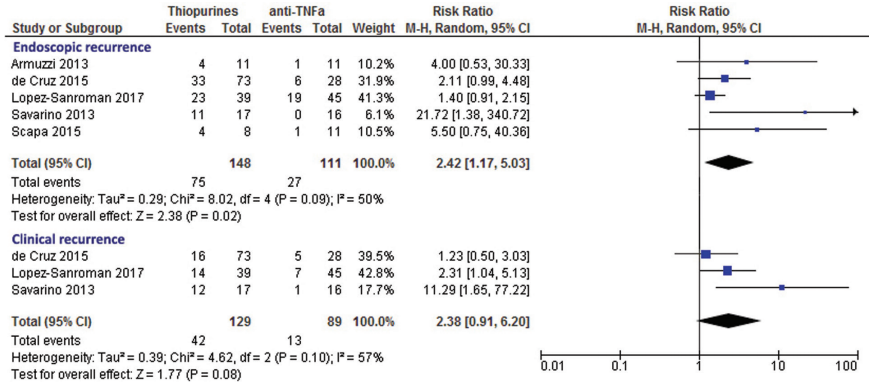
Abstract P697 – Study characteristics

Study name	Medication type and dose		FU (mo)	ER endpoint	CR endpoint	High risk n(%)
Armuzzi, JCC, 2013	AZA	2.5 mg/kg/d	12	≥i2	HBI≥8	11 (100)
	IFX	5 mg/kg/8w				11 (100)
De Cruz, AP&T, 2015	AZA/MP	2/1.5 mg/kg/d	6	≥i2b	CDAI>200	73 (100)
	ADA	40 mg/2w				28 (100)
Lopez-Sanroman, JCC, 2017	AZA	2.5 mg/kg/d	12	≥i2	CDAI>200	22 (56.4)
	ADA	40 mg/2w				29 (64.4)
Savarino, Am J Gastroenterol, 2013	AZA	2 mg/kg/d	24	≥i2	CDAI>200	N/A
	ADA	40 mg/2w				
Scapa, JCC abstract, 2015	MP	1.5 mg/kg/d	6	≥i2	CDAI>200	N/A
	ADA	40 mg/2w				

AZA = Azathioprine, MP = Mercaptopurine, IFX = Infliximab, ADA = Adalimumab, FU = follow-up, ER = endoscopic recurrence, CR = clinical recurrence, HBI = Harvey Bradshaw Index, CDAI = Crohn's disease activity index, High risk = presence of one or more risk factors (smoking, penetrating disease, previous resection), N/A = not available

Abstract P697 – Relative risk of endoscopic and clinical recurrence for thiopurines vs. anti-TNFa



higher in patients treated with thiopurines as compared with anti-TNFa (RR 2.38, 95% CI 0.91–6.02, p = 0.08), although not statistically significant. The quality of evidence was modelled to be moderate for assessing ER and low for CR.

Conclusions: Meta-analysis of available published data suggests that anti-TNFa is superior to thiopurines in the prevention of postoperative ER. However, for a reliable preference in optimal postoperative treatment strategy, individual patient data analysis is required to account for confounding factors (e.g. prior medication, therapy optimisation) and risk factors associated with postoperative CD recurrence.

P698

Early dose optimisation in non-responders to golimumab induction treatment for ulcerative colitis is supported by pharmacokinetic data

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Background: In the PURSUIT study, ulcerative colitis (UC) patients who were non-responders to golimumab (GLM) induction treatment at Week 6 (by full Mayo score) were given GLM 100 mg q4w from Week 6 through Week 54. It was previously shown that 28% of the non-responders at Week 6, after two post-induction doses of GLM 100 mg, became responders (by partial Mayo score) at Week 14.[1] We used serum GLM levels to assess the exposure-response relationship in patients who were either Responders or Non-responders to GLM induction treatment (based on Clinical Response using full Mayo score) at Week 6.

Methods: GLM levels were measured (as µg/ml) in Wk6-Responders and Wk6-Nonresponders. In this post hoc analysis, median trough levels (TL) were examined at Week 6, Week 10, and Week 14 (when steady-state levels are achieved on maintenance treatment). Also, subgroups based on body weight (BW) <80 kg and ≥80 kg) kg were examined; the 80 kg cut-point was selected based on the maintenance doses currently approved in the EU: either 50 mg for BW<80 kg, or 100 mg for BW ≥80 kg.

Results: When examined initially without regard to BW: At Week 6 (post-induction), the TL in Wk6-Nonresponders (1.31) was lower than in Wk6-Responders to 100 or 50 mg GLM (2.50 and 2.28, respectively), suggesting that Wk6-Nonresponders have higher clearance than Wk6-Responders. At Week 14 (steady-state), the TL in Wk6-Nonresponders on 100 mg (0.93) was lower than in Wk6-Responders on 100 mg (1.44) but similar to the TL in Wk6-Responders on 50 mg (0.83), further supporting higher clearance in Wk6-Nonresponders. When examined in subgroups based on BW: At Week 6, data in Wk6-Nonresponders on 100 mg with BW <80 kg (TL=1.40) support higher clearance compared with Wk6-Responders receiving maintenance doses approved in EU (TL=2.35 on 50 mg in BW <80 kg; TL=2.14 on 100 mg in BW ≥80 kg). At Week 14, Wk6-nonresponders on 100 mg with BW< 80 kg show a similar TL (1.03) compared with Wk6-responders receiving the EU-approved doses (TL = 0.92 on 50 mg in BW < 80 kg; TL = 1.24 on 100 mg in BW ≥80 kg).

Serum Golimumab Concentrations (Trough Levels, µg/mL) Based on Clinical Response Status, Maintenance Dose, and Body Weight										
		Week-6 Responders[a] 50 mg Maintenance			Week-6 Responders[a] 100 mg Maintenance			Week-6 Nonresponders[a] 100 mg Maintenance		
		All	Weight Subgroups		All	Weight Subgroups		All	Weight Subgroups	
			<80 kg	≥80 kg		<80 kg	≥80 kg		<80 kg	≥80 kg
Week 6 (post-induction)	Data available	N=153	N=109	N=44	N=153	N=100	N=53	N=396	N=252	N=144
	Median IQR	**2.28** 1.03-4.32	**2.35** 1.18-4.62	**1.88** 0.95-3.38	**2.50** 1.13-4.36	**2.54** 1.13-4.52	**2.14** 1.13-4.31	**1.31** 0.62-2.68	**1.40** 0.61-2.79	**1.18** 0.63-2.41
Week 10	Data available	N=150	N=107	N=43	N=148	N=96	N=52	N=361	N=234	N=127
	Median IQR	**1.04** 0.61-1.56	**1.06** 0.69-1.75	**0.94** 0.56-1.31	**1.43** 1.14-2.10	**1.62** 1.12-2.13	**1.32** 1.17-1.92	**0.99** 0.54-1.59	**1.05** 0.64-1.78	**0.86** 0.41-1.34
Week 14 (steady-state)	Data available	N=133	N=95	N=38	N=140	N=94	N=46	N=312	N=198	N=114
	Median IQR	**0.83** 0.48-1.20	**0.92** 0.52-1.35	**0.67** 0.46-0.88	**1.44** 1.04-2.07	**1.61** 1.12-2.13	**1.24** 0.93-1.59	**0.93** 0.54-1.49	**1.03** 0.59-1.67	**0.82** 0.43-1.16

*Responder status at Week 6 based on achieving a Clinical Response (defined as: Decrease [from the Week-0 full Mayo score] of ≥30% and >3 points, with either a rectal bleeding subscore of 0 or 1 or a decrease in the rectal bleeding subscore of ≥1)
N=number of patients with serum golimumab concentration data available, IQR=interquartile range.

Conclusions: GLM TL data provide evidence for higher clearance in Wk6-Nonresponders, compared with Wk6-Responders. These data further suggest that Wk6-Nonresponders with BW <80 kg may require the GLM 100 mg maintenance dose to achieve TL similar to the TL in Wk6-Responders receiving the maintenance doses currently approved in EU (either 50 mg for BW <80 kg, or 100 mg for BW ≥80 kg).

Reference

1. Rutgeerts. How long should golimumab treatment be continued in patients with ulcerative colitis who do not respond to initial induction therapy? *UEG*, 2014.

P699

Radiologic response reduces the risk of small-bowel surgery in Crohn's disease

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Background: The aim of the present study was (1) to identify factors associated with radiologic response and (2) to assess if radiologic response was associated with better long-term outcomes in Crohn's disease (CD) patients.

Methods: We performed a prospective study from 2011 to 2017 in the tertiary centre of Lille Hospital, including all patients with small-bowel (SB) CD who underwent two magnetic resonance imaging (MRI) within 3–6 months delay, with a follow-up for at least one year after the second MRI. Signs of radiologic inflammation were identified by an expert radiologist in CD. At second MRI, complete responders had all improved lesions, non-responders equal or worsening lesions, and partial responders other scenarios. Radiologic response included patients with complete and partial response. Factors associated with radiologic response were studied using multivariable Cox model. Rate of pejorative CD-related outcomes, i.e. hospitalisation, medical therapeutic optimisation, SB surgery, and endoscopic dilations were assessed using multivariable Cox models and were compared between radiologic responders and non-responders.

Results: A total of 115 SB CD patients were included: 55% had previous intestinal resection, 43% previous failure to immunosuppressant, 33% failure to at least one biologic. At the first MRI, 32% had stricturing disease and 25% penetrating disease. Median time between the two MRIs was 266 days (IQR 211–324), and median follow-up duration after the second MRI 17 months (IQR 11,6–28.3). At the second MRI, 18% had normal MRIs, 3% were complete radiologic responders, 26% were partial responders, 36% had stable abnormal MRIs and 17% presented worsening lesions. At the end, 54 (47%) patients were considered as responders and 61 (53%) as non-responders. In univariate analysis, use of anti-TNF treatment and a CRP ≥5 mg/l at the first MRI were associated with a decreased risk of radiologic response. In multivariate analysis, only a CRP ≥5 mg/l was associated with a decreased risk of radiologic response (OR 0.31; IC 1.10–0.96). At 1 year, 15 (13%) patients were hospitalised, 54 (47%) had medical therapy optimisation, 14 (12%) underwent surgery or endoscopic dilation. In univariate analysis, presence of a fistula or a stricture at the first MRI were associated with an increased risk of surgical or endoscopic procedure. On the opposite, radiologic response was associated with a decreased risk of surgery or endoscopic procedure in univariate and in multivariate analysis (OR 0.15; IC 0.03–0.73).

Conclusions: We here report that radiologic response assessed by MRI decreased the risk of SB surgical resection or endoscopic dilation and should be considered as a therapeutic target in CD patients.

P700

A high CRP before surgery and early medical prophylaxis predict postoperative endoscopic Crohn's disease recurrence

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Background: Early postoperative endoscopic recurrence (EPER) within the first year after a Crohn's disease (CD) resection can be as high as 90%. Established risk factors include smoking, previous resections, perforating disease, extent of resection and the presence of myenteric plexitis. Equivocal data exist, however, on the impact that the type of surgical anastomosis or the early use of medical prophylaxis has on the incidence of EPER. Our primary aim was to evaluate whether the type of anastomosis and the early use of biologic/immunosuppressant modified the risk of developing EPER.

Methods: This was a retrospective cohort study of Western Australian CD patients who had an ileo-colic resection from January 2012 to June 2017 across two tertiary centres. Included subjects had no macroscopic evidence of residual disease and had a colonoscopy within 12 months of surgery. Endoscopic recurrence was defined as a Rutgeerts score ≥ i2. Variables examined included the type of surgical anastomosis, the presence of at least one high-risk factor (smoking, perforating disease and/or a previous bowel resection), disease duration, peak CRP within 3 months of surgery, presence of histological inflammation at the resection margin, length of bowel resected and the early commencement of medical prophylaxis before the first colonoscopy. Univariate analyses were assessed by Fisher's exact test. Significant co-variates were examined by logistic regression analysis.

Results: The mean age of the cohort (n = 97) was 43 years. (19–80) and 53% were males. 75.3% had at least one high-risk factor. Overall, 49.5% had endoscopic recurrence. 54.5% had an end to end anastomosis. Univariate analysis showed that histologically