Poster D0398

Dose Escalation of Biologic Therapies in Biologic Treatment-Naïve Patients with Crohn's Disease: Results from the ODESSA-CD Study

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Background

- Several biologics are available for the induction and maintenance of remission in patients with moderate to severe Crohn's disease (CD)[1]
- Although biologics are effective treatment options, patients may lose response to a biologic during maintenance therapy and require dose escalation to reinduce and maintain remission[2]
- Existing data on the rates of biologic dose escalation in patients with CD are predominantly restricted to anti-tumor necrosis α (TNFα) treatments,[3–5] and outcomes after dose escalation have not been well characterized

Aim

- The ODESSA-CD (real wOrld Dose EScalation and outcomeS with biologics in inflammatory bowel disease pAtients) study aimed to investigate dose escalation of biologics and outcomes after dose escalation in biologic-naïve patients with CD

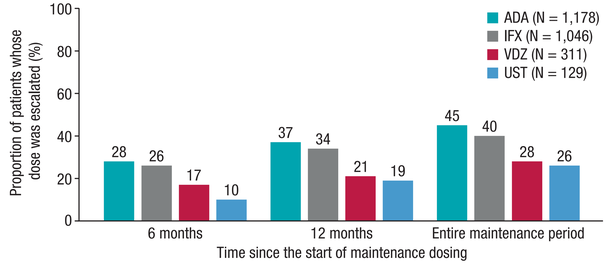
Methods

- ODESSA-CD was a retrospective observational cohort study conducted using administrative claims data from IBM® MarketScan® databases
- Adult patients with at least one claim for adalimumab, infliximab, vedolizumab, or ustekinumab between January 1, 2017, and December 31, 2018, were included, with the first claim date defined as index date 1 (**Supplemental Figure 1**)
- Patients were eligible if they had at least two diagnosis claims for CD at least 10 days apart, identified using CD diagnosis codes, with at least one claim on or before index date 1, and met all selection criteria (**Supplemental Figure 1**)
- Dose escalation was defined as an increase of at least 20% in average daily dose relative to expected daily dose based on prescribing information for CD during the maintenance period
- The maintenance period began on index date 2, which was defined as the date of the third (adalimumab) or fourth (infliximab or vedolizumab) claim or the first subcutaneous dose after an intravenous dose (ustekinumab) after index date 1
- The proportions of patients whose dose was escalated were compared among the study drugs at 6 months and 12 months of maintenance dosing, as well as over the entire maintenance period
- Time to dose escalation in the 12 months after initiation of the maintenance period was compared for vedolizumab versus anti-TNFα treatments (adalimumab and infliximab), and vedolizumab versus ustekinumab, using Kaplan–Meier unadjusted curves
- Cox proportional hazards regression models, adjusted for covariates, were used to compare the risk of dose escalation for vedolizumab versus anti-TNFα treatments, and for vedolizumab versus ustekinumab, 12 months after initiation of the maintenance period
- Drug costs after dose escalation were calculated from the paid amount captured in medical or pharmacy claims

Results

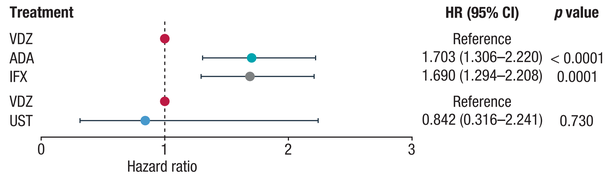
- In total, 2,664 eligible patients with CD were identified (**Supplemental Figure 1**), of whom 1,178 (44.2%), 1,046 (39.3%), 311 (11.7%), and 129 (4.8%) received adalimumab, infliximab, vedolizumab, and ustekinumab, respectively
- The proportions of patients whose dose was escalated were lower for patients who received vedolizumab and ustekinumab than for those who received adalimumab and infliximab at all time points analyzed (**Figure 1**)
- After adjustment for covariates, the hazard ratio of dose escalation was significantly higher for adalimumab and infliximab than for vedolizumab; there was no significant difference in the hazard ratio of dose escalation between vedolizumab and ustekinumab (**Figure 2**)
- Time to dose escalation was significantly longer for patients who received vedolizumab than an anti-TNFα treatment; there was no significant difference between patients who received vedolizumab and those who received ustekinumab (**Figure 3**)
- Among patients whose dose was escalated, mean study drug costs per patient per month after dose escalation ranged from US$4,503.78 for vedolizumab to US$13,800.81 for ustekinumab (**Table 1**)

Figure 1. Proportion of patients with Crohn's disease whose dose was escalated



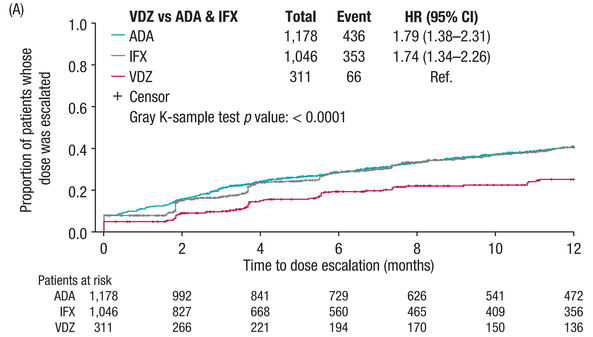
ADA, adalimumab; IFX, infliximab; UST, ustekinumab; VDZ, vedolizumab.

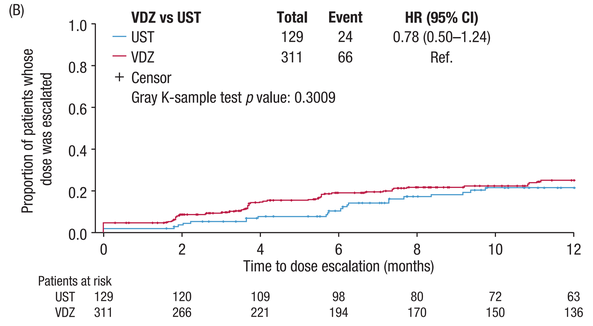
Figure 2. Adjusted risk of dose escalation in patients with Crohn's disease



Cox proportional hazards regression models adjusted for age, sex, baseline IBD-related hospitalization, mental disorder, anemia, adjusted Charlson Comorbidity Index, claim for an immunosuppressant or immunomodulatory agent, perianal disease, fistula, abscess, stricturing, disease location, and other pharmacy costs per patient per month. Cost of first maintenance dose was also included in the VDZ versus UST model only.
ADA, adalimumab; CI, confidence interval; HR, hazard ratio; IBD, inflammatory bowel disease; IFX, infliximab; UST, ustekinumab; VDZ, vedolizumab.

Figure 3. Kaplan–Meier unadjusted curves for time to dose escalation for (A) vedolizumab vs adalimumab and infliximab and (B) vedolizumab vs ustekinumab





ADA, adalimumab; CI, confidence interval; HR, hazard ratio; IFX, infliximab; Ref., reference; UST, ustekinumab; VDZ, vedolizumab.

Table 1. Mean study drug costs after dose escalation in patients with Crohn's disease

Study drug	Overall cohort, N	Mean (SD) unweighted study drug cost per patient, US$
ADA	1,178	36,045.07 (68,787.33)
IFX	1,046	22,469.39 (58,648.70)
VDZ	311	12,717.97 (30,936.18)
UST	129	33,339.80 (99,630.47)
Study drug	**Patients whose dose was escalated, N**	**Mean (SD) study drug cost per patient per month, US$**
ADA	436	6,467.41 (2,936.65)
IFX	353	4,617.56 (4,119.17)
VDZ	66	4,503.78 (1,817.49)
UST	24	13,800.81 (6,587.90)

ADA, adalimumab; IFX, infliximab; SD, standard deviation; UST, ustekinumab; VDZ, vedolizumab.

Summary and Conclusions

- This real-world study of US claims data demonstrates that dose escalation of biologics is required by at least a quarter of patients with CD during maintenance
- Vedolizumab was associated with a significantly lower need for dose escalation than anti-TNFα treatments, whereas there was no significant difference compared with ustekinumab
- Study drug costs after dose escalation were lower for vedolizumab than ustekinumab
- These findings may help to inform clinicians' choice of treatment and positioning of biologics in patients with CD

References

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Supplemental Content

To request the Supplemental Material, please contact Takeda US Medical Information (medinfoUS@takeda.com).

Disclosures

Noa Krugliak Cleveland: served as a consultant for Arena Pharmaceuticals, NeuroLogica, and Takeda Pharmaceuticals U.S.A., Inc., and received a speaker's fee from Bristol Myers Squibb. Niranjan Kathe: employee of Amgen, former salaried employee of Complete HEOR Solutions, North Wales, PA, USA, and received financial compensation for conducting the study analysis. Kandavadivu Umashankar: former employee of University of Illinois, Chicago, IL, USA, supported by a Takeda Pharmaceuticals U.S.A., Inc. fellowship at the time of the study. Kirti Mirchandani and Arunima Hait: employees of Complete HEOR Solutions, North Wales, PA, USA and received financial compensation for conducting the study analysis. Riyanka Paul: former employee of Complete HEOR Solutions, North Wales, PA, USA, and received financial compensation for conducting the study analysis. Sabyasachi Ghosh: former employee of Takeda Pharmaceuticals U.S.A., Inc. and holds stock or stock options. Ninfa Candela and Tao Fan: employees of Takeda Pharmaceuticals U.S.A., Inc. and hold stock or stock options. David T Rubin: received grant support from Takeda Pharmaceuticals U.S.A., Inc. and has served as a consultant for AbbVie, AltruBio, Arena Pharmaceuticals, Bristol Myers Squibb, Genentech/Roche, Gilead Sciences, Iterative Scopes, Janssen Pharmaceuticals, Lilly, Pfizer, Prometheus Biosciences, Takeda, and TechLab, Inc.

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