

## CONFER Cases Round 12

### Description

#### Case 1

<b>Case Title</b>	Metastatic Crohn's disease – a rare extraintestinal manifestation challenging diagnosis and management
<b>Principal Investigator</b>	Raman Nitskovich
<b>Case Manager</b>	Marie Truyens, Konrad Lewandowski
<b>Case Description</b>	Metastatic Crohn's Disease (MCD) is the rarest extraintestinal manifestation of inflammatory bowel disease (IBD), characterised by non-caseating granulomatous lesions similar to those seen in the intestines in skin or mucosal sites without anatomical continuity with intestinal lesions. Clinical presentation is highly heterogeneous and often misdiagnosed for years, most frequently as infectious dermatoses or hidradenitis suppurativa. Lesions may occur at any age, are resistant to treatment, and sometimes leave permanent disfigurement of the anogenital region and face. Importantly, cutaneous activity often dissociates from luminal disease and may precede intestinal involvement by several years, complicating diagnosis and management. Since the first description in 1965, only 300–350 cases have been reported worldwide, predominantly as single case reports. Management requires a multidisciplinary approach involving dermatology, gastroenterology, and pathology. To date, treatment remains empirical, including topical corticosteroids, antibiotics, systemic immunosuppressants, and advanced therapies such as anti-TNF agents, IL-12/23 and IL-23 inhibitors, and JAK inhibitors. No validated therapeutic algorithm exists.
<b>Main Clinical Question</b>	Through ECCO's collaborative network, we aim to collect the largest case series to date, refine diagnostic criteria, identify predictors of therapeutic response, and assess the role and safety of novel advanced therapy in MCD.
<b>Inclusion criteria</b>	<ol style="list-style-type: none"> <li><b>Metastatic Crohn's disease:</b> Cutaneous and/or mucosal lesions not contiguous with the gastrointestinal tract, compatible with metastatic Crohn's disease or histological findings compatible with metastatic Crohn's disease (non-caseating granulomas)</li> <li><b>Diagnosis of IBD:</b> either before, after, or concomitant with the skin lesions</li> <li><b>Data availability:</b> of basic clinical information, including treatment and follow-up</li> </ol>
<b>Literature on the topic</b>	<p>MCD is highly heterogeneous, under-recognised, and often dissociated from intestinal disease activity. Evidence remains limited to single case reports and small series, precluding evidence-based recommendations. The recently published Delphi consensus (2025) established diagnostic criteria, but validation in larger cohorts is urgently needed. Pooling cases within the ECCO network could fill this gap and guide clinical practice.</p> <p>Key references:</p>

1. Ebriani J, Santiago-Soltero K, Anshelevich EE, et al. Delphi panel for the development of diagnostic criteria for metastatic cutaneous Crohn disease: a consensus statement. *JAMA Dermatol.* 2025;161(6):642–7.
2. Palamaras I, El-Jabbour J, Pietropaolo N, et al. Metastatic Crohn’s disease: a review. *J Eur Acad Dermatol Venereol.* 2008;22:1033–43.
3. Ickrath F, Stoevesandt J, Schulmeyer L, et al. Metastatic Crohn’s disease: an underestimated entity. *J Dtsch Dermatol Ges.* 2021;19(7):973–82.
4. Honap S, Meade S, Spencer A, et al. Anogenital Crohn’s disease and granulomatosis: a systematic review of epidemiology, clinical manifestations, and treatment. *J Crohns Colitis.* 2022;16:822–34.
5. Boxhoorn L, Stoof TJ, de Meij T, et al. Dutch initiative on Crohn and colitis, clinical experience and diagnostic algorithm of vulval Crohn’s disease. *Eur J Gastroenterol Hepatol.* 2017;29:838–43.

## Case 2

<b>Case Title</b>	Dupilumab Monotherapy and in Combination with Other Biologic/Small-Molecule Therapy in Patients with Coexisting IBD and EoE: A Multicentre Case Series
<b>Principal Investigator</b>	Asaf Levartovsky
<b>Case Manager</b>	Thomas Greuter
<b>Case Description</b>	<p>Patients with concomitant inflammatory bowel disease (IBD) and eosinophilic esophagitis (EoE) represent a rare but increasingly recognized clinical overlap. Both conditions share immune-mediated pathways yet differ in dominant cytokine profiles. Dupilumab, an IL-4Ra antagonist approved for EoE, is effective in inducing clinical and histologic remission in EoE. Its role in IBD, however, remains uncertain: while preclinical rationale suggests possible benefit in ulcerative colitis, isolated case reports describe dupilumab-associated colitis. Beyond monotherapy, data on combining dupilumab with established IBD therapies (anti-TNF<math>\alpha</math>, anti-IL-23, anti-IL-12/23, anti-integrin, or small molecules) is lacking. Isolated reports of dual therapy in atopic dermatitis exist, but no systematic evidence has been published in patients with concurrent IBD and EoE. The feasibility, effectiveness, and safety of such combination regimens in this specific population therefore remain undefined. Given the importance of this immune overlap and the paucity of clinical experience, we propose a multicentre case series describing clinical outcomes and adverse events in patients with coexistent IBD and EoE treated with dupilumab alone or in combination with another biologic or small-molecule agent.</p>
<b>Main Clinical Question</b>	<ol style="list-style-type: none"> <li>1. In patients with coexisting IBD and EoE, is dupilumab therapy effective across both diseases?</li> <li>2. Is combination therapy of dupilumab with another biologic or small-molecule agent effective across both diseases?</li> <li>3. Is combination therapy of dupilumab with another biologic or small-molecule agent safe in patients with with concomitant IBD and EoE?</li> <li>4. Which patient- or therapy-related factors predict success or adverse outcomes?</li> </ol>
<b>Inclusion criteria</b>	<ul style="list-style-type: none"> <li>• Age <math>\geq</math>18y at dupilumab initiation</li> <li>• Confirmed IBD Dx by standard criteria</li> <li>• Confirmed EoE Dx (symptoms + biopsy proven <math>\geq</math>15 eos/hpf)</li> <li>• Received <math>\geq</math>1 dose of dupilumab for EoE with documented start date and planned maintenance regimen</li> <li>• Minimum follow-up of <math>\geq</math>12 weeks after dupilumab start or until discontinuation d/t adverse event or lack of response</li> </ul>
<b>Literature on the topic</b>	<ol style="list-style-type: none"> <li>1. Yanofsky R, Jogendran R, Hoxha T, Pathak A, Orchanian-Cheff A, Chhibba T, Sasson AN, Tandon P. The Association of Inflammatory Bowel Disease and Eosinophilic Esophagitis: A Systematic Review and Meta-analysis. <i>Inflamm Bowel Dis</i>. 2025 Jun 4;:izaf095. doi: 10.1093/ibd/izaf095. Epub ahead of print. PMID: 40468892.</li> <li>2. Malik A, Liu BD, Zhu L, Kaelber D, Song G. A Comprehensive Global Population-Based Analysis on the Coexistence of Eosinophilic Esophagitis and Inflammatory Bowel Disease. <i>Dig Dis Sci</i>. 2024 Mar;69(3):892-900. doi: 10.1007/s10620-024-08283-2. Epub 2024 Jan 13. PMID: 38218734; PMCID: PMC10960894.</li> </ol>



3. Mintz MJ, Ananthakrishnan AN. Phenotype and Natural History of Inflammatory Bowel Disease in Patients With Concomitant Eosinophilic Esophagitis. *Inflamm Bowel Dis*. 2021 Mar 15;27(4):469-475. doi: 10.1093/ibd/izaa094. PMID: 32430501; PMCID: PMC7957221.
4. Spencer EA, Dolinger MT, Dubinsky MC. A Single-Center Experience with Dupilumab for Atopic or Psoriasiform Dermatitis in Patients with Inflammatory Bowel Disease. *Dig Dis Sci*. 2023 Apr;68(4):1121-1124. doi: 10.1007/s10620-022-07684-5. Epub 2022 Sep 5. PMID: 36064828.
5. Rachel Drayne, Rosalind Hughes, Deirdre O'Donovan, BG08 Drug-induced colitis secondary to dupilumab prescribed for pompholyx eczema–bullous pemphigoid overlap: a case report, *British Journal of Dermatology*, Volume 193, Issue Supplement\_1, July 2025, lja085.354,
6. Gisondi P, Maurelli M, Costanzo A, Esposito M, Girolomoni G. The Combination of Dupilumab with Other Monoclonal Antibodies. *Dermatol Ther (Heidelb)*. 2023 Jan;13(1):7-12. doi: 10.1007/s13555-022-00851-6. Epub 2022 Nov 10. PMID: 36355314; PMCID: PMC9823163.