CORTICOSTEROID-SPARING EFFECTS OF USTEKINUMAB FOR ULCERATIVE COLITIS THROUGH 4 YEARS: UNIFI LONG-TERM EXTENSION

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M.T. Abreu,[1] E.J. Scherl,[2] D. Rowbotham,[3] S. Danese,[4] W.J. Sandborn,[5] Y. Miao,[6] H. Zhang,[6] R. Panaccione,[7] W. Afif,[8] T. Hisamatsu,[9] R.W. Leong,[10] B.E. Sands,[11] R.P. Arasaradnam,[12] C. Marano[6]

[1]University of Miami Miller School of Medicine, Miami, FL, USA; [2]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY, USA; [3]Auckland City Hospital, Auckland, NZ; [4]Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Milano, Italy; [5]Division of Gastroenterology, University of California San Diego, La Jolla, CA, USA; [6]Janssen Research & Development, LLC, Spring House, PA, USA; [7]University of Calgary, Calgary, Alberta, Canada; [8]Division of Gastroenterology, McGill University Health Centre, Montreal, Quebec, Canada; [9]Department of Gastroenterology and Hepatology, Kyorin University School of Medicine, Tokyo, Japan; [10]Concord Hospital and Macquarie University Hospital, Sydney, New South Wales, Australia; [11]Dr. Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [12]Warwick Medical School, University of Warwick & University Hospital Coventry, Coventry Warwickshire, UK

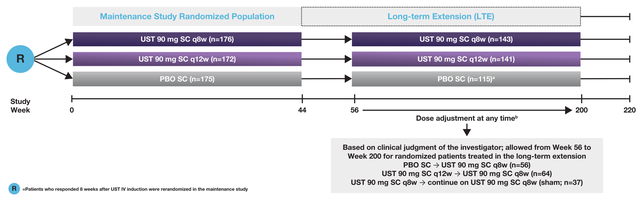
BACKGROUND/OBJECTIVE

- Ustekinumab (UST) is an interleukin-12/23p40 antagonist that is approved for the treatment of Crohn's disease and ulcerative colitis (UC)
- In the UNIFI maintenance study of patients with moderate-to-severe UC, >90% of UST-treated patients who achieved clinical remission at Week 44 were corticosteroid-free, an important therapeutic goal[1,2]
- **In this analysis, we describe the corticosteroid-sparing effects of UST treatment through 4 years among patients who were treated in the UNIFI long-term extension (LTE)**

METHODS

- A total of 284 UST-treated patients completed Week 44 and were treated in the LTE
- Placebo (PBO) patients were discontinued after study unblinding following completion of the Week 44 analysis
- Efficacy was evaluated using symptomatic remission
  - Mayo stool frequency subscore of 0 or 1 and rectal bleeding subscore of 0
- On entry into the maintenance study, all patients receiving corticosteroids were required to initiate tapering as per protocol
- Through Week 200 of the LTE, symptomatic remission endpoints were analyzed using treatment failure and missing data nonresponder imputation
  - Dose adjustment was not considered to be a treatment failure

Figure 1. UNIFI Study Design



q8w, every 8 weeks; q12w, every 12 weeks; UST, ustekinumab.
[a]Patients who remained on PBO were discontinued from the LTE after maintenance study unblinding, which occurred after analysis of the maintenance Week 44 study data
[b]Those patients randomized to PBO and those rerandomized to UST q8w were only eligible for dose adjustment prior to unblinding

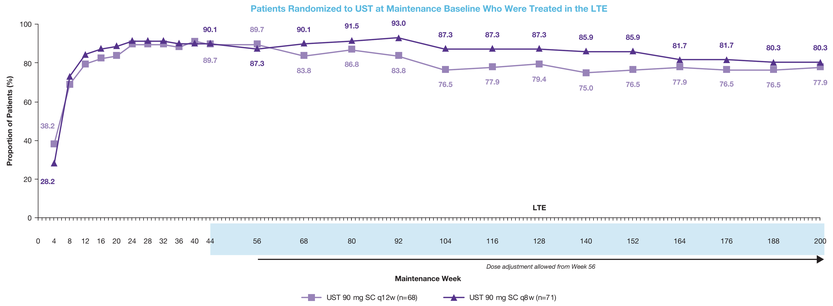
CONCLUSIONS

- **Both q8w and q12w dosing regimens of UST maintenance therapy were effective in reducing and eliminating the use of corticosteroids in patients with UC through 4 years**
- **The majority (~95%) of patients in symptomatic remission were corticosteroid-free through 4 years of UST treatment**

RESULTS

- Of the 284 patients randomized to UST and treated in the LTE, 139 patients were receiving corticosteroids at maintenance baseline
- Among patients receiving corticosteroids at maintenance baseline, 79.1% (n=110) of UST patients (combined dosing groups of every 12 weeks [q12w] and every 8 weeks [q8w]) were no longer receiving corticosteroids at Week 200
  - 77.9% (53/68) of the q12w group and 80.3% (57/71) of the q8w group were corticosteroid-free at Week 200 (**Figure 2**)

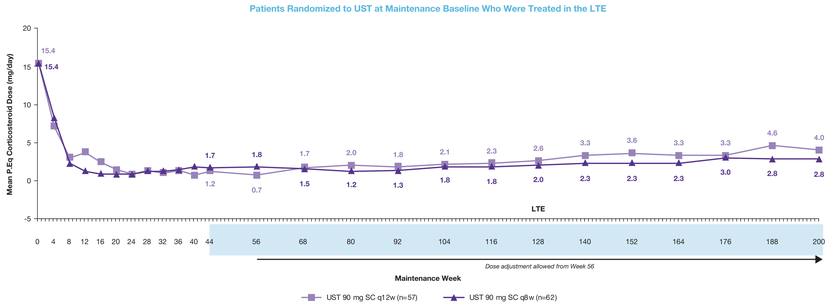
Figure 2. Corticosteroid-free Patients Through Week 200 Among Patients Receiving Corticosteroids at Maintenance Baseline[a,b,c,d]



[a]According to randomized group at maintenance Week 0 regardless if patients had a dose adjustment during the LTE
[b]Patients who had an ostomy or colectomy, or discontinued study agent due to lack of therapeutic effect or due to an adverse effect of worsening UC prior to the designated timepoint were not considered to be corticosteroid-free at that timepoint
[c]Patients who had a missing value in corticosteroid use prior to the designated timepoint had their last available value carried forward to that timepoint
[d]Denominator is the number of patients who were receiving concomitant corticosteroids at maintenance baseline

- In the q8w group, average P.Eq doses were 15.4 mg/day at maintenance baseline, and 1.7, 2.3, and 2.8 mg/day at Weeks 44, 152, and 200, respectively (**Figure 3**)
- In the q12w group, average P.Eq doses were 15.4 mg/day at maintenance baseline, and 1.2, 3.6, and 4.0 mg/day at Weeks 44, 152, and 200, respectively

Figure 3. Daily Prednisone-Equivalent Corticosteroid Dose (mg/day) Through Week 200 Among Patients Receiving Corticosteroids Other Than Budesonide and Beclomethasone Diproprionate at Maintenance Baseline[a,b,c]



[a]According to randomized group at maintenance Week 0 regardless if patients had a dose adjustment during the LTE
[b]Patients who had an ostomy or colectomy, or discontinued study agent due to lack of therapeutic effect or due to an adverse effect of worsening UC prior to the designated visit had their Week 0 value of the induction study carried forward to that timepoint
[c]Patients who had a missing value in corticosteroid use at a timepoint had their last available value carried forward to that timepoint

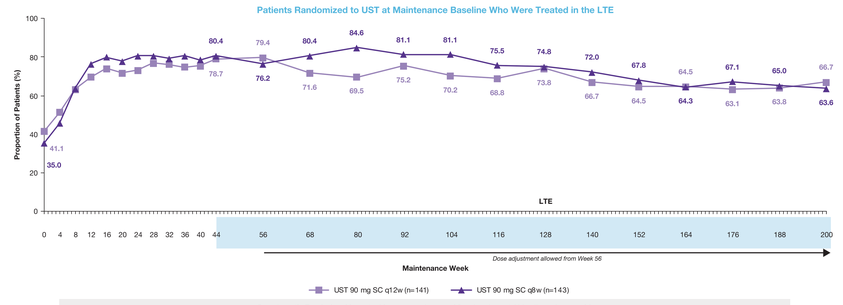
- Rates of corticosteroid-free symptomatic remission from Week 44 through Week 200 were generally sustained and similar for the q8w and q12w maintenance doses (**Table 1; Figure 4; Figure 5**)

Table 1. Summary of Symptomatic Remission and Corticosteroid-Sparing Effects in Patients Randomized to UST in Maintenance and Treated in the LTE

	90 mg UST SC q12w[a]	90 mg UST SC q8w[a]	Combined UST
Patients randomized to UST at maintenance baseline who were treated in the LTE, N	141	143	284
Patients in symptomatic remission, n/N (%)[b,c,d]			
Week 44	117/141 (83.0)	119/143 (83.2)	236/284 (83.1)
Week 200	96/141 (68.1)	96/143 (67.1)	192/284 (67.6)
Patients in symptomatic remission and not receiving corticosteroids, n/N (%)[b,c,d,e]			
Week 44	111/141 (78.7)	115/143 (80.4)	226/284 (79.6)
Week 200	94/141 (66.7)	91/143 (63.6)	185/284 (65.1)
Patients in symptomatic remission and not receiving corticosteroids among patients receiving corticosteroids at maintenance baseline, n/N (%)[b,c,d,e,f]			
Week 44	49/68 (72.1)	56/71 (78.9)	105/139 (75.5)
Week 200	39/68 (57.4)	47/71 (66.2)	86/139 (61.9)
Patients who eliminated the use of corticosteroids, n/N (%)[e,f]			
Week 44	61/68 (89.7)	64/71 (90.1)	125/139 (89.9)
Week 200	53/68 (77.9)	57/71 (80.3)	110/139 (79.1)

[a]According to randomized group at maintenance Week 0 regardless of whether patients had a dose adjustment during the LTE.
[b]Symptomatic remission is defined as a Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0.
[c]Patients who had both stool frequency and rectal bleeding subscores missing at a visit were considered not to be in symptomatic remission for that visit.
[d]Patients who had an ostomy or colectomy, or discontinued study agent due to lack of therapeutic effect or due to an adverse event of worsening of UC prior to the designated visit were considered not to be in symptomatic remission and were also not considered to have eliminated the use of corticosteroids.
[e]Patients who had a missing value in corticosteroid use at the designated visit had their last available value carried forward to the designated visit.
[f]Denominator is the number of patients who were receiving concomitant corticosteroids at maintenance baseline

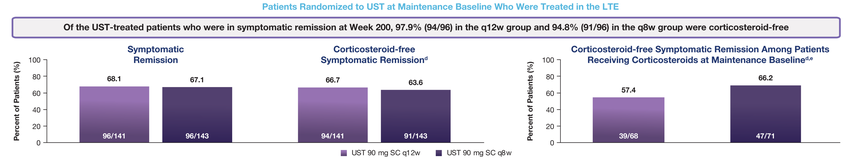
Figure 4. Corticosteroid-free Symptomatic Remission Through Week 200[a,b,c,d]



Symptomatic Remission: Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0

[a]According to randomized group at maintenance Week 0 regardless of whether patients had a dose adjustment during the LTE.
[b]Patients who had both stool frequency and rectal bleeding subscores missing at a visit were considered not to be in symptomatic remission for that visit.
[c]Patients who had an ostomy or colectomy, or discontinued study agent due to lack of therapeutic effect or due to an adverse event of worsening of UC prior to the designated visit were considered not to be in symptomatic remission.
[d]Patients who had a missing value in corticosteroid use had their last value carried forward

Figure 5. Symptomatic Remission and Corticosteroid-free Symptomatic Remission at Week 200[a,b,c]



[a]Patients who had both stool frequency and rectal bleeding subscores missing at a visit were considered not to be in symptomatic remission for that visit.
[b]According to randomized group at maintenance Week 0 regardless of whether patients had a dose adjustment during the LTE.
[c]Patients who had an ostomy or colectomy, or discontinued study agent due to lack of therapeutic effect or due to an adverse event of worsening of UC prior to the designated visit, were considered not to be in symptomatic remission
[d]Patients who had a missing value in corticosteroid use at the designated visit had their last available value carried forward to the designated visit.
[e]Denominator is the number of patients who were receiving concomitant corticosteroids at maintenance baseline

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1. Sands B, et al. *N Engl J Med.* 2019;381:1201-1214
2. Abreu M, et al. *J Crohns Colitis.* 2022;Mar 3:jjac030. Online ahead of print https://doi.org/10.1093/ecco-jcc/jjac030

Acknowledgments

This presentation was supported and funded by Janssen Research & Development, LLC, Spring House, PA, USA

Medical writing support was provided by Kristin Ruley Sharples, PhD, of Janssen Scientific Affairs, LLC, and Linda J. Cornfield, PhD, of Certara Synchrogenix, under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2015;163:461-464) and was funded by Janssen Scientific Affairs, LLC

Disclosures

Maria T Abreu: Reports having received consulting fees from Janssen Research & Development, LLC. **Ellen J Scherl:** Reports having received grant support from Janssen Research & Development, LLC and received consulting fees from Janssen. **David S Rowbotham:** Reports having received speaker fees from and served as an advisory board member for Janssen Research & Development, LLC. **Silvio Danese:** Reports having received consultancy fees from Janssen and Johnson & Johnson and received lecture fees from Janssen. **William J Sandborn:** Reports grants from Janssen and consulting fees from Janssen. **Ye Miao, Hongyan Zhang, Colleen Marano:** All are employees of Janssen Research & Development, LLC and own stock/stock options in Johnson & Johnson. **Remo Panaccione:** Reports having received consulting fees, speaker fees, and research/educational support from Janssen and served on an advisory board for Janssen. **Waqqas Afif:** Reports having received grant support from Janssen Research & Development, LLC. **Tadakazu Hisamatsu:** Reports having received consulting fees from Janssen Research & Development, LLC. **Rupert W Leong:** Reports having received grant support from Janssen and received consulting fees from Janssen Research & Development, LLC. **Bruce E Sands:** Reports having received grants, personal fees, and other from Janssen. **Ramesh P Arasaradnam:** Reports having received grant support and consulting fees from Janssen Research & Development, LLC.

American College of Gastroenterology 2022; October 21-26, 2022.
Originally presented at United European Gastroenterology Week 2022; October 8-11, 2022.