Abstract for DDW and ECCO 2019 (ECCO submission deadline: Nov 22, 2018)

Maintenance of efficacy following tofacitinib dose reduction in patients with ulcerative colitis in stable remission

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Word/Character count:

Background: Tofacitinib is an oral, small molecule JAK inhibitor approved in several countries for the treatment of ulcerative colitis (UC). Safety and efficacy of tofacitinib 5 and 10 mg twice daily (BID) were evaluated in two Phase 3 induction studies (OCTAVE Induction 1 & 2, NCT01465763 & NCT01458951), a 52-week (wk), Phase 3 maintenance study (OCTAVE Sustain, NCT01458574), and an ongoing open-label, long-term extension (OLE) study (NCT01470612). Here, we assess maintenance of remission following

tofacitinib dose reduction from 10 mg BID in OCTAVE Sustain to 5 mg BID in the OLE study, and explore potential predictors of successful dose reduction.

Methods: Patients (pts) in remission (total Mayo score ≤2 with no individual subscore >1, and rectal bleeding subscore of 0) at Wk52 of OCTAVE Sustain (central read) received tofacitinib 5 mg BID in the OLE study. We present remission rates (local read; as observed and with non-responder imputation) with tofacitinib 5 mg BID in the OLE study (as of 10 Nov 2017) among pts who achieved remission with tofacitinib 10 mg BID in OCTAVE Sustain, and evaluate characteristics of these pts, stratified by whether they subsequently maintained remission (local read; as observed) with 5 mg BID at Month (M)12 of the OLE study.

Results: Of 76 pts treated with tofacitinib 10 mg BID who were in remission at Wk52 of OCTAVE Sustain and received tofacitinib 5 mg BID in the OLE study, 82% and 76% (as observed) were in remission at M12 and M24 of the OLE study, respectively (Table). Pt characteristics by remission status at M12 of the OLE study are shown in the Table. Among pts in remission at baseline, Wk24 and Wk52 of OCTAVE Sustain (remission ≥12 months prior to dose reduction), 91% (21/23) maintained remission at M12 of the OLE study, vs 82% (18/22) who were not in remission at OCTAVE Sustain baseline but in remission at both Wk24 and Wk52 (remission 6–<12 months prior to dose reduction), and 71% (15/21) who were in remission at Wk52 but not Wk24 (remission <6 months prior to dose reduction).

Conclusion: In this post-hoc analysis, the majority of pts with UC who achieved remission with tofacitinib 10 mg BID in OCTAVE Sustain and reduced to 5 mg BID in the OLE study maintained remission through M24 of the OLE study. Although pt numbers were small, maintenance of remission following dose reduction was numerically more likely for pts who

had been in remission for ≥6 months than for those in remission for <6 months prior to dose reduction. Further studies are needed to evaluate flexible dosing of tofacitinib in pts with UC.

Table. Remission at M12 and M24 in the OLE study and patient characteristics by M12 remission status among patients who achieved remission at Wk52 of OCTAVE Sustain with tofacitinib 10 mg BID and reduced to 5 mg BID in the OLE study

Remission in the OLE study	**Patients in remission at Wk52 of OCTAVE Sustain after receiving tofacitinib 10 mg BID, who reduced to 5 mg BID in the OLE study[a] (N=76)**	
Remission at M12 of OLE study[b]		
As observed, n/N1 (%)	56/68 (82)	
NRI, n/N2 (%)	56/73 (77)	
Remission at M24 of OLE study[b]		
As observed, n/N1 (%)	32/42 (76)	
NRI, n/N2 (%)	32/52 (62)	
Patient characteristics	**OLE study M12 remission status (as observed)**	
	In remission at M12 of OLE study[b] (N=56)	**Not in remission at M12 of OLE study[b] (N=12)**
Male, n (%)	25 (45)	5 (42)
Age at induction study baseline (years), mean (SD)	46.0 (14.8)	42.4 (16.2)
Total Mayo score at induction study baseline, mean (SD)	8.7 (1.6)	8.0 (1.3)
Duration of remission in OCTAVE Sustain , n/N1 (%)[c]		
≥12 months prior to dose reduction (remission at Sustain baseline, Wk24 and Wk52)	21/54 (39)[#]	2/12 (17)
6–<12 months prior to dose reduction (remission at both Wk24 and Wk52, but not at Sustain baseline)	18/54 (33)[#]	4/12 (33)
<6 months prior to dose reduction (remission at Wk52 but not Wk 24, regardless of remission status at Sustain baseline)	15/54 (28)[#]	6/12 (50)
Endoscopic subscore at OLE study baseline, n (%)		

0	17 (30)	5 (42)
1	39 (70)	7 (58)
CRP at OLE study baseline, n/N1 (%)		
<3 mg/L	49/56 (88)	9/10 (90)
≥3 mg/L	7/56 (13)	1/10 (10)
Extent of disease at induction study baseline, n/N1 (%)		
Proctosigmoiditis	11/55 (20)	5/12 (42)
Left-sided colitis	16/55 (29)	5/12 (42)
Extensive colitis/pancolitis	28/55 (51)	2/12 (17)
Prior TNFi failure at induction study baseline, n (%)	25 (45)	6 (50)

[#]N=54 due to 2 patients with missing data at Wk24

[a]All OCTAVE Sustain remitters received tofacitinib 5 mg BID in the OLE study, per OLE study design

[b]Remission status in the OLE study was based on local read of endoscopy

[c]Remission status in OCTAVE Sustain was based on central read of endoscopy

Remission was defined as a total Mayo score of ≤2 with no individual subscore >1, and a rectal bleeding subscore of 0. PMS remission was defined as a PMS of ≤2 with no individual subscore >1

BID, twice daily; CRP, C-reactive protein; M, Month; N, number of evaluable patients;

N1, number of patients with non-missing data; N2, number of patients with non-missing data who could have reached the specified time point; n, number of patients in the given category; NRI, non-responder imputation;

OLE, open-label, long-term extension; PMS, partial Mayo score; SD, standard deviation;

TNFi, tumour necrosis factor inhibitor; Wk, Week