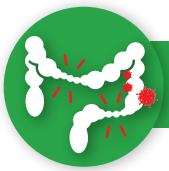
Focus on Ulcerative Colitis and Crohn's Disease

Recent events such as clinical trial failures, new pipeline assets, and data readouts will impact the future landscape for Ulcerative colitis (UC) and Crohn's disease (CD).



Ulcerative Colitis

While competition in UC is intense and new assets continue to be added to the pipeline, efficacy benchmarks have not moved based on data from pre-registration assets, filgotinib and ozanimod. However, promising early efficacy signals have been demonstrated by **SHR0302/Reistone Biopharma** and **Olamkicept/I-Mab Biopharma** on clinical response, clinical remission, and endoscopic remission/mucosal healing in the induction phase.

SHR0302: In a Phase II study, with endpoint assessment at week 8, SHR0302 met its primary [Clinical response] and key secondary [Clinical remission] endpoints. Although not a head-to-head comparison, the efficacy demonstrated in this study is less than the current benchmark, infliximab, in the biologic-naïve patient segment.[1]

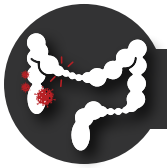
- Clinical response (% patients): SHR0302 8 mg QD, 4 mg BID, 4 mg QD (46.3%, 46.3%, 43.9%) vs. placebo (26.8%), respectively. Placebo subtracted difference (PSD) for each active arm was 19.8% ($p = 0.066$), 20.1% ($p = 0.059$), and 17.7% ($p = 0.095$) respectively.
- Clinical remission (% patients): SHR0302 8 mg QD, 4 mg BID, 4 mg QD (22.0%, 24.4%, 24.4%) vs. placebo (4.9%), respectively. PSD for each active arm was 17.5% ($p = 0.020$), 19.6% ($p = 0.013$), and 19.9% ($p = 0.011$) respectively.

Olamkicept: In a Phase II study, with endpoint assessment at week 12, efficacy of olamkicept was better than the current benchmark, tofacitinib, in the biologic-experienced patient segment on key secondary endpoints, clinical remission and mucosal healing. Although not a head-to-head comparison, the efficacy (PSD) of olamkicept vs. tofacitinib at week 8 (21% vs. 13% and 31% vs. 17%) on clinical remission and mucosal healing endpoints, respectively, is superior. However, data from larger clinical studies will determine whether olamkicept will reset the efficacy/safety thresholds or change the treatment paradigm.[2]

- Clinical response: Olamkicept 600 mg (58.6%) vs. placebo (34.5%), [PSD: 24.1], $p = 0.032$
- Clinical remission: Olamkicept 300 mg (6.7%), olamkicept 600 mg (20.7%) vs. placebo (0%), [PSD: 20.7], $p < 0.001$
- Mucosal healing: Olamkicept 300 mg (10%), olamkicept 600 mg (34.5%) vs. placebo (3.4%), [PSD: 31.1], $p < 0.001$
- Development of multiple Phase II assets has been discontinued in UC. Dekavil/Pfizer, KHK-4083/Kyowa Hakko Kirin, Vamorolone/ReveraGen BioPharma, and Tulinercept/Protalix are no longer included in the respective company pipelines.

STI-0529/Sublimity Therapeutics Phase IIa trial was terminated due to lack of efficacy:

- Treatment remission difference of 9.6% for 75 mg BID vs. placebo (due to an increase in placebo response rate) was determined not sufficient to continue the study.[3]



Crohn's Disease

Three new assets have been added to the existing 55 assets in the CD pipeline, while 2 assets have advanced to the next phase of clinical development.

Multiple IL-23 antagonists with encouraging efficacy signals (**Guselkumab/Janssen Biotech**, Phase II, **Mirikizumab/Eli Lilly**, Phase II, and **Risankizumab/AbbVie**, Phase III), are in development for moderately to severely active CD. While data from larger clinical studies for guselkumab and mirikizumab are needed to determine whether these assets will reset the efficacy/safety thresholds or change the treatment paradigm, risankizuamb has demonstrated the best efficacy data among pipeline assets for induction on clinical response and endoscopic response endpoints.[4]

In the biologic-naïve/refractory patient segment:

- **Clinical response:** Risankizumab 600 mg (45%) vs. placebo (25%), PSD: 20%
- **Endoscopic response:** Risankizumab 600mg (45%) vs. placebo (25%), PSD: 20%

Although not a head-to-head comparison, the efficacy of risankizumab is significantly higher in comparison to the current benchmark, ustekinumab, in the biologic-refractory patient segment:

- **Clinical response:** Risankizumab, PSD at week 12 (23%) vs. ustekinumab, PSD at week 8 (14%)
- **Endoscopic response:** Risankizumab PSD at week 12 (18%) vs. ustekinumab, PSD at week 8 (9%)

Amiselimod/Mitsubishi Tanabe Pharma, Phase II, failed to achieve the primary endpoint vs. placebo in moderate-to-severe active CD and its development has been discontinued.

References:

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3. ClinicalTrials.gov. A study evaluating the efficacy and safety of ST-0529 in subjects with moderately to severely active ulcerative colitis. Available at: https://clinicaltrials.gov/ct2/show/NCT03844932.
4. Geert R. D'Haens et al., Risankizumab induction therapy in patients with moderate-to-severe Crohn's disease with intolerance or inadequate response to conventional and/or biologic therapy: results from the Phase III ADVANCE study. DDW 2021. Available at: https://eventpilotadmin.com/web/planner.php?id=DDW21LITE.
5. ClinicalTrials.gov.
6. Company Websites.

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