Supplementary Table

	Compound	EIM	Study design	Study population	Outcome
Anti-TNF					
Brooklyn et al 2006[1]	Infliximab	PG	RCT, 2 weeks	30 patients (19 with IBD, 13 CD, 6 UC)	Clinical improvement in 46 vs. 6%
Kaufmann et al 2005[2]	Infliximab	Arthritis Arthralgia Inflammatory back pain PG	Open-label, 2 weeks	22 CD, 1 UC	Clinical remission of arthritis in 33% (1/3), clinical improvement of arthralgia in 63.6% (7/11), improvement of inflammatory back pain in 63.6% (7/11), and improvement of PG in 100% (4/4). In 1 patient, clinical remission of PG was achieved
Brooklyn et al 2006[1]	Infliximab	PG	Open-label, 4 weeks (extension of RCT)	29 patients	Clinical improvement of PG in 69% and remission in 21%
Rispo et al 2005[3]	Infliximab	Arthritis Arthralgia Cutaneous EIM Uveitis	Open-label, 10 weeks	15 CD	Improvement rates of 60-80% (arthritis), and remission rates of 100% (arthralgia 6/6, cutaneous manifestations, 4/4 and uveitis, 2/2)
Herfarth et al 2002[4]	Infliximab	Arthritis, inflammatory arthralgia	Open-label, 12 weeks	59 CD	Improvement and remission rates for arthritis/inflammatory arthralgia of 36/59 (61%) and 27/59 (46%), respectively
Generini et al. 2004[5]	Infliximab	Arthritis	Open-label, 6 months	24 CD	Decreasing prevalence rates from 58 down to 12.5%
Löfberg et al 2012[6]	Adalimumab	Arthralgia Arthritis Sacroiliitis EN	Open-label, 20 weeks	945 CD	Decreasing frequency for most EIM compared to baseline: arthralgia 47.1 vs. 26.8%, arthritis 8.7 vs. 2.1%, sacroiliitis 3.6 vs. 1.9%, and EN 2.4 vs. 0.4%.
Barreiro-de-Acosta et al[7]	Adalimumab	Arthritis Anklylosing spondylitis Uveitis PG	Open-label, 6 months	42 CD	Improvement/remission rates of 61% (arthritis,n=7) and 100% (ankylosing spondylitis, n=1, uveitis, n=1 and PG, n=2).
Anti-integrins					
Phillips et al 2020[8]	Vedolizumab	PG EN	Case series	5 cases	PG with Non-response 1/1 (PG), EN with response in 50% (2/4).
Tadbiri et al 2018[9]	Vedolizumab	Arthritis Inflammatory arthralgia Cutaneous manifestations	Observational cohort, 54 weeks	49 IBD	Clinical remission rates were 44.7% for arthritis/inflammatory arthralgia (n=47) and 75% for cutaneous manifestations (n=4).
Feagan et al 2019[10]	Vedolizumab	Arthritis Arthralgia EN PG Uveitis	RCT (post-hoc), 52 weeks	273 UC (GEMINI I) 553 CD (GEMINI II) 288 CD (GEMINI III)	Vedolizumab-treated CD patients were less likely to show new or worsening arthritis/arthralgia compared to placebo (HR 0.63). Sustained resolution rates between for arthritis/arthralgia were not significantly different from placebo (GEMINI trial III 22% vs. 16%).
JAK-inhibitors					
Rubin et al 2020[11]	Tofacitinib	Arthritis	RCT (post hoc), 52 weeks	1139 (OCTAVE I and II) 592 (OCTAVE Sustain)	Improvement of arthritis in 16.7% (1/6, 5mg bid) and 33.3% (1/3, 10mg bid), whereas worsening of symptoms was reported with placebo in 18.2% (2/11).

Kochar et al 2018[12]	Tofacitinib	PG	Case series	3 CD	Improvement of PG in 3 patients
Anti-IL12/23					
Philipps et al 2020[8]	Ustekinumab	PG EN	Case series	8 cases	PG with remission in 100% (3/3), EN with remission in 80% (4/5, 1 patient with response)

Supplementary Table: Main prospective studies and case series for biologic and small molecule treatment for extraintestinal manifestations of inflammatory bowel diseases. All these studies were performed to specifically look at treatment of IBD-related EIM. CD, Crohn's disease; EIM, extraintestinal manifestation; EN, erythema nodosum; IBD, inflammatory bowel disease; PG, pyoderma gangrenosum; RCT, randomized-controlled trial; UC, ulcerative colitis

REFERENCES

1. Brooklyn TN, Dunnill MG, Shetty A, et al. Infliximab for the treatment of pyoderma gangrenosum: a randomised, double blind, placebo controlled trial. *Gut.* 2006;55(4):505-509.
2. Kaufman I, Caspi D, Yeshurun D, Dotan I, Yaron M, Elkayam O. The effect of infliximab on extraintestinal manifestations of Crohn's disease. *Rheumatol Int.* 2005;25(6):406-410.
3. Rispo A, Scarpa R, Di Girolamo E, et al. Infliximab in the treatment of extra-intestinal manifestations of Crohn's disease. *Scand J Rheumatol.* 2005;34(5):387-391.
4. Herfarth H, Obermeier F, Andus T, et al. Improvement of arthritis and arthralgia after treatment with infliximab (Remicade) in a German prospective, open-label, multicenter trial in refractory Crohn's disease. *Am J Gastroenterol.* 2002;97(10):2688-2690.
5. Generini S, Giacomelli R, Fedi R, et al. Infliximab in spondyloarthropathy associated with Crohn's disease: an open study on the efficacy of inducing and maintaining remission of musculoskeletal and gut manifestations. *Ann Rheum Dis.* 2004;63(12):1664-1669.
6. Löfberg R, Louis EV, Reinisch W, et al. Adalimumab produces clinical remission and reduces extraintestinal manifestations in Crohn's disease: results from CARE. *Inflamm Bowel Dis.* 2012;18(1):1-9.
7. Barreiro-de-Acosta M, Lorenzo A, Domínguez-Muñoz JE. Efficacy of adalimumab for the treatment of extraintestinal manifestations of Crohn's disease. *Rev Esp Enferm Dig.* 2012;104(9):468-472.
8. Phillips FM, Verstockt B, Sebastian S, et al. Inflammatory cutaneous lesions in inflammatory bowel disease treated with Vedolizumab or Ustekinumab: an ECCO CONFER multicentre case series. *J Crohns Colitis.* 2020.
9. Tadbiri S, Peyrin-Biroulet L, Serrero M, et al. Impact of vedolizumab therapy on extra-intestinal manifestations in patients with inflammatory bowel disease: a multicentre cohort study nested in the OBSERV-IBD cohort. *Alimentary pharmacology & therapeutics.* 2018;47(4):485-493.
10. Feagan BG, Sandborn WJ, Colombel JF, et al. Incidence of Arthritis/Arthralgia in Inflammatory Bowel Disease with Long-term Vedolizumab Treatment: Post Hoc Analyses of the GEMINI Trials. *J Crohns Colitis.* 2019;13(1):50-57.
11. Rubin DT, Reinisch W, Greuter T, et al. THE EFFECT OF TOFACITINIB ON EXTRAINTESTINAL MANIFESTATIONS AT BASELINE IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS IN THE OCTAVE PROGRAM. Gastroenterology.2020;158(6):S1195-96.
12. Kochar B, Herfarth N, Mamie C, Navarini AA, Scharl M, Herfarth HH. Tofacitinib for the Treatment of Pyoderma Gangrenosum. *Clin Gastroenterol Hepatol.* 2018.