Supplementary Material

Tofacitinib as Induction and Maintenance Therapy in Japanese Patients with Active Ulcerative Colitis

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Methods

Eligibility

Patients in OCTAVE Induction 1 were ≥ 18 years of age, with an ulcerative colitis (UC) diagnosis for ≥ 4 months, and moderately to severely active disease (total Mayo score of ≥ 6, rectal bleeding subscore of ≥ 1, and endoscopic subscore of ≥ 2), based on centrally read Mayo endoscopic subscore.

Prohibited Medications

The washout periods for tumor necrosis factor inhibitors and immunomodulators were 8 weeks and 2 weeks, respectively.

Exclusion Criteria

Key exclusion criteria were: patients with indeterminate, microscopic, ischemic, or infectious colitis; patients with Crohn's disease; patients with UC limited to distal 15 cm of colon; and patients who had surgery for UC, or were likely to require surgery during the study. Patients with a history of lymphoma, lymphoproliferative disorders, or malignancies were excluded (except for adequately treated or excised non-metastatic basal cell or squamous cell skin cancer) [1].

Reference

1 Sandborn WJ, Su C, Sands BE, D'Haens GR, Vermeire S, Schreiber S, Danese S, Feagan BG, Reinisch W, Niezychowski W, Friedman G, Lawendy N, Yu D, Woodworth D, Mukherjee A, Zhang H, Healey P, Panés J: Tofacitinib as induction and maintenance therapy for ulcerative colitis. N Engl J Med 2017;376:1723–1736.

Tables

Supplementary Table 1. Definitions of endpoints based on Mayo score

Remission	Total Mayo score ≤ 2, with no individual subscore > 1, and a rectal bleeding subscore of 0
Mucosal healing	Mayo endoscopic subscore ≤ 1
Partial Mayo score	Mayo score excluding endoscopic subscore
Clinical response	≥ 30% and ≥ 3-point decrease from induction study baseline total Mayo score, plus decrease in rectal bleeding subscore ≥ 1 or absolute subscore ≤ 1
Endoscopic remission	Mayo endoscopic subscore of 0
Clinical remission	Total Mayo score of ≤ 2 points, with no individual subscore > 1
Symptomatic remission	Total Mayo score of ≤ 2 points with no individual subscore > 1 and both rectal bleeding and stool frequency subscore of 0
Deep remission	Total Mayo score of ≤ 2 points, with no individual subscore > 1, and endoscopic and rectal bleeding subscores of 0

Sustained steroid-free remission	Proportion of patients who achieve remission and are steroid-free for ≥ 4 weeks prior to the visit at both week 24 and week 52
Sustained remission	Proportion of patients who achieve remission at both week 24 and week 52
Sustained mucosal healing	Proportion of patients who achieve mucosal healing at both week 24 and week 52

Supplementary Table 2. Country of enrollment for patients randomized in OCTAVE Induction 1 and OCTAVE Sustain

Region/country, *n* (%)	OCTAVE Induction 1 *N* = 614	OCTAVE Sustain *N* = 593
Europe	359 (58.5)	346 (58.3)
Austria	29 (4.7)	13 (2.2)
Belgium	50 (8.1)	30 (5.1)
Croatia	1 (0.2)	1 (0.2)
Czech Republic	10 (1.6)	7 (1.2)
Denmark	8 (1.3)	7 (1.2)
Estonia	5 (0.8)	4 (0.7)
France	13 (2.1)	19 (3.2)
Germany	23 (3.7)	25 (4.2)
Great Britain	15 (2.4)	14 (2.4)

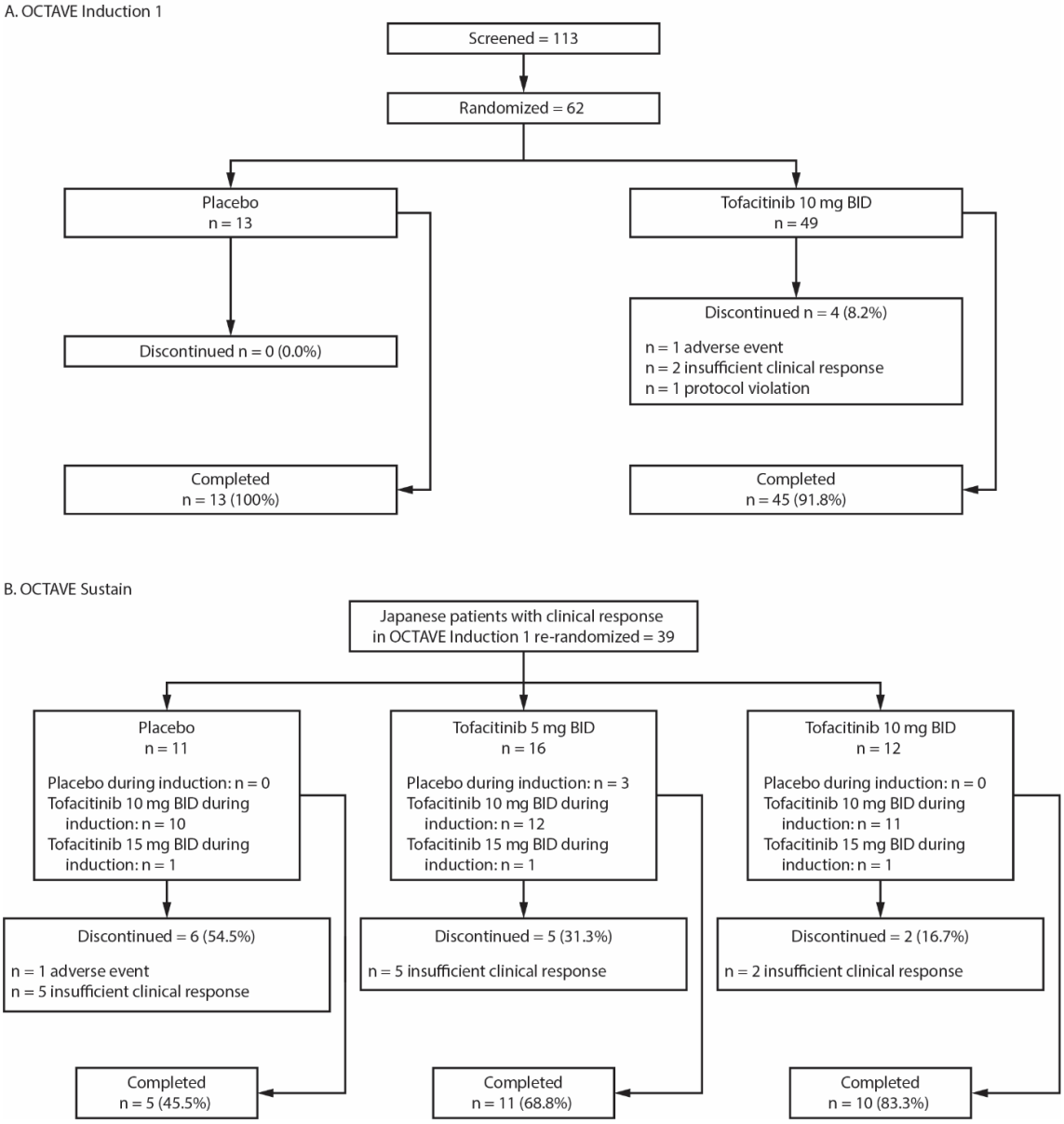
Hungary	9 (1.5)	23 (3.9)
Israel	3 (0.5)	7 (1.2)
Italy	34 (5.5)	22 (3.7)
Latvia	1 (0.2)	1 (0.2)
The Netherlands	2 (0.3)	14 (2.4)
Poland	22 (3.6)	40 (6.7)
Romania	9 (1.5)	6 (1.0)
Russia	23 (3.7)	19 (3.2)
Serbia	34 (5.5)	20 (3.4)
Slovakia	9 (1.5)	26 (4.4)
Spain	20 (3.3)	9 (1.5)
Ukraine	39 (6.4)	39 (6.6)

North America	143 (23.3)	128 (21.6)
Canada	23 (3.7)	14 (2.4)
USA	120 (19.5)	114 (19.2)
Other	112 (18.2)	119 (20.1)
Australia	12 (2.0)	15 (2.5)
Brazil	0 (0.0)	1 (0.2)
Colombia	1 (0.2)	1 (0.2)
Japan	65 (10.6)	39 (6.6)
Korea	0 (0.0)	23 (3.9)
New Zealand	19 (3.1)	17 (2.9)
South Africa	15 (2.4)	22 (3.7)
Taiwan	0 (0.0)	1 (0.2)

N, number of randomized patients; *n*, number of patients in the specified category.

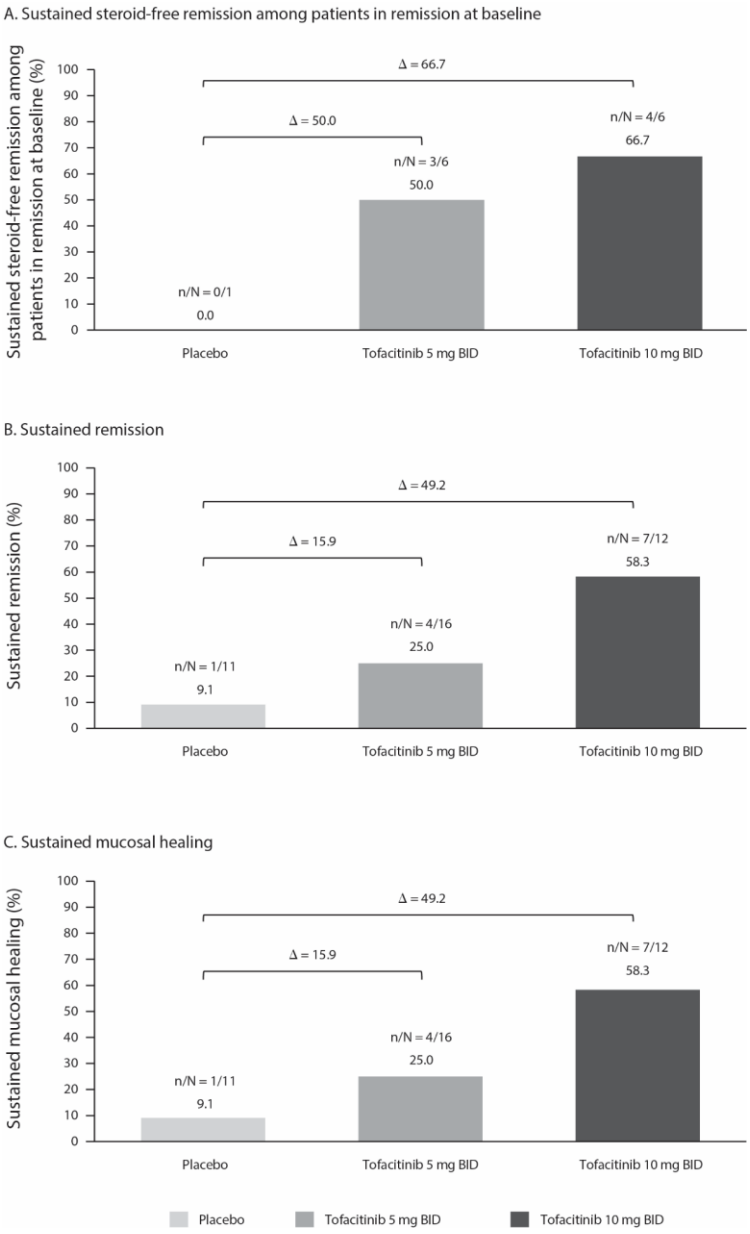
Figures

Supplementary Fig. 1. Japanese patient flow during (A) OCTAVE Induction 1 and (B) OCTAVE Sustain



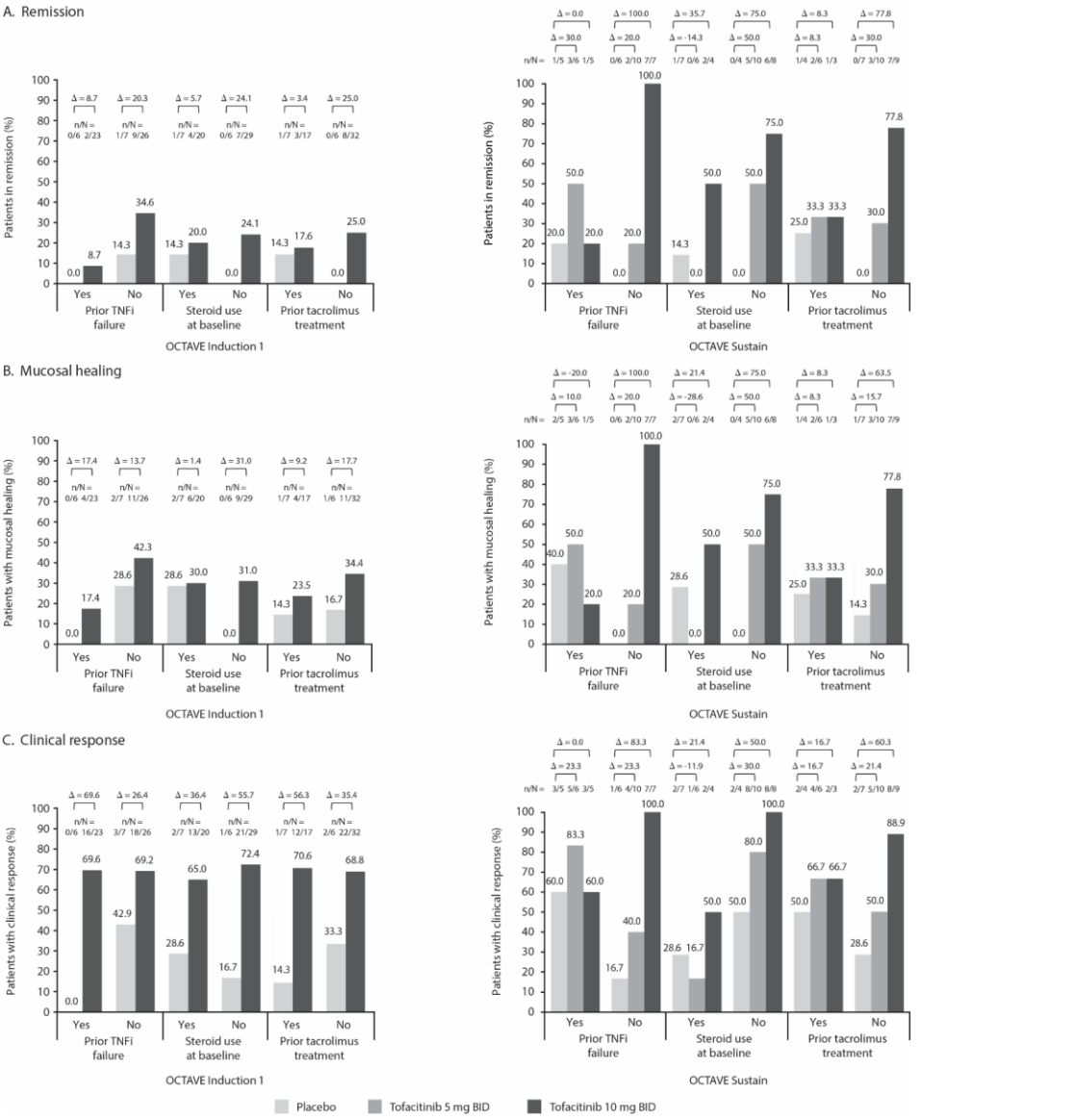
BID, twice daily; *n*, number of patients in the specified category.

Supplementary Fig. 2. Proportion of Japanese patients achieving (A) sustained steroid-free remission, (B) sustained remission, and (C) sustained mucosal healing at week 52 (OCTAVE Sustain), by treatment group



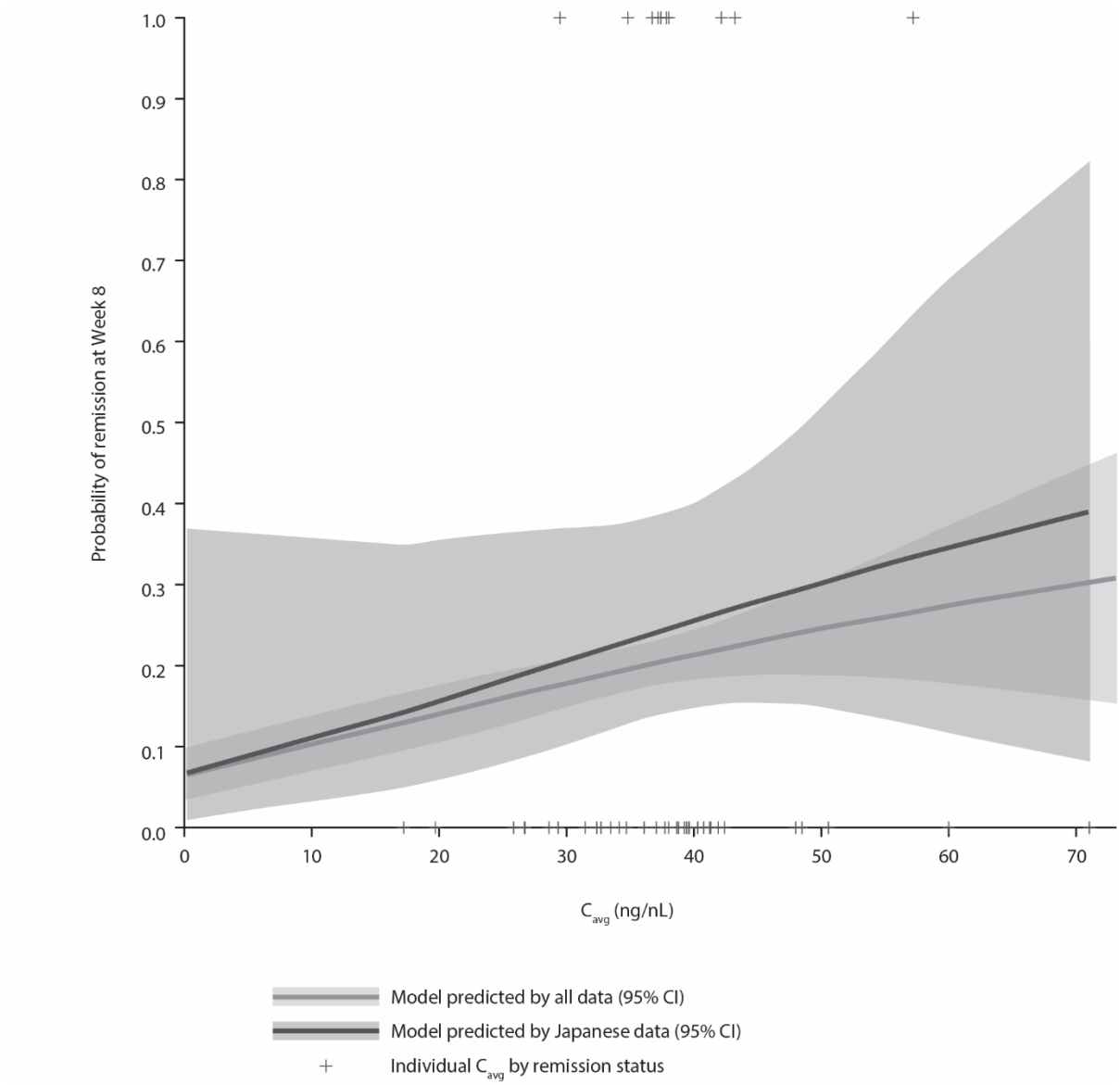
Δ, treatment difference; BID, twice daily; *N*, number of evaluable patients in each subgroup; *n*, number of patients with response.

Supplementary Fig. 3. Proportion of Japanese patients achieving (A) remission, (B) mucosal healing, and (C) clinical response at week 8 (OCTAVE Induction 1) and week 52 (OCTAVE Sustain), by treatment group



Data are full analysis set with non-responder imputation, central read. Δ, treatment difference; BID, twice daily; *N*, number of evaluable patients in each subgroup; *n*, number of patients with response; TNFi, tumor necrosis factor inhibitor.

Supplementary Fig. 4. Exposure-response modeling of the proportion of Japanese patients achieving remission compared with all data at week 8 of OCTAVE Induction 1



C_{avg}, average concentration; CI, confidence interval.