

**Supplementary Material. Gala M. Godoy Brewer. USTEKINUMAB IS EFFECTIVE FOR PERIANAL FISTULIZING CROHN'S DISEASE: A REAL-WORLD EXPERIENCE AND SYSTEMATIC REVIEW WITH META-ANALYSIS**

**Supplementary Table 1. Multivariable analysis of factors associated with fistula response to ustekinumab at 6 months.**

		OR (response)	95% CI	P
<b>Male</b>		1.52	0.29	0.58
			8.51	
<b>Race</b>	Caucasian	ref		
	African	0.54	0.07	0.46
	American		3.23	
	Other	0.88	0.07	0.90
			10.40	
<b>Smoking status</b>	Never	ref		
	Current	2.33	0.15	0.46
			83.62	
	Former	1.27	0.21	0.77
			7.66	
<b>Age at induction</b>		1.18	0.24	0.81
			5.97	

<b>Disease duration</b>	2.49	0.49	0.23
		14.11	
<b>Prior IBD surgery</b>	0.48	0.09	0.33
		2.29	
<b># prior biologics</b>	0.56	0.08	0.47
		3.10	
<b>Concurrent immunomodulator</b>	2.95	0.55	0.23
		19.16	
<b>Dose escalation</b>	1.53	0.21	0.67
		14.97	

Supplementary Table 2. Adverse events

Adverse event	Number of patients	Percentage	Type of adverse event
Infections	6	22	Perianal abscess , abdominal abscess and sepsis, sinus infection
Infusion reactions	2	7.4	Flushing and redness, numbness and tingling
Other adverse events	6	22	Chronic fevers, hypereosinophilia

			with hypereosinophilic gastro-esophagitis, flare of hemolytic uremic syndrome, headache, nausea and shortness of breath, bloating, vomiting and fatigue.
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**Supplementary Table 3. Quality assessment performed using the New-Castle Ottawa Scale (NOS)**

Study ID	Representativeness of exposed cohort (Maximum: ★)	Selection of non-exposed cohort (Maximum: ★)	Ascertainment of exposure (maximum: ★)	Outcome of interest was not present at start of study (Maximum: ★)	Comparability of cohorts on the basis of design or analysis (Maximum: ★★)	Assessment of outcomes (Maximum: ★)	Follow-up period long enough for outcome to occur (Maximum: ★)	Adequacy of follow-up period among cohorts (Maximum: ★)	Quality Score (TOTAL SCORE= 9)
HARRIS 2019	★	–	★	★	--	★	★	★	★★★★★ ★
WEAVER 2019	★	–	★	★	--	★	★	--	★★★★★
CHAVANNES 2019	★	--	★	★	--	★	★	★	★★★★★ ★
KRUGLIAK 2018	★	–	★	★	--	★	★	★	★★★★★ ★
SATYAM 2018	★	–	★	★	--	★	★	★	★★★★★ ★
BATTAT 2017	★	–	★	★	--	★	★	★	★★★★★ ★
TSISTRAKIS 2017	★	–	★	★	--	★	★	★	★★★★★ ★
MA 2017	★	–	★	★	--	★	★	★	★★★★★ ★
KHORRAMI 2016	★	–	★	★	--	★	★	★	★★★★★ ★
BISHOP 2016	★	–	★	★	--	★	★	★	★★★★★ ★
WILS 2016	★	–	★	★	--	★	★	★	★★★★★ ★

KOPYLOV 2015	★	--	★	★	--	★	★	★	★★★★★ ★
ATTAUABI 2020	★	--	★	★	--	★	★	★	★★★★★ ★
STRAATMIJE R 2021	★	--	★	★	--	★	★	★	★★★★★ ★
PLEVRIS 2020	★	--	★	★	--	★	★	★	★★★★★ ★
BAR-GIL SHIRIT 2020	★	--	★	★	--	★	★	★	★★★★★ ★
TURSI 2021	★	--	★	★	--	★	★	★	★★★★★ ★
MIYAZAKI 2019	★	--	★	★	--	★	★	--	★★★★★
BACAKSIZ 2019	★	--	★	★	--	★	★	★	★★★★★ ★
MARQUES- CAMI 2020	★	--	★	★	--	★	★	--	★★★★★
MANLAY 2021	★	--	★	★	--	★	★	★	★★★★★ ★
YOKOYAMA 2021	★	--	★	★	--	★	★	★	★★★★★ ★
CHAPUIS- BIRON 2019	★	--	★	★	--	★	★	★	★★★★★ ★
TAKEUCHI 2020	★	--	★	★	--	★	★	★	★★★★★ ★

**Supplementary Table 4. Quality Assessment performed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework**

**USTEKINUMAB COMPARED TO PLACEBO FOR THE TREATMENT OF PERIANAL FISTULAS AT 8 WEEKS**

OUTCOMES	Study event rates, n (%)		Relative effect, RR (95% CI)	No. of participants (Studies)	Quality of the evidence (GRADE)
	Risk with placebo	Risk with ustekinumab			
<b>FISTULA HEALING</b>	12/71	39/150	1.53 (0.85 to 2.75)	1306 (3 studies)	LOW (due to indirectness (-1) and imprecision(-1))
<b>FISTULA REMISSION</b>	10/71	37/150	1.75 (0.95 to 3.31)	1306 (3 studies)	LOW

(due to  
indirectness (-1)  
and imprecision (-1))

**USTEKINUMAB COMPARED TO PLACEBO FOR THE TREATMENT OF PERIANAL FISTULAS AT 22 WEEKS**

OUTCOMES	Study event rates, n (%)		Relative effect, RR (95% CI)	No. of participants (Studies)	Quality of the evidence (GRADE)
	Risk with placebo	Risk with ustekinumab			
<b>FISTULA HEALING</b>	6/20	9/19	1.57 (0.69 to 3.58)	39 (1 study)	VERY LOW (due to indirectness (-1) and serious imprecision (-2))

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