Poster #A0601

Real-World Ustekinumab Use in Pediatric Patients with Crohn's Disease

Timothy E. Ritter, MD;[1] Harry E. Sarles, MD, FACG;[1] Annette E. Whitney, MD;[1] Dawn N. Kim-Romo, PharmD, PhD, MS;[2] Lucinda J. Van Anglen, PharmD[2]

[1]GI Alliance, Southlake, Texas; [2]Healix Infusion Therapy, LLC, Sugar Land, Texas

Introduction

Ustekinumab (UST), a humanized IgG1κ monoclonal antibody antagonist of interleukin-12 and interleukin-23, is currently approved for patients (pts) 18 years and older with moderate-to-severe Crohn's disease (CD) [1]. Promising clinical results have been reported in the literature with UST in pediatric CD patients [2-5].

The purpose of this study was to evaluate the real-world experience of UST in pediatric CD patients treated at large gastroenterology private practices.

Methods

A retrospective, observational analysis was conducted in pediatric CD pts (aged ≤18 years) receiving UST therapy.

Patients were initiated and required to have a minimum of 52 weeks (wks) of UST therapy (or until discontinuation). Additional analyses were conducted for those with 104 wks of data. Patient data was obtained via electronic medical records.

Study data included:

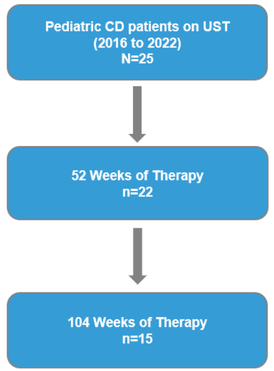
- Demographics and disease characteristics
- Previous CD therapy
- UST utilization
- Adverse events
- Short pediatric CD activity index (sPCDAI) [6]

The sPCDAI was used to assess disease activity at UST induction, 52 wks, and 104 wks. Clinical remission was based on sPCDAI scores <15. Corticosteroid (CS) use was evaluated at each time point.

Descriptive statistics included means, standard deviations (SD), medians, interquartile ranges (IQR), frequencies, and percentages. Wilcoxon rank sum tests were used to compare sPCDAI scores at 52 wks and 104 wks versus baseline.

Study Cohort

Figure 1. Patient Cohort



Results

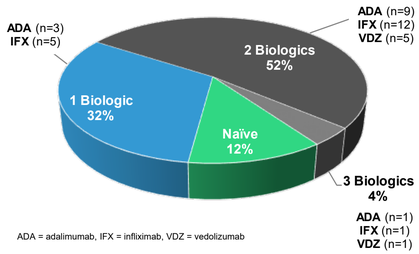
Patient and Therapy Characteristics

Table 1. Demographics and Disease Characteristics

Parameter	Pediatric UST N=25
Age (years), mean ± SD	16.5 ± 2.3
Male, n (%)	13 (52%)
Weight (kg), median [IQR]	62.1 [45-69]
Disease duration (years), mean ± SD	3.3 ± 2.8
Age at diagnosis (years), mean ± SD	13.1 ± 4.1
Baseline CS use, n (%)	11 (44%)

- Mean age at initiation of UST was 16.5 years, with a disease duration of 3.3 years
- Almost half were on oral corticosteroids at initiation of UST
- Baseline CS included prednisone (n=10) and budesonide (n=1)

Figure 2. Biologic Exposure Prior to UST



ADA = adalimumab, IFX = infliximab, VDZ = vedolizumab

- IFX was the most used biologic in experienced pts (n=18, 72%), then ADA (n=13, 52%), and VDZ (n=6, 24%)
- Biologics received just prior to UST were ADA (n=10), IFX (n=6), and VDZ (n=6)
- VDZ was used only as 2nd or 3rd line biologic
- Reasons for switching to UST were failed response in 14 pts and intolerance in 8

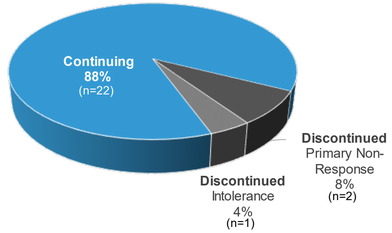
Table 3. Ustekinumab Dosing

Parameter	Pediatric UST N=25
Induction dose, n (%)	
260 mg (≤55kg)	10 (40%)
390 mg (>55 to 85 kg)	13 (52%)
520 mg (>85 kg)	2 (8%)

- All pts received intravenous induction doses, followed by subcutaneous maintenance doses of 90 mg
- Doses were escalated prior 52 wks in 2 and then in 4 more pts prior to week 104 (one was re-induced at week 98 due to sub-par drug levels)
- Following intravenous induction, 4 pts received subcutaneous injections in the office; the remainder self-administered all maintenance therapy at home

Discontinuations

Figure 3. UST Discontinuations at 52 Weeks



Prior to 52 wks, 3 pts discontinued UST

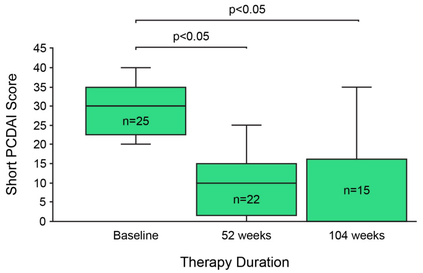
- 1 discontinued due to an infusion reaction during induction
- 2 discontinued due to lack of response at wks 10 and 21
- The remaining 22 pts continued therapy
- Of those continuing, no adverse events were noted

At 104 wks, 15 of 22 remained on therapy

- No patients discontinued between 52 and 104 wks
- Between wks 52 to 104, 1 transferred care, 1 was lost to follow-up, and 5 had not reached 104 wks of therapy

Disease Activity

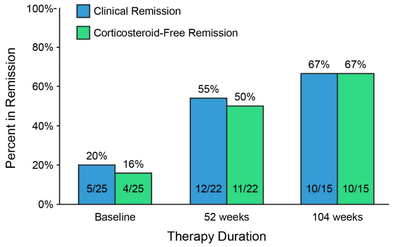
Figure 4. Change in Disease Activity



- Disease activity was measured at baseline, 52 wks, and 104 wks
- A significant 62% reduction in mean sPCDAI scores was observed from baseline to 52 wks (p<0.05)
- Disease activity scores from baseline to 104 wks were also significantly reduced by 67% percent (p<0.05)
- Biologic-naïve pts had reductions in mean sPCDAI scores from baseline to 52 wks and baseline to 104 wks at 54% and 31%, respectively
- Similarly, biologic-experienced scores decreased by 62% (52 wks) and 70% (104 wks) from baseline

Clinical Remission

Figure 5. Clinical Remission



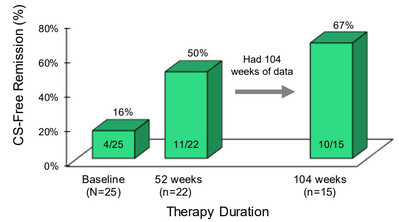
At 52 wks, 55% (12/22 pts) were in clinical remission

- 58% of biologic-experienced pts (11/19) achieved remission and 33% of biological naïve pts (1/3)
- 50% of pts with dose escalations (1/2) achieved remission

At 104 wks, 67% (10/15 pts) were in clinical remission

- 7 pts retained remission from week 52 to 104
- 3 with mild disease activity at week 52 achieved remission by week 104
- Of those who did not reach remission, 2 had mild disease, and 3 worsened but have remained on therapy
- 100% of biological naïve pts (2/2) and 62% of biologic-experienced pts (8/13) were in remission at 104 wks
- 50% of pts (2/4) with dose escalation after 52 wks had clinical remission at 104 wks

Figure 6. Corticosteroid-Free Remission



At 52 wks, 50% (11/22 pts) were in CS-free remission

- 53% biologic-experienced (10/19); 33% biologic-naïve (1/3)
- 50% with dose escalations (1/2) had CS-free remission

At 104 wks, 67% (10/15) were in CS-free remission

- All 10 pts in clinical remission were also CS-free at 104 wks
- 6 pts had CS-free remission at both wks 52 and 104
- 100% of biologic-naïve, 62% of biologic experienced, and 50% with dose escalation had CS-free remission by 104 wks

Discussion

We present long-term outcomes of pediatric patients with CD who received UST for up to 104 wks through a large gastroenterology private practice.

- Patients had a mean age of 17 yrs at the start of UST and were majority male and diagnosed with CD for over 3 years.
- As with previous studies [2-3], most pts had been exposed to anti-TNF agents prior to UST.
- One pt experienced an infusion reaction at induction but no other safety concerns were noted.
- UST use resulted in significant decreases in disease activity scores at wks 52 and 104 (p<0.05) compared to baseline.
- The majority of pts achieved clinical remission at 52 wks and this was sustained at 104 wks, similar other data [2,3].
- Although our numbers were small, clinical remission rates were higher for those on prior biologics than biologic-naïve pts. This differs from other reports at 52 wks [3].
- Six pts overall had dose escalations, with 4 resulting in CS-free remission and 2 with mild disease.
- CS-free remission occurred in half of pts at 52 wks, increased to two-thirds at 104 wks, and was comparable to other studies [2-3]. CS-free remission rates were higher for those on prior biologics compared to biologic-naïve, which differs from previous data [3].
- Limitations of this study are the small sample size and the retrospective, observational design. Safety-related data may have been missed due to self-administration of therapy at home. The sPCDAI was used rather than the PCDAI, and endoscopic and biochemical remission was not assessed due to limited availability of necessary data.

Conclusion

Pediatric patients receiving UST experienced significant improvement in disease activity scores at both 52 and 104 weeks.

Long-term UST data at 2 years show continued clinical remission and CS-free remission in pediatric CD patients. Further studies in this population are warranted.

References

1. Janssen Biotech, Inc. Horsham, PA Stelara® (ustekinumab) prescribing information. Accessed May 2022.
2. Chavannes M, et al. *J Crohn's and Colitis* 13(5), 2019.
3. Dayan JR, et al. *J Pediatr Gastroenterol Nutr.* 69 (1), 2019.
4. Bishop C, et al. *J Pediatr Gastroenterol Nutr.* 63 (3), 2016.
5. Cohen A, et al. *Intest Res.* 19 (2), 2021.
6. Kappelman MD, et al. *Inflamm Bowel Dis.* 17 (1), 2011.

Disclosures: TER is a speaker and/or advisor for AbbVie, Arena, BI, BMS, Ferring, Genentech, Gilead, Gossamer, Intercept, Janssen, Lilly, Pfizer, Prometheus and Sanofi and Takeda. The other authors have no disclosures.