European Crohn's and Colitis Organisation

EFFICACY AND SAFETY OF AN ADDITIONAL 8 WEEKS OF TOFACITINIB INDUCTION THERAPY: RESULTS OF THE OCTAVE OPEN STUDY FOR TOFACITINIB 8-WEEK INDUCTION NON-RESPONDERS

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Disclosures

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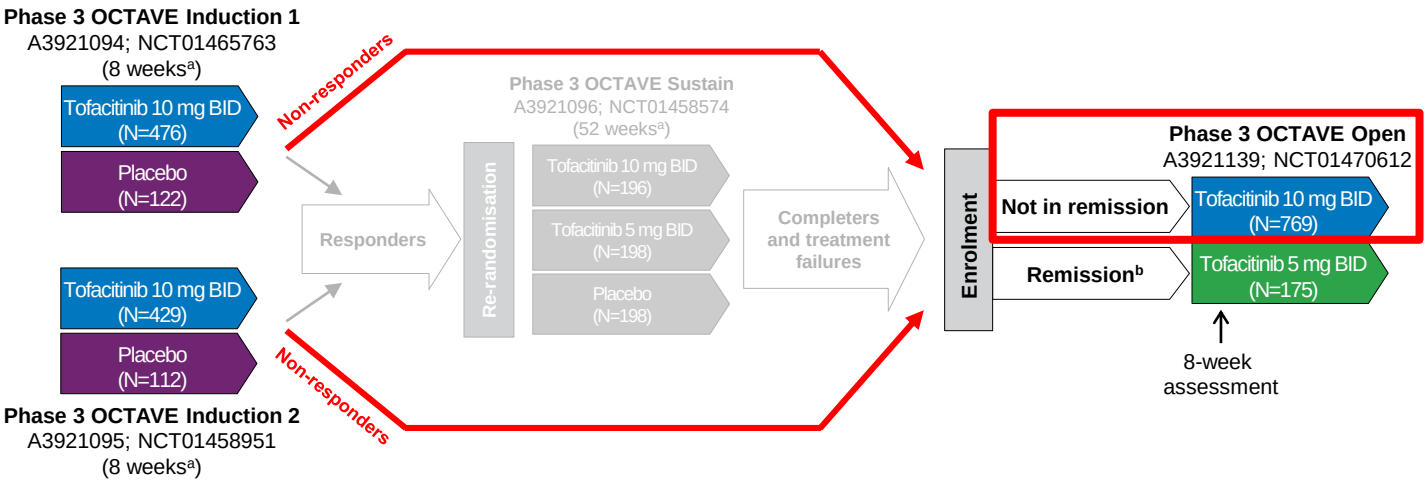
Background

- Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for UC
- Efficacy and safety of tofacitinib was demonstrated for induction and maintenance therapy for UC[1]
- Patients who did not achieve a clinical response after 8 weeks of tofacitinib 10 mg BID induction treatment could enter the Phase 3, open-label LTE and receive an additional 8 weeks of tofacitinib 10 mg BID[2]

Objective: To describe preliminary data for induction non-responder patients to tofacitinib who subsequently enrolled in the LTE

1. Sandborn WJ et al. N Engl J Med 2017;376:1723-1736; 2. Lichtenstein GR et al. Am J Gastroenterol 2017;112(S1):Abstract 714
BID, twice daily; JAK, Janus kinase, LTE, long-term extension; UC, ulcerative colitis

Phase 3 OCTAVE programme



- Patients who did not respond after 8 weeks of induction therapy with tofacitinib 10 mg BID received tofacitinib 10 mg BID in OCTAVE Open
  - Patients who were still non-responders at Week 8 of LTE were required to discontinue as per the protocol
- Interim safety and efficacy data are reported up to 2 years (as of 8 July 2016; from the unlocked database)

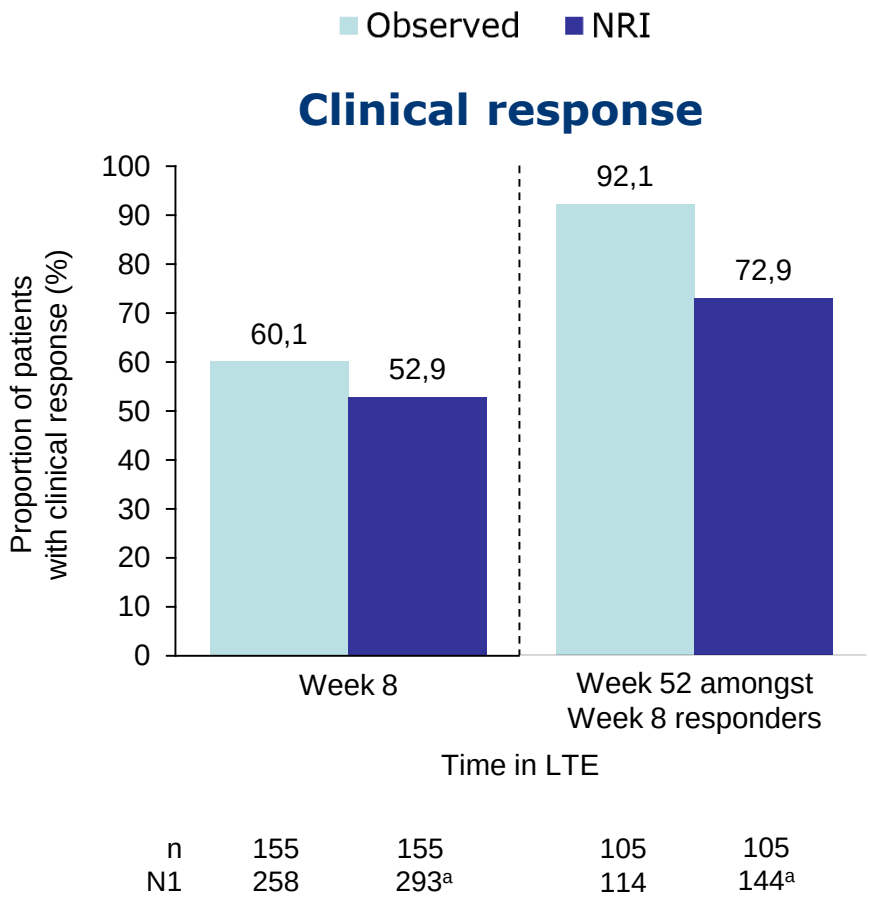
Responders were defined as patients with ≥3 points and ≥30% decrease from baseline total Mayo score and a decrease in rectal bleeding subscore ≥1 point or absolute rectal bleeding subscore of 0 or 1
[a]Final complete efficacy assessment at Week 8 / 52. Treatment continued up to Week 9 / 53;
[b]Remission was defined by a total Mayo score ≤2 with no individual subscore >1, and rectal bleeding subscore of 0, centrally read
BID, twice daily; LTE, long-term extension

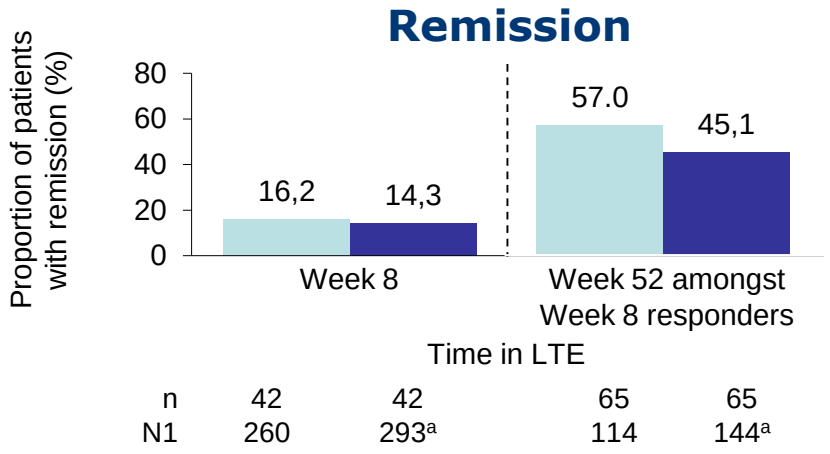
Baseline characteristics

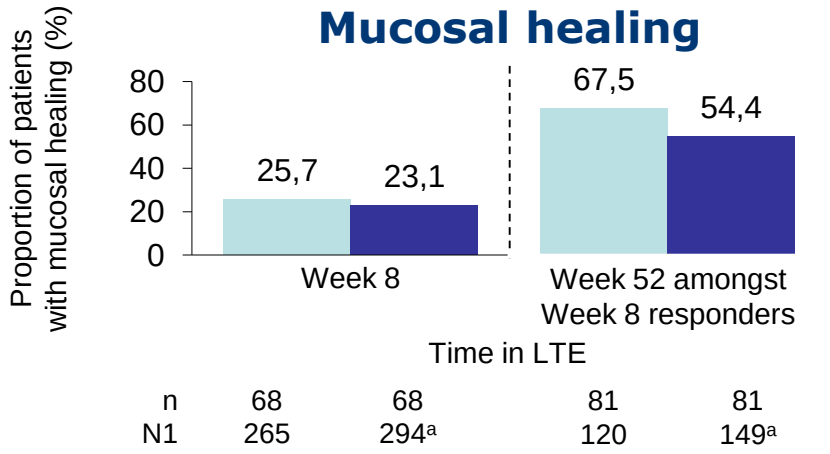
Characteristic	OCTAVE Induction 1 & 2 (N=1139)	Tofacitinib Induction non-responders (8 weeks of open label treatment with tofacitinib 10 mg BID, after 8 weeks of blinded tofacitinib 10 mg BID induction)[a] (N=295)
Female, n (%)	471 (41.4)	111 (37.6)
Age (years), mean (SD)	41.2 (13.9)	38.9 (13.4)
Duration of diagnosis (years), mean (SD)	8.1 (7.0)	7.6 (6.6)
Extent of disease[b]		
Proctosigmoiditis	167 (14.7)	48 (16.3)
Left-sided colitis	383 (33.7)	107 (36.3)
Extensive colitis / pancolitis	585 (51.5)	140 (47.5)
Prior TNFi failure, n (%)	589 (51.7)	181 (61.4)
Oral corticosteroid use at baseline, n (%)	525 (46.1)	116 (39.3)
Baseline total Mayo score, mean (SD)	9.0 (1.4)	9.2 (1.4)

[a]Non-responder patients from OCTAVE Induction 1 & 2 who previously received tofacitinib 10 mg BID;
[b]One patient with proctitis was enrolled into the induction study as a protocol deviation
N, number of patients in the specified category; n, number of patients; SD, standard deviation; TNFi, tumour necrosis factor inhibitor

Non-responders after 8 weeks of induction therapy achieve and maintain response in LTE







[a]Number of subjects who could have reached timepoint (based on enrolment dates and last non-missing full total Mayo score); Full analysis set data were based on local read of endoscopy; Data are reported as per the 8 July 2016 data cut; M, Month; M2 responders, patients in clinical response at Month 2 per central read of endoscopy (although data presented here are based on local read); n, number of patients with the specified response within the given category; N1, number of patients in the specified category with non-missing data; NRI, non-responder imputation

Safety data for tofacitinib Induction patients

n (%)	Tofacitinib OCTAVE Induction 1 & 2 (full study cohort - 8 weeks of tofacitinib 10 mg BID induction therapy)[a] (N=905)	Tofacitinib Induction non-responders (8 weeks of open label treatment with tofacitinib 10 mg BID, after 8 weeks of blinded tofacitinib 10 mg BID induction)[a] (N=295)
All-causality AEs		
Any AE	501 (55.4)	154 (52.2)
Any serious AE	34 (3.8)	11 (3.7)
Discontinuation[b]	35 (3.9)	7 (2.4)
Deaths	1 (0.1)[c]	0 (0.0)
AEs of special interest		
Serious infection	7 (0.8)	2 (0.7)
Herpes zoster (all)	5 (0.6)	1 (0.3)
Malignancy (excluding NMSC)[d]	0 (0.0)	1 (0.3)
NMSC[d]	2 (0.2)	0 (0.0)
MACE[d]	4 (0.4)	0 (0.0)
Gastrointestinal perforation[d]	1 (0.1)[e]	1 (0.3)

Data are reported as per the 16 December 2016 data cut; [a]Patients who received tofacitinib 10 mg BID in OCTAVE Induction 1 & 2; [b]Includes discontinuations due to worsening UC; [c]Reported in OCTAVE Induction 1. Cause was dissecting aortic aneurysm, not considered related to study drug by the investigator; [d]Based on adjudication; [e]Perforation reported for a patient with a history of cytomegalovirus colitis who had been receiving concomitant oral prednisone at baseline. The patient stated that the event occurred after lifting a 150 kg object. The patient underwent a colectomy and had a perforation in the descending colon, which had been affected by colitis

AE, adverse event; BID, twice daily; MACE, major adverse cardiovascular events; N, number of patients in the specified category; n, number of patients; NMSC, non-melanoma skin cancer; UC, ulcerative colitis

Conclusions

- Over half of patients who did not respond to 8 weeks of induction therapy with tofacitinib 10 mg BID achieved a clinical response with an additional 8 weeks of open-label tofacitinib 10 mg BID
    - The efficacy achieved with the extended induction was maintained through to Week 52 of LTE
- The rates of AEs and safety events of special interest were similar between the initial and additional 8 weeks of induction
- Tofacitinib induction treatment had an early onset of action and most patients achieved a clinical response with 8 weeks of tofacitinib 10 mg BID induction treatment
    - Patients who do not demonstrate a clinical response to the initial 8 weeks of treatment may benefit from an additional 8 weeks of tofacitinib induction therapy

AEs, adverse events; BID, twice daily; LTE, long-term extension

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