I. Introduction

Vedolizumab (VDZ), an anti-α4β7 integrin monoclonal antibody, is indicated for moderate to severe ulcerative colitis and Crohn's disease. Therapeutic drug monitoring (TDM) assays to measure VDZ and anti-vedolizumab drug antibodies (ADAb) in patient serum are utilized to manage lack or loss of response and to proactively optimize dosing. Here, 2239 VDZ patient results were analyzed.

II. Methods

Measurements of drug and ADAb levels were performed by lab developed chemiluminescent immunomassays.[1] The VDZ drug assay is two-site immunoassay on a Meso-Scale Discovery platform. The ADAb assay utilizes a solution phase bridging method and has demonstrated drug tolerance. All ADAb positive samples are confirmed by a signal suppression test. Precision, accuracy and lower limits of quantitation are shown in Table 1. Clinical histories and blood collection timing are unknown.

The occurrence of ADAb was low (43/2239, 1.9%) with ADAb levels ranging from 25 to >18,000 ng/mL (Table 2). Importantly, we found that samples with the highest titers of ADAb (>1000 ng/mL) had undetectable VDZ (mean <1.5 µg/mL); ADAb-positive samples with the lowest titers (<100 ng/mL) had VDZ drug levels (mean 15.6 µg/mL) that were closest to the mean VDZ of ADAb-free samples (22 µg/mL). Samples with intermediate ADAb titers between 5 and 20 µg/mL had VDZ levels of <1.5 µg/mL. As a general trend, higher titers of anti-vedolizumab antibodies were associated with lower VDZ drug levels using our ADAb assay which measures free, antibody-unbound drug. However, the sample size here was small.

We analyzed 2239 patient samples for vedolizumab and anti-vedolizumab antibodies. Collection timing and clinical histories are not known. Of all ADAb-free samples, about 48% of all samples were between 5 and 20 µg/mL; 37% were >20 µg/mL; about 15% were undetectable or less than 5 µg/mL.

We observed a low incidence of immunogenicity (1.9%) less than that of GEMINI 1 and 2 (4%) [2] of all 2239 samples, only 43 exhibited anti-vedolizumab antibodies using our drug tolerant assay. ADAb titers in excess of 1000 ng/mL occurred with undetectable drug levels of <1.5 µg/mL. As a general trend, higher titers of anti-vedolizumab antibodies were associated with lower VDZ drug levels using our ADAb assay which measures free, antibody-unbound drug.

Some of our 2239 samples were serial measurements; 74 patients had sera collected on at least two different dates. Of those, the majority (70%) of patients demonstrated an increased serum VDZ level on the latter collection, suggesting the use of VDZ TDM to escalate dosing to achieve higher serum drug levels. Additionally, 8 patients with serial measurements had positive ADAb; in 4 of the 8 (50%), the positive ADAb (ranging from 25 to 111 ng/mL) became negative on the latter samples, suggesting that some low anti-vedolizumab antibodies may be transient or treated away.

III. Results

The median VDZ drug level was 16.0 µg/mL with a range of <1.5 to 308 µg/mL. The distribution of 2239 VDZ concentration measurements is shown in Table 2. Of note, 5% of patient samples had undetectable VDZ and 15% were less than 5 µg/mL. If we separated our results into drug concentration categories from GEMINI 1 quartiles, we found that 51% (1483) were in the lowest category of < 17 µg/mL (median 8.9 µg/mL) while only 15% (450) of our samples had VDZ levels in the highest drug concentration category of 36 - 45 µg/mL (median 50 µg/mL). The remaining 34% of samples were in the interquartile drug concentration range: 19% (548) of VDZ drug levels were 17 – 34 g/mL (median 20 µg/mL); 15% (411) were 25 – 36 µg/mL (median 30 µg/mL).[2]

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IV. Conclusion

We analyzed 2239 patient samples for vedolizumab and anti-vedolizumab antibodies. Collection timing and clinical histories are not known. Of all ADAb-free samples, about 48% of all samples were between 5 and 20 µg/mL; 37% were >20 µg/mL; about 15% were undetectable or less than 5 µg/mL.

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Well-defined target concentration ranges have yet to be established for vedolizumab induction and maintenance; however, VDZ trough concentration thresholds of 30 µg/mL at week 2, 24 µg/mL at week 6, and 14 µg/mL during maintenance have been proposed [3]. Our analysis of 2239 samples suggests that physicians are already utilizing VDZ TDM to assess patients' pharmacokinetic, pharmacodynamic and immunogenic status in order to inform dosing and other clinical decisions.

V. References