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MP083

VEDOLIZUMAB THERAPEUTIC DRUG MONITORING AND REAL-WORLD OUTCOMES IN INFLAMMATORY BOWEL DISEASE

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Introduction: The present study evaluates the relationships between post-induction vedolizumab trough concentrations (VTC) and real-world outcomes in inflammatory bowel disease (IBD), including biomarkers of inflammation and clinical disease scores.

Aims & Methods: Participants in the Takeda Canada Patient Support Program who were treated with vedolizumab for Crohn's disease (CD) and ulcerative colitis (UC) were assessed at defined timepoints from 2018-2020. Post-induction VTC (Week 14), baseline albumin (Week 0), faecal calprotectin (FC; Week 0 and 30), C-reactive protein (CRP; Week 0 and 30), Harvey-Bradshaw Index (HBI; Week 0 and 30) and Partial Mayo Scores (PMS; Week 0 and 30) were collected. Remission was defined by CRP (<5mg/L), FC (<250µg/g), HBI (<5), or PMS (<3) at Week 30. Receiver operating characteristic (ROC) curve analyses were used to measure the sensitivity, specificity, and optimal cut-point value of VTC for multiple definitions of remission. In multivariate analyses, covariates included optimal VTC threshold, age, sex, disease subtype, baseline albumin, disease duration, and biologic treatment exposure.

Results: IBD patients who achieved CRP remission at Week 30 had higher Week 14 VTC levels than those who did not (n=210, p=0.0001). Among all patients, a Week 14 VTC cut-off of 17.35µg/mL (n=210, Area Under the ROC (AUROC): 0.67, 95% Confidence Interval (CI): 0.59-0.74, p<0.001) best predicted CRP remission by multivariate analysis (p=0.001). VTC cut-offs best predicting CRP remission were similar between subgroups (CD VTC>19.60µg/mL, p=0.01 (AUROC: 0.69, 95% CI: 0.60-0.78, p<0.001); UC VTC>17.35µg/mL, p=0.005 (AUROC: 0.64, 95% CI: 0.52-0.76, p<0.001)). Patients with Week 14 VTC levels above the determined cut-off remained on vedolizumab treatment for longer than those below this cut-off (n=210; VTC>17.35µg/mL Hazard Ratio: 0.44, 95% CI: 0.20-0.99, log-rank p=0.04). Week 14 VTC levels were higher in IBD patients who achieved FC remission compared with those who did not (n=144, p=0.02). A Week 14 cut-off of 18.55µg/mL (n=144, AUROC: 0.61, 95% CI: 0.52-0.70, p<0.001) was associated with FC remission by univariate (p=0.005) analysis, but not in multivariate analysis. In all patients, baseline albumin levels were independently associated with FC remission by multivariate analysis (n=144, p=0.03). In CD patients, FC remission was associated with baseline albumin levels (n=79, p=0.04) and female sex (n=79, p=0.02), both by multivariate analysis. There were no associations found between Week 14 VTC and Week 30 disease activity index scores in UC or CD patients by multivariate analysis.

Conclusion: Monitoring VTC in early treatment of CD and UC may predict patient outcomes as measured by CRP. Baseline normal albumin in all patients and female sex in CD patients are associated with improved FC remission, likely related to decreased clearance of vedolizumab.

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MP084

EFFECTIVENESS OF USTEKINUMAB DOSE ESCALATION IN CROHN'S DISEASE PATIENTS WITH INSUFFICIENT RESPONSE TO STANDARD-DOSE SUBCUTANEOUS MAINTENANCE THERAPY: AN OBSERVATIONAL MULTICENTRE STUDY

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Introduction: Ustekinumab is a human monoclonal antibody that targets interleukin (IL)-12 and IL-23 and it is effective for the treatment of Crohn's disease (CD). However, a group of patients will not respond or over time will experience loss of response (LOR) to ustekinumab. Evidence supportting the effectiveness of ustekinumab dose escalation for LOR is scarce.

Aims & Methods: The aim of this study was to assess the effectiveness of ustekinumab dose escalation in a cohort of patients with active CD. Multicentric retrospective cohort study conducted in five tertiary Andalusian centers. Patients with active CD who received a standard-dose intravenous (IV) induction and at least one subcutaneous (SC) ustekinumab 90 mg dose were included.

All enrolled patients received dose escalation by either shortening the interval between the maintenance doses to every 4 or 6 weeks, IV reinduction or a combination of strategies. The primary outcome of the study was to asses corticosteroid (CS)-free remission (HBI ≤4) at week 16.

Secondary outcomes were CS-free response (decrease in the HBI ≥ 3 points from baseline) at week 16 and on the last follow-up, CS-free remission on the last follow-up and ustekinumab persistence after dose escalation.

Results: A total of 84 patients were included (table 1). Patients were dose-escalated after a median treatment duration of 37 weeks (IQR 23-54). At week 16 from dose escalation the proportion of patients in CS-free response was 50/84 (59%) including 18/84 (21,4%) in CS-free remission. Follow-up data beyond week 20 were available for 61/84 patients (72.6%). On the last follow-up visit, 29/61 (47,5%) patients responded to treatment without concomitant CS of which 19/61 (31%) were in CS-free clinical remission. Systemic CS were discontinued in 21/44 (47,7%) patients who were on CS at the time of dose escalation. Ustekinumab was discontinued in 14/84 (17%) of the patients due to clinical non-response (ustekinumab persistence 81% at 14 months of follow-up). Adverse events following dose escalation were reported in 4 of the 84 patients (7.7%), none of them were serious.

Age at treatment onset, years (median, IQR)	40 (33-50)
Disease duration, years (median, IQR)	13,5 (9-18,75)
Gender (n, %)	
Male	38 (45,2)
Female	46 (54,8)
Behaviour (n, %)	
Nonstricturing nonpenetrating	36 (43)
Stricturing	29 (34,5)
Penetrating	19 (22,5)
Smoking (n, %)	
Active smoker	22 (26,2)
History of previous abdominal surgery (n, %)	40 (47,6)
Type of dose escalation (n,%)	
Q4w	49 (58,3)
Q4w + IV reinduction	13 (15,5)
Q6w	22 (26,2)
Systemic corticosteroids at escalation (n, %)	45 (53,6)
Concomitant immunomodulators at escalation (n, %)	21 (25)

Conclusion: Dose escalation of ustekinumab maintenance was effective in over 50% of the patients and the treatment persistence was high. This strategy should be considered in patients who are not responsive or have LOR to ustekinumab on an 8 week dose maintenance interval

Disclosure: Nothing to disclose.

Oesophageal motility

13:00-14:00 / Hall 5

MP085

CHANGES IN ESOPHAGEAL BODY MOVEMENT AFTER PERORAL ENDOSCOPIC MYOTOMY IN TYPE III ACHALASIA

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Introduction: Although peroral endoscopic myotomy (POEM) is reportedly effective, especially for type III achalasia, its effect on esophageal body movement is poorly understood.

Aims & Methods: This study aimed to evaluate the morphologic changes in cross-sectional movement in the esophageal body after POEM in type III achalasia in comparison to type I and II achalasia by analyzing intraluminal ultrasound (US) images temporally correlated with high-resolution impedance manometry (HRIM) data.

Intraluminal US images and impedance values from 17 achalasia patients who underwent POEM with pre- and post-POEM HRIM and intraluminal US examinations (mean age, 48.47 years (22 – 76); 7 males, 10 females; type I, n=4; type II, n=7; and type III, n=6) and eight normal subjects (mean age, 45.13 years (27 – 57); 3 males, 5 females) were analyzed. Intraluminal US image parameters included the esophageal muscle thickness (MT), lumen cross-sectional area (LCSA), contractility/distensibility indices, swallow-to-distension interval and distension duration.