2020. CONDUCT

Phase 2b RCT/Cobitolimod/UC/ Induction

Cobitolimod for moderate-to-severe, left-sided UC (CONDUCT): a phase 2b randomised, double-blind, placebo-controlled, dose-ranging induction trial

Randomized placebo-controlled tria. Patients with left side UC were randomised to:
5 arms: cobitolimod 2 ×31 mg group, 2 × 125 mg group, 4 × 125 mg group, 2 × 250 mg group or placebo.
Active study drug was administered week 0 and week 3 (cobitolimod 2 × 31 mg, 2 × 125 mg, and 2 × 250 mg groups), or at weeks 0, 1, 2, and 3 (4 × 125 mg group). Drug applied by enema in hospital.

<u>Primary endpoint:</u>
Clinical remission at w6, defined by Mayo subscores for rectal bleeding of 0, for stool frequency of 0 or 1 (with ≥1-point decrease from baseline), and for endoscopy of 0 or 1.

Results:
- Clinical remission w6: 21% cobitolimod 2x250 vs 7% placebo, p=0.025
- No significant difference in the proportion of cobitolimod 2x31 or 4x125 against placebo.

<u>Conclusion</u>:
Two topical administrations of cobitolimod 250 mg were well tolerated and more effective than placebo in inducing clinical remission w6 after the start of treatment. TLR9 activation is a promising novel therapeutic target in ulcerative colitis and warrants further testing, with phase 3 trials of cobitolimod planned.

	Cobitolimod 2 × 31 mg			Cobitolimod 2 × 125 mg			Cobitolimod 4 × 125 mg			Cobitolimod 2 × 250 mg			Placebo
	n/N (%)	OR (80% CI)	p value	n/N (%)	OR (80% CI)	p value	n/N (%)	OR (80% CI)	p value	n/N (%)	OR (80% CI)	p value	n/N (%)
Primary endpoint													
Clinical remission*	5/40 (13%)	2·0 (0·7–5·5)	0·18	2/43 (5%)	0·7 (0·2–2·2)	0·66	4/42 (10%)	1·4 (0·5–3·9)	0·33	9/42 (21%)	3·8 (1·5–9·5)	0·025†‡	3/44 (7%)
Absolute difference vs placebo	6 percentage points	–	–	−2 percentage points	–	–	3 percentage points	–	–	15 percentage points	–	–	–
Secondary endpoints§													
Mayo clinical remission	5/33 (15%)	1·9 (0·7–5·0)	0·21	1/41 (2%)	0·3 (0·1–1·3)	0·85	3/39 (8%)	1·0 (0·3–2·8)	0·52	7/35 (20%)	2·6 (1·0–6·6)	0·098*	3/39 (8%)
Symptomatic remission	10/37 (27%)	1·5 (0·7–2·9)	0·23	11/42 (26%)	1·4 (0·7–2·7)	0·25	10/40 (25%)	1·2 (0·6–2·4)	0·35	13/37 (35%)	1·8 (1·0–3·5)	0·12	9/43 (21%)
Clinical response	17/33 (51%)	0·9 (0·5–1·5)	0·63	18/41 (44%)	0·8 (0·4–1·4)	0·71	15/39 (38%)	0·6 (0·4–1·2)	0·83	20/35 (57%)	1·3 (0·7–2·3)	0·27	20/39 (51%)
Endoscopic improvement	7/34 (21%)	0·6 (0·3–1·3)	0·80	5/41 (12%)	0·3 (0·2–0·7)	0·97	10/39 (26%)	0·8 (0·4–1·6)	0·65	15/37 (41%)	1·5 (0·8–2·8)	0·20	12/40 (30%)
Histological improvement	4/35 (11%)	0·4 (0·2–0·9)	0·92	5/41 (12%)	0·4 (0·2–0·9)	0·92	7/39 (18%)	0·7 (0·3–1·4)	0·74	8/37 (22%)	0·8 (0·4–1·6)	0·66	10/41 (24%)

Results are presented according to observed data except where indicated. OR was calculated using the Cochran-Mantel-Haenszel test, adjusted for stratification factors. OR=odds ratio. *With non-responder imputation for missing data for presentation of outcome percentages and calculation of OR. †One-sided p<0·10 indicates a statistically significant result. ‡Two-sided test p=0·049. §With placebo multiple imputation for missing data for calculation of OR.

Table 2: **Clinical remission (primary endpoint) and main secondary endpoints at week 6 for all cobitolimod groups compared with placebo (full analysis set)**

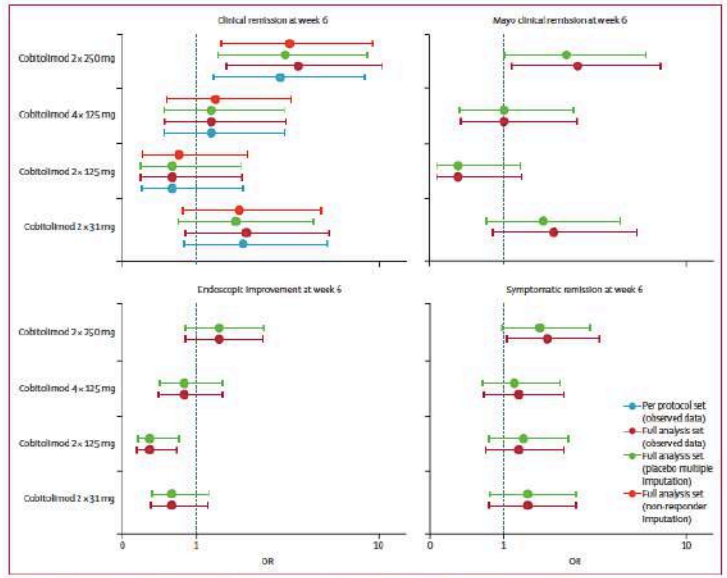

Figure 2: **ORs with 80% CIs for the primary endpoint and major secondary endpoints at week 6 with placebo as the comparator**
ORs were adjusted for stratification factors. OR=odds ratio.

Atreya R et al. Lancet. 2020;1063-1075