated which included: patient data overview, team workload, resource management, quality of care, and trends and patterns.

We discussed this project with the senior divisional management and have utilised this data at local commissioning meetings.

Results: At the start of the project the staffing numbers was 2.6 whole time equivalent (wte) band 7 nurses with no designated administration support for the team. According to Crohn's & Colitis UK the required staffing numbers for our catchment population was 7.5 wte nurses, which meant we were drastically under-resourced. We were able to utilise the data provided to convene a meeting with key stake holders including general manager, clinical lead, divisional director and medical director. This meeting focussed on the data provided and reviewing the workload. To enable the team to provide a safe service, the IBD Nurse clinics were suspended until safer staffing numbers were increased. This enabled the nursing team to focus on the helpline service and to plan a new service with safer staffing numbers. This was agreed by the divisional management team and a recruitment strategy was planned. The patients whose clinic appointments were cancelled were given access to the IBD helpline, to provide support if required. The IDB Data dashboard enabled the team to provide the essential data to be able to increase staff numbers, both nursing and administration to provide a safer service.

Discussion/Conclusion: The objectives of the project was to provide a safer IBD service and to increase staffing numbers by utilising a Dashboard system. This project's primary endpoint was to increase staffing numbers to provide a safer service. The staffing numbers were increased from 2.6 x band 7 nurses to 1.0 x band 8A, 3.6 x band 7 nurses, 1.0 band 6 biological nurse, 1.0 band 4 IBD Coordinator and a designated secretary for each nurse. The IBD Dashboard System is still being utilised to provide essential information to the divisional management team, primary care teams about the capacity and demand of the service. This project could be further developed to monitor other activities for future business planning.

This project has improved patient care as we now have a fully funded service providing safer care to patients. We were also able to provide a development day for all staff to compile a safe job plan and to focus on how the new service will work. It provides dedicated clinical administration time and dedicated learning and development time for staff to continue with professional development. This project could be transferrable to any speciality or location.

58. Clinical outcomes of potential coeliac disease: A systematic review and meta-analysis

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Introduction: Potential coeliac disease (PCD) is charactarised by positive serological and genetic markers of coeliac disease with architecturally preserved duodenal mucosa. The clinical outcomes and rates of progression to overt coeliac disease in patients with PCD remain uncertain. In this systematic review and meta-analysis, we aimed to evaluate the clinical outcomes of patients with PCD.

Methods: We searched Medline, Embase, Scopus, and Cochrane Library from 1991 through May 2024 to identify studies evaluating the clinical outcomes of PCD patients. The progression rates to villous atrophy, seroconversion and response to a gluten-free diet (GFD) were analysed. A random-effects meta-analysis was performed, and the results were reported as pooled proportions with 95% confidence intervals (CIs).

Results: Seventeen studies comprising 1010 patients with PCD were included in the final analyses. The pooled prevalence of PCD among patients with suspected coeliac disease was 16% (95% CI: 10–22%). During follow-up, 33% (95% CI: 18–48%; I2 = 96.4%) of patients with PCD on a gluten-containing diet developed villous atrophy, and 33% (95% CI: 17–48%; I2 = 93.0%) had normalisation of serology. Among those who adhered to a GFD, 88% (95% CI: 79–97%; I2 = 93.2%) reported symptomatic improvement.

Discussion/Conclusion: Almost a third of patients with PCD develop villous atrophy over time, whereas a similar proportion experience normalisation of serology despite a gluten-containing diet. Most symptomatic patients benefit from a GFD. These findings highlight the importance of structured follow-up and individualised management for patients with PCD.

59. Predictive factors for non-response to corticosteroids in microscopic colitis

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Introduction: Microscopic colitis (MC), including collagenous colitis (CC) and lymphocytic colitis (LC), often presents with chronic diarrhea that is typically managed with corticosteroids. However, a subset of patients does not respond to corticosteroid therapy. Identifying predictive factors for non-response can help tailor treatment strategies and improve patient outcomes.

Methods: A retrospective analysis was conducted on patients diagnosed with MC at a tertiary care center over a 5-year period. Data on demographics, clinical presentation, histological subtypes, laboratory results, and treatment outcomes were collected. Logistic regression was used to identify factors predictive of non-response to corticosteroids.

Results: Out of 84 patients with MC, 21 (25%) were non-responders to corticosteroid therapy. Multivariate analysis identified several predictive factors for non-response: younger age at diagnosis (mean age 42.7 years; $p < 0.01$), presence of concomitant autoimmune diseases (OR = 2.5; 95% CI: 1.4–4.4; $p = 0.002$), higher baseline fecal calprotectin levels (OR = 2.2; 95% CI: 1.3–3.8; $p = 0.003$), and diagnosis of lymphocytic colitis (OR = 1.8; 95% CI: 1.0–3.2; $p = 0.045$). Histopathological analysis showed that greater intraepithelial lymphocyte counts in LC and thicker subepithelial collagen bands in CC were also associated with non-response ($p < 0.05$).

Discussion/Conclusion: Younger age, presence of concomitant autoimmune diseases, higher baseline fecal calprotectin levels, and diagnosis of lymphocytic colitis are significant predictors of non-response to corticosteroid therapy in patients with microscopic colitis. Recognizing these factors can aid clinicians in anticipating corticosteroid non-response and considering alternative therapeutic approaches.

60. Role of capsule endoscopy in the evaluation and management of celiac disease

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Introduction: Even though capsule endoscopy (CE) is not a first-line tool in the evaluation of celiac disease (CD), it is recommended in cases of equivocal diagnosis, and is particularly valuable for patients with non-responsive or complicated CD. This study aims to assess the diagnostic utility, clinical impact, and safety of CE in patients with celiac disease.

Methods: A retrospective cohort study was conducted involving 34 patients with confirmed or suspected celiac disease who underwent CE between 2019 and 2023 at a tertiary care center. Data collected included patient demographics, indications for CE, diagnostic findings, histopathological correlation, changes in clinical management, and follow-up outcomes.

Results: The study included 34 patients, with a mean age of 32 years (range, 18–65 years) and a female predominance (60%). Indications for CE included persistent symptoms despite a gluten-free diet (50%), evaluation of complicated CD (30%), and assessment of mucosal healing (20%). CE had a completion rate of 92%. The diagnostic yield of CE was 70%, identifying villous atrophy, mucosal scalloping, and other characteristic features of CD in 60% of patients with non-responsive CD. CE also detected additional findings such as ulcerations, strictures, and lymphomas in 20% of patients with complicated CD. CE findings led to a change in clinical management in 56% of cases, including reinforcement of the gluten-free diet in 30%, initiation of immunosuppressive therapy in 15%, and surgical intervention in 9%. In patients assessed for mucosal healing, CE confirmed complete healing in 41% and partial healing in 59%. Capsule retention occurred in one case, representing 3% of patients, necessitating endoscopic retrieval. No other significant complications were reported.

Discussion/Conclusion: Capsule endoscopy is a valuable diagnostic tool in the management of celiac disease, particularly for patients with non-responsive or complicated forms of the disease. It provides a high diagnostic yield and significantly impacts clinical management by detecting both typical and atypical features of CD. CE is generally safe, with a low complication rate. Further studies are warranted to refine its role in routine clinical practice and to establish standardized protocols for its use in celiac disease.

61. Use of incisional therapy in pediatric gastrointestinal endoscopic dilation

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Introduction: Pediatric gastrointestinal (GI) luminal strictures are caused by a variety of conditions, such as inflammation, chemical injury, surgery, congenital malformations, and others. Pediatric GI strictures are not uncommon, and result in compromised elasticity of the narrowed GI organ, significant disruption of motility, or stiff obstruction. Treatment options include mainly different dilation techniques, and if failed, surgery. The main dilation method is

by pneumatic balloon. Recently, incisional therapy, using an endoscopic diathermy knife, has been reported as an optional treatment for refractory esophageal strictures. However, there is very limited data and scarce reports on the use of this technique in pediatrics.

The most common endoscopic GI dilation technique is balloon dilation, where the balloon exerts 360° radial pressure equally on the GI walls. However, the stricture is often asymmetric, so that softer parts are dilated more by the balloon, while stiffer, more fibrotic parts, remain unchanged. Incisional therapy, using a diathermy system and an endoscopic knife, might have an advantage over balloon dilation since one can direct the therapy anatomically towards the most resistant parts. This will assumingly result in further reduction of focal stiffness, better dilation and improvement in local compliance. Moreover, in some cases the anatomy of the stricture (e.g., angles, the extent of obstruction, etc.) might limit the use of balloon. In this case, incisional therapy might be the only available endoscopic option. In this study, we aimed to assess the safety of incisional therapy in pediatric GI strictures.

Methods: The study is a retrospective cohort study. The local electronic medical record were searched for pediatric patients undergoing incisional therapy for GI strictures in the years 2019 to present (August 2023). Medical background and complications (including perforations, local infection, bleeding, fever, significant pain requiring more than basic analgesics, or admissions) were collected.

Results: Between the years 2019 and 2023, we identified 23 pediatric patients who underwent 87 endoscopic GI dilations by incisional therapy. Fourteen were males and 9 females. Mean age at the procedure was 5.5 years (median = 3 years, range, < 1 to 23 years) and the youngest was 11 months old. Twelve patients had post tracheoesophageal fistula repair stricture, 5 had post-caustic ingestion strictures. Other etiologies included Epidermolysis Bullosa, Dyskeratosis Congenita, battery ingestion, graft versus host disease (post bone marrow transplant), congenital esophageal web, congenital duodenal web – one patient each. Most of the strictures were at the middle esophagus, others at upper or lower esophagus or duodenum. The average number of procedures per patient was 3.7 (median = 2, range, 1 to 14). The following technique has been practiced – radial cuts at the narrowed area, using an endoscopic diathermy knife with the following settings: monopolar cutting mode, ERBE Endocut, I mode (= blended, predominantly cutting mode) set to effect 2, 3 sec intervals and duration.The effect of the dilation has not been studied objectively; however all procedures have been reported effective (as a single step or part of multistep dilations) by the performing endoscopist. There were no complications in the 87 procedures.

Discussion/Conclusion: Endoscopic GI dilation by incisional therapy is safe in pediatric patients and offers an alternative endoscopic dilation technique. This study sets a basis for immediate optional use of this procedure, as well as for future studies on the efficacy of this technique, by establishing the safety potential of the procedure.

62. Assessment of the histologic activity index (HAI) in biopsy colonoscopic specimens obtained from children with ulcerative colitis in North-Eastern Poland

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Introduction: Inflammatory bowel disease (IBD) is an inflammatory autoimmune gastrointestinal disease composed of ulcerative colitis (UC), Crohn's disease (CD) and IBD unclassified (IBDU) that may begin in childhood. The major pathomorphological characteristic is transmural infiltration of polymorphonuclear neutrophils and monocellular cells, frequently with marked content of eosinophils. It has been emphasized in literature that there are no

formal validated definitions of mild, moderate, or severe IBD even though many treatment algorithms in IBD start with patients' classification by disease severity. Taking the above into account, the major purpose of the study was to determine the severity of inflammation, i.e. the degree of inflammation, in each biopsy specimen obtained from 40 UC pediatric patients who underwent surveillance colonoscopy (in total 192 examinations) using the histologic activity index (HAI) and classification according to Gupta RB et al. (2007) applied in adult patients with this pathology. The current study is a continuation of our pathomorphological research into the pediatric form of UC.

Methods: The degree of inflammation in each biopsied segment of the colon was scored as follows: 0, inactive/absence; 1, mild (neutrophil infiltration of ≤ 50% of sampled crypts or cross sections; no ulcers or erosions); 2, moderate (neutrophil infiltration of ≥ 50% of sampled crypts or cross sections; no ulcers or erosions); 3, severe (erosion or ulceration, irrespective of other features). Histopathological assessment of colonoscopic specimens was performed in the Department of Medical Pathomorphology, Medical University of Bialystok.

Results: The current findings obtained on the basis of the conducted assessment of HAI showed that in 192 surveillance examinations, like in analogous preliminary observations performed in biopsy colonoscopic specimens obtained from children 2 years earlier, mildly active colitis was most exhibited, corresponding to the 1st grade of histological activity according to Gupta RB et al. (2007). It was followed by inactive colitis with no cryptitis or crypt abscesses and then by moderately active colitis with cryptitis or crypt abscesses involving ≥ 50% of crypts. The least exhibited was severely active colitis with erosion or ulceration.

Discussion/Conclusion: The currently used relatively simple histologic activity index i.e. the histologic scoring system to determine the severity of inflammation in biopsy colonoscopic specimens has allowed for better knowledge of the pathomorphological pattern of CU and understanding of the disease dynamics in children. We hope that it may also help in CU therapy.

63. Distribution of esophageal inflammation in patients with eosinophilic esophagitis and its impact on diagnosis and outcome

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Introduction: This study aimed to assess the distribution of esophageal inflammation in patients with eosinophilic esophagitis (EoE) and its impact on diagnosis and outcome.

Methods: Data from consecutive adult EoE patients who were followed-up at four Italian referral centers from October 2022 to October 2023 were retrospectively collected.

Results: One hundred forty-nine patients were included. Proximal EoE was observed in 8.1% of patients; distal EoE in 27.5%; and and diffuse EoE in 64.4%. Allergic rhinitis was more prevalent in distal and diffuse than proximal EoE (72.5% vs. 61.5% vs. 33.3%; p = 0.049). The prevalence of asthma, atopic dermatitis, oral allergy syndrome, and gastroesophageal reflux disease was not significantly different among the three EoE extent groups. Endoscopic inflammatory features at diagnosis were more prevalent in proximal EoE (91.7% vs. 53.8% distal [p = 0.01] vs. 66% diffuse [p = 0.05]). No significant differences in fibrotic features and esophageal stenoses were observed. The clinical remission rate after first-line therapy was comparable in all groups (75.0%, 70.7%, and 69.8%; p = 0.93). Patients with proximal EoE had a higher endoscopic fibrotic remission rate after therapy than distal and diffuse EoE (100.0% vs. 35.7% vs. 13.8%; p = 0.0001).

Discussion/Conclusion: The inflammation of the esophagus in EoE more frequently involves the distal esophagus than in the proximal esophagus. There was no clear correlation between the histologic extent of EoE and comorbidities or response to treatment.

64. The expression of the hydroxycarboxylic acid receptors 2 and 3 is upregulated in inflammatory bowel diseases: The role of stromal cells

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Introduction: Microbial Metabolite Receptors (MMRs) participate in microbiota-host interactions, and in a previous in silico study, we identified the dysregulated expression of Hydroxycarboxylic acid receptors 2 (HCAR2) and 3 (HCAR3) in the inflamed colon of IBD patients. Our aim was to investigate the expression of these receptors in human intestinal mucosa and the cellular mechanisms that regulate it.

Methods: The expression of HCAR2 and HCAR3 was examined ex vivo in colonic biopsies from 6 Crohn's disease patients, 13 with ulcerative colitis and 11 healthy individuals using qRT-PC. Their cellular expression was investigated via in silico deconvolution analysis of RNA-sequencing data using the xCell software and Spearman correlation between MMR genes and cell populations. Subsequently, regulation of HCAR2 and HACR3 expression was analyzed through qRT-PCR in primary human subepithelial myofibroblasts (SEMFs) and intestinal epithelial colonoids (HC) from healthy individuals, prior and after pro-inflammatory and pro-fibrotic stimulation.

Results: HCAR2 and HCAR3 exhibited significantly upregulated mRNA levels [HCAR2 Fold induction (FI) = 40x, $p < 0.01$; HCAR3 FI = 45x, $p < 0.01$] in inflamed colonic mucosa of IBD patients compared to healthy individuals. Bioinformatics analysis revealed HCAR2 and HCAR3 expression was significantly correlated with fibroblasts and negatively corelated with epithelial cells. In cell cultures of non-stimulated SEMFs as well as HC, HCAR2 and HCAR3 showed minimal expression, whereas stimulation with TNF-α and IL-1α significantly upregulated their mRNA in SEMFs (HCAR2 FI = 13x, $p < 0.01$; HCAR3 FI = 12x, $p < 0.05$) but not in HC, confirming our in silico findings. On the other hand, pro-fibrotic stimulation of SEMFs with TGF-β had no effect on HCAR2 or HCAR3, indicating that their expression might be more associated with inflammatory rather than fibrotic mechanisms.

Discussion/Conclusion: These findings suggest that HCAR2 and HCAR3 are up-regulated in the inflamed mucosa of IBD patients, probably via the inflammatory stimulation of resident stromal cells, introducing these genes as possible disease biomarkers and future therapeutic candidates.

65. The role of intraepithelial lymphocytes in inflammatory bowel disease

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Introduction: Intraepithelial lymphocytes (IELs) are T cells that patrol within the intestinal epithelial layer, serving as a primary defense against pathogens. These antigen-experienced CD8+ T cells are implicated in the pathogenesis of inflammatory bowel diseases (IBD) through potential overreaction or dysfunction. The chemokine CXCL10 is known to attract immune cells to inflamed areas, thereby exacerbating local inflammation. The specific interaction between CXCL10 and IELs in IBD patients remains unclear.

Methods: Primary IELs and intestinal epithelial organoids (IECs) were freshly isolated from mucosal biopsies of IBD patients during routine colonoscopy of the terminal ileum. Molecular characteristics and gene expression of IELs were analyzed using quantitative PCR, flow cytometry, and confocal microscopy with immunofluorescent staining. Further molecular analysis was conducted in silico using the IBD patient database, IBDome.

Results: In vitro studies indicated that CXCL10 expression was significantly induced in human IECs, especially with combined stimulation by IFNγ and TNFα. A positive correlation was observed between inflammation severity and CXCL10 expression in IBD patients. Autologous co-culture experiments with IELs and IECs demonstrated higher CXCL10 expression at both RNA and protein levels in IBD patients with active inflammation compared to those without. Additionally, IELs from highly inflamed patients produced increased levels of IFNγ and TNFα compared to controls. Notably, lower CXCL10 levels were observed in patients undergoing anti-TNF therapy compared to those not receiving such treatment.

Discussion/Conclusion: This study highlights the potentional dysregulation of the IFNγ/TNFα and CXCL10 axis in the crosstalk between IELs and IECs in IBD patients with active inflammation. Further research is necessary to elucidate the functions and pathological roles of IELs in both healthy and diseased states, potentially leading to novel therapeutic strategies for IBD.

66. Disparities in healthcare services usage for inflammatory bowel disease patients between urban and rural areas from Northeastern Romania

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Introduction: The rural population in Romania often encounter barriers to accessing health services due to various socio-economic factors. Our aim was to assess the differences in health service utilization between rural and urban residents diagnosed with inflammatory bowel disease (IBD) in a tertiary care center in northeastern Romania.

Methods: We carried out a restrospective study using the administrative health database of our center. We analyzed a period of 7 years between January 2017 and February 2023. The following factors were evaluated: sex, age, family history, smoking, Montreal categorization, extraintestinal symptoms, treatment. Data regarding gastroenterology visits, lower endoscopies, IBD-specific and IBD-related hospitalizations, and surgeries where also collected.

Results: We identified 117 cases of IBD, 67 (57.2%) being diagnosed with ulcerative colitis (UC). Most of the patients had urban residence (60%). The findings were divided into two main categories: before and after COVID-19 outbreak (2017–2020 and 2020–2023). In the first category there was significant differences between the rural and urban populations, the latter having more gastroenterology outpatient visits ($p < 0.005$), less IBD – specific and IBD - related hospitalizations ($p = 0.044$), more lower endoscopies ($p < 0.005$) and higher rates of biologic therapies ($p < 0.005$). There was no significant difference regarding surgery in the two groups. The COVID-19 outbreak made a change in the approach of patients` medical care, namely the outpatients gastroenterology visits of rural IBD patients have increased with a decrease in the IDB – related hospitalization. An increase in the rate of biologic therapies prescriptions is noted among the rural population, fact that is probably linked to the expansion of therapeutic choices.

Discussion/Conclusion: The differences in healthcare service usage between rural and urban IBD populations are a significant issue in our region, which is also greatly affected by low socio-economic conditions.

67. The occurrence of thromboembolic events in patients with inflammatory bowel disease

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Introduction: Inflammatory bowel disease is an independent risk factor for thromboembolic events. This study aimed to evaluate the prevalence and possible risk factors associated with thromboembolic events in patients at our clinic with inflammatory bowel disease.

Methods: All patients with inflammatory bowel disease who had experienced any type of thromboembolic event were retrospectively assessed by a specialized unit in an independent, tertiary hospital.

Results: Data from 163 patients were retrospectively collected between January 2019 and December 2023. As per standard diagnostic criteria, 61% were diagnosed with ulcerative colitis (UC) and 39% with Crohn's disease (CD). Of all, 65% were male, with an average age of 46 years for the UC group (range, 35–68) and 51 years (range, 25–74) for the CD group. Of the CD patients, 58% had B1 disease behavior, 25% had B2 and 17% had B3. Disease location was: L1: 17%, L2: 33%, L3: 50%. Of the UC patients, classifications were: E3: 78%, E2: 11%, E1: 11%; S0: 22%, S1: 22%, S2: 11%, S3: 44%. At the time of the occurrence of the thromboembolic event, 48% had mild to moderate activity and 22% had severe activity. In our cases, the most common thromboembolic event was deep vein thrombosis (30%), followed by pulmonary thromboembolism (14%). Only one death occurred due to thromboembolism, involving a patient with ulcerative pancolitis with mild to moderate activity who was treated with corticosteroids. When the events occurred, 52.3% of the patients were being treated with corticosteroids, 30.4% were receiving immunosuppressive therapy and 17.3% were receiving anti-TNF therapy.

Discussion/Conclusion: Inflammatory bowel disease is a risk factor for the occurrence of thromboembolic events. In our cases, the patients at greatest risk were males, those with CD, and those with active phase disease. No other associated risk factors were found.

68. iNKT cell immunomodulation and mucosal healing by microbiota-derived lactate

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Introduction: Invariant natural killer T (iNKT) cells play a critical role in mucosal immune homeostasis. Although iNKT cells release proinflammatory cytokines in response to the altered gut microbiota of IBD patients, exposure to microbiota-derived metabolites can promote homeostatic IL10-mediated iNKT cell responses resulting in better clinical outcomes in Crohn's disease (CD) patients. Thus, understanding the mechanisms leading to iNKT cells' functional shaping by microbiota-derived metabolites is important to design novel therapies for IBD patients.

Methods: We hypothesised that iNKT cells, serving as sentinels of tissue integrity, are the primary immune cells sensing microbiota-derived metabolic signals promoting the resolu-

tion of inflammation in IBD. In particular, we show that microbiota-derived lactate can control iNKT cell functions promoting iNKT cell-mediated mucosal tolerance while preventing T-cell-mediated overt inflammation and tissue injury.

We performed immunophenotyping of iNKT cells by multiparametric flow-cytometry from surgical specimens of CD patients and correlated NKT10 responses with intra-colonic levels of lactate, gut microbiome composition and tissue injury/healing by spatial biology techniques. We studied the molecular pathway determining the NKT10 phenotype in a lactate-enriched microenvironment by RNA-seq and CHIP-seq. We validated the role of NKT10 responses by microbiota-derived lactate by using in-vivo experimental colitis models.

Results: Our data suggest that microbiota-derived lactate plays a role in the epigenetic control of the immunoregulatory phenotype of iNKT cells through histone lactylation, thereby protecting animals from intestinal inflammation. On overall our data show i) how microbiota-derived lactate modulates the immunophenotype of iNKT cells, ii) the mechanisms underlying sensing of microbiota-derived lactate by iNKT cells, iii) iNKT cells role in inflammation resolution.

Discussion/Conclusion: This project is redefining the role of iNKT cells in IBD, changing the paradigm that Tregs are the primary T-cells promoting homeostasis during chronic inflammation. Understanding the mechanisms by which iNKT cells sense the intestinal microenvironment will enable the targeted manipulation of these cells to develop new microbiome-targeted and adoptive cell therapies (ACT) in IBD.

69. The common and distinct microbiota features and colonic resistance in IBD and PSC

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Introduction: There are multiple GI conditions which are considered to have at least some immune-mediated pathogenetic mechanisms in common. Among them the combination of primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD) represents a well-known disease constellation. Whereas, IBD is present in over 50% of patients with PSC, on the contrary, it is diagnosed in only about 10% of IBD patients, mainly in ulcerative colitis. The existing relationship between PSC and IBD raises the question of whether PSC may be considered as yet another extra-intestinal manifestation of IBD, or PSC and IBD are two separate conditions, which only share a common susceptibility, or if IBD is among the causative/trigger factors for PSC development. Furthermore, exact factors, which may explain their common and distinct features, remain unclear. The intestinal microbiota has been suggested to play a well-established role in both IBD and PSC pathogenesis, determining the gut microbiota vs. host immune system interaction, and implicating the gut-liver axis as translocated substances are commonly found in patients with PSC. In addition, colonic resistance formed by indigenous microbiota plays specific role in both intestinal inflammation and gut leakage. The aim of this study was to identify gut microbial features and colonic resistance of both IBD and PSC patients in attempt to better understand of what is distinct and mutual in their pathogenesis.

Methods: The study included 15 – IBD (10 – CD, 5 – UC), 16 PSC patients with concomitant IBD (9 – UC, 7 – CD) and 6 PSC patients. 70 healthy individuals formed control. PSC diagnosis followed established guidelines, CD or UC was confirmed by a combination of endoscopy, histopathology and radiological and biochemical investigations in accordance to ECCO

Guidelines. Colonic resistance studied in mucosal bioptates obtained during endoscopic examination. Standard aerobic and anaerobic microbiology techniques with taxonomy identification and quantity composition of microbiota as well as microecology indices calculation were used.

Results: Major autochthonic species (14 in total) were present in all samples: among them Lactobacteria, Bifidobacteria, E. coli, several other anaerobic species were dominating. However, Lacto- and Bifidobacteria were found in significantly lower levels compared to control subjects (p = 0.02–0.0031). The general tendency for colonic resistance in IBD was decrease of autochthonic anaerobes (Bifido-, Lactobacteria, Bacteroides spp, Clostridia spp, Bacillae spp.) and significant growth of allochtonic aerobes and facultative anaerobes (E. coli Hly+, Pseudomonas, Serratia, Hafniae, P. mirrabilis and other conditionally pathogenic Enterobacteriaceae). Enterococci were present in 60.0% of control and 7.14–20.69% of study groups. Staphylococci were present only in study groups (17.24–31.58%). When compared to control, PSC displayed increased abundance of Enterococcus, Fusobacterium, Lactobacillus, Morganella and Streptococcus, decreased Anaerostipes (p = 0.0002–0.046). Similar tendency was found for Enterococcus, Fusobacterium, Lactobacillus and Streptococcus when comparing PSC-IBD (PSC-UC and PSC-CD) with control. Enterococcus, Streptococcus, Lactobacillus and Fusobacterium were significantly altered in colonic mucosa in all the PSC and PSC-IBD patients compared to control, demonstrating tighter association with PSC-related dysbiosis, and not with IBD dysbiosis.

Discussion/Conclusion: The data from this study both variates and confirms the findings from other studies, which may be explained by different methods, and because mostly the transient faecal microbiota is studied, which is more variable and differs from the adherent (colonic mucosal) and more stable microbiota. This study confirms certain similarities and differences between PSC and IBD. Both diseases are characterized by decreased biovariability and biodiversity in colonic microbiome. Interestingly, microbial changes under PSC present strong similarities with other liver diseases and IBD, obtained in other studies. In contrast, we were unable to confirm underrepresentation of an uncultured Clostridiales II in PSC, which was previously named as a sole association to PSC in colonic mucosa. This study has several important limitations based on cohort sizes, exclusion of treatment peculiarities and methods use.

70. The thymic stromal lymphopoietin receptor gene's nucleotide polymorphism in eosinophilic esophagitis and inflammatory bowel disease

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Introduction: Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of immune/atopic genesis, basically associated with oesophageal mucosal eosinophil accumulation and Th2-related immune pathogenesis. Expected genetic background of EoE is based on connections to other atopic diseases, and population GWAS studies. The thymic stromal lymphopoietin receptor (TSLPR) attracts major attention as there is evidence that the TSLP signalling pathway may contribute to the formation of perverted immune response in EoE, while exact polymorphisms and their roles have to be determined. In terms of IBD, the Th1 immune response is considered to greatly contribute to the pathogenesis of CD, whereas the Th2 immune mechanisms are considered to participate to UC. Moreover, some recent studies showed decreased mRNA expression levels of TSLP and a negative correlation between expression of TSLP and severity of UC disease. Therefore, we aimed on studying TSLPR genet-

ic single nucleotide polymorphisms (SNP) in both EoE and IBD patients in attempt to clarify its possible role in their pathogenesis.

Methods: The study consists of two parts. As for the EoE part, we observed 75 schoolchildren with symptoms of food allergy (FA) based on clinical symptoms and prick skin testing as major criteria for FA. Based on questioning, clinical and laboratory observations, individuals were divided into following groups: 1st group included 68 FA patients with FA without EoE; 2nd group (7 patients, all males) – FA+EoE. EoE diagnosed based on symptoms and oesophageal endoscopy with biopsies (not less than 15 eosinophils per ×400 hpf in at least one sample). In addition, 36 IBD patients (17 – CD, 19 – UC) participated in the study and formed study groups 3 and 4, respectively. IBDQ and CDAI were used to evaluate disease severity, IBD diagnosis according to ECCO Guidelines. Twenty-three practically healthy individuals formed the control group. TSLPR gene's single nucleotide polymorphism (rs36133495) was selected following literature search and studied in lymphocytes by PCR.

Results: The A-allele of the TSLPR gene was detected in 88.89% of group 1, 14.29% of group 2, 88.2% of group 3, 42.1% of group 4, and 91.30% of controls. Minor G-allele was found in 11.11% of group 1, 85.71% of group 2, 11.8% of group 3, 57.9% of group 4, and 8.70% of controls, respectively. No GG-genotype carriers observed in control. The likelihood of EoE increases in G-allele carriers of the TSLPR gene (OR = 2.46; 95% CI: 0.43–6.16; $p < 0.001$). However, emphasizing IBD, TSLPR gene's polymorphism doesn't show remarkable association (OR close to 1 even in UC group – 1.26), which may be explained by the fact that besides pro-inflammatory activity, TSLP may play an anti-inflammatory and tolerogenic role, too. Moreover, there were statistically valid differences in genotypes and alleles between 3rd (CD) and 4th (UC) groups. The distribution pattern of SNP in studied population meets the Hardy-Weinberg equilibrium ($p > 0.05$) with a slight excess of heterozygosity, which generally does not disturb the population balance.

Discussion/Conclusion: TSLP is mainly expressed by epithelial cells, especially those located in the gut. Some of the studies have tied the genetic variations of TSLP/TSLPR with a wide range of Th2 determined GI diseases, including EoE, IBD and even colorectal cancer. This study shows that the particular rs36133495 (A/G) TSLPR genetic polymorphism may be involved in the development of both EoE and partially IBD and requires further investigation emphasizing possibilities for associated treatment approaches. A/G SNP (rs36133495) in the TSLPR gene suggests a potential mechanism for the difference between CD and UC.

71. Eotaxin, eosinophils and TGF-β interplay in intestinal inflammation

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Introduction: Gastrointestinal disorders associated with type 2 immunity and eosinophilic involvement include allergic vasculitis, EoE, eosinophilic gastroenteritis, carcinomatosis, drug-related conditions, inflammatory bowel disease and others. The increased number of eosinophils is described in IBD, in both active disease and in remission. In addition, a set of molecules participate in pathogenesis, among them different chemokines, which form the largest subgroup of cytokines, consisting of about 45 currently identified in humans. Their main role is the recruitment and activation of leukocytes during the inflammatory process, additionally, they modulate various biological effects, such as T-lymphocyte activation, angiogenesis, and hematopoiesis via interaction with different receptors expressed on different types of leukocytes. Recent studies showed eosinophilic activation and accumulation in IBD potentially involving certain chemokines in the pathophysiology of IBD. Eotaxin, has low activity on neutrophils and monocytes but it does show a certain degree of chemotactic

activity toward Th2 cells and basophils. The role of eosinophils in IBD was demonstrated in recent studies, alongside with the eotaxin's significance in selective recruitment of eosinophils. Furthermore, dysregulation of TGF-β signalling is observed in IBD patients, too. Whereas there are multiple studies on the issue, present data is still confusing. Therefore, the aim of this study was to investigate eotaxin, eosinophils and TGF-β interplay in IBD patients.

Methods: Thirty-six IBD patients (17 – UC, 19 – CD) participated in the study. IBDQ and CDAI were used to evaluate disease severity. 24 and 12 were in remission or have active disease, respectively, 13 – receive corticosteroids. 30 practically healthy individuals formed control group. Cells subpopulations were determined in fresh blood samples in an automated analyser, serum quantitative assay for eotaxin by solid phase sandwich ELISA. Colonic biopsies (screening colonoscopies in practically healthy adults as controls) were used to immunohistochemically (double immunostaining) identify and quantify eosinophils, and TGF-β1+ cells via immunofluorescence method in 10–20 high power fields of view in each sample using automated computer-assisted visual analysis system.

Results: Significantly increased eotaxin levels ($p < 0.01–0.05$) were observed in both CD (301.2 3 135.0 pg/ml) and UC patients (218.4 3 142.5 pg/ml) when compared to controls (145.2 3 112.7 pg/ml). Active IBD demonstrated higher eotaxin levels than patients with quiescent disease – 395.1 3 172.3 pg/ml vs. 118.5 3 63.7 pg/ml in CD and 289.5 3 152.8 versus 143.6 3 95.7 pg/ml in UC, respectively ($p < 0.05$). A significant dominance of eosinophils was observed in the colonic bioptates in active CD patients (537.5 3 913 cells per sq. mm) and UC (299.4 3 45.1 cells per sq. mm) compared to controls (52.6 3 7.4 cells per sq. mm), $p < 0.05$. However, eosinophils' number significantly ($p < 0.001–0.01$) dropped in remission (221.6 3 31.1 and 72.1 3 8.1 cells per sq. mm in CD and UC, respectively), still remaining higher than in control. Ratio of eosinophils expressing TGF-β1 dropped significantly in all IBD patients with lowest figures observed in active IBD (12%). In remission, number of TGF-β1+ cells (48%) raised significantly closer to control (58%).

Discussion/Conclusion: This study shows that eotaxin is significantly increased in serum of patients with active IBD, suggesting that this cytokine may be responsible for the IBD activity. Previous studies have shown that TGF-β level is elevated in active IBD patients, but activation of TGF-β signalling is insufficient to suppress active IBD. Therefore, obtained data shows that eosinophils may play significant role in downregulating TGF-β release in IBD contributing into its pathogenesis via both pathways. These mechanisms may play the interconnecting role with other immuno-mediated GI conditions and beyond.

72. Endoscopic features of the intestinal mucosa in patients with ulcerative colitis depending on the level of IgG4

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Introduction: Despite the presence of elevated levels of IgG4-positive plasma cells in the intestinal mucosa (IM) according to few studies research, ulcerative colitis (UC) is not an IgG4-related disease because it does not have signs of storiform fibrosis and phlebitis, but researchers do not exclude the role of IgG4 in the pathogenesis of UC. The issue of correlating endoscopic signs in UC with the degree of infiltration of the intestinal mucosa with IgG4-positive plasma cells and the concentration of IgG4 in the blood remains open.

Methods: We examined 75 patients with UC. Patients were divided according to severity using the Mayo index for UC: 54 patients had moderate severity, 14 patients were diagnosed with severe UC and 7 patients had mild UC. Endoscopic examinations of the colon were performed according to generally accepted methods. The level of IgG4 in the blood serum was deter-

mined by enzyme-linked immunosorbent assay. The presence of IgG4-positive plasma cells was determined by immunohistochemical method using monoclonal rabbit anti-human IgG4. Tissue IgG4 was considered positive if more than 10 cells were present in the field of view

Results: An increase in IgG4 levels above 1.2 g/l was noted in 45 patients (%). Such endoscopic signs as hyperaemia, edema, haemorrhage and the presence of IM erosions were diagnosed 1.2 times ($p > 0.05$) more often in the group with elevated IgG4 levels. Both with elevated IgG4 levels in the blood and with normal levels, the frequency of detected pseudopolyps IM was almost the same in both groups and amounted to 26.7% and 23.3% of cases, respectively. At the same time, colonic ulcers IM were diagnosed 2 times ($\chi2 = 4.52$; $p = 0.033$) more often in patients with elevated IgG4 levels in the blood. Vascular abrasion was noted in the majority of patients with UC with a predominance of detection in the group with elevated IgG4 levels in the blood ($\chi2 = 4.42$; $p = 0.03$). Bleeding of the colon IM of the 2nd and 3rd degree was detected 1.6 times and 5 times more often (> 0.05) in the group with elevated IgG4, respectively, while bleeding of the 1st degree was diagnosed 2 times more often in the group with normal IgG4 levels ($p = 0.049$). Positive tissue IgG4 was found in 33.3% of patients with UC. The main endoscopic signs of UC were detected in them more often than in the group with negative tissue IgG4: erasure of the vascular pattern – 1.5 times ($\chi2 = 7.41$; $p < 0.01$), haemorrhage – 1.3 times (> 0.05), presence of erosions – 1.2 times (> 0.05). Colonic ulcers were diagnosed 3.4 times ($\chi2 = 23.31$; $p < 0.001$) more often in patients with increased IgG4 content in colon biopsies. The 2nd and 3rd degree of bleeding was detected in the group with positive tissue IgG4, respectively, 2 times ($p = 0.035$) and 4 times ($p = 0.028$) more often than in the group with negative tissue IgG4.

In general, patients with positive tissue IgG4 in the colon mucosa were found to have 2.9 times more severe endoscopic UC activity (grade 3) ($\chi2 = 20.17$; $p < 0.001$)

Discussion/Conclusion: Thus, in patients with UC, an increase in the level of both serum and tissue IgG4 is accompanied by an increase in the frequency of detection of endoscopic signs of the disease, so that endoscopic activity of the 3rd degree was noted 2 ($p < 0.05$) and 2.9 times ($p < 0.001$) more often than in patients with normal IgG4 levels

73. Age-related immune cell dynamics in patients with Crohn's disease reveal CD8+CD28- T cells as potential mediators of clinical remission

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Introduction: Aging affects the organism at cellular and molecular levels, driving the development of a variety disorders such as cancer and cardiovascular disease. Aging can affect the immune system as well, leading to the development of inflammatory diseases like rheumatoid arthritis. Surprisingly, this is not the case for inflammatory bowel diseases (IBD), which are considered rather diseases of the young. This study aims to investigate immune cell dynamics in patients with Crohn's disease (CD), with a special focus on T cells.

Methods: We collected blood and tissue samples from patients with CD, age 19–80 years. Disease activity was assessed using Harvey-Bradshaw-Index (HBI < 5 was considered remission; HBI ≥ 5, active disease). Peripheral blood mononuclear cells (PBMCs) were evaluated for markers for T cell maturation and co-stimulatory molecules.

Results: Our results on PMBCs revealed no age-related changes in the relative numbers of CD4+ and CD8+ T cells. Interestingly, tSNE plots showed different clustering signatures in young (< 50 years old) CD patients compared to old ones (≥ 50 years old). Further analysis

based on the disease activity revealed that young patients with disease in remission have increased relative numbers of naïve CD8+ T cells that express CD27 and CD28 co-stimulatory molecule, while elderly CD patients in remission rather accumulate exhausted CD8+ T cells. We observed a similar phenotype in tissue samples from patients with CD, where CD8+CD28- T cells numbers significantly declined with age. Interestingly, increased numbers of CD8+CD27-CD28- T cells led to significantly less major adverse outcomes in patients with CD in remission monitored over a period of 18 months. In elderly patients with active CD, a specific cluster of cells with high expression of CD45RA and CD27, but not CD4 or CD8, was predominant, suggesting different modulatory mechanisms of disease in aging patients compared to the young ones.

Discussion/Conclusion: In conclusion, aging CD patients show different immune cell dynamics compared to the young ones, revealing CD8+CD28- T cells as potential mediators for clinical remission. Understanding the functional role of these cells might help for development of targeted therapies for CD.

74. Cell cycle regulation by p21 prevents the exhaustion of CD4+ T cells within the anti-tumor response to colorectal cancer

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Introduction: Colorectal cancer (CRC) arises as an effect of continuous DNA damage to the epithelial cells, leading to an uncontrolled cell growth of malignant cells. DNA damage accumulation is regulated by activation of cell cycle pathways such as p53/p21 or p16INKa/retinoblastoma pathways, which act as protective mechanisms against CRC development. Furthermore, CRC is also shaped by the interplay between T cells and tumor cells. Here, we aimed to understand the role of cell cycle regulation by p21 in CD4+ T cells during colorectal cancer development.

Methods: We have assessed the expression of p21 in CD4+ T cells on tissue samples from murine tumor models and human CRC. Furthermore, we used both in vivo orthotopic MC38 models and in vitro co-culture experiments to evaluate the response of p21-deficient CD4+ T cells to colorectal cancer.

Results: Immunohistological evaluation of human and murine models of CRC showed that CD4+ T cells found in the tumor microenvironment express nuclear and cytoplasmic p21. Furthermore, Rag1-/- mice reconstituted with p21-/- CD4+ T cells and exposed to MC38 orthotopic model showed increased tumor growth compared to the control ones. In human CRC, we observed that patients with low p21 expression in CD4+ T cells had significantly worse cancer-free survival compared to those with high p21. Functionally, p21-deficient CD4+ T cells expressed significantly less cytotoxic IFNγ and failed to induce tumor cell death, as shown by both in vivo orthotopic MC38 models and in vitro co-culture experiments. Furthermore, p21-/- CD4+ T cells were also more exhausted, with significantly increased numbers of effector/effector memory and CD27-CD28- T cells found at the tumor site. By targeting cell cycle regulation via CDK4/6 inhibition with commercially available inhibitors such as Palbociclib, we were able to restore the loss function of p21-deficient CD4+ T cells and reduce tumor growth in in vivo and in vitro tumor models.

Discussion/Conclusion: In conclusion, p21 expression in CD4+ T cells mediates their anti-tumor response to colorectal cancer. Targeting downstream molecules that modulate cell cycle such as CDK4/6 using Palbociclib might offer novel therapeutic strategies in CRC.

75. Diagnostic of complicated forms of acute diverticulitis according to the data of ultrasound examination of the organs of the abdominal cavity

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Introduction: In recent decades, the number of cases of diverticular disease and its complications has increased significantly. The frequency of diverticular disease is 1,2 cases per 1000 population, and among the elderly and senile age it reaches 7,5 per 1000 population. Complications of this disease develop in 5% of cases, and the risk of development purulent-inflammatory processes in the development of diverticular disease is 55–68%.

The progression of diverticulitis leads to the destruction of its wall with the development of a purulent-inflammatory process. In order to improve the results of the treatment of diverticular disease, for the early diagnosis of diverticulitis and its complications, we were used ultrasound examination of the organs of the abdominal cavity and pelvis.

Methods: Ultrasound is used for early diagnosis and classification of diverticulitis severity: limited (Hinchey I and II) and unlimited (Hinchey III and IV). In 114 patients, 64.9% had Hinchey I and II, and 35.1% had Hinchey III and IV. Ultrasound showed 89.5% sensitivity. With unlimited forms (Hinchey III and IV), such a nosological reason was indicated much less often – 77.5%, but the diagnosis of peritonitis was unambiguously established in all conclusions, which, in turn, active surgical tactics was caused in all patients of this category, and acute diverticulitis was diagnosed intraoperatively.

Spiral computed tomography of the abdominal cavity and pelvis with intravenous contrast was used as a method of second-line indirect imaging diagnosis in cases of indeterminate diagnosis according to ultrasound data and the absence of a clinic of unlimited peritonitis. Colonoscopy was performed when there was a clinically justified high probability of a tumor or inflammatory diseases of the large intestine.

Results: Abdominal ultrasound is the main screening method for early diagnosis of acute diverticulitis and its complications with a high sensitivity of 89.5%.

76. Blood eosinophils accurately predict a diagnosis of eosinophilic esophagitis among patients reporting dysphagia and treatment response in eosinophilic esophagitis: A prospective multicenter study

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Introduction: Upper endoscopy (EGD) with esophageal biopsies is required to rule out eosinophilic esophagitis (EoE) in patients reporting dysphagia. Moreover, EoE monitoring currently requires esophageal biopsies to assess treatment response based on eosinophil counts on histology. Non-invasive screening and monitoring strategies are needed to reduce the diagnostic delay and streamline the follow-up of patients with EoE.

Methods: In this prospective cross-sectional multicenter study conducted at three EoE-referral centers in Italy, we investigated whether absolute eosinophil count (AEC) and eosinophil percentage (EosPercent) could a) predict a diagnosis of EoE among patients referred for dysphagia, b) serve as a marker of histological remission in treated EoE patients. We enrolled consecutive patients undergoing EGD with six esophageal biopsies for suspected or

known EoE. For all patients, a full blood count was obtained prior to the EGD. A diagnosis of active EoE or histological remission was performed based on current guidelines. Non-EoE dysphagia (NED) patients were identified based on the presence of < 15 eosinophils/high-power field in all six esophageal biopsies while off eosinophil-depleting treatments. Demographic, clinical, AEC, and EosPercent data were collected. Kruskal-Wallis Rank Sum Test and Pearson's Chi-squared were used for comparisons as appropriate. ROC curve analysis was used to assess the diagnostic accuracy (AUC) of AEC and EosPercent. Significance threshold was $p < 0.05$.

Results: Of the 92 included patients, 33 had active EoE, 18 had EoE in histological remission while on budesonide orodispersible tablets (BOT) or proton pump inhibitors (PPI), and 41 had NED. Patients with EoE were younger and more frequently male and atopic compared to NED ($p < 0.01$ for all). Overall, 98% (50/51) of EoE had AEC, and 84.3% (43/51) had EosPercent within the normal range. Similarly, 100% (41/41) of NED had AEC, and 90.2% (37/41) had EosPercent within the normal range. There were no differences between EoE and NED in terms of proportion of patients with AEC or EosPercent above the upper limit of normal ($p > 0.4$ for all). Median AEC [380 (210, 460)/mm3 vs. 120 (70, 220)/mm3; $p < 0.001$) and EosPercent [5.40 (3.60, 7.05)% vs. 1.80 (0.8, 3.0)%; $p < 0.01$] were significantly higher in active EoE compared to NED. Based on ROC curve analysis, a cut-off of 155 eosinophils/mm3 segregated active EoE from NED with AUC of 0.82, specificity of 91.0%, and sensitivity of 65.8%, while a cut off value of 2.5% of EosPercent had AUC of 0.83 with 68.2% specificity and 93.5% sensitivity for the identification of EoE among patients with dysphagia. In terms of prediction of BOT or PPI response, median AEC (380 [210, 460]/mm3 vs. 150 [98, 268]/mm3; $p < 0.01$) and EosPercent (5.40 [3.60, 7.05]% vs. 1.85 [1.55, 4.47]%; $p < 0.01$) were significantly higher in active EoE compared to EoE in histological remission. Based on ROC curve analysis, a cut-off of 375 eosinophils/mm3 had AUC of 0.75 with 94.1% specificity and 54.5% sensitivity, while a cut off value of 2.25% of EosPercent had AUC of 0.79 with 93.5% specificity and 60.0% sensitivity for the identification of histological remission among EoE patients.

Discussion/Conclusion: AEC and EosPercent are within the normal range in most EoE patients regardless of histological disease activity. Nevertheless, AEC and EosPercent values accurately predict a diagnosis of EoE among patients reporting dysphagia, as well as histological remission among EoE patients. If these findings are replicated on a larger scale, AEC and EosPercent could be used as biomarkers in clinical practice.

77. Clinical significance of esophageal hypervigilance, anxiety, and adaptive behaviors in patients with eosinophilic esophagitis

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Introduction: There is a known discrepancy between symptoms reporting and histological disease activity in patients with eosinophilic esophagitis (EoE) such that patients with EoE in histological remission may still report symptoms while patients with histologically active EoE may report few or no symptoms. Esophageal symptom-specific anxiety, hypervigilance, and adaptive behaviours at mealtime may affect dysphagia reporting in EoE but this has not been investigated.

Methods: Consecutive adults (> 18 years) with histologically active or inactive EoE (i.e., ≥ 15 or < 15 eosinophils/high-power field) at their last upper endoscopy (EGD) were prospectively enrolled. For each patient, esophageal hypervigilance, anxiety, and adaptive behaviours

were assessed prior to the EGD by a physician who was blind to patients' treatment status and histological disease activity. Esophageal anxiety and hypervigilance were assessed using the validated Esophageal Hypervigilance and Anxiety Scale (EHAS) with a 30-day recall, while the validated Dysphagia Symptom Questionnaire (DSQ) and Dysphagia Symptom Score (DSS) were used for quantification of dysphagia. A structured interview (Pisa adaptation questionnaire, PiEAQ) was used for the assessment of adaptive behaviours (including drinking water to push the bolus, lubricating food, chewing for long, and blending food) over the 30 days prior to the EGD. Kruskal-Wallis Rank Sum Test and Pearson's Chi-squared were used for comparisons as appropriate. ROC curve analysis was used to calculate the diagnostic accuracy (AUROC). Significance threshold was $p < 0.05$.

Results: Of the 95 included patients, 56/95 patients (58.9%) had histologically active EoE, while 39/95 patients (41.0%) were in histological remission. Based on EHAS scores, 46.3% (44/95) had high esophageal anxiety and 47.4% (45/95) had high esophageal hypervigilance. Overall, 55.8% (53/95) of patients reported at least one adaptive behaviour at mealtime, while 44.2% (42/95) did not report any adaptive behaviour. Patients with histologically active EoE had significantly higher scores of DSQ, DSS, and EHAS compared to patients in histological remission ($p < 0.001$ for DSQ and DSS; $p = 0.03$ for EHAS). Adaptive behaviors were significantly more prevalent among patients with histologically active EoE compared to patients in histological remission (76.8% vs. 25.6%, $p < 0.001$). Based on ROC curve analysis, for the assessment of histological disease activity, the AUROC of the DSQ was 77.7% (95% CI: 68.7–86.7), with sensitivity, specificity, PPV and NPV of 80.3%, 66.6%, 77.6%, and 70.3%, respectively. The AUROC of the DSS was 75.3% (DeLong 95% CI: 65.5–85.2), with sensitivity, specificity, PPV and NPV of 80.3%, 66.6%, 77.6%, and 70.3%, respectively. DSQ and DSS performed comparably for predicting histological disease activity in EoE ($p = 0.3$). Using a model that integrates DSQ or DSS measurements with individual patients' data of esophageal anxiety, hypervigilance, and adaptive behaviors to the DSQ and DSS, the AUROC of DSQ was significantly increased to 86.6% (95% CI: 78.9–94.4), with sensitivity, specificity, PPV and NPV of 78.6%, 72.7%, 86.2%, and 72.7%, respectively, and the AUROC of DSS was significantly increased to 84.3% (95% CI: 76.1–92.6), with sensitivity, specificity, PPV and NPV of 67.8%, 84.6%, 86.3%, 64.7%, respectively.

Discussion/Conclusion: Esophageal anxiety, hypervigilance and adaptive behaviors are highly prevalent in patients with EoE. Higher EHAS scores and the use of adaptive behaviors are associated with active EoE and represent clinical markers of disease activity. Integrating the assessment of EHAS and adaptive behaviors significantly improves the accuracy of DSQ and DSS for predicting HDA in EoE.

78. Lymphocytic esophagitis is clinically and endoscopically different from eosinophilic esophagitis

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Introduction: Lymphocytic and eosinophilic esophagitis (LyE and EoE) are immune-mediated esophageal diseases. LyE has been proposed as a variant of EoE but differences and similarities between the diseases have been poorly investigated. We aimed to compare clinical characteristics, endoscopic findings, and treatment response in patients with LyE versus EoE.

Methods: Consecutive patients diagnosed with LyE (i.e., ≥ 30 lymphocytes/high-power field, HFP) or EoE (i.e., ≥ 15 eosinophils/HPF) without evidence of candida esophagitis were enrolled at three esophageal tertiary referral centres in the UK and Italy (London, Pisa, and

Padua). For each patient, the following data were retrospectively extracted: clinical characteristics, endoscopy findings at index endoscopy, histology response to proton pump inhibitors (PPIs) based on at least six esophageal biopsies, and symptoms response. Treatment efficacy was assessed after a minimum of 12 weeks of treatment. Histological response was defined as lymphocytes < 30/HPF for LyE and as eosinophils < 15/HPF for EoE. Symptom response was based on patients' perception of resolution or persistence/worsening of symptoms. Data are described as median and interquartile range (Q1–Q3) or as counts and percent. Kruskal-Wallis Rank Sum Test was used for continuous data, while Pearson's Chi-Square test (with continuity correction) and Fisher's exact test were used for counts. Significance was set at $p < 0.05$.

Results: Thirty LyE and 59 EoE patients were included. Patients with Lye were older (53 yrs [33–61] vs. 38 [25–47]; $p = 0.005$] and more frequently female (46.7% vs. 18.6%; $p < 0.01$) compared to EoE. Dysphagia and food bolus impaction requiring endoscopic removal were less common in LyE than EoE ($p < 0.01$ and $p < 0.001$), while heartburn and chest pain had similar prevalence in the two cohorts. Patients with LyE had autoimmune diseases more often than EoE ($p = 0.001$). LyE patients less frequently had atopy and increased serum IgE ($p < 0.001$ for both), while the prevalence of nasal polyposis or asthma was comparable to EoE (Table1). At index endoscopy, LyE patients less frequently had edema, rings, exudates, or furrows ($p < 0.05$ for all), but had a similar and low prevalence of strictures, or Schatzki rings (Table 1). Histological or symptomatic response to PPIs was consistently lower in LyE compared to EoE. These differences were statistically significant when any dose of PPI was considered (20 mg or 40 mg or 60 mg daily), but the differences were not statistically significant when only patients taking ≥ 40 mg/day were included in the analysis (Table 2).

Discussion/Conclusion: LyE and EoE patients are different in terms of demographics, comorbidities, clinical presentation, and endoscopic findings. This suggests different immunological phenotypes. Response to PPI seems lower in LyE, but further studies are needed to confirm these findings.

79. Serum eotaxin-3 and IL-10 are useful non-invasive biomarkers for the diagnosis and identification of histological remission of eosinophilic esophagitis: A prospective, longitudinal study

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Introduction: The diagnosis and follow-up of eosinophilic esophagitis (EoE) currently requires an esophagogastroduodenoscopy (EGD) with multiple esophageal biopsies. Since the follow-up of the disease is highly demanding in terms of healthcare resources, non-invasive biomarkers are needed to make the management of EoE less cumbersome. We investigated the utility of serum eotaxin-1, eotaxin-2, eotaxin-3, interleukin (IL)-4, IL-5, and IL-10 as biomarkers of EoE.

Methods: Consecutive adults (age > 18 years) with a new diagnosis of EoE [i.e., esophageal eosinophil counts per high-power field ≥ 15] were prospectively enrolled. At baseline (T0), patients underwent EGD with six esophageal biopsies to diagnose active EoE, as well as blood sampling within one week from the diagnosis of active EoE. Treatment was started following diagnosis of active EoE and histological response was assessed after 12 weeks of treatment (T1). Serum levels of eotaxin-1, eotaxin-2, eotaxin-3, IL-4, IL-5, and IL-10 were assessed at T0 and at T1. Baseline clinical data were recorded for each EoE patient. Age-, Sex-

, and atopy-matched subjects were used as healthy controls (HC). Kruskal-Wallis Rank Sum Test and Pearson's Chi-squared were used for comparisons as appropriate. ROC curve analysis was used to calculate the diagnostic accuracy (AUC) of the biomarkers. Significance threshold was $p < 0.05$.

Results: We enrolled 25 patients with active EoE and 14 HC, which were comparable in terms of age, sex, and atopy. At baseline (T0), patients with active EoE had significantly higher serum levels of eotaxin-3 compared to HC (501 pg/ml vs. 224 pg/ml; $p = 0.002$) and of IL-10 (100 pg/ml vs. 56 pg/ml; $p = 0.01$), while other biomarkers were not statistically different between active EoE and HC. Based on ROC curve analysis, a value of 389 pg/ml of etaxin-3 had AUC of 0.80 for the diagnosis of EoE with 93% specificity. A value of 168 pg/ml of IL-10 had AUC of 0.74 for the diagnosis of EoE with 100% specificity. Following treatment (T1), remission of EoE was achieved by 18/25 (72%) of EoE patients taking budesonide orodispersible tablets or PPIs. At T1, patients with EoE in histological remission had significantly lower serum levels of eotaxin-3 (252 pg/ml vs. 501 pg/ml; $p = 0.02$) and of IL-10 (67 pg/ml vs. 100 pg/ml; $p < 0.05$) compared to T0. A cut-off value of 241 pg/ml of eotaxin-3 had AUC of 0.7, and a cut-off value of 199.5 of IL-10 had AUC of 0.68 for the identification of histological remission at T1.

Discussion/Conclusion: Serum eotaxin-3 and IL-10 are promising non-invasive biomarkers for the diagnosis of EoE with high specificity. In addition, eotaxin-3 and IL-10 are accurate in monitoring therapeutic response in patients with EoE.

80. Evaluating the role of AI in IBD treatment decisions: A comparative analysis of ChatGPT recommendations and clinical practice

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Introduction: Selecting the right treatment strategy for inflammatory bowel disease (IBD) is crucial and can significantly impact the disease's progress. Advanced artificial intelligence language models like ChatGPT could help healthcare providers with this task. ChatGPT can access and summarize medical information from various sources, making it easier for practitioners to understand and utilize medical knowledge.

Methods: We conducted a ChatGPT-guided analysis of 149 IBD patients treated at the Clinical Department of Gastroenterology and Hepatology at University Medical Center "Zvezdara," Belgrade, to consider further treatment with certain biological drugs. Complete clinical and laboratory data were provided to ChatGPT so that a treatment proposal could be obtained. We then analyzed the alignment of decisions and assessed the treatment outcomes in groups where choices matched or differed.

Results: In 120 patients (81%), there was agreement between ChatGPT's treatment recommendation and the medical consultation, while in 29 patients, there were differences in the treatment approach. The most common difference in treatment modality was ChatGPT's recommendation of ustekinumab compared to our choice of vedolizumab for non-biologically naive patients with Crohn's disease, affecting seven patients with these characteristics. Additionally, for four patients with severe ulcerative colitis, ChatGPT recommended using Anti-TNFα, contrary to the medical consultation's decision to use cyclosporine in combination with vedolizumab. The group of patients where the artificial intelligence advice differed from the medical consultation was in a clinically more severe stage of the disease (CRP 12.4 vs. 10.1, $p = 0.024$), with worse endoscopic findings (proportion of severe endoscopic disease SES CD ≥ 33/Mayo score > 2, 57% vs. 29%, $p = 0.013$). Despite the baseline differences in these patient groups, multiple analyses of covariance did not reveal a significant difference in the ultimate treatment outcome, including proportions of endoscopic ($p = 0.547$) and clinical remission ($p = 0.304$) between patient groups.

Discussion/Conclusion: Integrating advanced artificial intelligence language models may be a promising approach to assisting practitioners in decision-making for IBD treatment. However, clinical experience should be a vital consideration in this process.

81. Multiple eosinophilic oesophagitis (EoE) guidelines – Have they changed our practice in Wales?

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Introduction: EoE is a common immune mediated inflammatory condition of the oesophagus, and meta-analysis showed an incidence of 3.64 per 100,000 person years. There has been significant variability in the induction and maintenance therapies delivered. In the UK, quality standards were published in 2017 stipulating the requirement for minimum number of oesophageal biopsies. We audited our current practice across multiple Welsh centres against the latest British guidelines (2022), and evaluated whether this has translated to real-world improvement in our practice.

Methods: We collaborated with pathology departments across Wales using codes including "eosinophilic", "eosinophilia", and "oesophagitis". Data were retrieved from January 2021 to May 2022 and August 2022 to December 2023.

Results: A total of 118 patients were identified across 5 Welsh centres (20 pre-guideline, 98 post-guideline). Correct biopsy protocol was observed in 65% and 47% of cases respectively. Average number of biopsies were 6.2 vs. 5.7 (SD 2.9 and 2.3). Improvement in histology reporting with quantitative measurement of eosinophilia was seen in 40% and 57%. The average duration of dysphagia reduced from a mean of 44 to 22 months and a median of 24 to 12 months. A similar proportion of patients was on PPI at index gastroscopy (30% vs. 28%). For induction therapies, more patients received either PPI or budesonide (73.6% vs. 81.4%). Variability in the choice of PPI was observed, and of those on omeprazole, 35% of patients were on the optimal regimen (20 mg BD or 40 mg BD). Induction budesonide was used in 27.6% and 6.1% in maintenance.

Discussion/Conclusion: Our audit has shown improvement in the histological diagnosis of PPI, an increased proportion of patients receiving induction therapies, and a reduction in dysphagia symptoms at index, challenges remain regarding biopsy protocol and abstinence from PPI prior to biopsy.

82. Novel transcriptomic panel identifies histologically active eosinophilic esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is characterized by symptoms of esophageal dysfunction and eosinophil tissue infiltration. The EoE Diagnostic Panel (EDP) can distinguish between active and non-active EoE using a set of 77 genes. Recently, the existence of distinct EoE variants featuring symptoms similar to EoE, such as esophageal dysfunction but lacking eosinophil infiltration, had been determined.

Methods: We used esophageal biopsies from patients with histologically active (n = 10) and non-active EoE (n = 9) as well as from healthy esophageal controls (n = 5) participating in the Swiss Eosinophilic Esophagitis Cohort Study (SEECS) and analyzed the gene expression profile in these biopsies by total RNAseq. Moreover, we employed the publicly accessible

RNASeq dataset (series GSE148381) as reported by Greuter et al., encompassing a comprehensive genomic profile of patients presenting with EoE variants.

Results: A novel, diagnostic gene expression panel that can effectively distinguish patients with histologically active conventional EoE not only from EoE patients in histological remission and control individuals, but also from three newly discovered EoE variants was identified. Histologically Active EoE Diagnostic Panel (HAEDP) consists of 53 genes that were identified based on differential expression between histologically active EoE, histologic remission, and controls (p-value ≤ 0.05). By combining the HAEDP with EDP, we expanded our knowledge about factors that may contribute to the inflammation in EoE and improved our understanding of the underlying mechanisms of the disease. Conversely, we suggested a compact group of genes common to both HAEDP and EDP to create a reliable diagnostic tool that might enhance the accuracy of EoE diagnosis.

Discussion/Conclusion: We identified a novel set of 53 dysregulated genes that are closely associated with the histological inflammatory activity of EoE. In combination with EDP, our new panel might be a valuable tool for the accurate diagnosis of EoE patients as well as for monitoring their disease course.

83. Analysing the effect of TIM genes and molecules on microscopic colitis

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Introduction: Microscopic colitis (mC) is an inflammatory bowel disease (IBD) that presents with watery non-bloody diarrhea and macroscopically normal intestinal mucosa. Its incidence reaches or even surpasses that of classic IBD Crohn's disease and ulcerative colitis. mC is discerned by histopathological features and subclassified as collagenous colitis (CC: thickened subepithelial collagenous band > 10 m) or lymphocytic colitis (LC: lymphocyte infiltration). Here, we aim at investigating the significance of TIM1/3 (T cell immunoglobin and mucin domain) molecules with its genes HAVCR1/2 in mC.

Methods: mC patient samples from colon tissue were analysed for the specific expression of HAVCR1/2 by RNA-sequencing. The cohort was divided into active/untreated (auCC, auLC), inactive/budenoside-treated (itCC) and active/refractory (aRCC) groups. Immunofluorescence staining of colon tissue from the patient groups was performed and analyzed for the distribution of TIM1/3+ CD3+ T cells

Results: HAVCR2 was found uniquely upregulated in inflammatory LC but not in CC or channelopathic LC (a recently proposed LC subtype lacking inflammation dominated by ion and organic acid dysregulation). Interestingly, IL-2 inducible T-cell kinase (ITK)-related gene LCP2 was found upregulated in all mC patient samples independently of the treatment. Other ITK-related genes were specifically upregulated for inflammatory LC (LCK, LCP2, LGALS9) or CC (SPI1, ZAP70). Based on the protein expression of the molecules in immunofluorescence staining, we found that TIM1 is significantly highly expressed in CD3+ T cells from auCC patietns compared to LC or controls. This is not reversed by budesonide treatment even if patients displayed a positive clinical response. However, CC patients how did not respond to budesonide show normal levels of TIM1.

Discussion/Conclusion: TIM molecules and signal cascade-related factors LCP2 and ZAP70 play an important role in mC and especially in CC subtype. They could serve as new targets for the prevention and future treatment of mC and - in the long term - replace systemic immunosuppressive therapy and its related side effects

84. Viscosity plane-wave ultrasound for the assessment of liver inflammation in patients with inflammatory bowel disease and hepatocitolysis syndrome

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Introduction: It is well-known that liver necroinflammation plays a key role in the process of hepatic fibrogenesis, thus there are several studies that assessed different methods for the evaluation of necroinflammatory activity in liver diseases. Viscosity Plane-wave UltraSound (Vi.PLUS) 2D imaging mode, a parameter embedded in 2D – ShearWave Elastography (2D-SWE) ultrasound machine allows the quantification of tissue viscosity, which has been demonstrated to be is associated with liver inflammation due to shear wave dispersion Hence, we aimed to assess the necroinflammatory activity in patients with inflammatory bowel disease (IBD) and hepatocytolysis syndrome.

Methods: We prospectively enrolled 83 IBD patients with high transaminase levels (ALT or AST ≥ 50 U/l) in Institute of Gastroenterology and Hepatology, Iași with high transaminase levels (ALT or AST ≥ 50 U/l), between January 2023 to Decembre 2023. All participants were evaluated using Aixplorer MACH 30 (Supersonic Imagine, Aix-en-Provence, France) ultrasound machine equipped with 2D-SWE.PLUS for quantifying liver fibrosis, Sound Speed Plane-wave UltraSound (SSp.PLUS) concomitant with Attenuation Plane-wave UltraSound (Att.PLUS) for liver steatosis, and Vi.PLUS for liver viscosity assessment.

Results: In total, 83 patients (54.2% females, mean age 55.2 3 15.05, BMI 25.69 3 4.77 kg/m2) were included in our study. Valid measurements, according to guidelines, were obtained in 81 (97.6%) patients, and they were included in the final analysis. Among them 18 (21.7%) patients declared chronic alcohol consumption (> 30 g/day), and 6 (7.2%) patients tested positive for viral hepatitis (2 patients with HBsAg, and 4 with HCV antibody). Forty-one (50.6%) patients were diagnosed with liver steatosis (SSp.PLUS ≤ 1537 Pa.s) with a mean SSp.PLUS of 1485 3 36.89 m/s, and Att.PLUS of 0.44 3 0.11 dB/cm/MHz. Regarding LSM, 61 (75.3%) patients had F0–1 (< 8 kPa), 19 (22.9%) F2–3 (8–12.4 kPa), and 1 (1.2%) in F4 (≥ 12.5 kPa) degree, with a mean 2D-SWE.PLUS of 8.3 3 7.18 kPa. Fifty (61.7%) patients present an increased liver viscosity (≥ 1.8 Pa.s.) with a mean Vi.PLUS of 1.96 3 0.50 Pa.s, being strongly correlated with ALT ($r = 0.405$, $p < 0.001$), AST ($r = 0.573$, $p < 0.001$), faecal calprotectin (FC) ($r = 0.284$, $p = 0.005$), CRP ($r = 0.803$, < 0.001), SSp.PLUS ($r = 0.413$, $p < 0.001$), and Att.PLUS ($r = -0.331$, $p = 0.003$). Participants with FC > 200 Qg/g and longer disease duration (> 7.2 years) had an increased Vi.PLUS (2.35 3 0.77 vs. 1.86 3 0.35 Pa.s [$p < 0.008$]) with an increased risk of liver necroinflammation (OR = 2.13, 0.62–7.32, $p < 0.001$). Moreover, patients with abnormal AST level had an increased risk of liver inflammation (OR = 1.34 CI: 0.52–3.42, $p = 0.031$), while an AST value of 72 U/l could modestly predict a ViPLUS score > 2.2 Pa.s (moderate liver inflammation) (ROC curve = 0.649, Sp = 75, Ss = 57%).

Discussion/Conclusion: Multiparametric liver ultrasonography is a valuable tool for detecting liver abnormalities in IBD patients, with a high prevalence of liver steatosis and fibrosis observed in this cohort. The study highlights the importance of routine liver monitoring in IBD patients, particularly those with longer disease duration, higher CRP levels, and increased FC level. Early identification and management of liver involvement can potentially improve patient outcomes and reduce the burden of liver-related complications in IBD.

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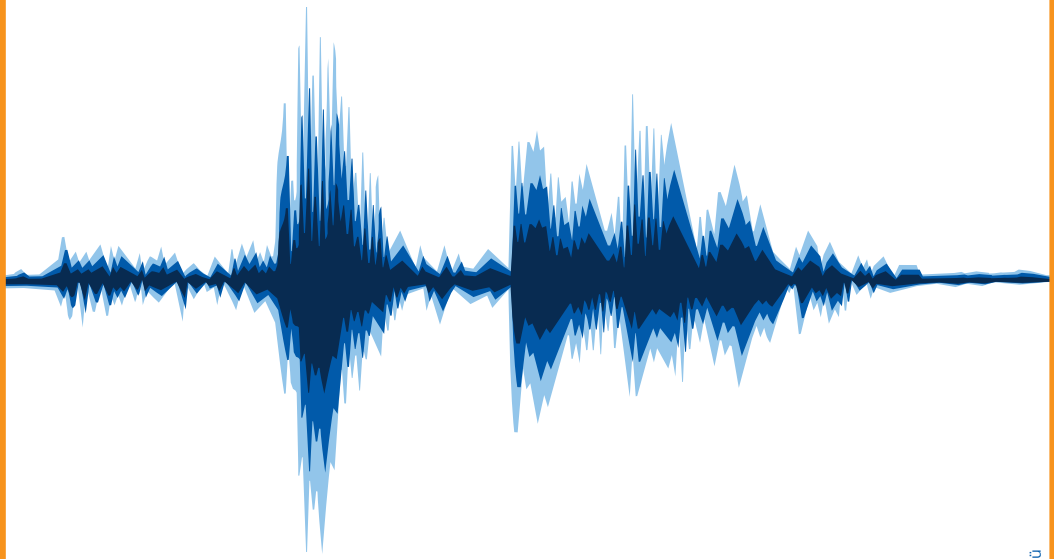
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