Background: Adhesion molecule α4β7 is a validated treatment target in inflammatory bowel diseases. We evaluated abirubicab, a fully human monoclonal antibody against α4β7, in patients with moderate to severe Crohn's disease (CD).

Methods: This phase 2b, randomised, multi-centre, double-blind, placebo (Pbo)-controlled study enrolled patients aged 18–65 years with moderate to severe CD (CDAI score 220–450) and evidence of active inflammation (by endoscopic evaluation, or elevated C-reactive protein or fecal calprotectin). In addition, patients must have had inadequate or loss of response or intolerance to immunosuppressives, TNF antagonists, or corticosteroids. Eligible patients were randomised to receive Pbo or abirubicab (21 or 70 mg) SC on day 1, weeks 2 and 4, and every 4 weeks (Q4W) for up to 24 weeks, or one dose of abirubicab 210 mg SC on day 1. The primary endpoint was CDAI remission (score <150) at week 8. Key secondary endpoints were remission at week 12 and CDAI response (reduction from baseline of ≥100) at weeks 8 and 12. CD4+ T cell subsets were enumerated and α4β7 receptor occupancy was measured in a subgroup of patients.

Results: This study enrolled 249 patients. Final randomisation allocation was affected by a systematic misalignment in investigational product, resulting in 98, 26, 84, and 41 patients in the Pbo, 21 mg Q4W, 70 mg Q4W, and 210 mg treatment groups, respectively. The study blind and randomisation were intact. Baseline demographics were similar. Statistically significant improvement was not achieved with the abirubicab 70 mg Q4W and Pbo arms for the primary endpoint (p=0.76 vs Pbo) (Table). However, higher rates of remission and response were observed in the active treatment arms at week 12, particularly in patients with prior failure of TNF antagonists assigned to the 210 mg abirubicab group. Maximal reduction of free α4β7 on naive CD4+ T cells in the peripheral blood was sustained from the first measurement at week 2 to week 8 for all dose groups, and through week 12 for the 21 mg Q4W and 70 mg Q4W groups. Abirubicab induced a significant post-dose increase in α4β7-high central memory CD4+ T cell counts between baseline and week 8. Adverse events were similar among treatment groups through week 24, with no cases of PML or deaths. No patients developed neutralizing antibodies to abirubicab.

Conclusions: Although the primary endpoint was not met, beneficial effects of abirubicab were observed for remission and response rates. There was no safety imbalance compared with Pbo.

Amen and AstraZeneca/MedImmune sponsored this study.

OP037
Infants born to mothers with inflammatory bowel disease exhibit distinct microbiome features that persist up to 3 months of life

J. Torres1, J. Hu2, C. Eisele2, N. Nair2, H. Panchal2, X. Bao2, X. Niu2, J. Côté-Daigneault1, B. JhaраЭ, E. Maser1, A. Kornbluth1, P. Legnani1, J. George1, M. Dubinsky1, J. Stone1, C.-L. Chen4, J. Clemente2, J.-F. Colombel1, J. Peter2

1Icahn School of Medicine at Mount Sinai, Gastroenterology, New York, United States; 2The Johns Hopkins University School of Medicine, Department of Pediatrics, Baltimore, United States; 3The Children’s Hospital at Westmead, Westmead, Australia; 4Fiona Stanley Hospital, Gastroenterology, Perth, Australia; 5University of Queensland, School of Medicine, Brisbane, Australia; 6The Royal Children’s Hospital, Department of Gastroenterology, Melbourne, Australia; 7University of North Carolina, Chapel Hill, United States; 8Rutgers University, New Brunswick, United States; 9Brigham and Women’s Hospital, Boston, United States; 10Istituto Giannina Gaslini, Genova, Italy; 11University of California, San Francisco, United States