European Crohn's and Colitis Organisation

EFFICACY AND SAFETY OF OPEN-LABEL TREATMENT WITH TOFACITINIB 10 MG TWICE DAILY IN PATIENTS WITH ULCERATIVE COLITIS WITH CLINICAL RESPONSE, BUT NOT REMISSION, AFTER 52 WEEKS OF MAINTENANCE THERAPY: DATA FROM THE OCTAVE STUDIES

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Disclosures

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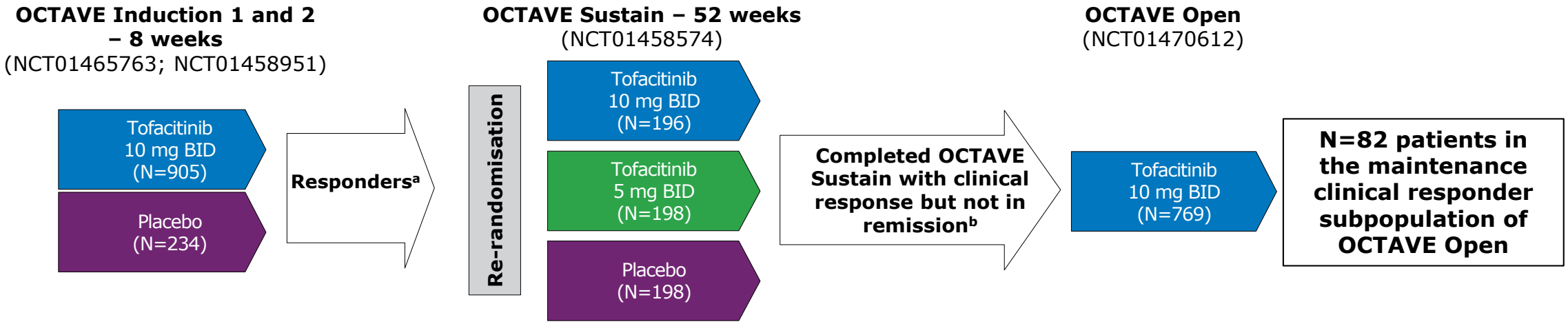
Background

- Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of UC
- The global, Phase 3, randomised, double-blind, placebo-controlled OCTAVE studies reported the efficacy and safety of tofacitinib as induction and maintenance therapy for patients with moderately to severely active UC[1]
- OCTAVE Open is an ongoing OLE study that enrolled patients who completed or failed treatment in OCTAVE Sustain, as well as non-responders from the OCTAVE Induction studies[2]

Objective: To evaluate the efficacy and safety of tofacitinib in patients with clinical response, but not in remission, after 52 weeks of maintenance therapy in the OCTAVE Sustain study, who subsequently received tofacitinib 10 mg BID in OCTAVE Open

OCTAVE Induction 1 and 2: NCT01465763 and NCT01458951; OCTAVE Sustain: NCT01458574; OCTAVE Open: NCT01470612
1. Sandborn WJ et al. N Engl J Med 2017;376:1723-1736; 2. Lichtenstein GR et al. Am J Gastroenterol 2018;113(Suppl 1):Abstract 571
BID, twice daily; JAK, Janus kinase; OLE, open-label, long-term extension; UC, ulcerative colitis

Maintenance clinical responder subgroup



- This analysis includes efficacy and safety data from the ongoing OCTAVE Open OLE study (data as of November 2017; database not locked)
- We evaluated patients who had clinical response, but who were not in remission, at Week 52 of OCTAVE Sustain, who subsequently received tofacitinib 10 mg BID in OCTAVE Open
- Remission / response status was based on central endoscopic reading at Week 52 of OCTAVE Sustain

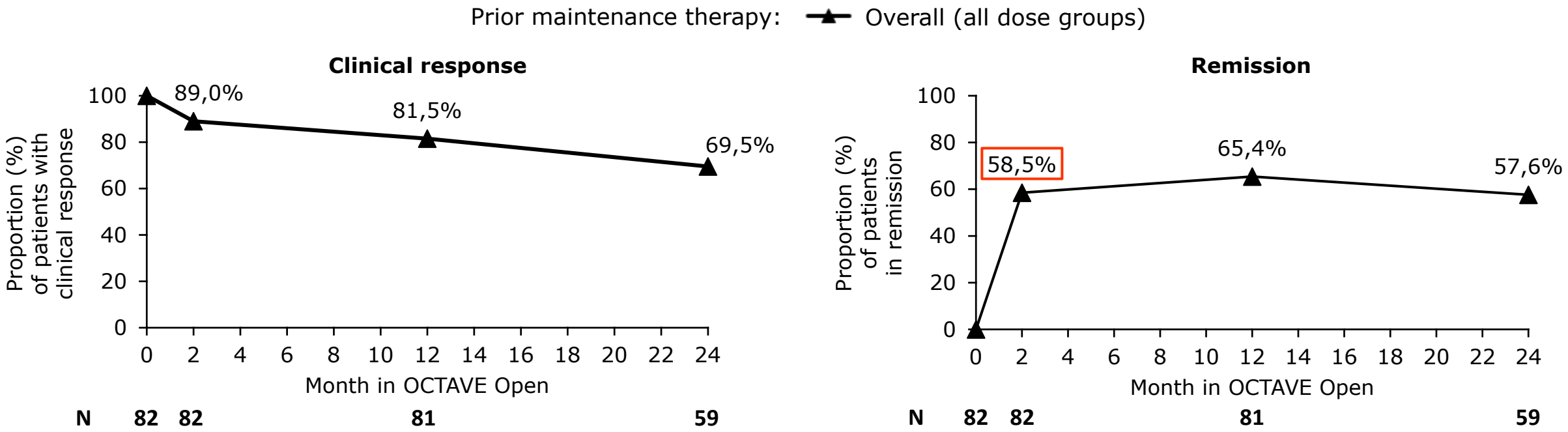
[a]Clinical response in OCTAVE Induction 1 and 2 was defined as a decrease from induction study baseline total Mayo score of ≥3 points and ≥30%, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1; [b]Remission was defined as a total Mayo score of ≤2 with no individual subscore >1, and a rectal bleeding subscore of 0
BID, twice daily; N, number of patients treated in each treatment group; OLE, open-label, long-term extension

Baseline characteristics

	Maintenance clinical responder subpopulation (N=82)[a]
Age (years), mean (SD)	43.1 (13.1)
Male, n (%)	48 (58.5)
Prior treatment in OCTAVE Sustain, n (%)	
Placebo	18 (22.0)
Tofacitinib 5 mg BID	28 (34.1)
Tofacitinib 10 mg BID	36 (43.9)
Total Mayo score at baseline of OCTAVE Open, median (range)	3.0 (2.0–7.0)
Prior corticosteroid failure, n (%)[b]	62 (75.6)
Corticosteroid use at baseline of OCTAVE Open, n (%)	0 (0.0)
Prior TNFi failure, n (%)[b]	38 (46.3)
Prior immunosuppressant failure, n (%)[b]	62 (75.6)
Extent of disease, n (%)[b]	
Proctosigmoiditis	8 (9.8)
Left-sided colitis	22 (26.8)
Extensive colitis / pancolitis	52 (63.4)

[a]Patients who had clinical response (neither in remission nor treatment failures), based on central endoscopic reading, at the OLE study baseline (all receiving tofacitinib 10 mg BID in the OLE study)
[b]Data at baseline of induction studies
BID, twice daily; N, number of patients in the maintenance clinical responder subpopulation; n, number of patients in the specified category; SD, standard deviation; TNFi, tumour necrosis factor inhibitor

Maintenance of clinical response and improvement to remission



- Clinical response was maintained at Month 24 by 69.5% of patients (41 / 59) overall

Data are FAS, NRI. Data for Month 0 (ie Week 52 of OCTAVE Sustain) are based on central read endoscopy; efficacy from OCTAVE Open are reported based on local endoscopic reading
BID, twice daily; FAS, full analysis set; N, number of evaluable patients; NRI, non-responder imputation; TNFi, tumour necrosis factor inhibitor

Summary of safety

	Overall tofacitinib 10 mg BID OLE (N=769)
Duration (days) of exposure, median (range)	562 (1-1793)
Adverse events, n (%)	607 (78.9)
Serious adverse events, n (%)	119 (15.5)
Discontinuations, n (%)	448 (58.3)
Due to adverse events (excluding worsening UC)	53 (6.9)
Due to insufficient clinical response (including worsening UC)	312 (40.6)
Serious infections, n (%)	23 (3.0)
Opportunistic infections,[a] n (%)	13 (1.7)[b]
Herpes zoster (non-serious and serious), n (%)	47 (6.1)
Herpes zoster serious adverse events	4 (0.5)
Malignancies (excluding non-melanoma skin cancer),[a] n (%)	12 (1.6)[c]
Non-melanoma skin cancer,[a] n (%)	9 (1.2)
Major adverse cardiovascular events,[a] n (%)	1 (0.1)
Gastrointestinal perforation,[a,d] n (%)	1 (0.1)
Deaths, n (%)	4 (0.5)[e]

[a]Adjudicated events; [b]herpes zoster (n=7), herpes zoster meningitis (n=1), herpes zoster cutaneous disseminated (n=1), ophthalmic herpes zoster (n=1), cytomegalovirus hepatitis (n=1), herpes zoster disseminated (n=1), histoplasmosis (n=1); [c]cervical dysplasia (n=1), hepatic angiosarcoma (n=1), invasive ductal breast carcinoma (n=1), adenocarcinoma of colon (n=2), essential thrombocythemia (n=1), acute myeloid leukemia (n=1), cholangiocarcinoma (n=1), leiomyosarcoma (n=1), Epstein-Barr virus-associated lymphoma (n=1), renal cell carcinoma (n=1), malignant melanoma (n=1); [d]Revised definition excludes fistulae and perianal abscesses; [e]Investigator-reported preferred terms: hepatic angiosarcoma (n=1), acute myeloid leukemia (n=1; reported 27 days after the last dose of tofacitinib), pulmonary embolism (n=1; in a patient with cholangiocarcinoma and peritoneal carcinomatosis), malignant melanoma (n=1)

BID, twice daily; N, number of patients in the treatment group; n, number of unique patients with event; OLE, open-label, long-term extension; UC, ulcerative colitis

Limitations

- Due to the relatively small number of patients in the maintenance clinical responder subpopulation and the short duration of exposure, efficacy and safety analyses should be interpreted with caution

Conclusions

- Among patients with UC who completed OCTAVE Sustain as clinical responders, 69.5% maintained clinical response at Month 24 while receiving tofacitinib 10 mg BID in the OLE study
- A majority (58.5%) further improved to remission within 2 months while receiving tofacitinib 10 mg BID in the OLE study. The rate of remission at Month 24 was 57.6%
- Efficacy was observed regardless of whether patients had failed prior therapy with TNFi agents or not
- The safety profile of the overall tofacitinib 10 mg BID OLE cohort was consistent with previous safety analyses from the OCTAVE program[1]

1. Sandborn WJ et al. Clin Gastroenterol Hepatol 2018: Epub ahead of print

BID, twice daily; JAK, Janus kinase; OLE, open-label, long-term extension; TNFi, tumour necrosis factor inhibitor; UC, ulcerative colitis

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