Introduction: The Phase 3b SEQUENCE study directly compared efficacy and safety of risankizumab (RZB, IL-23p19 inhibitor), and ustekinumab (UST, IL-12/23p40 inhibitor), in patients (pts) with moderate-to-severe Crohn's disease (CD).

Methods: SEQUENCE, an open-label, multicentre, randomised, efficacy assessment-blinded study, enrolled pts with moderate-to-severe CD who previously failed ≥1 anti-tumour necrosis factor (TNF) agents. In Part 1 of the trial, pts were randomised 1:1 to receive RZB (600 mg IV at weeks [wks] 0, 4 and 8, followed by 360 mg SC every 8 wks [Q8W] from wk12) or UST (single weight-based IV dose at wk0, followed by 90 mg SC Q8W from wk8) over 48 wks. Mandatory steroid tapering started at wk2. Primary endpoints were clinical remission at wk24 (non-inferiority of RZB vs UST in 50% of planned pts) and endoscopic remission at wk48 (superiority of RZB vs UST). Safety was assessed throughout.

Results: 255 (RZB) and 265 (UST) patients were assessed. The primary endpoints of the study were met. At wk24 clinical remission (CD Activity Index <150) rates were 58.6% (75/128) for RZB and 39.5% (54/137) for UST (∆18.4, non-inferiority met with the pre-defined margin of 10% in 50% of enrolled patients). At wk48, endoscopic remission rates were 31.8% (81/255) for RZB and 16.2% (43/265) for UST (∆15.6%, p<0.0001 for superiority). RZB was superior to UST for all secondary endpoints (all p<0.0001). Exposure-adjusted adverse event (AE) rates (Events [E/100PYs]) were comparable between RZB (879 [341.2]) and UST (763 [282.7]). Serious AEs and AEs leading to discontinuation were numerically higher with UST vs RZB.

Conclusions: RZB demonstrated non-inferiority to UST for wk24 clinical remission, superiority for wk48 endoscopic remission, and superiority in secondary endpoints in moderate-to-severe CD refractory to anti-TNFs. RZB and UST were well tolerated.