Abstract citation ID: jjac190.0922

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Pharmacokinetics and clinical evaluation of vedolizumab based on real-life routine monitoring data in IBD patients

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Background: Vedolizumab (VDZ) is recommended for induction of remissionin patients with inflammatory bowel disease (IBD). Therapeutic drug monitoring (TDM) based on pharmacokinetic measurements of VDZ trough plasma concentrations adds-up on routine patients' clinical follow-up. Great interpatient variability in VDZ serum concentrations is observed. Our aim was to investigate factors contributing to variations in VDZ levels by developing population pharmacokinetic model based on sparse TDM data, and understand its importance in reaching adequate response.

Methods: Retrospective data from IBD patients undergoing treatment with VDZ were reviewed, and patients with measured VDZ serum concentration were included in analysis. In addition, demographic, therapy and clinical characteristics were collected; including various inflammatory biomarkers such as platelets, leucocytes, C-reactive protein, sedimentation rate, fecal calprotectin, etc., and calculated Mayo, SES scores, where appropriate. VDZ dose of 300 mg was administered as 30-minutes infusion at week: 0, 2 and 6 during induction, with a 4-, 6- or 8-week dosing interval during maintenance phase. Population modeling approach was applied to characterize pharmacokinetic profile of VDZ. In addition, logistic analysis was implemented to test correlation among VDZ concentration, disease biomarkers, and appropriate clinical scores.

Results: In total, 115 VDZ trough concentrations obtained from 107 patients were analysed. Patients' characteristics are given in Table 1. VDZ concentrations were described by two-compartment model. Estimated typical value of VDZ clearance (CL) was 0.226 L/day, without any difference among ulcerative colitis (UC) and Crohn's disease (CD) patients. We identified that previous treatment with anti-TNF biologics increases CL by on average 24.8%. In addition, our preliminary analyses indicate higher probability of thrombocytosis with lower VDZ levels. Median VDZ concentration in patients whose platelets were above and below 350 (10^9/L) were 15.33 and 20.29 microg/mL, respectively (Figure 1).

Conclusion: Our preliminary results suggest that platelets account as inflammation burden marker and previous antiTNF treatment may be predictive factors for proactive VDZ optimization.