SUPPLEMENTARY DATA

SUPPLEMENTARY TABLE 1. Demographics, Baseline Characteristics, and Clinical Characteristics of the Induction Cohort[†]

	18 to < 30 years		30 to < 40 years		40 to < 50 years		50 to < 60 years		≥ 60 years	
	Placebo (*N* = 67)	Tofacitinib 10 mg BID (*N* = 216)	Placebo (*N* = 80)	Tofacitinib 10 mg BID (*N* = 251)	Placebo (*N* = 51)	Tofacitinib 10 mg BID (*N* = 210)	Placebo (*N* = 44)	Tofacitinib 10 mg BID (*N* = 149)	Placebo (*N* = 40)	Tofacitinib 10 mg BID (*N* = 112)
Age (years), mean (SD)	24.6 (3.2)	24.6 (3.3)	34.0 (2.9)	34.3 (2.7)	44.6 (2.7)	44.2 (2.9)	54.0 (2.8)	54.4 (2.8)	66.1 (5.3)	66.0 (4.8)
Male, *n* (%)	35 (52.2)	128 (59.3)	47 (58.8)	147 (58.6)	30 (58.8)	124 (59.0)	20 (45.5)	84 (56.4)	23 (57.5)	74 (66.1)
Race, *n* (%)										
White	53 (79.1)	183 (84.7)	66 (82.5)	195 (77.7)	40 (78.4)	171 (81.4)	37 (84.1)	119 (79.9)	33 (82.5)	88 (78.6)
Asian	9 (13.4)	21 (9.7)	7 (8.8)	33 (13.1)	5 (9.8)	29 (13.8)	4 (9.1)	17 (11.4)	3 (7.5)	14 (12.5)
Geographic region, *n* (%)										
Asia	9 (13.4)	17 (7.9)	6 (7.5)	30 (12.0)	5 (9.8)	23 (11.0)	3 (6.8)	14 (9.4)	3 (7.5)	11 (9.8)
Eastern Europe	19 (28.4)	63 (29.2)	37 (46.3)	80 (31.9)	13 (25.5)	68 (32.4)	12 (27.3)	44 (29.5)	9 (22.5)	28 (25.0)
Western Europe	24 (35.8)	73 (33.8)	19 (23.8)	79 (31.5)	18 (35.3)	56 (26.7)	10 (22.7)	46 (30.9)	8 (20.0)	27 (24.1)
North America	7 (10.4)	41 (19.0)	10 (12.5)	34 (13.5)	7 (13.7)	44 (21.0)	15 (34.1)	34 (22.8)	14 (35.0)	34 (30.4)
Rest of world	8 (11.9)	22 (10.2)	8 (10.0)	28 (11.2)	8 (15.7)	19 (9.0)	4 (9.1)	11 (7.4)	6 (15.0)	12 (0.7)
Disease duration (years), mean (SD)	4.8 (3.5)	4.8 (3.6)	7.7 (5.0)	7.2 (5.0)	8.0 (6.3)	9.5 (7.4)	11.7 (8.1)	11.8 (8.1)	10.9 (9.9)	10.1 (9.8)
Total Mayo score, mean (SD)	8.5 (1.5)	9.0 (1.5)	9.1 (1.4)	8.9 (1.4)	9.1 (1.5)	9.0 (1.4)	8.6 (1.5)	8.9 (1.5)	9.1 (1.6)	8.9 (1.4)
Baseline CRP (mg/L), median (range)	4.3 (0.1–73.4)	4.2 (0.1–102.0)	6.4 (0.3–76.3)	4.6 (0.2–156.0)	4.7 (0.4–82.5)	4.1 (0.3–124.6)	5.2 (0.3–47.9)	4.7 (0.2–208.4)	5.5 (0.2–205.1)	6.7 (0.4–94.6)

Prior TNFi treatment, *n* (%)	38 (66.7)	120 (57.1)	35 (53.0)	118 (48.4)	23 (53.5)	115 (57.5)	17 (47.2)	72 (50.7)	17 (53.1)	63 (57.8)
Prior immunosuppressant treatment, *n* (%)	38 (66.7)	157 (74.8)	51 (77.3)	178 (73.0)	31 (72.1)	163 (81.5)	19 (52.8)	112 (78.9)	21 (65.6)	73 (67.0)
Immunosuppressant treatment within 8 weeks prior to baseline, *n* (%)	20 (35.1)	61 (29.0)	13 (19.7)	72 (29.5)	13 (30.2)	66 (33.0)	6 (16.7)	38 (26.8)	4 (12.5)	22 (20.2)
Oral corticosteroid use at baseline, *n* (%)	27 (40.3)	107 (49.5)	38 (47.5)	117 (46.6)	25 (49.0)	88 (41.9)	16 (36.4)	62 (41.6)	21 (52.5)	56 (50.0)
Oral corticosteroid daily dose at baseline – prednisone equivalent (mg/day), mean (SD)‡	16.9 (6.6)	16.0 (6.3)	17.8 (5.6)	17.0 (6.3)	17.8 (7.2)	16.5 (6.3)	15.6 (6.1)	15.2 (6.5)	15.0 (6.0)	14.4 (6.7)
Extent of disease, *n* (%)										
Proctosigmoiditis	7 (12.3)	25 (12.0)	10 (15.2)	32 (13.1)	9 (20.9)	37 (18.5)	7 (19.4)	19 (13.4)	2 (6.5)	19 (17.6)
Left-sided colitis	16 (28.1)	61 (29.2)	16 (24.2)	70 (28.7)	15 (34.9)	80 (40.0)	14 (38.9)	51 (35.9)	15 (48.4)	45 (41.7)
Extensive/pancolitis	34 (59.6)	123 (58.9)	40 (60.6)	142 (58.2)	19 (44.2)	83 (41.5)	15 (41.7)	71 (50.0)	14 (45.2)	44 (40.7)
Proctitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
Smoking status, *n* (%)										
Current smoker	2 (3.0)	16 (7.4)	8 (10.0)	17 (6.8)	0 (0.0)	9 (4.3)	0 (0.0)	5 (3.4)	1 (2.5)	1 (0.9)
Ex-smoker	9 (13.4)	22 (10.2)	11 (13.8)	54 (21.5)	15 (29.4)	85 (40.5)	21 (47.7)	69 (46.3)	20 (50.0)	66 (58.9)
Never smoked	56 (83.6)	178 (82.4)	61 (76.3)	180 (71.7)	36 (70.6)	116 (55.2)	23 (52.3)	75 (50.3)	19 (47.5)	44 (39.3)

†Induction Cohort: placebo, *N* = 282; tofacitinib 10 mg BID, *N* = 938.

‡Based on prednisone-equivalent total daily doses, and excludes medications like budesonide and beclometasone.

BID indicates twice daily; CRP, C-reactive protein; *N*, total number of patients in the treatment group; *n*, number of patients in the specified category; SD, standard deviation; TNFi, tumor necrosis factor inhibitor.

SUPPLEMENTARY TABLE 2. Demographics, Baseline Characteristics, and Clinical Characteristics of the Maintenance Cohort[†]

	18 to <30 years			30 to <40 years			40 to <50 years			50 to <60 years			≥60 years		
	Placebo (*N* = 39)	Tofacitinib 5 mg BID (*N* = 44)	Tofacitinib 10 mg BID (*N* = 36)	Placebo (*N* = 48)	Tofacitinib 5 mg BID (*N* = 50)	Tofacitinib 10 mg BID (*N* = 56)	Placebo (*N* = 40)	Tofacitinib 5 mg BID (*N* = 46)	Tofacitinib 10 mg BID (*N* = 42)	Placebo (*N* = 42)	Tofacitinib 5 mg BID (*N* = 36)	Tofacitinib 10 mg BID (*N* = 31)	Placebo (*N* = 29)	Tofacitinib 5 mg BID (*N* = 22)	Tofacitinib 10 mg BID (*N* = 31)
Age (years), mean (SD)	24.9 (3.2)	25.2 (3.0)	24.3 (3.6)	34.6 (2.9)	34.2 (2.7)	34.8 (2.9)	44.1 (2.8)	44.5 (2.7)	44.5 (3.2)	54.3 (2.7)	54.6 (3.1)	53.5 (2.6)	66.0 (4.4)	66.6 (5.7)	67.1 (5.8)
Male, *n* (%)	20 (51.3)	28 (63.6)	18 (50.0)	27 (56.3)	25 (50.0)	33 (58.9)	25 (62.5)	22 (47.8)	25 (59.5)	24 (57.1)	14 (38.9)	15 (48.4)	20 (69.0)	14 (63.6)	19 (61.3)
Race, *n* (%)															
White	34 (87.2)	34 (77.3)	32 (88.9)	36 (75.0)	42 (84.0)	43 (76.8)	32 (80.0)	38 (82.6)	33 (78.6)	30 (71.4)	32 (88.9)	23 (74.2)	23 (79.3)	18 (81.8)	22 (71.0)
Asian	4 (10.3)	7 (15.9)	3 (8.3)	7 (14.6)	4 (8.0)	8 (14.3)	4 (10.0)	6 (13.0)	6 (14.3)	6 (14.3)	3 (8.3)	5 (16.1)	5 (17.2)	3 (13.6)	3 (9.7)
Geographic region, *n* (%)															
Asia	4 (10.3)	7 (15.9)	3 (8.3)	5 (10.4)	4 (8.0)	7 (12.5)	3 (7.5)	5 (10.9)	5 (11.9)	5 (11.9)	3 (8.3)	4 (12.9)	3 (10.3)	3 (13.6)	2 (6.5)
Eastern Europe	11 (28.2)	12 (27.3)	17 (47.2)	15 (31.3)	21 (42.0)	18 (32.1)	14 (35.0)	14 (30.4)	14 (33.3)	12 (28.6)	12 (33.3)	9 (29.0)	5 (17.2)	7 (31.8)	5 (16.1)
Western Europe	12 (30.8)	12 (27.3)	9 (25.0)	12 (25.0)	12 (24.0)	18 (32.1)	11 (27.5)	13 (28.3)	10 (23.8)	11 (26.2)	6 (16.7)	11 (35.5)	9 (31.0)	4 (18.2)	9 (29.0)
North America	8 (20.5)	6 (13.6)	6 (16.7)	10 (20.8)	8 (16.0)	9 (16.1)	8 (20.0)	7 (15.2)	10 (23.8)	10 (23.8)	13 (36.1)	6 (19.4)	9 (31.0)	5 (22.7)	13 (41.9)
Rest of world	4 (10.3)	7 (15.9)	1 (2.8)	6 (12.5)	5 (10.0)	4 (7.1)	4 (10.0)	7 (15.2)	3 (7.1)	4 (9.5)	2 (5.6)	1 (3.2)	3 (10.3)	3 (13.6)	2 (6.5)
Disease duration (years), mean (SD)	4.4 (3.5)	5.2 (3.0)	4.4 (3.1)	6.4 (4.5)	6.4 (4.4)	7.2 (5.1)	9.4 (7.3)	10.6 (7.5)	9.7 (7.1)	11.6 (6.4)	12.5 (10.7)	11.7 (7.5)	13.7 (11.8)	6.7 (6.0)	11.9 (9.4)
Total Mayo score, mean (SD)[‡]	3.5 (1.9)	3.7 (1.8)	2.8 (1.9)	2.9 (1.7)	2.9 (1.6)	3.3 (1.7)	3.2 (2.1)	3.3 (1.7)	4.2 (1.8)	3.6 (1.7)	3.1 (1.8)	3.5 (1.6)	3.1 (1.7)	3.4 (1.9)	3.5 (1.8)
Baseline CRP (mg/L), median (range)[‡]	0.5 (0.1-33.9)	0.9 (0.1-33.7)	0.7 (0.1-74.3)	1.2 (0.1-30.5)	0.8 (0.1-10.4)	1.0 (0.1-67.1)	1.1 (0.2-33.4)	0.6 (0.1-10.2)	2.6 (0.1-35.3)	0.9 (0.1-45.0)	1.2 (0.1-17.7)	0.5 (0.1-29.3)	1.3 (0.1-16.3)	0.4 (0.1-18.9)	1.0 (0.1-26.0)
Prior TNFi treatment, *n* (%)[§]	16 (41.0)	26 (59.1)	15 (41.7)	23 (47.9)	24 (48.0)	27 (48.2)	16 (40.0)	19 (41.3)	21 (50.0)	19 (45.2)	14 (38.9)	18 (58.1)	18 (62.1)	7 (31.8)	19 (61.3)

Prior immunosuppressant treatment, *n* (%)[§]	24 (61.5)	31 (70.5)	24 (66.7)	30 (62.5)	40 (80.0)	43 (76.8)	29 (72.5)	37 (80.4)	30 (71.4)	28 (66.7)	29 (80.6)	27 (87.1)	23 (79.3)	12 (54.5)	20 (64.5)
Immunosuppressant treatment within 8 weeks prior to baseline, *n* (%)[§]	9 (23.1)	13 (29.5)	10 (27.8)	7 (14.6)	12 (24.0)	13 (23.2)	11 (27.5)	9 (19.6)	17 (40.5)	10 (23.8)	8 (22.2)	10 (32.3)	7 (24.1)	3 (13.6)	6 (19.4)
Oral corticosteroid use at baseline, *n* (%)[‡]	22 (56.4)	22 (50.0)	18 (50.0)	26 (54.2)	30 (60.0)	20 (35.7)	18 (45.0)	26 (56.5)	17 (40.5)	15 (35.7)	13 (36.1)	16 (51.6)	19 (65.5)	10 (45.5)	15 (48.4)
Oral corticosteroid daily dose at baseline – prednisone equivalent (mg/day), mean (SD) [‡,¶]	17.2 (5.9)	14.8 (7.1)	12.2 (5.6)	16.8 (6.1)	14.8 (6.1)	17.6 (4.5)	14.6 (5.3)	15.1 (5.6)	15.8 (5.5)	17.5 (8.0)	15.0 (5.5)	12.5 (6.7)	13.7 (5.9)	14.4 (7.7)	13.0 (6.4)
Extent of disease, *n* (%)[§]															
Proctosigmoiditis	3 (7.7)	6 (14.0)	6 (16.7)	5 (10.4)	5 (10.0)	6 (10.7)	5 (12.5)	11 (23.9)	11 (26.2)	2 (4.8)	4 (11.1)	4 (12.9)	6 (20.7)	2 (9.5)	6 (20.0)
Left-sided colitis	14 (35.9)	10 (23.3)	11 (30.6)	13 (27.1)	13 (26.0)	12 (21.4)	14 (35.0)	20 (43.5)	15 (35.7)	15 (35.7)	12 (33.3)	11 (35.5)	12 (41.4)	11 (52.4)	11 (36.7)
Extensive/ pancolitis	22 (56.4)	27 (62.8)	19 (52.8)	30 (62.5)	32 (64.0)	38 (67.9)	21 (52.5)	15 (32.6)	16 (38.1)	24 (57.1)	20 (55.6)	16 (51.6)	11 (37.9)	8 (38.1)	13 (43.3)
Proctitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Smoking status, *n* (%)[§]															
Current smoker	2 (5.1)	1 (2.3)	2 (5.6)	4 (8.3)	3 (6.0)	3 (5.4)	2 (5.0)	1 (2.2)	1 (2.4)	3 (7.1)	2 (5.6)	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)
Ex-smoker	8 (20.5)	4 (9.1)	3 (8.3)	11 (22.9)	9 (18.0)	9 (16.1)	16 (40.0)	15 (32.6)	18 (42.9)	16 (38.1)	13 (36.1)	17 (54.8)	22 (75.9)	8 (36.4)	16 (51.6)
Never smoked	29 (74.4)	39 (88.6)	31 (86.1)	33 (68.8)	38 (76.0)	44 (78.6)	22 (55.0)	30 (65.2)	23 (54.8)	23 (54.8)	21 (58.3)	14 (45.2)	6 (20.7)	14 (63.6)	15 (48.4)

[†]Maintenance Cohort: placebo, *N* = 198; tofacitinib 5 mg BID, *N* = 198; tofacitinib 10 mg BID, *N* = 196; Tofacitinib All, *N* = 364.

[‡]Parameters based on baseline of the maintenance trial.

[§]Parameters based on baseline of the Induction trials (Phase 2 induction, OCTAVE Induction 1, and OCTAVE Induction 2).

[¶]Based on prednisone-equivalent total daily doses, and excludes medications like budesonide and beclometasone.

BID indicates twice daily; CRP, C-reactive protein; *N*, total number of patients in the treatment group; *n*, number of patients in the specified category; SD, standard deviation;

TNFi, tumor necrosis factor inhibitor.

SUPPLEMENTARY TABLE 3. Demographics, Baseline Characteristics, and Clinical Characteristics of the Overall Cohort[†]

	18 to < 30 years (*N* = 270)	30 to < 40 years (*N* = 311)	40 to < 50 years (*N* = 251)	50 to < 60 years (*N* = 181)	≥ 60 years (*N* = 144)
Age (years), mean (SD)	24.6 (3.3)	34.3 (2.8)	44.3 (2.9)	54.3 (2.8)	66.0 (4.8)
Male, *n* (%)	157 (58.1)	181 (58.2)	148 (59.0)	99 (54.7)	94 (65.3)
Race, *n* (%)					
White	224 (83.0)	244 (78.5)	201 (80.1)	145 (80.1)	113 (78.5)
Asian	32 (11.9)	39 (12.5)	34 (13.5)	21 (11.6)	18 (12.5)
Geographic region, *n* (%)					
Asia	28 (10.4)	35 (11.3)	28 (11.2)	17 (9.4)	15 (10.4)
Eastern Europe	76 (28.1)	103 (33.1)	77 (30.7)	51 (28.2)	35 (24.3)
Western Europe	94 (34.8)	94 (30.2)	69 (27.5)	55 (30.4)	32 (22.2)
North America	47 (17.4)	48 (15.4)	52 (20.7)	47 (26.0)	47 (32.6)
Rest of world	25 (9.3)	31 (10.0)	25 (10.0)	11 (6.1)	15 (10.4)
Disease duration (years), mean (SD)	4.7 (3.5)	7.4 (5.0)	9.3 (7.2)	11.6 (8.1)	10.6 (9.8)
Total Mayo score, mean (SD)[‡]	8.6 (1.9)	8.6 (1.9)	8.7 (2.0)	8.5 (2.1)	8.5 (1.9)
Baseline CRP (mg/L), median (range)[‡]	4.2 (0.1-102.0)	4.4 (0.2-156.0)	4.1 (0.2-124.6)	4.9 (0.2-208.4)	6.0 (0.3-94.6)
Prior TNFi treatment, *n* (%)[§]	155 (58.7)	153 (50.3)	137 (56.8)	87 (50.0)	80 (56.7)
Prior immunosuppressant treatment, *n* (%)[§]	194 (73.5)	227 (74.7)	192 (79.7)	131 (75.3)	94 (66.7)

Immunosuppressant treatment within 8 weeks prior to baseline, *n* (%)[§]	79 (29.9)	83 (27.3)	80 (33.2)	44 (25.3)	27 (19.1)
Oral corticosteroid use at baseline, *n* (%)[§]	129 (47.8)	141 (45.3)	108 (43.0)	76 (42.0)	69 (47.9)
Oral corticosteroid daily dose at baseline – prednisone equivalent (mg/day), mean (SD) [§, ¶]	15.8 (6.4)	17.1 (6.1)	16.3 (6.2)	15.4 (6.3)	13.9 (6.4)
Extent of disease, *n* (%)[§]					
Proctosigmoiditis	31 (11.8)	42 (13.8)	44 (18.3)	24 (13.8)	22 (15.8)
Left-sided colitis	75 (28.5)	84 (27.6)	96 (39.8)	65 (37.4)	60 (43.2)
Extensive/pancolitis	157 (59.7)	178 (58.6)	101 (41.9)	84 (48.3)	57 (41.0)
Proctitis	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Smoking status, *n* (%)[‡]					
Current smoker	17 (6.3)	26 (8.4)	9 (3.6)	5 (2.8)	2 (1.4)
Ex-smoker	28 (10.4)	62 (19.9)	98 (39.0)	87 (48.1)	82 (56.9)
Never smoked	225 (83.3)	223 (71.7)	144 (57.4)	89 (49.2)	59 (41.0)

[†]Overall Cohort: tofacitinib 5 mg BID, *N* = 198; tofacitinib 10 mg BID, *N* = 959; Tofacitinib All, *N* = 1157.

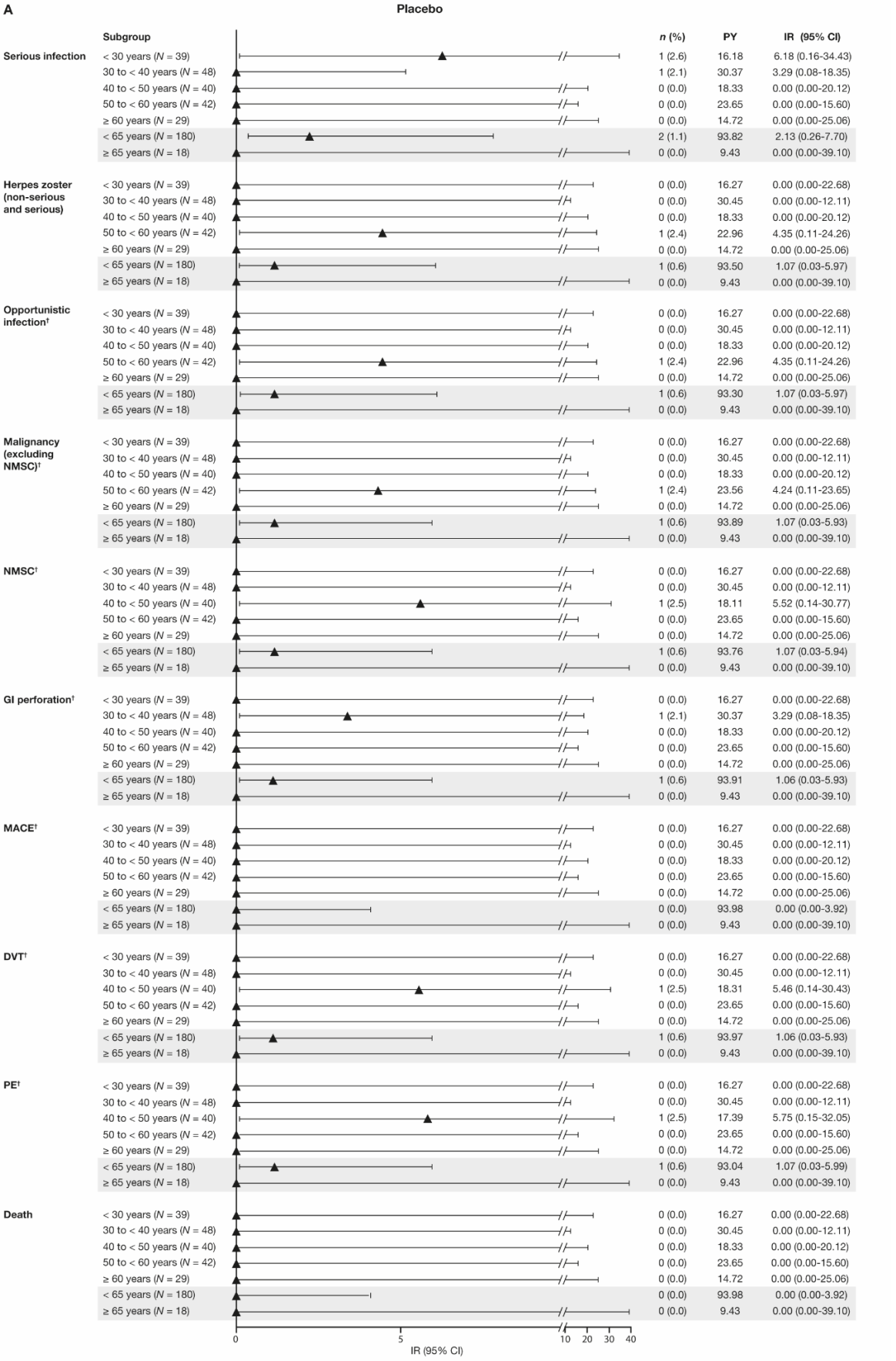
[‡]Parameters based on Day 1, start of active tofacitinib treatment in the UC program, smoking based on baseline of Induction trials.

[§]Parameters based on baseline of the Induction trials (Phase 2 induction, OCTAVE Induction 1, and OCTAVE Induction 2), with exception of oral corticosteroid use.

[¶]Based on prednisone-equivalent total daily doses, and excludes medications like budesonide and beclometasone.

BID indicates twice daily; CRP, C-reactive protein; *N*, total number of patients in the treatment group; *n*, number of patients in the specified category; SD, standard deviation; TNFi, tumor necrosis factor inhibitor; UC, ulcerative colitis.

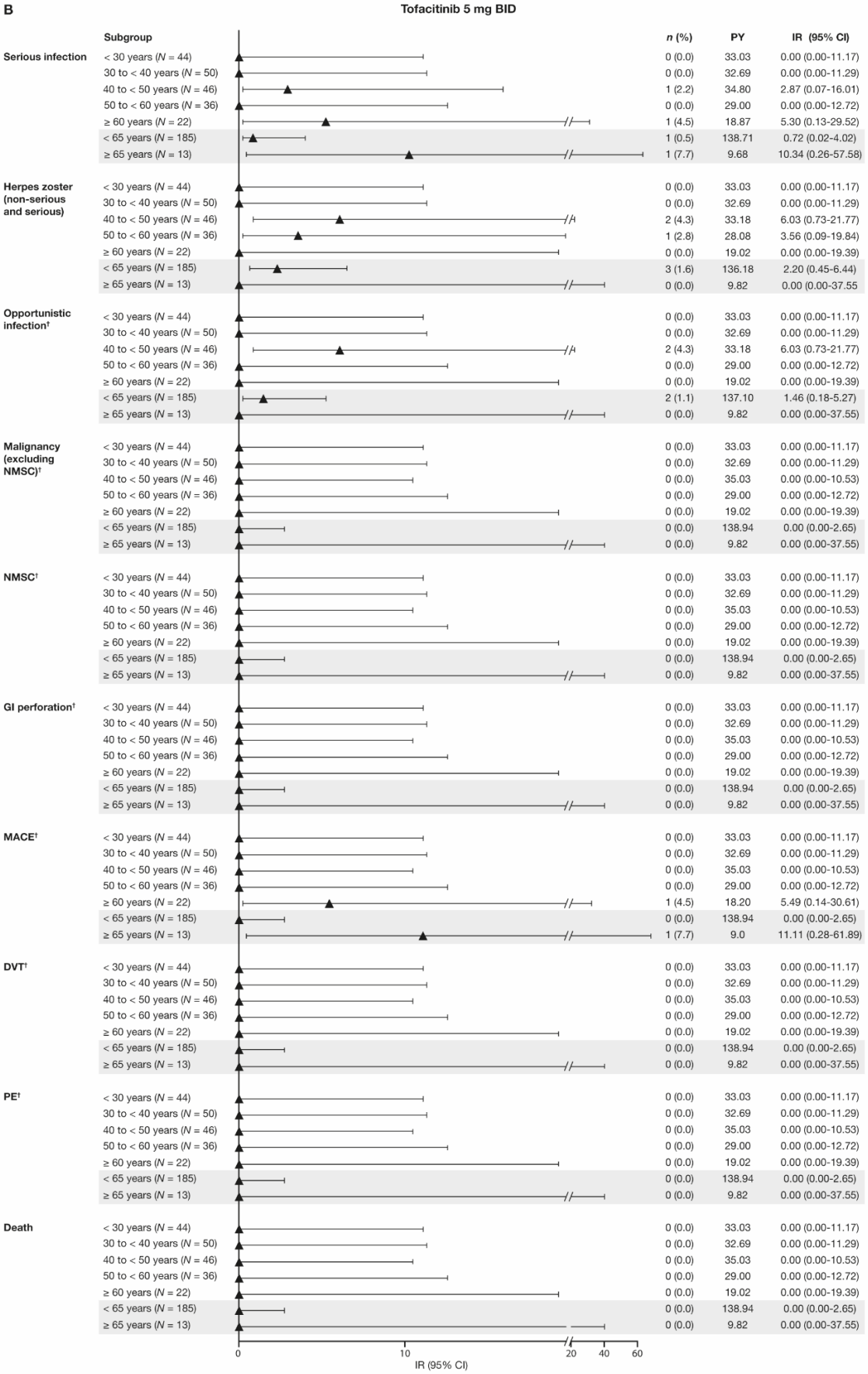
SUPPLEMENTARY FIGURE 1. AEs of special interest reported by age group in the Maintenance Cohort.



Events were counted to the earliest of: day of the first event, time to data cut-off or progression to next study, or up to 28 days beyond the last dose. IR was defined as the number of unique patients with events per 100 PY of exposure. Exact Poisson (adjusted for PY) 95% CIs are provided. †Adjudicated events. AE indicates adverse event; CI, confidence interval; IR, incidence rate; *N*, total number of patients; *n*, number of patients with the specified event; PY, patient-years; UC, ulcerative colitis.

SUPPLEMENTARY FIGURE 1. AEs of special interest reported by age group in the Maintenance Cohort.

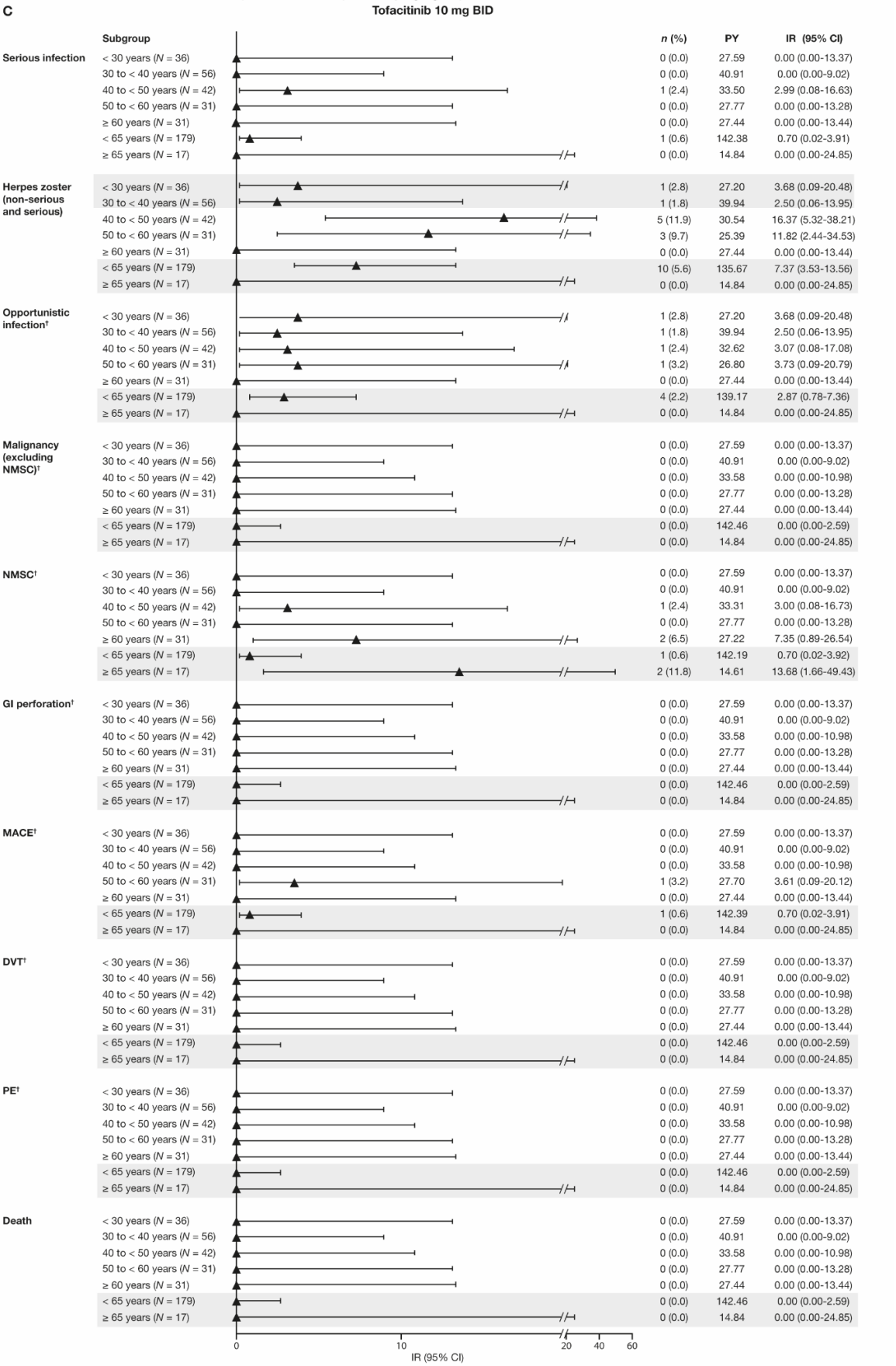
B



Events were counted to the earliest of: day of the first event, time to data cut-off or progression to next study, or up to 28 days beyond the last dose. IR was defined as the number of unique patients with events per 100 PY of exposure. Exact Poisson (adjusted for PY) 95% CIs are provided. †Adjudicated events. AE indicates adverse event; CI, confidence interval; IR, incidence rate; *N*, total number of patients; *n*, number of patients with the specified event; PY, patient-years; UC, ulcerative colitis.

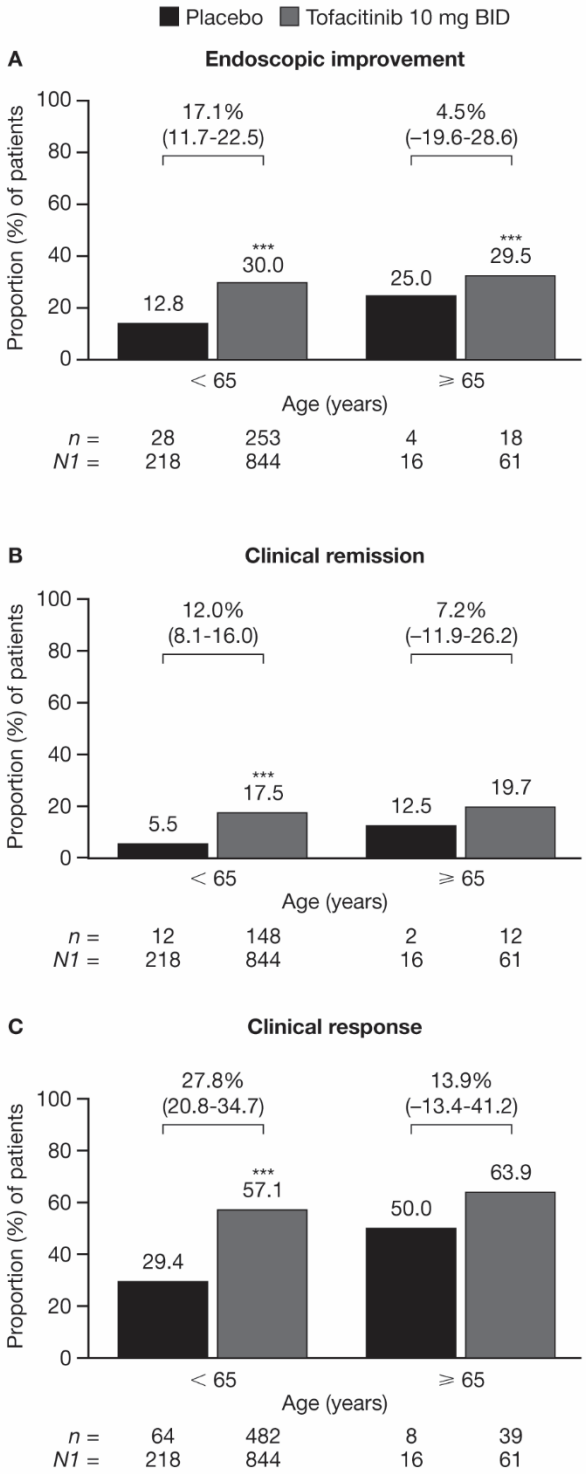
SUPPLEMENTARY FIGURE 1. AEs of special interest reported by age group in the Maintenance Cohort.

C



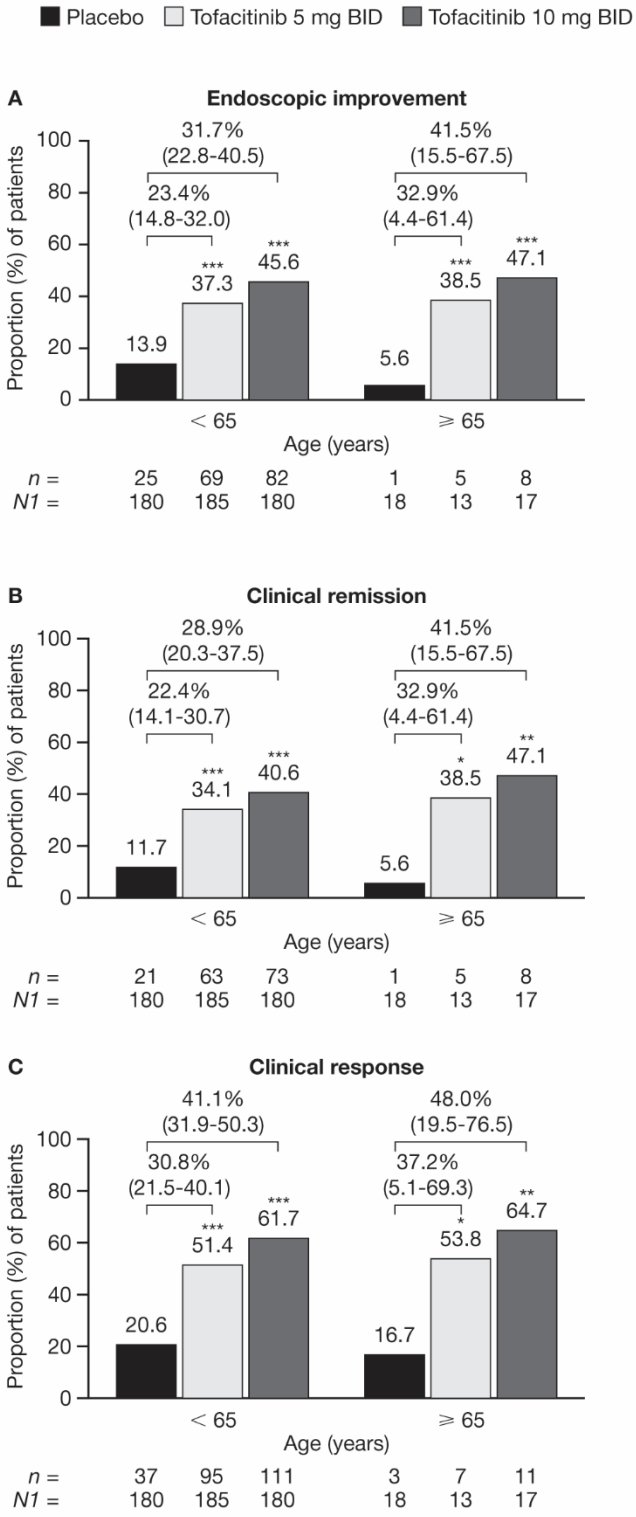
Events were counted to the earliest of: day of the first event, time to data cut-off or progression to next study, or up to 28 days beyond the last dose. IR was defined as the number of unique patients with events per 100 PY of exposure. Exact Poisson (adjusted for PY) 95% CIs are provided. †Adjudicated events. AE indicates adverse event; CI, confidence interval; IR, incidence rate; *N*, total number of patients; *n*, number of patients with the specified event; PY, patient-years; UC, ulcerative colitis.

SUPPLEMENTARY FIGURE 2. Proportions of patients in the < 65 and ≥ 65 years age groups receiving placebo or tofacitinib 10 mg BID, who achieved (A) endoscopic improvement, (B) clinical remission, or (C) clinical response at Week 8 in the Induction Cohort (FAS, NRI).



*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$ (P-values from Cochran-Mantel-Haenszel chi-squared test). Values above bars show the difference from placebo (95% CI). Endoscopic improvement was defined as a Mayo endoscopic subscore of 0 or 1. Clinical remission was defined as a total Mayo score of ≤ 2, with no individual subscore exceeding 1 point. Clinical response 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. BID indicates twice daily; CI, confidence interval; FAS, full analysis set; *N1*, number of patients in the specified category with non-missing data; *n*, number of patients with the specified response within the given category; NRI, non-responder imputation.

SUPPLEMENTARY FIGURE 3. Proportions of patients in the < 65 and ≥ 65 years age groups receiving placebo, tofacitinib 5 mg BID, or tofacitinib 10 mg BID, who achieved (A) endoscopic improvement, (B) clinical remission, or (C) clinical response at Week 52 in the Maintenance Cohort (FAS, NRI).



*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$ (P-values from Cochran-Mantel-Haenszel chi-squared test). Values above bars show the difference from placebo (95% CI). Endoscopic improvement was defined as a Mayo endoscopic subscore of 0 or 1. Clinical remission was defined as a total Mayo score of ≤ 2, with no individual subscore exceeding 1 point. Clinical response 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. BID indicates twice daily; CI, confidence interval; FAS, full analysis set; *N1*, number of patients in the specified category with non-missing data; *n*, number of patients with the specified response within the given category; NRI, non-responder imputation.

SUPPLEMENTARY APPENDIX

Concomitant and Prohibited Concomitant Medications in the Ulcerative Colitis (UC) Clinical Program

Concomitant Medications

Phase 2 Induction Study

All concomitant medication(s) taken during the study must be recorded with indication, daily dose, and start and stop dates of administration. All patients will be questioned about concomitant medication at each clinic visit. The following treatments for UC were allowed, provided that they were stable for the specified period of time:

- Oral 5-aminosalicylates (5-ASA) or sulfasalazine were allowed, provided that the dose was stable for ≥ 2 weeks prior to baseline and during the study treatment period
- Oral corticosteroids were allowed during the study up to a dose of 30 mg/day prednisolone or equivalent, provided that the dose was not commenced or increased within 2 weeks of baseline. Decrease of the steroid dose due to the tapering regime was allowed during the study. If the steroid tapering was commenced, the daily dose of prednisolone or equivalent should be decreased at a rate of 5 mg/week until the dose reached 20 mg/day, then reduced by 2.5 mg every week until the dose reached 0 mg.

OCTAVE Induction 1 and 2

The following treatments for UC were allowed, provided that they were stable for the specified period of time prior to the first dose of study medication and were not permitted to change (dose reduction or increase) during the study treatment period:

- Oral 5-ASA or sulfasalazine were allowed, provided that the dose was stable for ≥ 4 weeks prior to baseline
- Chronic treatment for UC with antibiotics (eg, metronidazole, rifaximin) was allowed, provided that the dose was stable for ≥ 2 weeks prior to baseline
- Oral corticosteroids were allowed during the study up to a dose of 25 mg/day oral prednisone or equivalent, and up to 9 mg/day budesonide, provided that the dose was stable within 2 weeks of baseline. Note: for patients taking more than 20 mg/day oral corticosteroids, the dose may be decreased down to 20 mg/day, at the Investigator's discretion, starting at Week 4/Visit 4 and stay at this reduced dose thereafter for the remainder of the induction study, provided that their partial Mayo score is ≤ 2, with no individual subscore > 1 and rectal bleeding subscore of 0 at Week 4. If the patient subsequently experiences worsening of UC signs or symptoms, in the opinion of the Investigator, due to reduction in corticosteroid daily dose, the daily corticosteroid dosage for the patient could be reverted to the preceding daily dosage instructed by the Investigator; however, in that case, no further dose decrease will be allowed for the remainder of the induction study.

OCTAVE Sustain

The following treatments for UC were allowed, provided their doses were not changed (dose reduction or increase), with the exception of oral corticosteroids (see below), during the study treatment period:

- Oral 5-ASA or sulfasalazine
- Chronic treatment for UC with antibiotics (eg, metronidazole, rifaximin)

- Oral corticosteroids were allowed during the study. Since the patients were transferred from OCTAVE Induction 1 and 2, the maximum corticosteroid dose was 25 mg/day oral prednisone or equivalent, and 9 mg/day budesonide. Tapering steroids was mandatory starting the first week of the study.

- The daily dose of oral prednisone or equivalent was decreased at a rate of 5 mg/week until the dose reached 20 mg/day, then reduced by 2.5 mg to 5.0 mg weekly until the dose reached 10 mg/day, and then reduced by 2.5 mg/week until the dose reached 0 mg.

OCTAVE Open

The following treatments for UC were allowed, provided their doses were not changed (reduced or increased), with the exception of oral 5-ASA or sulfasalazine and oral corticosteroids (see below), during the study treatment period:

- Oral 5-ASA or sulfasalazine dose modifications during the study were permitted

- Chronic treatment for UC with antibiotics (eg, metronidazole, rifaximin) if continued from the preceding study

- Oral corticosteroids were allowed for patients entering OCTAVE Open already on oral corticosteroids (maximum dose of 25 mg/day oral prednisone or equivalent) and tapering was required to commence starting the first week of the study

- The daily dose of oral prednisone or equivalent was decreased at a rate of 5 mg/week until the dose reached 20 mg/day, then reduced by 2.5 mg to 5.0 mg weekly until the dose reached 0 mg.

Prohibited Concomitant Medications

Phase 2 Induction Study

The following medications were prohibited throughout the duration of the study:

- Azathioprine, 6-mercaptopurine, and methotrexate within 7 days of baseline
- Cyclosporine, mycophenolate, and tacrolimus within 4 weeks of baseline
- Interferon within 8 weeks of baseline and tumor necrosis factor inhibitor therapy within 8 weeks of baseline
- Intravenous corticosteroids or rectally administered formulations of corticosteroids or 5-ASA within 2 weeks prior to baseline.

In addition, concomitant administration of CYP3A inducers and moderate to potent CYP3A inhibitors with systemic effects should be avoided for the duration of the study.

OCTAVE Induction 1 and 2, OCTAVE Sustain, and OCTAVE Open

The following medications were prohibited:

- Azathioprine, 6-mercaptopurine, and methotrexate
- Cyclosporine, mycophenolate mofetil/mycophenolic acid, and tacrolimus
- Interferon
- Anti-TNFi therapy (eg, infliximab, adalimumab, or certolizumab)
- Intravenous corticosteroids
- Rectally administered formulations of corticosteroids or 5-ASA
- Natalizumab, vedolizumab (only OCTAVE Open), or other anti-adhesion molecule therapy (including investigational agents)

- Other investigational or marketed immunosuppressants or biologics with immunomodulatory properties
- Leukocyte apheresis, including selective lymphocyte, monocyte, or granulocyte apheresis (eg, Cellsorba®) or plasma exchange
- Moderate to potent CYP3A inducers or inhibitors due to potential for drug interactions or confounding of data interpretation
- Antimotility agents for control of diarrhea (ie, diphenoxylate hydrochloride with atropine sulphate or loperamide) (not prohibited in OCTAVE Open).