2022. Spesolimab

RCT/Spesolimab/UC / Induction

Safety and tolerability of spesolimab in patients with ulcerative colitis

Phase II and IIA, randomised, double-blind trials.
Patients with mod-severe UC were randomized to:
Study 1: 300 mg single dose; 450 mg q4w; or 1,200 mg q4w, three doses). Patients who failed to biologics.
Study 2: phase IIa, (1,200 mg q4w). Patients were on antiTNF
Study 3: phase IIa OL, single-arm trial (1,200 mg q4w). AntiTNF naïve or not failed to antiTNF
Studies lasted 12 weeks, with a 12-, 24-, and 16-w safety follow-up.

Primary endpoints: Study 1:Dose-finding, efficacy (clinical remission w12), safety. Study 2: Efficacy & safety as add-on therapy. Study 3: mechanism of action

Results:
- Efficacy endpoints were not met. In Study 1, 1/24 (4.2%), 2/23 (8.7%), and 2/28 (7.1%) vs 0% placebo.
- Adverse event rates were similar for spesolimab vc placebo Study 1 (N = 98; 64.9%; 65.2%) & 2 (N = 22; 86.7%; 71.4%); all patients in Study 3 (N = 8) experienced AEs.
- The most frequent AEs were skin related

Conclusion:
Spesolimab was generally well tolerated, with no unexpected safety concerns. The safety data are consistent with studies in other inflammatory diseases.

*Spesolimab, a novel, humanized monoclonal immunoglobulin G1 antibody that specifically targets and blocks IL-36 R signaling.

Table 4. Overall summary of adverse events in clinical trials of intravenous spesolimab in patients with ulcerative colitis.

	Study 1 (1368–0005)		Study 2 (1368–0010)		Study 3 (1368–0004)
n (%)	Spesolimab (300 mg single dose, 450 mg q4w, or 1,200 mg q4w) (n = 74)	Placebo (n = 23)	Spesolimab (1,200 mg q4w) (n = 15)*	Placebo (n = 7)	Spesolimab (1,200 mg q4w) (n = 8)
Any AE	48 (64.9)	15 (65.2)	13 (86.7)	5 (71.4)	8 (100)
Severe AE (RCTC grade 3 or 4)	7 (9.5)	4 (17.4)	1 (6.7)	1 (14.3)	2 (25.0)
Investigator-defined, drug-related AE	16 (21.6)	2 (8.7)	3 (20.0)	1 (14.3)	6 (75.0)
AE leading to discontinuation of study treatment	6 (8.1)	2 (8.7)	2 (13.3)	1 (14.3)	2 (25.0)
SAEs	7 (9.5)	4 (17.4)	1 (6.7)	1 (14.3)†	2 (25.0)
Resulted in death	0	0	0	0	0
Was life-threatening	1 (1.4)	0	0	0	0
Required or prolonged hospitalization	6 (8.1)	2 (8.7)	0	1 (14.3)	2 (25.0)
Other medically important	1 (1.4)	2 (8.7)	1 (6.7)	1 (14.3)	0
TEAEs (system organ class; preferred term)					
Gastrointestinal disorders	20 (27.0)	5 (21.7)	6 (40.0)	1 (14.3)	3 (37.5)
Worsening of UC	12 (16.2)	1 (4.3)	3 (20.0)	1 (14.3)	1 (12.5)
Infections and infestations	19 (25.7)	2 (8.7)	4 (26.7)	2 (28.6)	7 (87.5)
Nasopharyngitis	5 (6.8)	0	3 (20.0)	1 (14.3)	4 (50.0)
Nausea	1 (1.4)	1 (4.3)	2 (13.3)	0	0
Skin and subcutaneous tissue disorders	13 (17.6)	2 (8.7)	4 (26.7)	2 (28.6)	2 (25.0)
Skin rash	5 (6.8)	0	0	1 (14.3)	1 (12.5)
Acne	1 (1.4)	0	2 (13.3)	0	1 (12.5)
Eczema	1 (1.4)	0	2 (13.3)	0	0
Eye disorders	0	0	0	0	2 (25.5)
Eye inflammation	0	0	0	0	2 (25.5)
Nervous system disorders	8 (10.8)	1 (4.3)	5 (33.3)	1 (14.3)	2 (25.0)
Headache	4 (5.4)	0	4 (26.7)	1 (14.3)	2 (25.0)
Blood and lymphatic system disorders	5 (6.8)	6 (26.1)	0	0	1 (12.5)
Anemia	1 (1.4)	6 (26.1)	1 (6.7)	0	1 (12.5)
UDAECs (system organ class; preferred term)					
Any UDAEC	10 (13.5)	2 (8.7)	3 (20.0)	1 (14.3)	3 (37.5)
Infusion or systemic hypersensitivity reactions, including anaphylactic reactions	10 (13.5)	1 (4.3)	2 (13.3)	1 (14.3)	2 (25.0)
Rash	5 (6.8)	0	0	1 (14.3)	1 (12.5)
Eczema	1 (1.4)	0	2 (13.3)	0	0

Ferrante M et al. Expert Opinion on Drug Safety. 2022