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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; ‡Study A3921139 (OCTAVE Open) was ongoing at the time of this analysis; §Remission was defined as a total Mayo score of ≤2 with no individual subscore >1, and a rectal bleeding subscore of 0 (centrally read). BID, twice daily; N, number of patients treated in each treatment group; UC, ulcerative colitis. 9

SUPPLEMENTARY FIGURE 2. Evaluation of CRP at Week 4 of the Phase 2 study in patients receiving tofacitinib 10 mg BID (N = 28), stratified by whether patients achieved clinical and endoscopic outcomes at induction Week 8 (full analysis set, observed case analysis). BID, twice daily; CRP, C-reactive protein; N, number of patients with non-missing data in each category; SD, standard deviation. 11

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SUPPLEMENTARY FIGURE 4. ROC curves for prior TNFi failure as a predictor of clinical and endoscopic outcomes (full analysis set, observed case analysis): A, at induction Week 8; B, at induction Week 16. ROC, receiver operating characteristic; TNFi, tumor necrosis factor inhibitor. 13

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SUPPLEMENTARY TABLE 1. Assessments of Early Markers of Disease Activity and Clinical and Endoscopic Outcomes in Patients Receiving Tofacitinib 10 mg BID Induction Therapy in the Phase 2, Phase 3 OCTAVE Induction 1 and 2, and OLE Studies.

	Phase 2 Study (NCT00787202)			OCTAVE Induction 1 and 2 (NCT01465763; NCT01458951)			OLE Study (NCT01470612)	
Tofacitinib Induction Therapy	Week 2	Week 4	Week 8	Week 2	Week 4	Week 8	Week 12	Week 16
Potential early markers of disease activity measured:								
CRP	-	Y	Y	-	Y	Y	-	-
PMS	Y	Y	Y	Y	Y	Y	Y	-
Outcomes assessed:								
Clinical response[†]	-	-	Y	-	-	Y	-	Y
Clinical remission[‡]	-	-	Y	-	-	Y	-	Y
Endoscopic improvement[§]	-	-	Y	-	-	Y	-	Y
Endoscopic remission[¶]	-	-	Y	-	-	Y	-	Y

[†]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.

[‡]Clinical remission was defined as a total Mayo score of ≤2 with no individual subscore >1.

[§]Endoscopic improvement (defined as mucosal healing per the original Phase 2 and OCTAVE protocols [NCT00787202; NCT01465763; NCT01458951] approved prior to publication of the US Food and Drug Administration draft guidance on the definition of mucosal healing) was defined as a Mayo endoscopic subscore of 0 or 1.

[¶]Endoscopic remission was defined as a Mayo endoscopic subscore of 0.

BID, twice daily; CRP, C-reactive protein; OLE, open-label, long-term extension; PMS, partial Mayo score; Y, yes.

SUPPLEMENTARY TABLE 2. Definition of Full Analysis Set for the Phase 3 OCTAVE Induction 1 and 2 and OLE Studies Within the Tofacitinib UC Clinical Program who were included in this analysis.

Study	Definition of Full Analysis Set
OCTAVE Induction 1 and 2 (NCT01465763; NCT01458951)[1]	All randomized patients assigned to tofacitinib 10 mg BID
OLE study (NCT01470612)[2]	All induction non-responders who received tofacitinib 10 mg BID in OCTAVE Induction 1 and 2 and received tofacitinib 10 mg BID

BID, twice daily; OLE, open-label, long-term extension; UC, ulcerative colitis.

SUPPLEMENTARY TABLE 3. Demographics and Clinical Characteristics of Tofacitinib Induction Non-Responders at Baseline of OCTAVE Induction 1 and 2, by Clinical Responder Status at Week 16 of Tofacitinib Induction (Non-Responder Imputation Last Observation Carried Forward).

	All N = 295	Complete Non-responder N = 147	Delayed Responder N = 148
Age, y, mean (SD)	38.9 (13.4)	37.4 (13.2)	40.4 (13.5)
Male, n (%)	184 (62.4)	90 (61.2)	94 (63.5)
Total Mayo score at baseline, mean (SD)[†]	9.2 (1.4)	9.4 (1.3)	9.1 (1.4)
Partial Mayo score at baseline, mean (SD)[†]	6.6 (1.2)	6.7 (1.2)	6.5 (1.2)
CRP >3 mg/L at baseline, n (%)[‡]	198 (67.6)	105 (71.4)	93 (63.7)
Prior TNFi failure, n (%)	181 (61.4)	96 (65.3)	85 (57.4)
Prior immunosuppressant failure, n (%)	235 (79.7)	117 (79.6)	118 (79.7)
Prior corticosteroid failure, n (%)	202 (68.5)	104 (70.7)	98 (66.2)
Oral corticosteroid use at baseline, n (%)	116 (39.3)	66 (44.9)	50 (33.8)
Extent of disease, n (%)			
Proctosigmoiditis	48 (16.3)	25 (17.0)	23 (15.5)
Left-sided colitis	107 (36.3)	54 (36.7)	53 (35.8)
Extensive colitis/pancolitis	140 (47.5)	68 (46.3)	72 (48.6)

Responder status was determined as of the May 27, 2019 data cut, database not locked.

[†]All, N = 293; complete non-responders, N = 145; delayed responders, N = 148.

[‡]All, N = 293; complete non-responders, N = 147; delayed responders, N = 146.

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

SUPPLEMENTARY TABLE 4. Univariate Logistic Regression Analysis Results from the Phase 2 Study for CRP and PMS in Patients Receiving Tofacitinib 10 mg BID, by Week 8 Efficacy Endpoints (Full Analysis Set, Observed Case Analysis).

Odds Ratio (95% CI)	CRP (mg/L) Week 4 N = 28	PMS Week 2 N = 25	PMS Week 4 N = 26
Clinical response	0.73 (0.44, 1.19)	0.70 (0.45, 1.09)	0.57* (0.35, 0.95)
Clinical remission	0.58* (0.34, 0.99)	0.50* (0.29, 0.86)	0.46* (0.25, 0.85)
Endoscopic improvement	0.80 (0.49, 1.30)	0.63 (0.39, 1.01)	0.65 (0.41, 1.03)
Endoscopic remission	0.73 (0.43, 1.25)	0.75 (0.48, 1.15)	0.64 (0.37, 1.10)

Log-transformed data were used for CRP analysis. Odds ratios <1 signify that a decrease in CRP or PMS (per unit) is associated with an increase in the odds of response.

*$P < 0.05$.

BID, twice daily; CI, confidence interval; CRP, C-reactive protein; N, number of patients in the analysis population; PMS, partial Mayo score.

SUPPLEMENTARY TABLE 5. ROC Analysis For Ability of TNFi To Predict Clinical and Endoscopic Outcomes At Weeks 8 and 16 of Tofacitinib Induction (Full Analysis Set, Observed Case Analysis).

	AUC	SE	95% CI	Sensitivity	Specificity	PPV	NPV
Efficacy outcomes at Week 8							
Clinical response	0.576	0.018	0.54, 0.61	0.545	0.608	0.693	0.451
Clinical remission	0.613	0.021	0.57, 0.65	0.669	0.557	0.261	0.878
Endoscopic improvement	0.599	0.018	0.56, 0.63	0.620	0.578	0.410	0.763
Endoscopic remission	0.639	0.029	0.58, 0.70	0.742	0.535	0.112	0.963
Efficacy outcomes at Week 16							
Clinical response	0.524	0.031	0.46, 0.59	0.426	0.623	0.612	0.437
Clinical remission	0.587	0.053	0.48, 0.69	0.560	0.615	0.136	0.928
Endoscopic improvement	0.528	0.043	0.44, 0.61	0.450	0.606	0.171	0.859
Endoscopic remission	0.603	0.101	0.40, 0.80	0.800	0.406	0.026	0.991

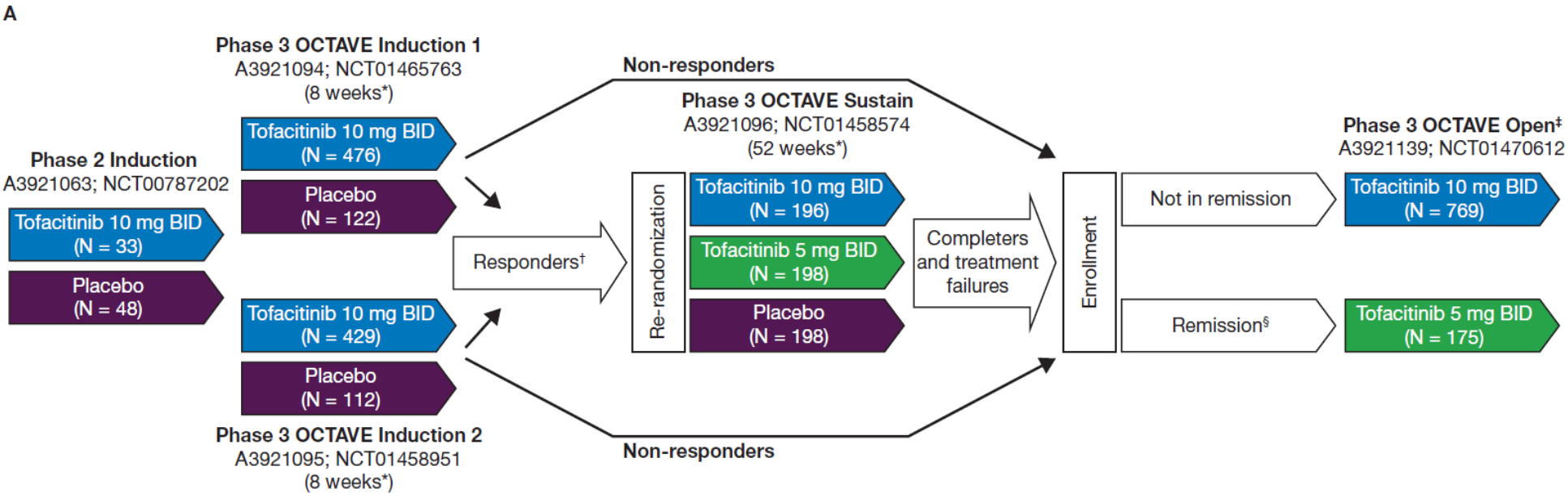
AUC values between 0.9 and 1.0 = outstanding predictive value; between 0.8 and 0.9 = excellent predictive value; between 0.7 and 0.8 = acceptable predictive value; >0.5–0.7 = poor predictive value; ≤0.5 = no discrimination

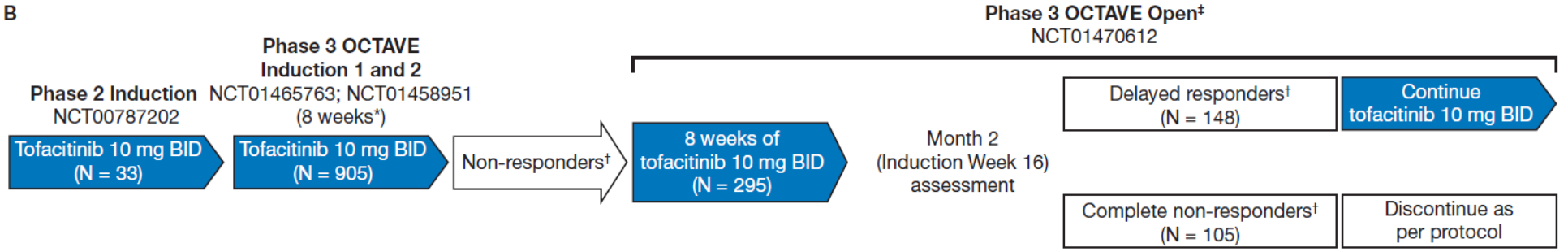
AUC, area under the curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic; SE, standard error; TNFi, tumor necrosis factor inhibitor.

SUPPLEMENTARY FIGURE 1. A, Overview of the tofacitinib UC clinical program. Adapted from Winthrop KL, Melmed GY, Vermeire S, et al. Inflamm Bowel Dis. 2018;24:2258–65 (in accordance with the CC BY-NC license); B, overview of the patient population in this post hoc analysis.

[*]Final complete efficacy assessment at Week 8/52. Treatment continued up to Week 9/53; [†]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; [‡]Study A3921139 (OCTAVE Open) was ongoing at the time of this analysis; [§]Remission was defined as a total Mayo score of ≤2 with no individual subscore >1, and a rectal bleeding subscore of 0 (centrally read).

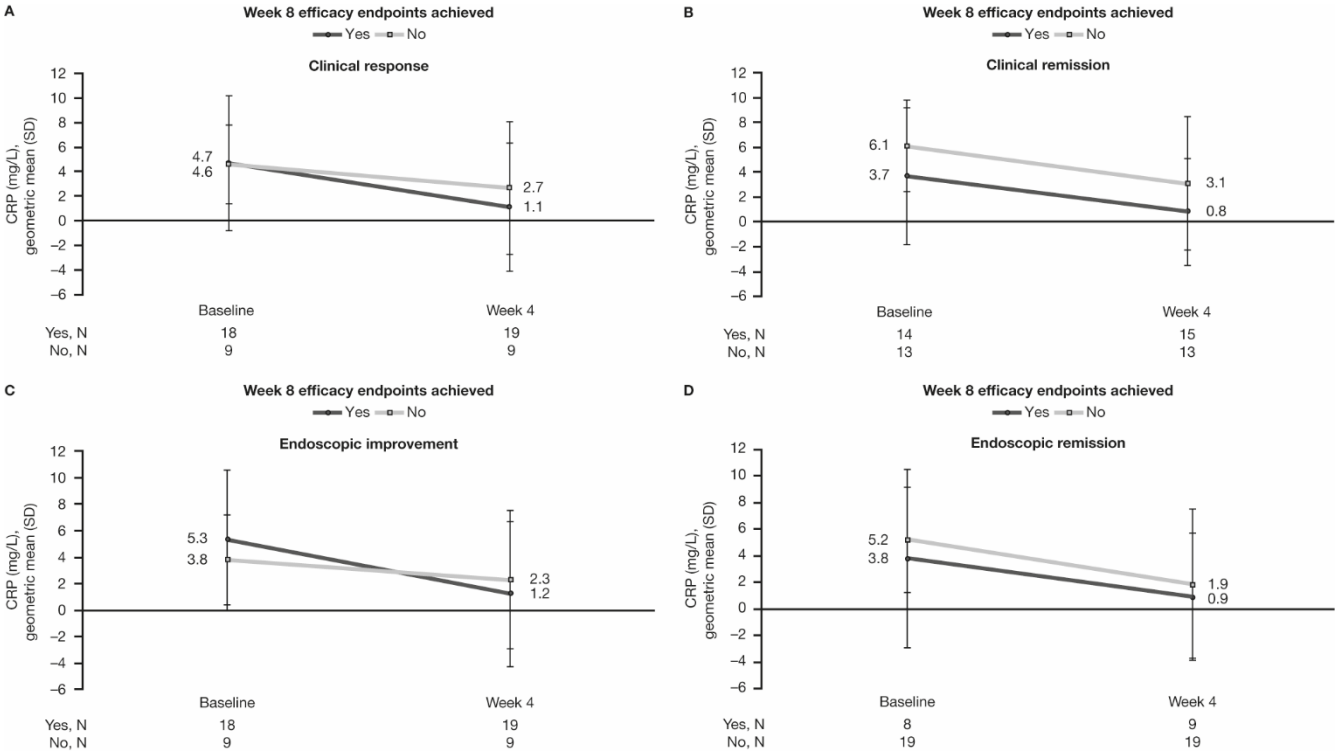
BID, twice daily; N, number of patients treated in each treatment group; UC, ulcerative colitis.


A
Phase 3 OCTAVE Induction 1
A3921094; NCT01465763
(8 weeks*)
Phase 2 Induction
A3921063; NCT00787202
Tofacitinib 10 mg BID
(N = 33)
Placebo
(N = 48)
Tofacitinib 10 mg BID
(N = 476)
Placebo
(N = 122)
Tofacitinib 10 mg BID
(N = 429)
Placebo
(N = 112)
Phase 3 OCTAVE Induction 2
A3921095; NCT01458951
(8 weeks*)
Non-responders
Responders†
Phase 3 OCTAVE Sustain
A3921096; NCT01458574
(52 weeks*)
Re-randomization
Tofacitinib 10 mg BID
(N = 196)
Tofacitinib 5 mg BID
(N = 198)
Placebo
(N = 198)
Non-responders
Completers
and treatment
failures
Enrollment
Not in remission
Remission§
Phase 3 OCTAVE Open‡
A3921139; NCT01470612
Tofacitinib 10 mg BID
(N = 769)
Tofacitinib 5 mg BID
(N = 175)


B
Phase 2 Induction
NCT00787202
Tofacitinib 10 mg BID
(N = 33)
Phase 3 OCTAVE
Induction 1 and 2
NCT01465763; NCT01458951
(8 weeks*)
Tofacitinib 10 mg BID
(N = 905)
Non-responders†
8 weeks of
tofacitinib 10 mg BID
(N = 295)
Month 2
(Induction Week 16)
assessment
Phase 3 OCTAVE Open‡
NCT01470612
Delayed responders†
(N = 148)
Continue
tofacitinib 10 mg BID
Complete non-responders†
(N = 105)
Discontinue as
per protocol

SUPPLEMENTARY FIGURE 2. Evaluation of CRP at Week 4 of the Phase 2 study in patients receiving tofacitinib 10 mg BID (N = 28), stratified by whether patients achieved clinical and endoscopic outcomes at induction Week 8 (full analysis set, observed case analysis).

BID, twice daily; CRP, C-reactive protein; N, number of patients with non-missing data in each category; SD, standard deviation.



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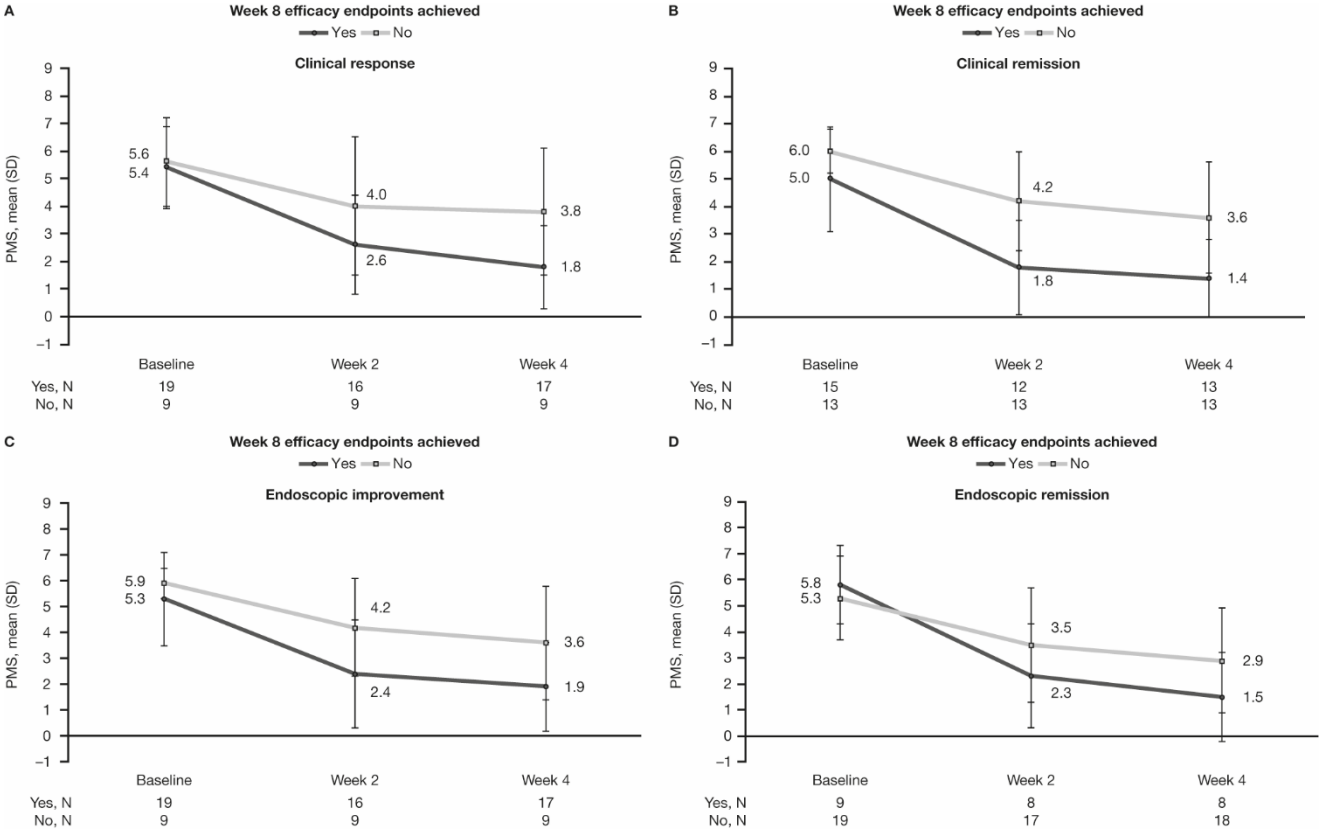

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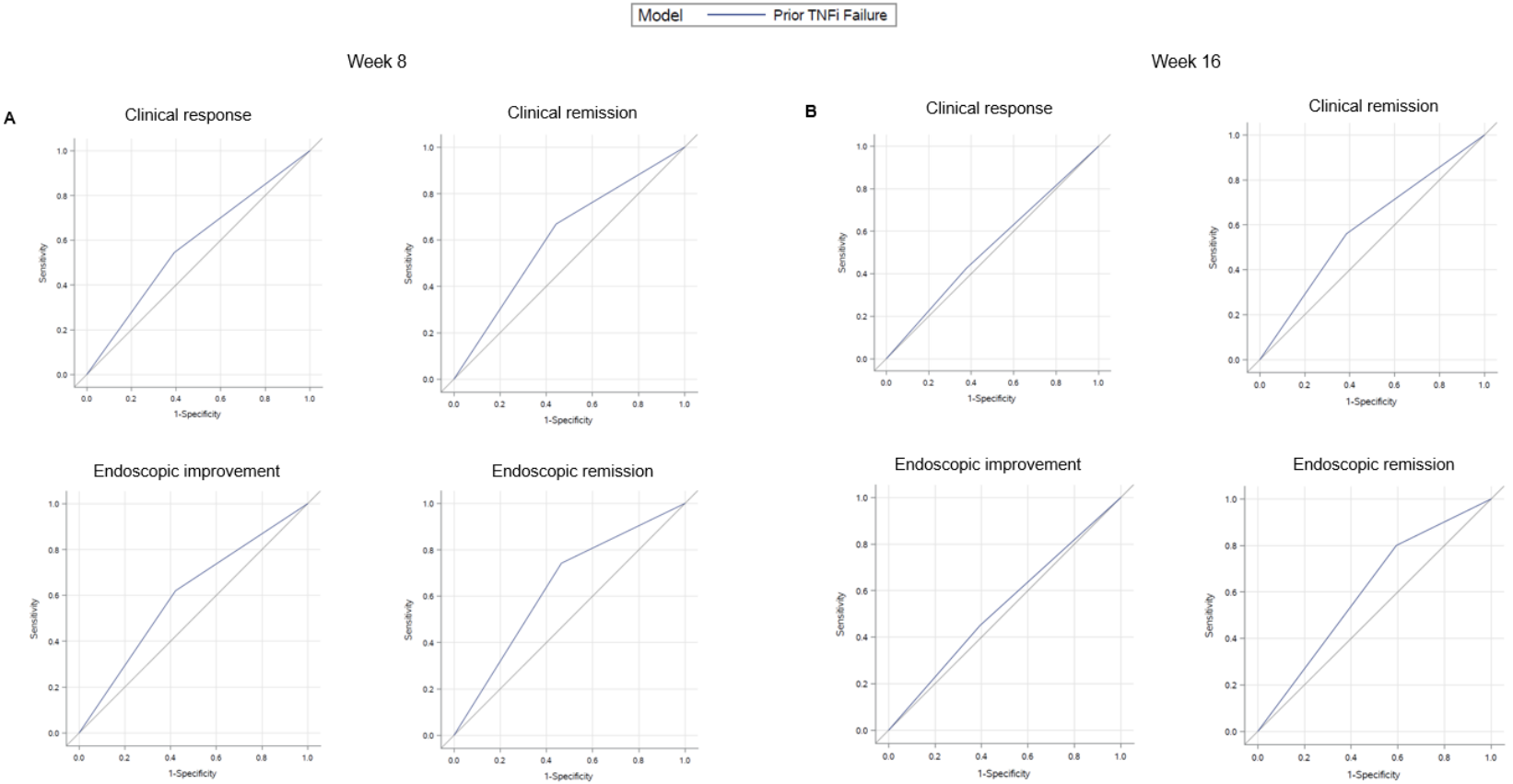

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