2017.TURANDOT

Phase 2/ PF-00547659/ UC / Induction

Anti-MAdCAM antibody (PF-00547659) for ulcerative colitis (TURANDOT) phase 2, randomised, double-blind, placebo controlled trial

Randomized, double-blind, placebo-controlled trial.
UC extending more than 15cm from anal verge who failed/were intolerant to at least one conventional therapy were randomized to:
Subcutaneous injection of 7.5 mg, 22.5 mg, 75 mg, or 225 mg PF-00547659 or placebo at baseline, then every 4 weeks.

Primary endpoint: proportion of patients achieving remission at w12 (total Mayo score ≤2 with no individual subscore >1 and rectal bleeding subcscore ≤1)

Results:

- Remission rates w12 placebo 2.7% vs 7.5mg 11.3% vs 22.5 mg 16.7% vs 75mg 15.5% vs 225mg 5.7%. All treatment (but not 225mg dose) arms better than placebo p<0.05
- No safety signal was observed for the study drug

Conclusions:
PF-00547659 was safe and well tolerated in this patient population, and better than placebo for induction of remission in patients with moderate to severe UC. The greatest clinical effects were observed with the 22.5 mg and 75 mg dose

	Placebo (n=73)	PF-00547659			
		7·5 mg (n=71)	22·5 mg (n=72)	75 mg (n=71)	225 mg (n=70)
Central endoscopy reading					
Remission rate, n/N					
Overall	2/73 (2·7%)	8/71 (11·3%)	12/72 (16·7%)	11/71 (15·5%)	4/70 (5·7%)
Anti-TNFα-naive, n/N	2/31 (6·5%)	5/30 (16·7%)	8/31 (25·8%)	7/30 (23·3%)	3/30 (10·0%)
Anti-TNFα-experienced, n/N	0/42 (0·0%)	3/41 (7·3%)	4/41 (9·8%)	4/41 (9·8%)	1/40 (2·5%)
Risk difference vs placebo (90% CI)*	–	0·08 (0·019 to 0·14)	0·128 (0·056 to 0·199)	0·118 (0·048 to 0·188)	0·026 (−0·012 to 0·064)
p value†	–	0·0425	0·0099	0·0119	0·1803
Response rate, n/N	21/73 (28·8%)	27/71 (38·0%)	39/72 (54·2%)	32/71 (45·1%)	35/70 (50·0%)
Risk difference vs placebo (90% CI)*	–	0·089 (−0·037 to 0·214)	0·254 (0·121 to 0·388)	0·163 (0·032 to 0·293)	0·213 (0·08 to 0·347)
p value†	–	0·1379	0·0044	0·0479	0·0157
Mucosal healing rate, n/N	6/73 (8·2%)	11/71 (15·5%)	20/72 (27·8%)	18/71 (25·4%)	10/70 (14·3%)
Risk difference vs placebo (90% CI)*	–	0·081 (0 to 0·162)	0·187 (0·091 to 0·284)	0·159 (0·068 to 0·25)	0·069 (−0·013 to 0·151)
p value†	–	0·0099	0·0038	0·0080	0·0099
Local endoscopy reading					
Remission rate, n/N					
Overall	4/73 (5·5%)	10/71 (14·1%)	17/72 (23·6%)	13/71 (18·3%)	9/70 (12·9%)
Anti-TNFα-naive, n/N	2/31 (6·5%)	6/30 (20·0%)	9/31 (29·0%)	8/30 (26·7%)	6/30 (20·0%)
Anti-TNFα-experienced, n/N	2/42 (4·8%)	4/41 (9·8%)	8/41 (19·5%)	5/41 (12·2%)	3/40 (7·5%)
Risk difference vs placebo (90% CI)*	–	0·08 (0·002 to 0·159)	0·178 (0·083 to 0·272)	0·122 (0·036 to 0·208)	0·066 (−0·009 to 0·142)
p value†	–	0·0927	0·0056	0·0375	0·0927
Response rate, n/N	24/73 (32·9%)	27/70 (38·6%)	39/72 (54·2%)	34/70 (48·6%)	36/70 (51·4%)
Risk difference vs placebo (90% CI)*	–	0·056 (−0·075 to 0·186)	0·212 (0·077 to 0·347)	0·156 (0·022 to 0·290)	0·185 (0·050 to0·320)
p value†	–	0·2617	0·0231	0·0652	0·0435
Mucosal healing rate, n/N	16/73 (21·9%)	16/71 (22·5%)	27/72 (37·5%)	25/71 (35·2%)	20/70 (28·6%)
Risk difference vs placebo (90% CI)*	–	0·001 (−0·111 to 0·114)	0·154 (0·030 to 0·278)	0·130 (0·008 to 0·253)	0·066 (−0·053 to 0·186)
p value†	–	0·5225	0·0982	0·1393	0·4000

TNFα=tumour necrosis factor-α. *The stratum-adjusted risk difference and the corresponding 90% CIs were obtained with the Cochran-Mantel-Haenszel test.[28] †One-sided adjusted p value due to the Hochberg step up method.

Table 2: **Remission, response, and mucosal healing rates at week 12 with central and local endoscopy readings**

Vermeire S et al.Lancet 2017.390; 135-144