Οι 5 καλύτερες δημοσιεύσεις κλινικής έρευνας την χρονιά που πέρασε

Μ. ΜΥΛΩΝΑΚΗ

Γαστρεντερολόγος

Τ. Επιμελήτρια Α'

Γενικό Νοσοκομείο Νίκαιας Πειραιάς

Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease

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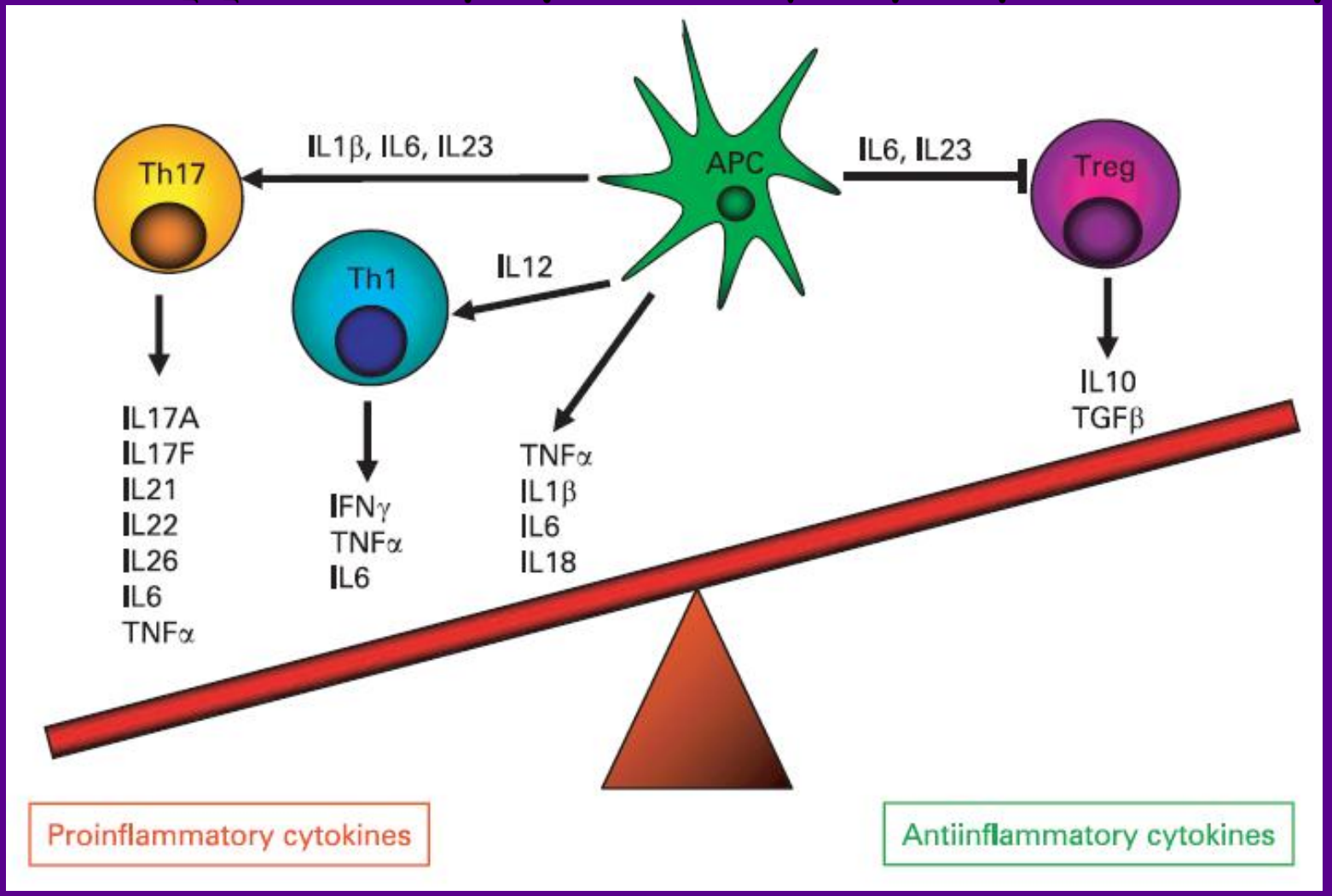
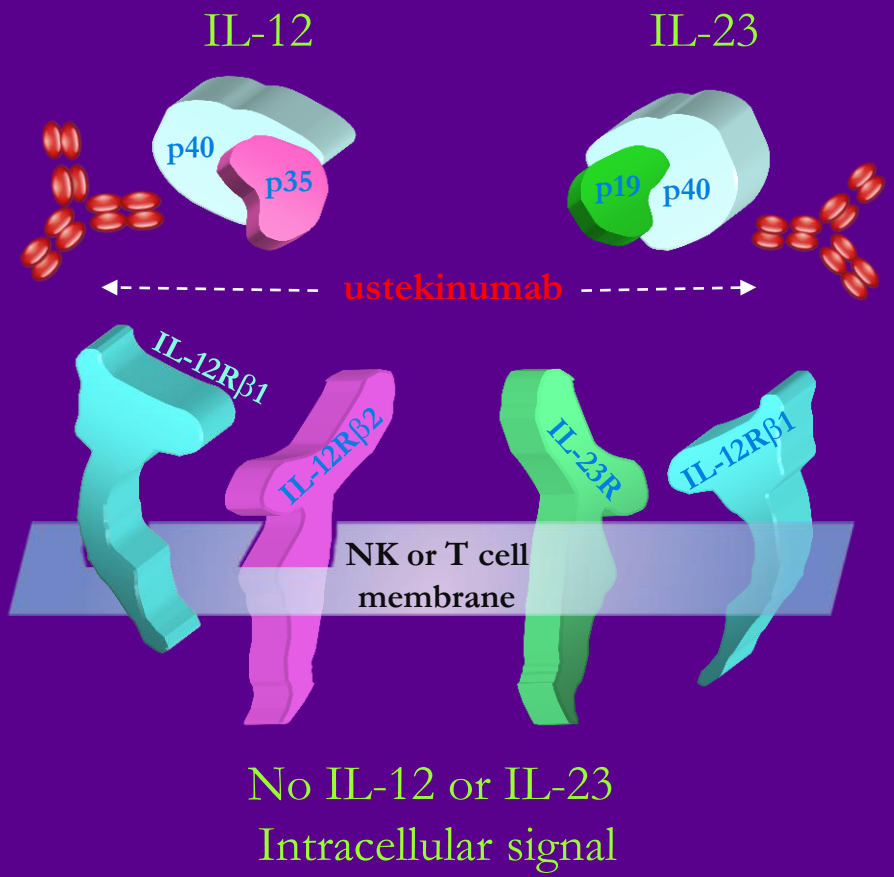
N Engl J Med 2016; 375(20):1946-1960

Παθογένεια των ΙΦΝΕ:
Ανισορροπία της φυσιολογικής ομοιόστασης



Brand S Gut 2009;58:1152-67.

Ustekinumab: Μηχανισμός δράσης



- IL-12 & IL-23 are key cytokines in the pathogenic immune cascade of Crohn's disease
- Ustekinumab is a fully human IgG1k monoclonal antibody binding the p40 subunit of Interleukins-12 & 23
- Inhibits IL-12- and IL-23-mediated signaling, cellular activation, and downstream cytokine production

Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease

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ABSTRACT

BACKGROUND
Ustekinumab, a monoclonal antibody to the p40 subunit of interleukin-12 and interleukin-23, was evaluated as an intravenous induction therapy in two populations with moderately to severely active Crohn's disease. Ustekinumab was also evaluated as subcutaneous maintenance therapy.

METHODS
We randomly assigned patients to receive a single intravenous dose of ustekinumab (either 130 mg or approximately 6 mg per kilogram of body weight) or placebo in two induction trials. The UNITI-1 trial included 741 patients who met the criteria for primary or secondary nonresponse to tumor necrosis factor (TNF) antagonists or had unacceptable side effects. The UNITI-2 trial included 628 patients in whom conventional therapy failed or unacceptable side effects occurred. Patients who completed these induction trials then participated in IM-UNITI, in which the 397 patients who had a response to ustekinumab were randomly assigned to receive subcutaneous maintenance injections of 90 mg of ustekinumab (either every 8 weeks or every 12 weeks) or placebo. The primary end point for the induction trials was a clinical response at week 6 (defined as a decrease from baseline in the Crohn's Disease Activity Index [CDAI] score of ≥100 points or a CDAI score <150). The primary end point for the maintenance trial was remission at week 44 (CDAI score <150).

RESULTS
The rates of response at week 6 among patients receiving intravenous ustekinumab at a dose of either 130 mg or approximately 6 mg per kilogram were significantly higher than the rates among patients receiving placebo (in UNITI-1, 34.3%, 33.7%, and 21.5%, respectively, with $P \leq 0.003$ for both comparisons with placebo; in UNITI-2, 51.7%, 55.5%, and 28.7%, respectively, with $P < 0.001$ for both doses). In the groups receiving maintenance doses of ustekinumab every 8 weeks or every 12 weeks, 53.1% and 48.8%, respectively, were in remission at week 44, as compared with 35.9% of those receiving placebo ($P = 0.005$ and $P = 0.04$, respectively). Within each trial, adverse-event rates were similar among treatment groups.

CONCLUSIONS
Among patients with moderately to severely active Crohn's disease, those receiving intravenous ustekinumab had a significantly higher rate of response than did those receiving placebo. Subcutaneous ustekinumab maintained remission in patients who had a clinical response to induction therapy. (Funded by Janssen Research and Development; ClinicalTrials.gov numbers, NCT01369329, NCT01369342, and NCT01369355.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Feagan at Robarts Clinical Trials, Robarts Research Institute, Western University, 100 Perth Dr., London, ON N6A 5K8, Canada, or at brian.feagan@robartsinc.com; or to Dr. Sandborn at the Division of Gastroenterology, University of California, San Diego, 9500 Gilman Dr., La Jolla, CA 92093-0956, or at wsandborn@ucsd.edu.

*A complete list of the investigators in UNITI-1, UNITI-2, and IM-UNITI is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Feagan and Sandborn contributed equally to this article.

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Περιλαμβάνει

3 μελέτες φάσης 3 με **1409 ασθενείς** με μέτρια-σοβαρά ενεργή νόσο του Crohn

- Δύο μελέτες 8 εβδομάδων ενδοφλέβιας επαγωγής (UNITI-1 και UNITI-2)
  - ✓ UNITI-1: ασθενείς με αποτυχία ή δυσανεξία σε προηγούμενη θεραπεία με αντι-TNFα
  - ✓ UNITI-2: ασθενείς με αποτυχία σε τουλάχιστον μία συμβατική θεραπεία, συμπεριλαμβανομένων των κορτικοστεροειδών ή των ανοσορρυθμιστικών παραγόντων, και είτε δεν είχαν λάβει στο παρελθόν αντι-TNFα , είτε είχαν λάβει στο παρελθόν θεραπεία με αντι-TNFα αλλά δεν απέτυχε
- Μια μελέτη 44 εβδομάδων υποδόριας τυχαιοποιημένης θεραπείας συντήρησης (IM-UNITI)

N Engl J Med 2016; 375(20):1946-1960

Baseline Characteristics of the Study Population.

Table 1. Baseline Characteristics of the Study Population.*

Characteristic	UNITI-1			UNITI-2			IM-UNITI		
	Placebo	Ustekinumab		Placebo	Ustekinumab		Placebo	Ustekinumab	
	(N=247)	130 mg (N=245)	6 mg/kg† (N=249)	(N=210)	130 mg (N=209)	6 mg/kg† (N=209)	(N=133)	90 mg/12 wk (N=132)	90 mg/8 wk (N=132)
Male sex — no. (%)	118 (47.8)	98 (40.0)	101 (40.6)	99 (47.1)	104 (49.8)	90 (43.1)	59 (44.4)	56 (42.4)	58 (43.9)
Age — yr	37.3±11.8	37.4±11.8	37.3±12.5	40.2±13.1	39.1±13.8	38.4±13.1	39.5±12.7	37.9±13.2	38.6±13.7
Weight — kg	71.5±17.7	68.4±17.4	69.5±19.5	74.0±19.9	74.4±21.3	71.9±18.8	72.3±17.3	70.6±16.9	70.0±19.6
Duration of disease — yr‡	12.1±8.4	11.8±8.3	12.7±9.2	10.4±9.8	8.7±8.5	8.7±8.4	10.6±9.5	10.3±8.7	9.5±8.7
CDAI§	319.0±59.7	321.0±64.7	327.6±62.0	302.2±61.7	304.1±57.0	302.2±58.9	319.1±60.8	320.4±66.7	313.1±58.0
Median C-reactive protein — mg/liter	8.5	10.4	9.9	8.5	7.4	7.8	9.6	8.8	9.1
Median fecal calprotectin — mg/kg	515.8	399.9	530.2	415.5	519.6	523.2	587.4	536.5	567.5
GI areas involved — no. (%)									
Total	246	245	249	210	208	209	133	132	132
Ileum only	28 (11.4)	38 (15.5)	37 (14.9)	44 (21.0)	53 (25.5)	49 (23.4)	19 (14.3)	26 (19.7)	19 (14.4)
Colon only	48 (19.5)	36 (14.7)	40 (16.1)	37 (17.6)	44 (21.2)	43 (20.6)	28 (21.1)	23 (17.4)	29 (22.0)
Ileum and colon	166 (67.5)	171 (69.8)	171 (68.7)	129 (61.4)	109 (52.4)	117 (56.0)	86 (64.7)	83 (62.9)	84 (63.6)
Proximal GI tract	45 (18.3)	57 (23.3)	54 (21.7)	32 (15.2)	34 (16.3)	29 (13.9)	28 (21.1)	18 (13.6)	19 (14.4)
Perianal GI tract	107 (43.5)	107 (43.7)	107 (43.0)	57 (27.1)	60 (28.8)	61 (29.2)	43 (32.3)	39 (29.5)	46 (34.8)
Medications for Crohn's disease taken at baseline — no. (%)									
One or more medications	185 (74.9)	178 (72.7)	174 (69.9)	158 (75.2)	161 (77.0)	170 (81.3)	101 (75.9)	106 (80.3)	108 (81.8)
Immunosuppressant¶	81 (32.8)	74 (30.2)	78 (31.3)	73 (34.8)	74 (35.4)	72 (34.4)	47 (35.3)	52 (39.4)	44 (33.3)
Aminosalicylate	54 (21.9)	50 (20.4)	50 (20.1)	89 (42.4)	89 (42.6)	93 (44.5)	46 (34.6)	47 (35.6)	49 (37.1)
Glucocorticoid‖	111 (44.9)	121 (49.4)	108 (43.4)	75 (35.7)	80 (38.3)	92 (44.0)	59 (44.4)	58 (43.9)	64 (48.5)
History of disease refractory to treatment with TNF antagonist — no. (%)	246 (99.6)	243 (99.2)	246 (98.8)	NA	NA	NA	61 (45.9)	59 (44.7)	58 (43.9)
No history of TNF antagonist treatment — no. (%)	NA	NA	NA	131 (62.4)	152 (72.7)	144 (68.9)	52 (39.1)	53 (40.2)	52 (39.4)
History of TNF antagonist treatment failure — no. (%)**									
Patients who received 1 drug	112 (45.3)	124 (50.6)	120 (48.2)	NA	NA	NA	NA	NA	NA
Patients who received 2 or 3 drugs	134 (54.3)	119 (48.6)	126 (50.6)	NA	NA	NA	NA	NA	NA
Primary nonresponse	74 (30.0)	70 (28.6)	72 (28.9)	NA	NA	NA	NA	NA	NA
Secondary nonresponse	170 (68.8)	173 (70.6)	171 (68.7)	NA	NA	NA	NA	NA	NA
Unacceptable side effects	87 (35.2)	78 (31.8)	105 (42.2)	NA	NA	NA	NA	NA	NA

* Plus–minus values are means ±SD. There were no significant differences among the treatment groups in the three trials. GI denotes gastrointestinal, NA not applicable, and TNF tumor necrosis factor.
† Weight-range–based doses of ustekinumab approximate 6 mg per kilogram of body weight (with 260 mg prescribed for patients weighing ≤55 kg, 390 mg for patients weighing >55 kg and ≤85 kg, and 520 mg prescribed for patients weighing >85 kg).
‡ In UNITI-1, data on duration of disease were available for 246 patients in the placebo group.
§ The Crohn's Disease Activity Index (CDAI) consists of eight factors, with each factor totaled after adjustment with a weighting factor ranging from 1 to 30. CDAI scores range from approximately 0 to 600, with higher scores indicating more severe disease activity.
¶ The immunosuppressants included azathioprine, mercaptopurine, and methotrexate.
‖ The glucocorticoids included budesonide.
** Patients may have reported more than one reason for treatment failure. Primary nonresponse refers to the absence of an initial response. Secondary nonresponse refers to an initial response that was not maintained.

Feagan BG et al. N Engl J Med 2016;375:1946-1960

Σχεδιασμός μελέτης

Δύο μελέτες θεραπείας εφόδου

Μία μελέτη θεραπείας συντήρησης

UNITI-1: *Πληθυσμός με αποτυχία σε ανταγωνιστές του* TNF

- **UST ~ 6 mg/kg † IV** (n=225)*
- **UST 130 mg IV** (n=225)*
- **PBO IV** (n=225)*

UNITI-2: Πληθυσμός με αποτυχία σε συμβατική θεραπεία

- **UST ~ 6 mg/kg IV** (n=200)
- **UST 130 mg IV**(n=200)
- **PBO IV** (n=200)

R

Ανταποκρινόμενοι την Εβδ. 8

IM-UNITI

Τυχαιοποιημένη μελέτη απόσυρσης της θεραπείας συντήρησης

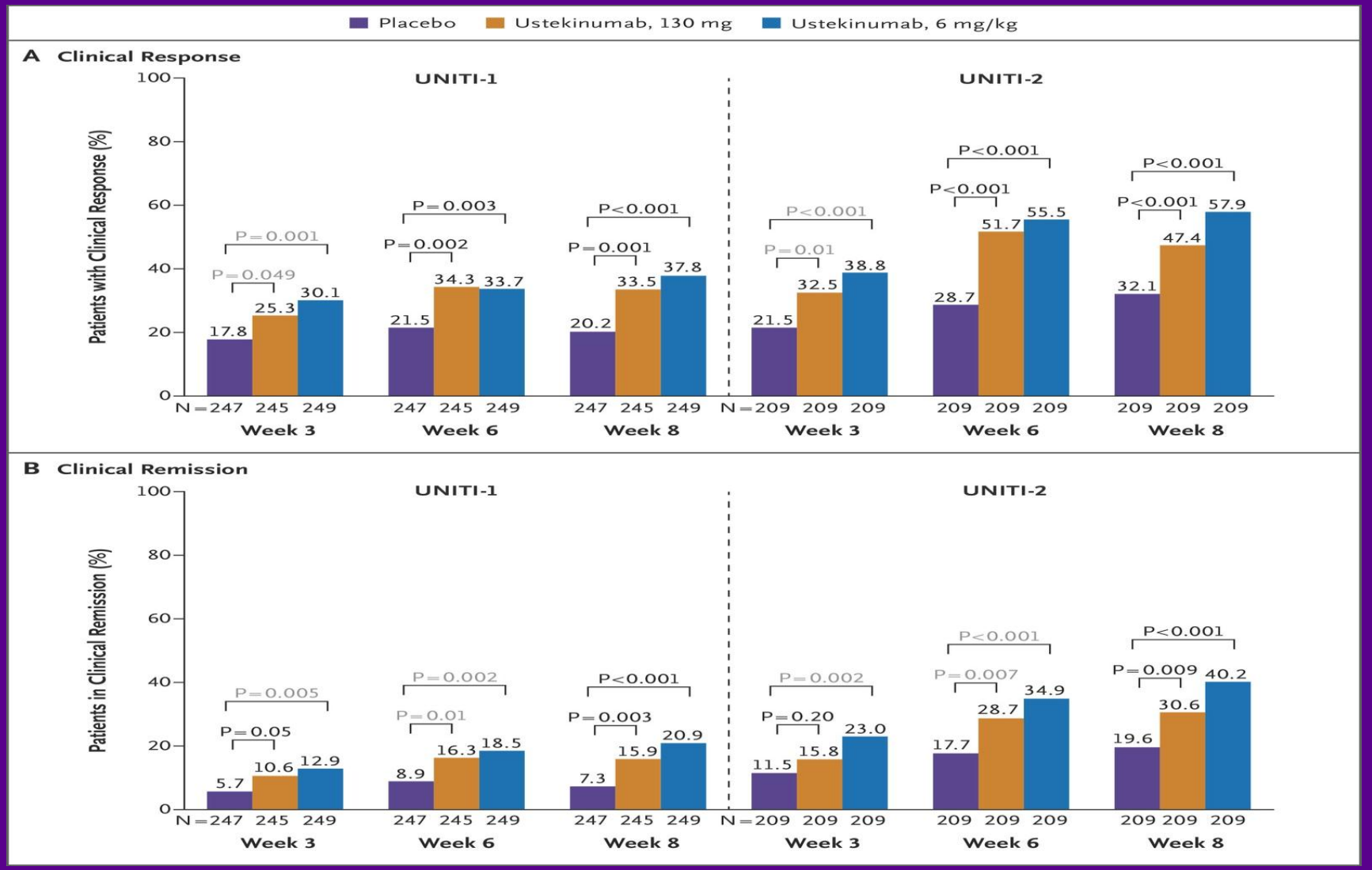
R

- UST 90 mg SC q8w
- UST 90 mg SC q12w
- PBO SC

Μελέτη συντήρησης 44 εβδομάδων

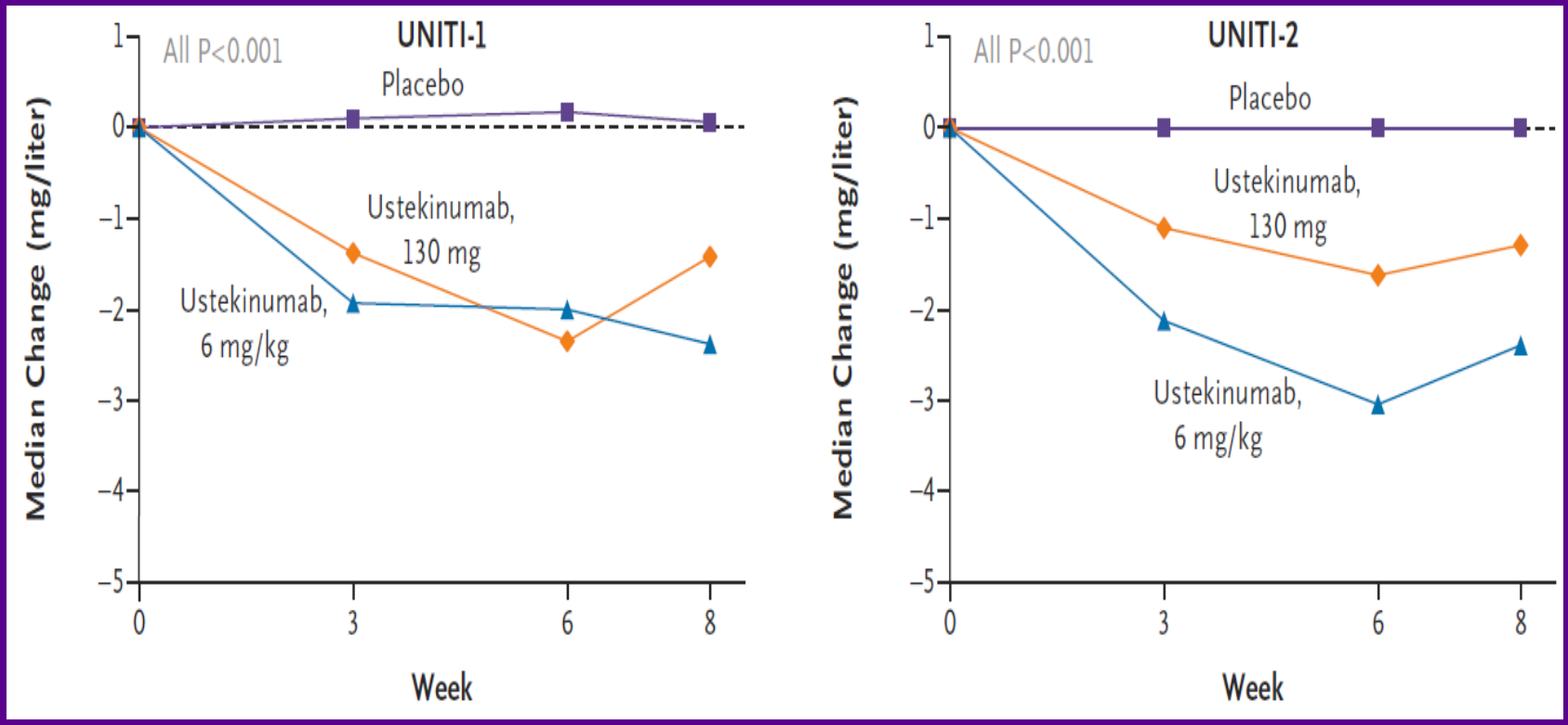
Feagan BG. et al. N Engl J Med 2016 Nov 17;375(20):1946-1960

USTEKINUMAB: ΑΝΤΑΠΟΚΡΙΣΗ - ΥΦΕΣΗ



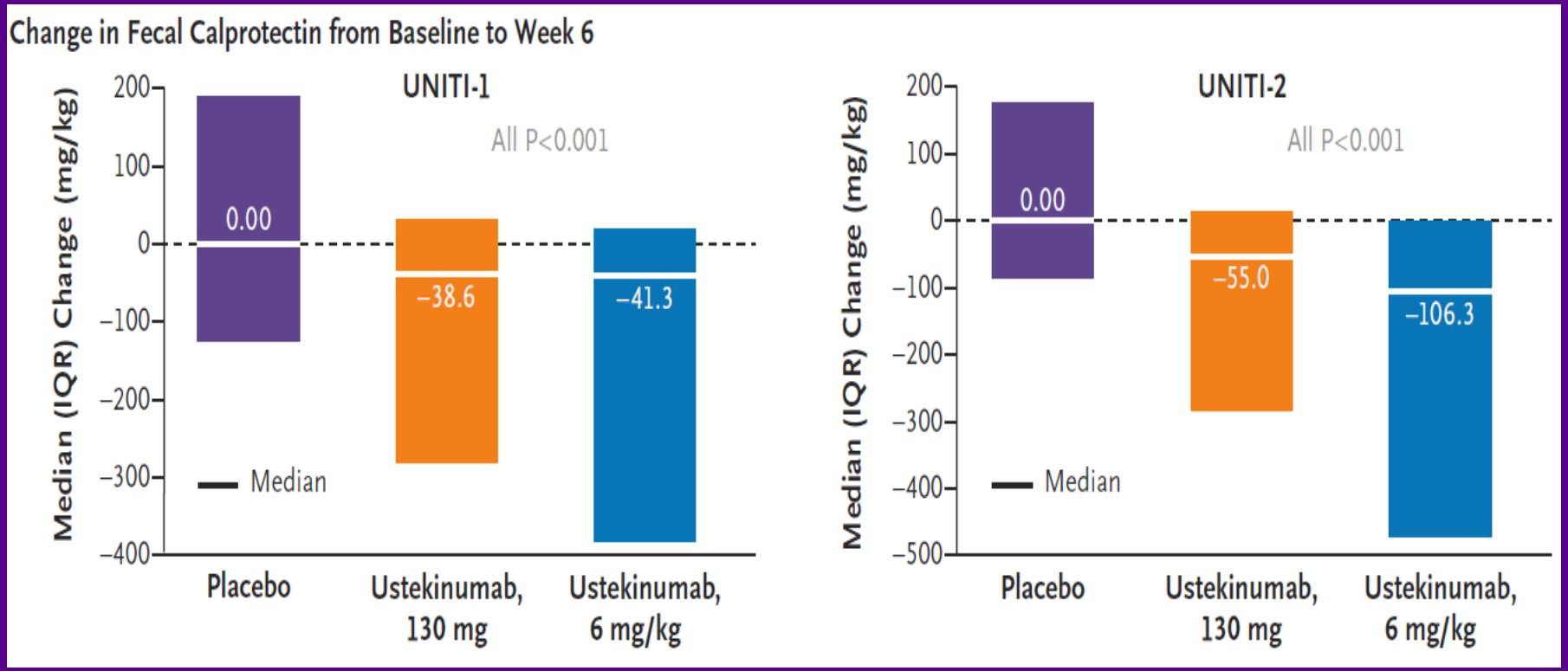
Feagan BG et al. N Engl J Med 2016;375:1946-1960

Ustekinumab: κλινική ανταπόκριση και πτώση της CRP



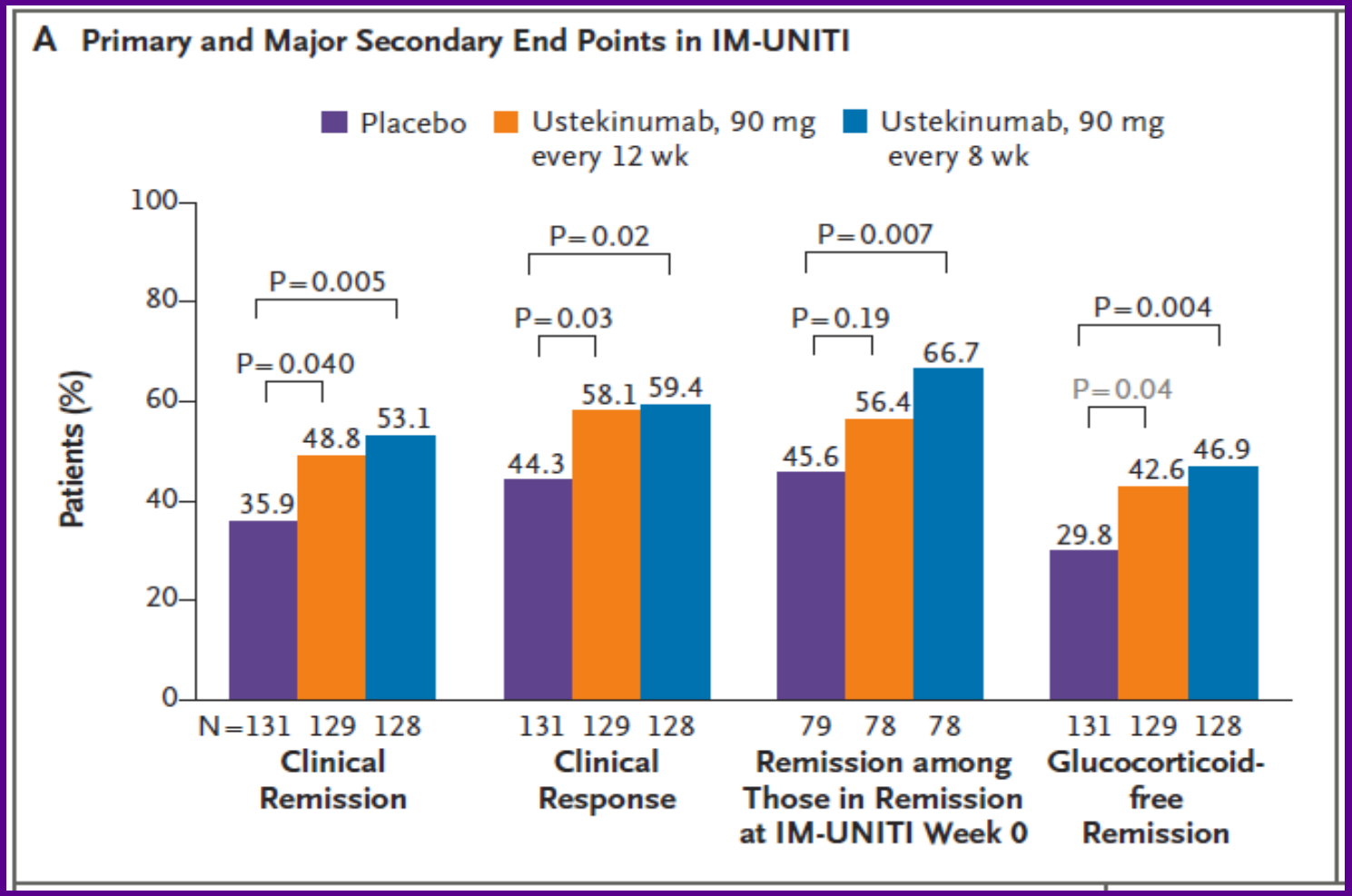
Feagan BG et al. NEJM 2016;375:1946-60

Ustekinumab: κλινική ανταπόκριση και πτώση της καλπροτεκτίνης των κοπράνων



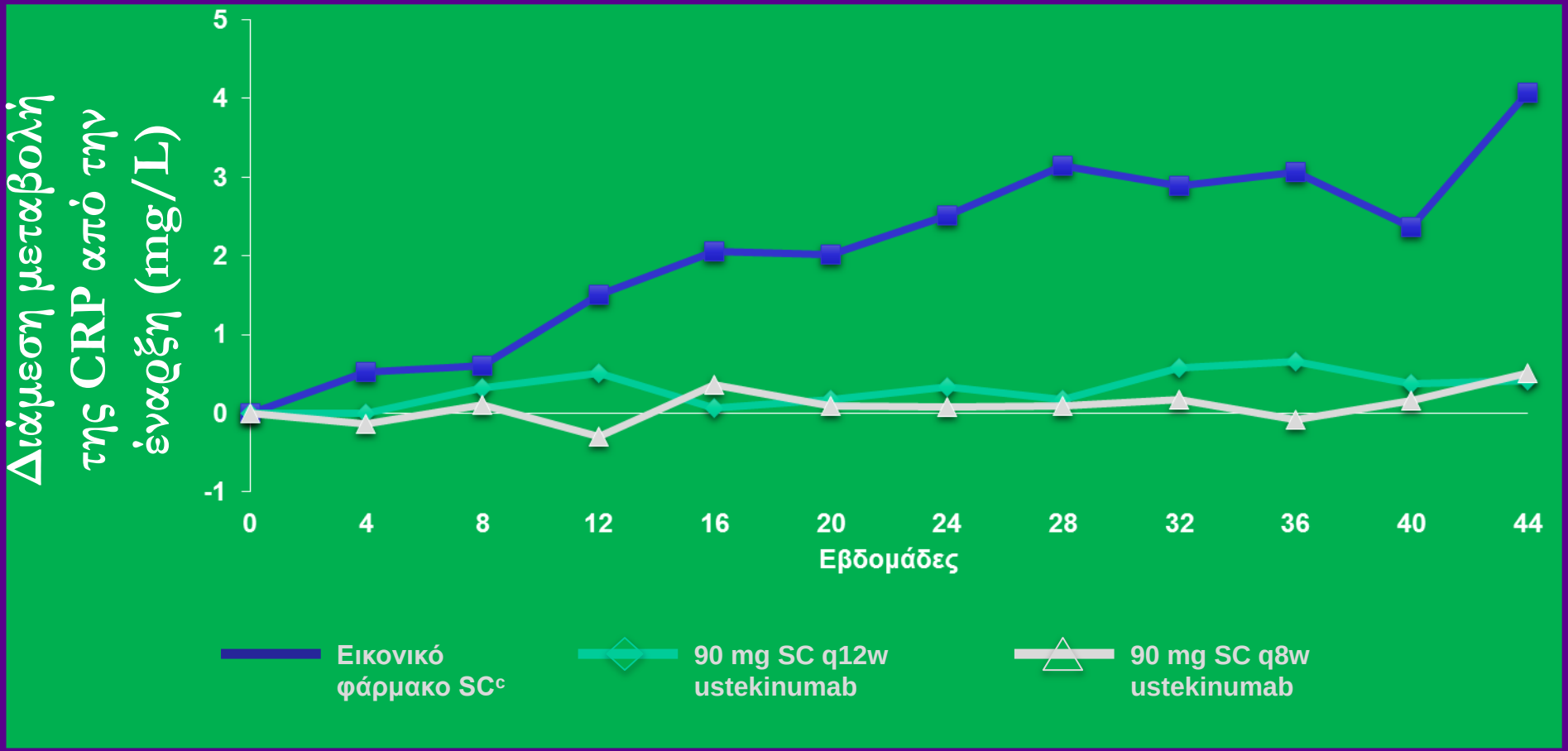
Feagan BG et al. NEJM 2016;375:1946-60

Ustekinumab: Διατήρηση της ύφεσης



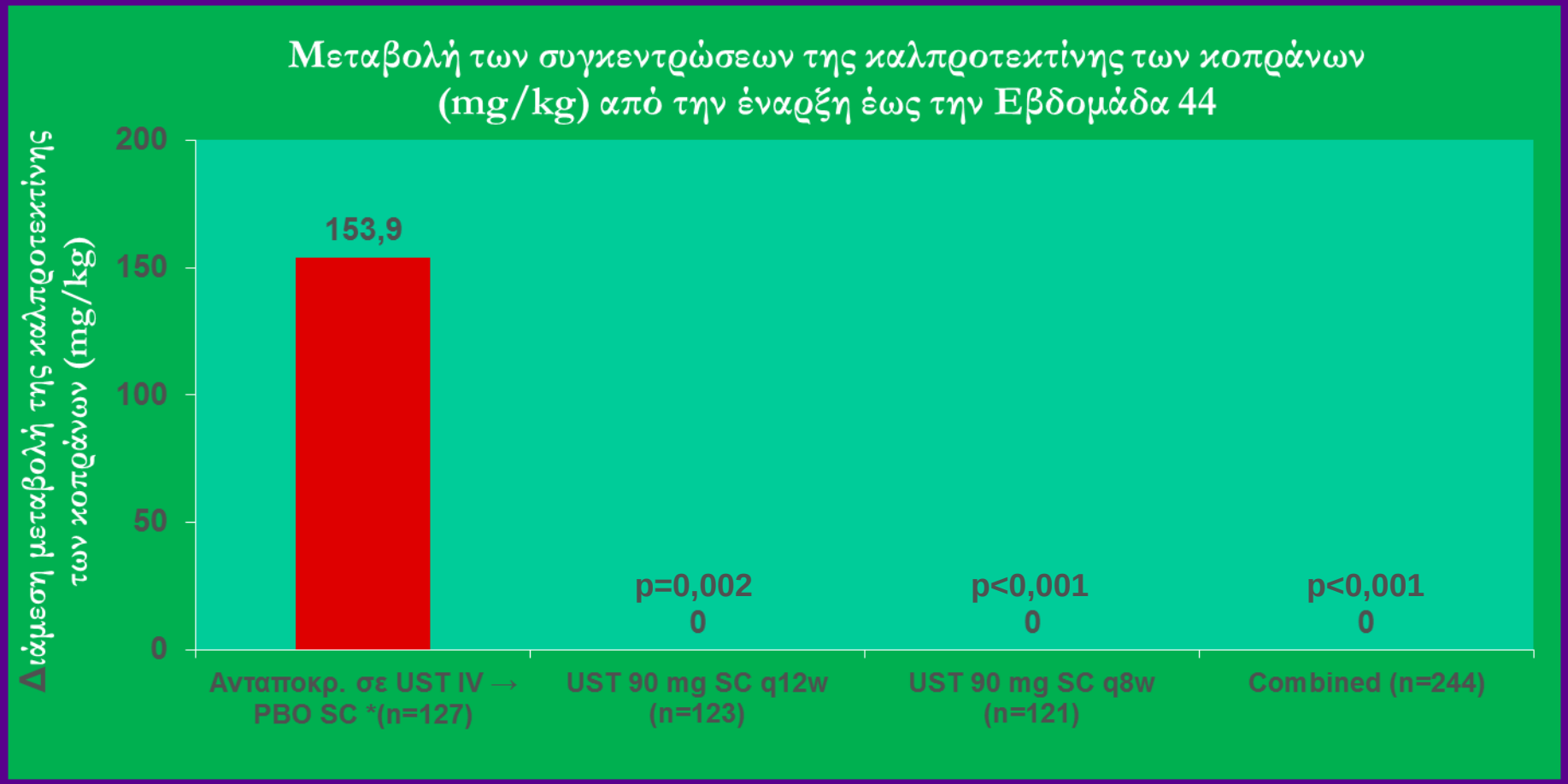
Feagan BG et al. NEJM 2016;375:1946-60

Μεταβολή της συγκέντρωσης της CRP



Sandborn W.J., et al. DDW 2016. Presentation 768.

Μεταβολή της καλπροτεκτίνης των κοπράνων



Adverse Events through Week 8 in UNITI-1 and UNITI-2 and through Week 44 in IM-UNITI.

Table 2. Adverse Events through Week 8 in UNITI-1 and UNITI-2 and through Week 44 in IM-UNITI.

Event	UNITI-1			UNITI-2			IM-UNITI		
	Placebo	Ustekinumab		Placebo	Ustekinumab		Placebo	Ustekinumab	
	(N=245)	130 mg (N=246)	6 mg/kg (N=249)	(N=208)	130 mg (N=212)	6 mg/kg (N=207)	(N=133)	90 mg/12 wk (N=132)	90 mg/8 wk (N=131)
	number (percent)								
Any adverse event	159 (64.9)	159 (64.6)	164 (65.9)	113 (54.3)	106 (50.0)	115 (55.6)	111 (83.5)	106 (80.3)	107 (81.7)
Common adverse events*									
Arthralgia	18 (7.3)	26 (10.6)	15 (6.0)	4 (1.9)	8 (3.8)	9 (4.3)	19 (14.3)	22 (16.7)	18 (13.7)
Headache	22 (9.0)	20 (8.1)	20 (8.0)	14 (6.7)	20 (9.4)	10 (4.8)	15 (11.3)	15 (11.4)	16 (12.2)
Nausea	18 (7.3)	20 (8.1)	13 (5.2)	5 (2.4)	7 (3.3)	11 (5.3)	9 (6.8)	10 (7.6)	4 (3.1)
Pyrexia	15 (6.1)	14 (5.7)	15 (6.0)	10 (4.8)	6 (2.8)	11 (5.3)	10 (7.5)	11 (8.3)	8 (6.1)
Nasopharyngitis	13 (5.3)	12 (4.9)	11 (4.4)	10 (4.8)	10 (4.7)	14 (6.8)	10 (7.5)	17 (12.9)	14 (10.7)
Abdominal pain	13 (5.3)	9 (3.7)	13 (5.2)	7 (3.4)	5 (2.4)	10 (4.8)	16 (12.0)	13 (9.8)	11 (8.4)
Crohn's disease event	24 (9.8)	13 (5.3)	6 (2.4)	10 (4.8)	8 (3.8)	7 (3.4)	19 (14.3)	16 (12.1)	16 (12.2)
Fatigue	13 (5.3)	6 (2.4)	9 (3.6)	4 (1.9)	3 (1.4)	4 (1.9)	6 (4.5)	8 (6.1)	6 (4.6)
Infections†									
Any	58 (23.7)	57 (23.2)	64 (25.7)	48 (23.1)	31 (14.6)	45 (21.7)	66 (49.6)	61 (46.2)	63 (48.1)
Serious	3 (1.2)	3 (1.2)	7 (2.8)	3 (1.4)	3 (1.4)	1 (0.5)	3 (2.3)	7 (5.3)	3 (2.3)
Serious adverse events	15 (6.1)	12 (4.9)	18 (7.2)	12 (5.8)	10 (4.7)	6 (2.9)	20 (15.0)	16 (12.1)	13 (9.9)
Adverse events associated with infusion or injection-site reactions‡	5 (2.0)	11 (4.5)	9 (3.6)	6 (2.9)	5 (2.4)	3 (1.4)	1 (0.8)	3 (2.3)	9 (6.9)

* The listed adverse events were reported by at least 5% of the patients in any group.
† Infections were assessed by the investigator.
‡ Adverse events associated with infusions in UNITI-1 and UNITI-2 refer to events that occurred within 1 hour after infusion. Adverse events summarized for IM-UNITI refer to injection-site reactions.

Feagan BG et al. N Engl J Med 2016;375:1946-1960

IM-UNITI

Θεραπεία διατήρησης της ύφεσης: Ανεπιθύμητες ενέργειες

	Εικονικό φάρμακο SC*	Ustekinumab		
		90 mg SC q12w	90 mg SC q8w	Συνδυασμός
Συμμετέχοντες που έλαβαν θεραπεία και που τυχαιοποιήθηκαν (n)	133	132	131	263
Μέσος όρος διάρκειας παρακολούθησης (εβδομάδες)	32,0	36,6	35,2	35,9
Συμμετέχοντες με (%)				
Θάνατο	0%	0%	0%	0%
AE	83,5%	80,3%	81,7%	81,0%
SAE	15,0%	12,1%	9,9%	11,0%
Λοιμώξεις	49,6%	46,2%	48,1%	47,1%
Σοβαρές λοιμώξεις	2,3%	5,3%	2,3%	3,8%
Διακοπή λόγω AE	6,0%	7,6%	3,1%	5,3%
Κακοήθειες	0,8%	0%	0,8%	0%

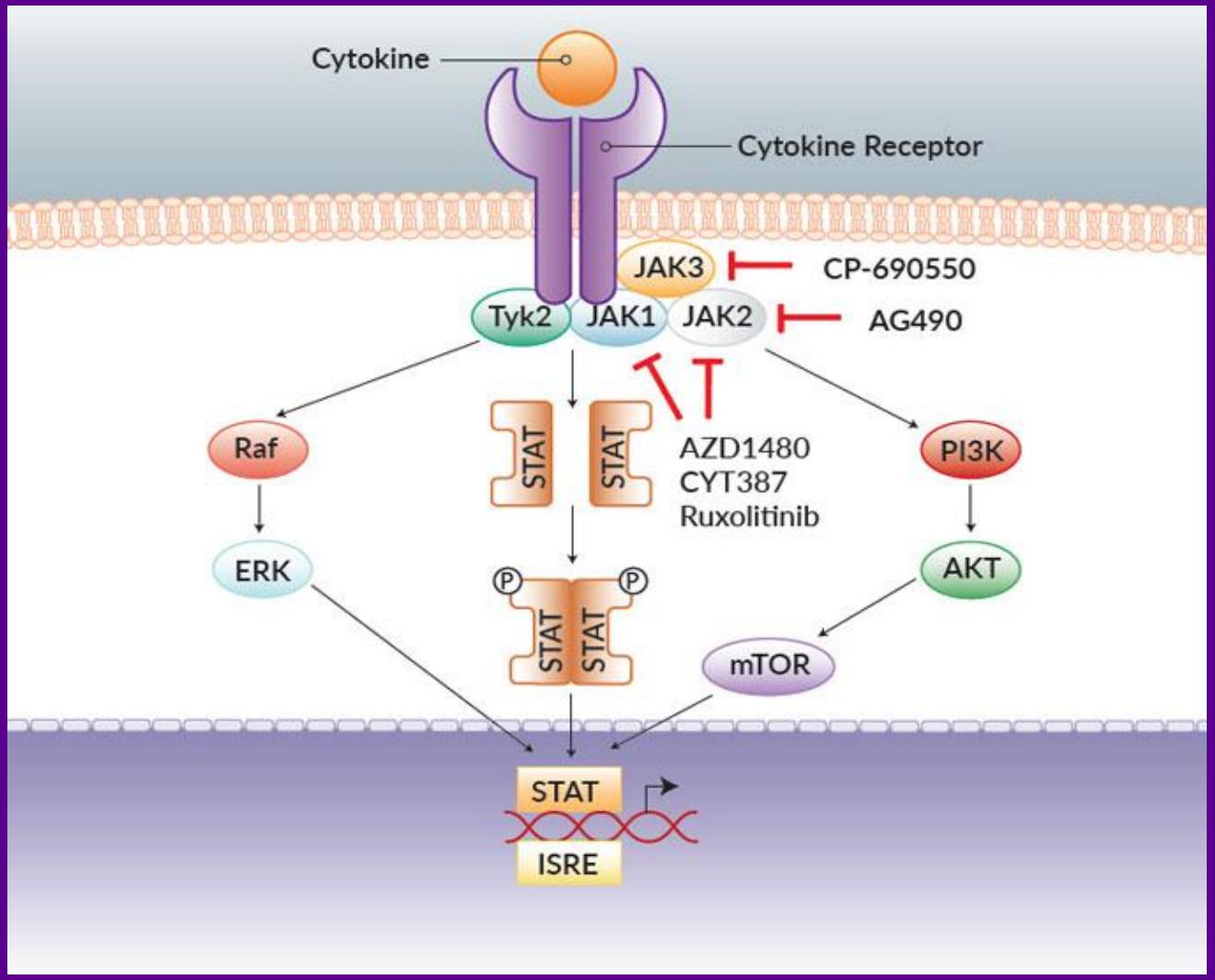
Sandborn W.J., et al. DDW 2016. Presentation 768.

Tofacitinib as Induction and Maintenance Therapy for Ulcerative Colitis

William J. Sandborn, M.D., Chinyu Su, M.D., Bruce E. Sands, M.D., Geert R. D'Haens, M.D., Séverine Vermeire, M.D., Ph.D., Stefan Schreiber, M.D., Silvio Danese, M.D., Brian G. Feagan, M.D., Walter Reinisch, M.D., Wojciech Niezychowski, M.D., Gary Friedman, M.D., Nervin Lawendy, Pharm.D., Dahong Yu, M.D., Ph.D., Deborah Woodworth, M.B.A., Arnab Mukherjee, Ph.D., Haiying Zhang, Ph.D., Paul Healey, M.D., Julian Panés, M.D., for the OCTAVE Induction 1, OCTAVE Induction 2, and OCTAVE Sustain Investigators

N Engl J Med Volume 376(18):1723-1736May 4, 2017

Tofacitinib: Μηχανισμός δράσης



Baseline Demographic and Disease Characteristics of the Patients in the OCTAVE Induction 1, OCTAVE Induction 2, and OCTAVE Sustain Trials

Table 1. Baseline Demographic and Disease Characteristics of the Patients in the OCTAVE Induction 1, OCTAVE Induction 2, and OCTAVE Sustain Trials.*

Characteristic	OCTAVE Induction 1		OCTAVE Induction 2		OCTAVE Sustain		
	Placebo (N=122)	Tofacitinib, 10 mg (N=476)	Placebo (N=112)	Tofacitinib, 10 mg (N=429)	Placebo (N=198)	Tofacitinib, 5 mg (N=198)	Tofacitinib, 10 mg (N=197)
Male sex — no. (%)†	77 (63.1)	277 (58.2)	55 (49.1)	259 (60.4)	116 (58.6)	103 (52.0)	110 (55.8)
Age — yr‡	41.8±15.3	41.3±14.1	40.4±13.2	41.1±13.5	43.4±14.0	41.9±13.7	42.9±14.4
Induction-trial group assignment — no. (%)							
Placebo	—	—	—	—	24 (12.1)	22 (11.1)	24 (12.2)
Tofacitinib, 10 mg twice daily	—	—	—	—	167 (84.3)	170 (85.9)	167 (84.8)
Tofacitinib, 15 mg twice daily	—	—	—	—	7 (3.5)	6 (3.0)	6 (3.0)
Remission at maintenance-trial entry — no. (%)	—	—	—	—	59 (29.8)	65 (32.8)	55 (27.9)
Duration of disease — yr‡							
Median	6.0	6.5	6.2	6.0	7.2	6.5	6.8
Range	0.5–36.2	0.3–42.5	0.4–27.9	0.4–39.4	0.6–42.7	0.6–40.3	0.6–35.7
Extent of disease — no./total no. (%)§¶							
Proctosigmoiditis	19/122 (15.6)	65/475 (13.7)	16/111 (14.4)	67/428 (15.7)	21/198 (10.6)	28/196 (14.3)	33/196 (16.8)
Left-sided colitis	37/122 (30.3)	158/475 (33.3)	39/111 (35.1)	149/428 (34.8)	68/198 (34.3)	66/196 (33.7)	60/196 (30.6)
Extensive colitis or pancolitis	66/122 (54.1)	252/475 (53.1)	56/111 (50.5)	211/428 (49.3)	108/198 (54.5)	102/196 (52.0)	103/196 (52.6)
Total Mayo score‡‖	9.1±1.4	9.0±1.4	8.9±1.5	9.0±1.5	3.3±1.8	3.3±1.8	3.4±1.8
Partial Mayo score‡‖	6.5±1.2	6.3±1.2	6.4±1.2	6.4±1.3	1.8±1.4	1.8±1.3	1.8±1.3
C-reactive protein — mg/liter‡							
Median	4.7	4.4	5.0	4.6	1.0	0.7	0.9
Range	0.1–82.5	0.1–208.4	0.2–205.1	0.2–156.0	0.1–45.0	0.1–33.7	0.1–74.3
Oral glucocorticoid use at baseline — no. (%)‡	58 (47.5)	214 (45.0)	55 (49.1)	198 (46.2)	100 (50.5)	101 (51.0)	87 (44.2)
Previous treatment with TNF antagonist — no. (%)§	65 (53.3)	254 (53.4)	65 (58.0)	234 (54.5)	92 (46.5)	90 (45.5)	101 (51.3)
Previous treatment failure — no. (%)§**							
TNF antagonist	64 (52.5)	243 (51.1)	60 (53.6)	222 (51.7)	89 (44.9)	83 (41.9)	93 (47.2)
Glucocorticoid	98 (80.3)	350 (73.5)	83 (74.1)	303 (70.6)	151 (76.3)	145 (73.2)	149 (75.6)
Immunosuppressant††	83 (68.0)	360 (75.6)	75 (67.0)	301 (70.2)	129 (65.2)	143 (72.2)	141 (71.6)

* Plus–minus values are means ±SD. There were no significant differences between groups within each trial unless otherwise noted. TNF denotes tumor necrosis factor.
† In the OCTAVE Induction 2 trial, there was a significant difference between groups in the proportion of male patients (P=0.03).
‡ For the OCTAVE Sustain trial, the baseline values were obtained at the time of entry in the OCTAVE Sustain trial.
§ For the OCTAVE Sustain trial, the baseline values were obtained at the time of entry into one of the induction trials (OCTAVE Induction 1 or 2).
¶ Data on extent of disease are missing for three patients.
‖ The total Mayo score ranges from 0 to 12 and the partial Mayo score (i.e., the total Mayo score excluding the endoscopic subscore) ranges from 0 to 9, with higher scores indicating more severe disease.
** Previous treatment failure was determined by the investigator.
†† Immunosuppressants included agents such as azathioprine and mercaptopurine and did not include biologic agents (e.g., TNF antagonists) or glucocorticocoids.

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Efficacy Outcomes in the OCTAVE Induction 1 and OCTAVE Induction 2 Trials.

Table 2. Efficacy Outcomes in the OCTAVE Induction 1 and OCTAVE Induction 2 Trials.*

End Point	OCTAVE Induction 1				OCTAVE Induction 2			
	Placebo (N=122)	Tofacitinib, 10 mg (N=476)	Difference (95% CI)	P Value	Placebo (N=112)	Tofacitinib, 10 mg (N=429)	Difference (95% CI)	P Value
			percentage points				*percentage points*	
Based on Mayo score†								
Primary end point: remission at wk 8 — no. (%)	10 (8.2)	88 (18.5)	10.3 (4.3 to 16.3)	0.007	4 (3.6)	71 (16.6)	13.0 (8.1 to 17.9)	<0.001
Mucosal healing at wk 8 — no. (%)	19 (15.6)	149 (31.3)	15.7 (8.1 to 23.4)	<0.001	13 (11.6)	122 (28.4)	16.8 (9.5 to 24.1)	<0.001
Clinical response at wk 8 — no. (%)	40 (32.8)	285 (59.9)	27.1 (17.7 to 36.5)	<0.001	32 (28.6)	236 (55.0)	26.4 (16.8 to 36.0)	<0.001
Clinical remission at wk 8 — no. (%)	10 (8.2)	88 (18.5)	10.3 (4.3 to 16.3)	0.007	4 (3.6)	72 (16.8)	13.2 (8.3 to 18.1)	<0.001
Endoscopic remission at wk 8 — no. (%)	2 (1.6)	32 (6.7)	5.1 (1.9 to 8.3)	0.04	2 (1.8)	30 (7.0)	5.2 (1.8 to 8.6)	0.04
Symptomatic remission at wk 8 — no. (%)	7 (5.7)	56 (11.8)	6.0 (1.0 to 11.1)	0.06	3 (2.7)	46 (10.7)	8.0 (3.9 to 12.2)	0.009
Deep remission at wk 8 — no. (%)	0	31 (6.5)	6.5 (4.3 to 8.7)	0.004	2 (1.8)	22 (5.1)	3.3 (0.1 to 6.6)	0.14
Change from baseline in total Mayo score at wk 8	−1.8±0.3	−3.8±0.1	−1.9 (−2.5 to −1.4)	<0.001	−2.1±0.3	−3.7±0.1	−1.6 (−2.2 to −1.0)	<0.001
Based on IBDQ score‡								
Remission at wk 4 — no. (%)	27 (22.1)	167 (35.1)	13.0 (4.4 to 21.5)	0.008	9 (8.0)	124 (28.9)	20.9 (14.3 to 27.5)	<0.001
Remission at wk 8 — no. (%)	32 (26.2)	206 (43.3)	17.0 (8.1 to 26.0)	<0.001	20 (17.9)	173 (40.3)	22.5 (14.0 to 30.9)	<0.001
Treatment response at wk 4 — no. (%)	55 (45.1)	299 (62.8)	17.7 (7.9 to 27.6)	<0.001	44 (39.3)	266 (62.0)	22.7 (12.6 to 32.9)	<0.001
Treatment response at wk 8 — no. (%)	56 (45.9)	307 (64.5)	18.6 (8.8 to 28.4)	<0.001	54 (48.2)	288 (67.1)	18.9 (8.7 to 29.2)	<0.001

* Plus–minus values are least-squares means ±SE.

† Definitions of all efficacy end points that are based on the Mayo score are provided in Table S1 in the Supplementary Appendix. The total Mayo score ranges from 0 to 12, with higher scores indicating more severe disease.

‡ The Inflammatory Bowel Disease Questionnaire (IBDQ) score ranges from 32 to 224, with higher scores indicating better quality of life. An IBDQ score of 170 or higher is indicative of remission, and an IBDQ score at least 16 points higher than the baseline score in the induction trial is indicative of a treatment response.

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Efficacy Outcomes in the OCTAVE Sustain Trial

Table 3. Efficacy Outcomes in the OCTAVE Sustain Trial.

End Point	OCTAVE Sustain						
	Placebo (N=198)	Tofacitinib, 5 mg (N=198)	Difference vs. Placebo (95% CI)	P Value	Tofacitinib, 10 mg (N=197)	Difference vs. Placebo (95% CI)	P Value
			percentage points			*percentage points*	
Based on Mayo score*							
Primary end point: remission at wk 52 — no. (%)	22 (11.1)	68 (34.3)	23.2 (15.3–31.2)	<0.001	80 (40.6)	29.5 (21.4–37.6)	<0.001
Sustained remission — no. (%)	10 (5.1)	44 (22.2)	17.2 (10.6–23.7)	<0.001	50 (25.4)	20.3 (13.5–27.1)	<0.001
Remission at wk 52 among patients in remission at baseline — no./total no. (%)	6/59 (10.2)	30/65 (46.2)	36.0 (21.6–50.3)	<0.001	31/55 (56.4)	46.2 (31.0–61.4)	<0.001
Sustained remission among patients in remission at baseline — no./total no. (%)	3/59 (5.1)	24/65 (36.9)	31.8 (18.8–44.8)	<0.001	26/55 (47.3)	42.2 (27.9–56.5)	<0.001
Sustained and glucocorticoid-free remission among patients in remission at baseline — no./total no. (%)	3/59 (5.1)	23/65 (35.4)	30.3 (17.4–43.2)	<0.001	26/55 (47.3)	42.2 (27.9–56.5)	<0.001
Mucosal healing at wk 52 — no. (%)	26 (13.1)	74 (37.4)	24.2 (16.0–32.5)	<0.001	90 (45.7)	32.6 (24.2–41.0)	<0.001
Sustained mucosal healing — no. (%)	13 (6.6)	55 (27.8)	21.2 (14.1–28.3)	<0.001	65 (33.0)	26.4 (19.0–33.8)	<0.001
Mucosal healing at wk 52 among patients with mucosal healing at baseline — no./total no. (%)	12/101 (11.9)	44/105 (41.9)	30.0 (18.7–41.4)	<0.001	49/89 (55.1)	43.2 (31.1–55.3)	<0.001
Sustained mucosal healing among patients with mucosal healing at baseline — no./total no. (%)	9/101 (8.9)	35/105 (33.3)	24.4 (13.8–35.0)	<0.001	44/89 (49.4)	40.5 (28.7–52.3)	<0.001
Clinical response at wk 52 — no. (%)	40 (20.2)	102 (51.5)	31.3 (22.4–40.2)	<0.001	122 (61.9)	41.7 (32.9–50.5)	<0.001
Sustained clinical response — no. (%)	38 (19.2)	97 (49.0)	29.8 (20.9–38.7)	<0.001	117 (59.4)	40.2 (31.4–49.0)	<0.001
Based on IBDQ score†							
Remission at wk 52 — no. (%)	29 (14.6)	76 (38.4)	23.7 (15.4–32.1)	<0.001	95 (48.2)	33.6 (25.0–42.1)	<0.001
Treatment response at wk 52 — no. (%)	38 (19.2)	92 (46.5)	27.3 (18.4–36.1)	<0.001	106 (53.8)	34.6 (25.8–43.5)	<0.001

* Definitions for all efficacy end points that are based on the Mayo score are provided in Table S1 in the Supplementary Appendix. End points were considered to be sustained if they occurred at both 24 and 52 weeks and were considered to be glucocorticoid-free if they occurred without the administration of glucocorticoids for at least 4 weeks before the assessment. Baseline information was obtained at entry in the OCTAVE Sustain trial.

† The Inflammatory Bowel Disease Questionnaire (IBDQ) score ranges from 32 to 224, with higher scores indicating better quality of life. An IBDQ score of 170 or higher is indicative of remission, and an IBDQ score at least 16 points higher than the baseline score in the induction trial is indicative of a treatment response.

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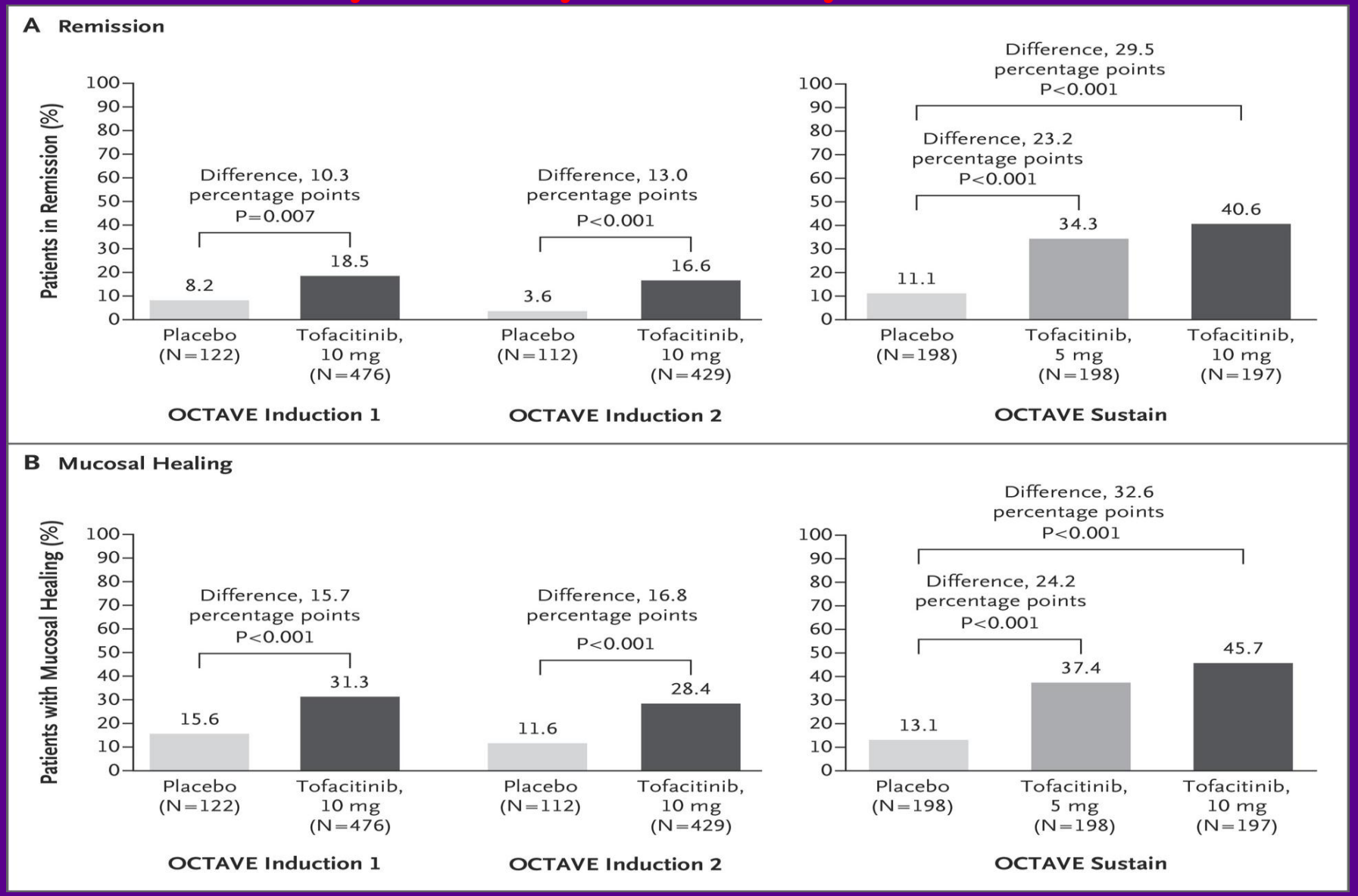
Primary and Key Secondary End Points.



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Safety Outcomes at 8 Weeks in the OCTAVE Induction 1 and 2 Trials and at 52 Weeks in the OCTAVE Sustain Trial

Table 4. Safety Outcomes at 8 Weeks in the OCTAVE Induction 1 and 2 Trials and at 52 Weeks in the OCTAVE Sustain Trial.*

End Point	OCTAVE Induction 1		OCTAVE Induction 2		OCTAVE Sustain		
	Placebo (N=122)	Tofacitinib, 10 mg (N=476)	Placebo (N=112)	Tofacitinib, 10 mg (N=429)	Placebo (N=198)	Tofacitinib, 5 mg (N=198)	Tofacitinib, 10 mg (N=196)
Adverse events — no. (%)	73 (59.8)	269 (56.5)	59 (52.7)	232 (54.1)	149 (75.3)	143 (72.2)	156 (79.6)
Serious adverse events — no. (%)	5 (4.1)	16 (3.4)	9 (8.0)	18 (4.2)	13 (6.6)	10 (5.1)	11 (5.6)
Most frequent adverse events — no. (%)†							
Worsening ulcerative colitis	5 (4.1)	11 (2.3)	6 (5.4)	13 (3.0)	71 (35.9)	36 (18.2)	29 (14.8)
Nasopharyngitis	9 (7.4)	34 (7.1)	4 (3.6)	21 (4.9)	11 (5.6)	19 (9.6)	27 (13.8)
Arthralgia	6 (4.9)	14 (2.9)	6 (5.4)	11 (2.6)	19 (9.6)	17 (8.6)	17 (8.7)
Headache	8 (6.6)	37 (7.8)	9 (8.0)	33 (7.7)	12 (6.1)	17 (8.6)	6 (3.1)
Infections — no. (%)							
Any infection	19 (15.6)	111 (23.3)	17 (15.2)	78 (18.2)	48 (24.2)	71 (35.9)	78 (39.8)
Serious infection‡	0	6 (1.3)	0	1 (0.2)	2 (1.0)	2 (1.0)	1 (0.5)
Herpes zoster	1 (0.8)	3 (0.6)	0	2 (0.5)	1 (0.5)	3 (1.5)	10 (5.1)
Adverse events of special interest — no.							
Intestinal perforation§	0	1	1	0	0	0	0
Cancer other than nonmelanoma skin cancer¶	0	0	0	0	1‖	0	0
Nonmelanoma skin cancer¶	0	1	0	1	1	0	3
Cardiovascular events¶	0	2	0	2	0	1	1
Adverse events leading to discontinuation — no. (%)**	2 (1.6)	18 (3.8)	8 (7.1)	17 (4.0)	37 (18.7)	18 (9.1)	19 (9.7)
Abnormal laboratory test results — no./total no. (%)††							
Total cholesterol >1.3× ULN	11/122 (9.0)	80/471 (17.0)	6/111 (5.4)	73/424 (17.2)	16/198 (8.1)	54/198 (27.3)	44/195 (22.6)
Low-density lipoprotein >1.2× ULN	11/122 (9.0)	91/471 (19.3)	12/111 (10.8)	92/424 (21.7)	37/198 (18.7)	62/198 (31.3)	55/195 (28.2)
High-density lipoprotein <0.8× LLN	2/122 (1.6)	6/471 (1.3)	1/111 (0.9)	7/424 (1.7)	12/198 (6.1)	9/198 (4.5)	3/195 (1.5)
Triglycerides >1.3× ULN	1/122 (0.8)	15/471 (3.2)	2/111 (1.8)	12/424 (2.8)	7/198 (3.5)	9/198 (4.5)	15/195 (7.7)
Creatine kinase >2× ULN	2/122 (1.6)	45/474 (9.5)	10/112 (8.9)	40/425 (9.4)	14/198 (7.1)	37/198 (18.7)	54/195 (27.7)
Addition or increase in dose of lipid-lowering agent — no. (%)	0	4 (0.8)	1 (0.9)	2 (0.5)	3 (1.5)	2 (1.0)	8 (4.1)

* LLN denotes lower limit of the normal range, and ULN upper limit of the normal range.
† The rates of the four most frequent adverse events occurring in the OCTAVE Sustain trial are listed for all three trials.
‡ A list of serious infections that occurred during the trials is provided in Table S6 in the Supplementary Appendix.
§ These events were determined on the basis of the *Medical Dictionary for Regulatory Activities* preferred term.
¶ These events were determined on the basis of external adjudication.
‖ The cancer was invasive ductal breast carcinoma.
** These data include patients who discontinued treatment because of worsening ulcerative colitis.
†† Laboratory data were missing for some patients.

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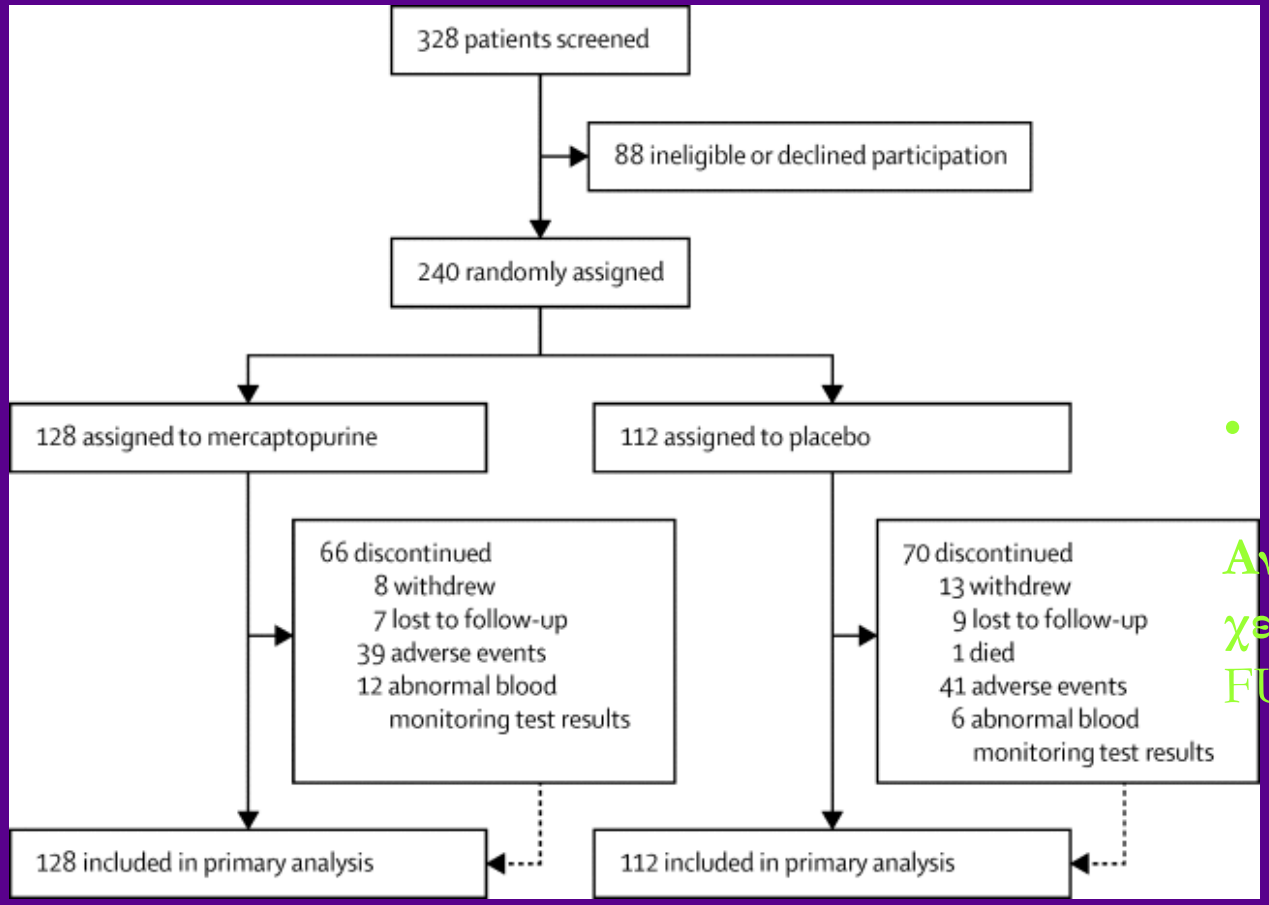
Mercaptopurine versus placebo to prevent recurrence of Crohn's disease after surgical resection (TOPPIC): a multicentre, double-blind, randomised controlled trial

Craig Mowat, MD, Ian Arnott, MD, Aiden Cahill, MB, Malcolm Smith, MBChB, Tariq Ahmad, DPhil, Sreedhar Subramanian, MD, Simon Travis, FRCP, John Morris, FRCP, John Hamlin, PhD, Anjan Dhar, DM, Chuka Nwokolo, MD, Cathryn Edwards, DPhil, Tom Creed, MD, Stuart Bloom, FRCP, Mohamed Yousif, FRCP, Linzi Thomas, MD, Simon Campbell, MD, Stephen J Lewis, FRCP, Shaji Sebastian, FRCP, Sandip Sen, MRCP, Simon Lal, PhD, Prof Chris Hawkey, FMedSci, Charles Murray, PhD, Fraser Cummings, DPhil, Jason Goh, MD, James O Lindsay, PhD, Naila Arebi, PhD, Lindsay Potts, MBChB, Aileen J McKinley, MBChB, John M Thomson, PhD, John A Todd, MD, Mhairi Collie, MD, Prof Malcolm G Dunlop, MD, Prof Ashley Mowat, MBChB, Daniel R Gaya, FRCP, Jack Winter, MD, Graham D Naismith, MBChB, Holly Ennis, PhD, Catriona Keerie, MSc, Steff Lewis, PhD, Prof Robin J Prescott, PhD, Nicholas A Kennedy, MBBS, Prof Jack Satsangi, DPhil

The Lancet Gastroenterology & Hepatology 2016; 1(4): 273-282

Σχεδιασμός μελέτης



29 νοσοκομεία (UK)

Ειλεοκολική ή εκτομή λεπτού εντέρου < 3 μήνες

MP:1mg/Kg ΒΣ ή placebo

- **CDAI >150 +**

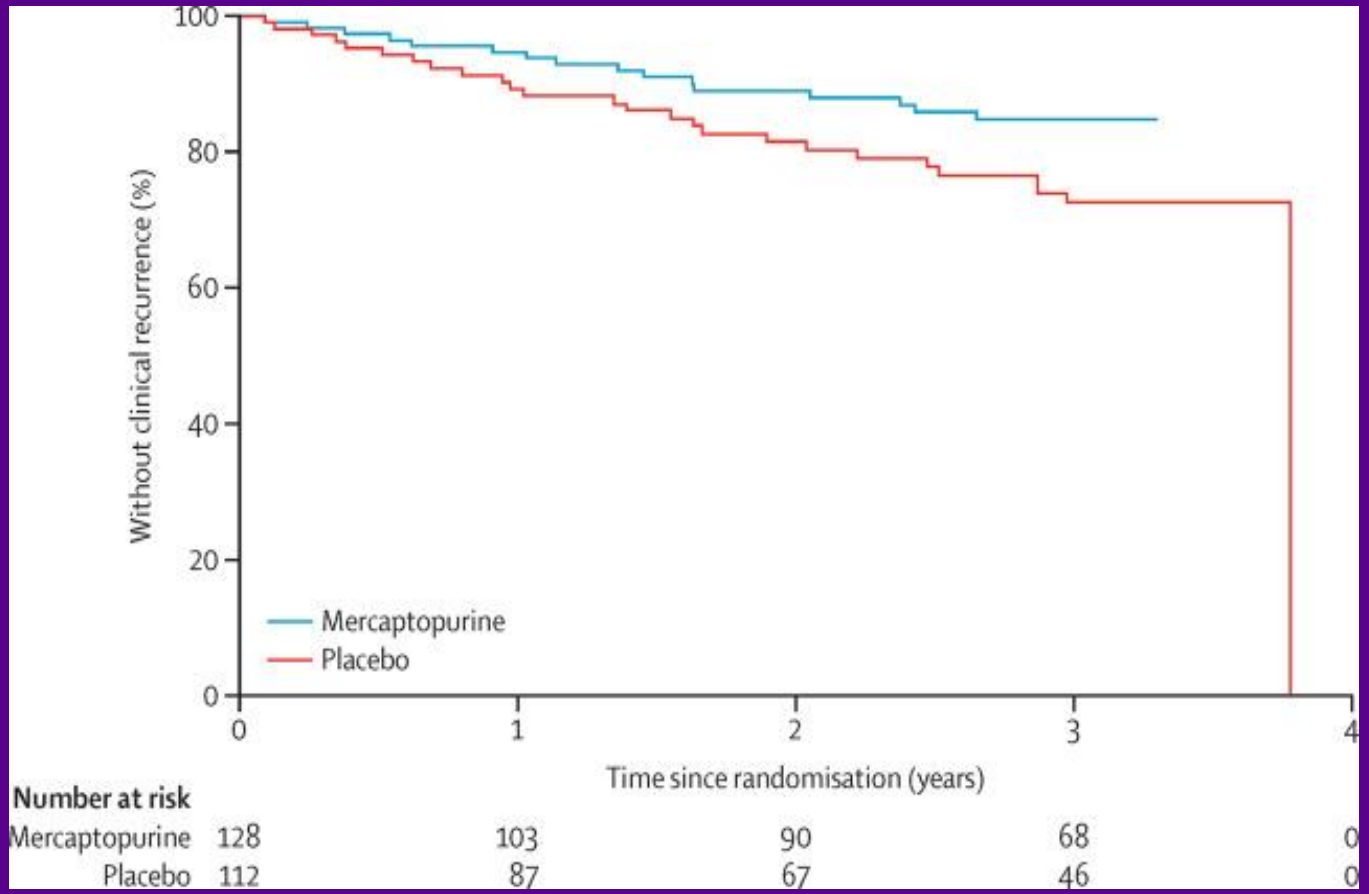
CDAI >100 +

Ανάγκη για χορήγηση θεραπείας ή χειρουργική επέμβαση

FU: 36 μήνες

The Lancet Gastroenterology & Hepatology 2016; 1 (4), 273-282

Μετεγχειρητική κλινική υποτροπή



Καπνιστές:
NNT: 3
Μη καπνιστές
NNT: 31

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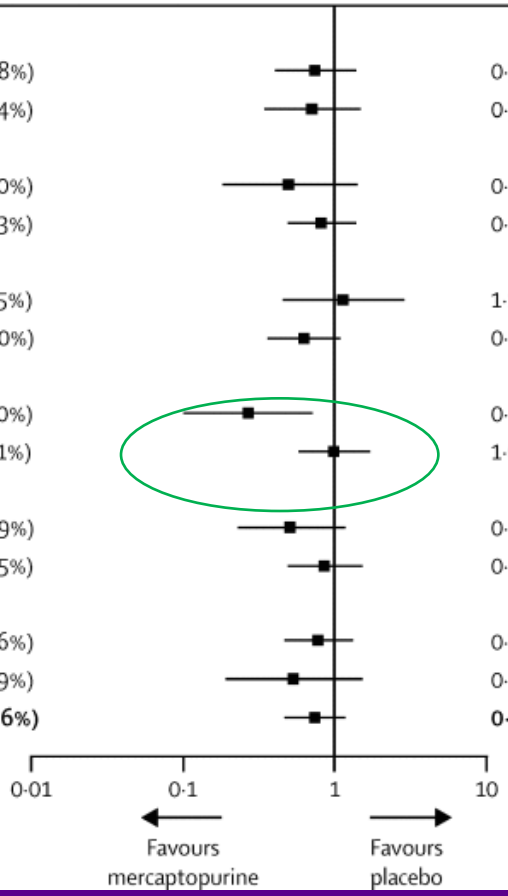
Μετεγχειρητική υποτροπή

	Mercaptopurine		Placebo		Hazard ratio (95% CI)	$p_{interaction}$
	Number of patients	Number (%) experiencing outcome	Number of patients	Number (%) experiencing outcome		
Previous treatment with thiopurines						0·96
Yes	81	23 (28%)	50	19 (38%)	0·74 (0·40–1·38)	
No	47	11 (23%)	61	21 (34%)	0·71 (0·34–1·47)	
Previous treatment with infliximab or methotrexate						0·39
Yes	26	6 (23%)	20	10 (50%)	0·51 (0·18–1·42)	
No	102	28 (27%)	91	30 (33%)	0·82 (0·49–1·37)	
Previous surgery						0·28
Yes	46	13 (28%)	28	7 (25%)	1·14 (0·46–2·87)	
No	82	21 (26%)	83	33 (40%)	0·63 (0·36–1·09)	
Present smoker						0·033
Yes	29	6 (21%)	26	13 (50%)	0·27 (0·10–0·72)	
No	99	28 (28%)	86	27 (31%)	1·00 (0·58–1·70)	
Duration of disease						0·38
≤1 year	37	9 (24%)	41	16 (39%)	0·52 (0·23–1·17)	
>1 year	91	25 (27%)	69	24 (35%)	0·86 (0·49–1·52)	
Age at diagnosis						0·57
≤40 years	103	28 (27%)	87	31 (36%)	0·79 (0·47–1·32)	
>40 years	25	6 (24%)	23	9 (39%)	0·53 (0·19–1·51)	
Overall	**128**	**34 (27%)**	**112**	**40 (36%)**	**0·75 (0·47–1·18)**	



The Lancet Gastroenterology & Hepatology 2016; 1 (4), 273-282

Ενδοσκοπική υποτροπή

- Wk: 157 (MP: 69, placebo: 59)
- Colonoscopy : Rutgeerts score: 124pts (MP: 67, PL: 57)
  - Score >i0 : 77 (47% MP vs 48%PL)
  - Score > i2: 29 (43%)MP vs 28 (49%)PL, p=0.38
- Πρόβλεψη ενδοσκοπικής ύφεσης με καλπροτεκτίνη κοπράνων:
  - NPV(50μg/g): 81% (95% CI 75-87.7)
  - NPV (100μg/g): 84% (95% CI 77-91)

The Lancet Gastroenterology & Hepatology 2016; 1 (4), 273-282

Μετεγχειρητική υποτροπή Συμπεράσματα

- Ίσως είναι προτιμότερη η έναρξη MP/AZA μετά από ενδοσκόπηση σε 6-12 μήνες σε μη καπνιστές
- Σημαντικό όφελος στην έναρξη MP/AZA σε καπνιστές οι οποίοι δεν διακόπτουν το κάπνισμα
- Η καλπροτεκτίνη δεν μπορεί να αντικαταστήσει την ενδοσκόπηση σε ασθενείς μετά από χειρουργείο

The Lancet Gastroenterology & Hepatology **2016; 1 (4), 273-282**

Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial

Julian Panıs, Damian Garcva-Olmo, Gert Van Assche, Jean Frederic Colombel, Walter Reinisch, Daniel C Baumgart, Axel Dignass, Maria Nachury, Marc Ferrante, Lili Kazemi-Shirazi, Jean C Grimaud, Fernando de la Portilla, Eran Goldin, Marie Paule Richard, Anne Leselbaum, Silvio Danese, for the ADMIRE CD Study Group Collaborators

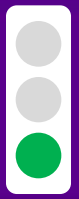
Lancet **2016; 388: 1281–90**

Study Overview

	Summary
Status[1]	24-week primary analysis results published; ongoing long-term (2 years) follow-up
Condition[1]	Complex perianal fistulas in patients with CD
Study design[1]	▪ Phase 3, randomized, double-blind, placebo-controlled ▪ All fistula tracts treated; single intralesional injection[a]
Enrollment[1]	289 patients recruited
Number of sites[1]	49 hospitals; 7 European countries and Israel
Primary endpoint[1]	Combined remission at Week 24
Secondary endpoints at Week 24, 52 and 104[1,2]	▪ Clinical remission ▪ Response ▪ Relapse ▪ Time to combined remission / to clinical remission / to response / to relapse ▪ PDAI, CDAI, IBDQ, and van Assche score ▪ Safety

Lancet 2016; 388: 1281–90

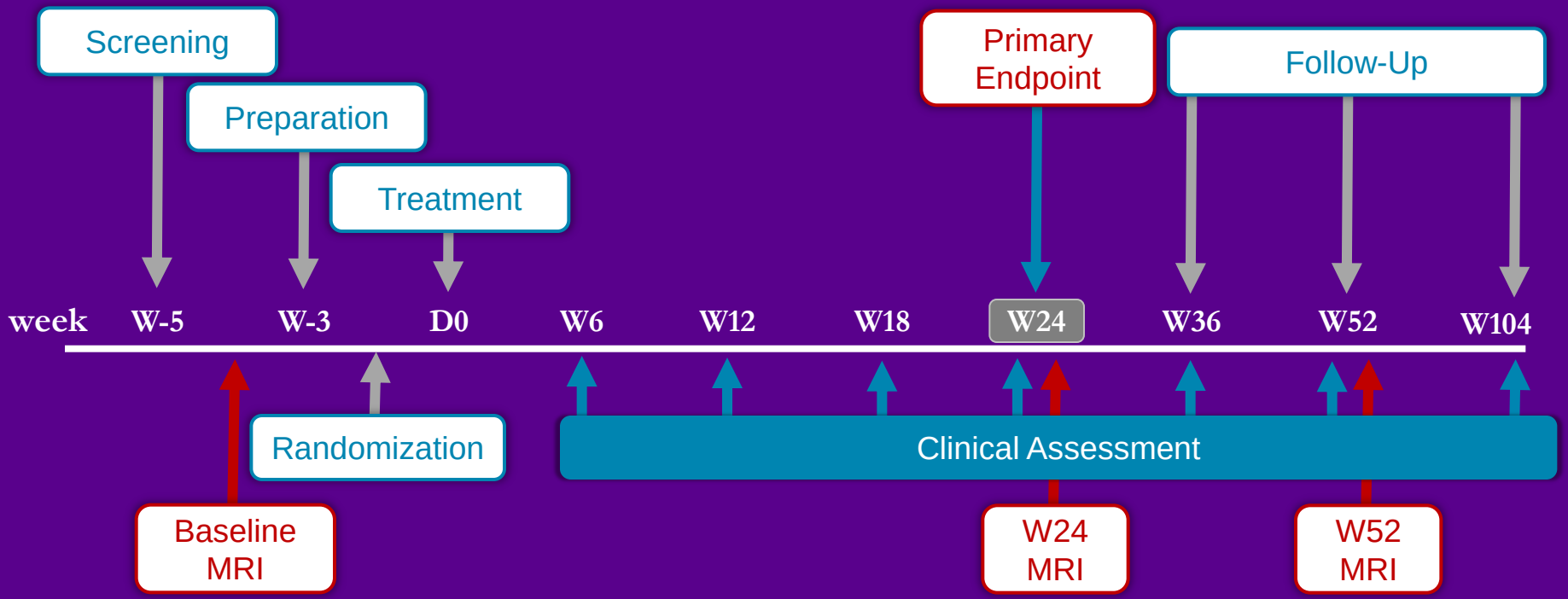
Key Inclusion Criteria



- Adults ≥18 years
- Nonactive/mildly active luminal CD disease for ≥6 months (CDAI ≤220)
- Presence of complex perianal fistulas defined as ≥1 of the following:
  - High inter-sphincteric, high trans-sphincteric, extra-sphincteric, supra-sphincteric origin
  - ≥2 external openings
  - Associated collections
- Fistulas had to have a maximum of 2 internal and 3 external openings, and draining for ≥6 weeks before inclusion
- Refractory to ≥1 of the following:
  - Antibiotics ciprofloxacin or metronidazole (no response after 1 month)
  - Immunomodulators AZA, 6-MP, or MTX (no response after 3 months)
  - Anti-TNFs (induction or maintenance)

Study Design

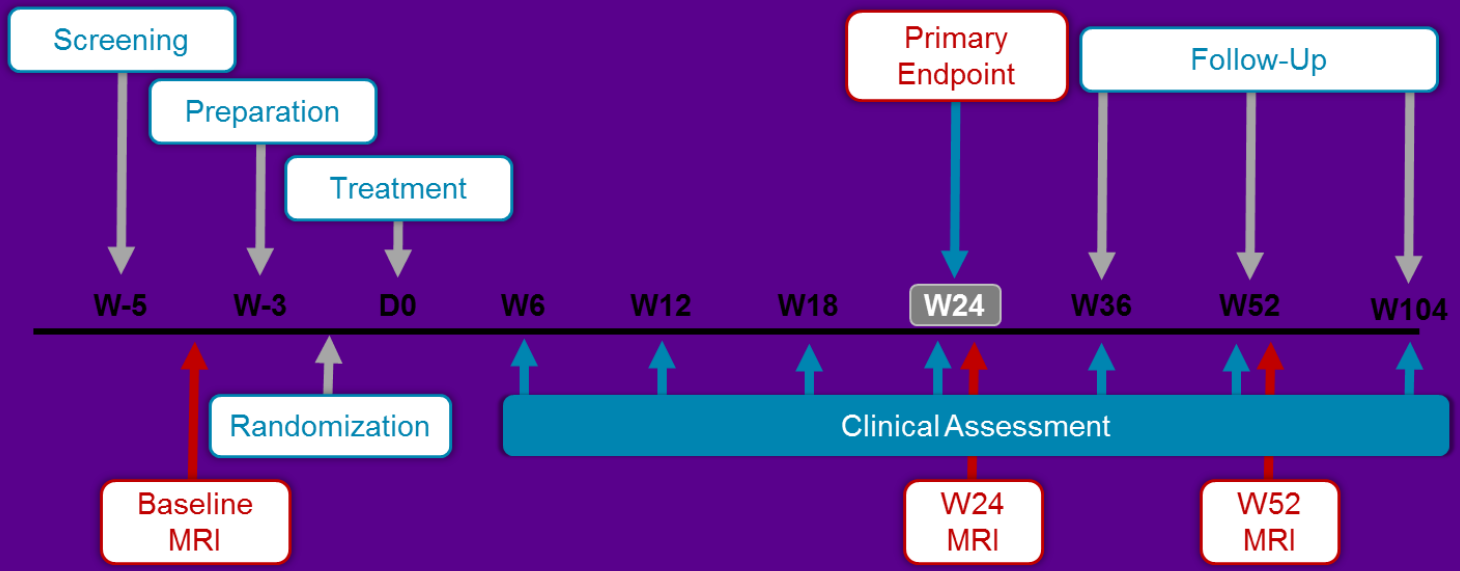
- Double-blind, placebo-controlled, randomized, parallel-arm, multicenter, phase 3 study (NCT01541579)
  - Single local injection of $120x10^6$ eASC or placebo
  - Primary endpoint: 24 weeks



Panés J, et al. *Lancet*. 2016;388:1281-90

Procedures: Screening and Preparation visit

- Screening visit
  - Pelvic MRI scan to guide surgical procedure and assess abscesses
- Fistula preparation visit
  - Examination under anaesthesia, fistula curettage, seton placement as clinically indicated ≥2 weeks before investigational product administration

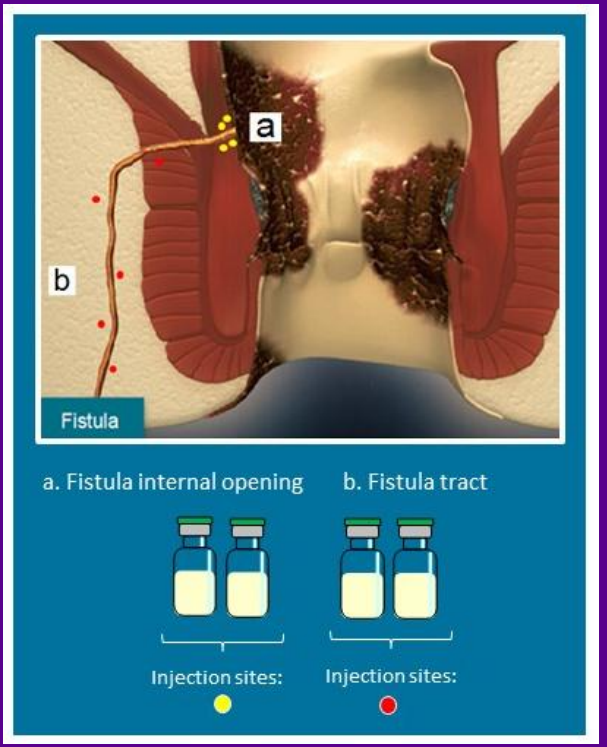


Panés J, et al. *Lancet.* 2016;388:1281-90

Procedures: Treatment Administration Visit

- **Conditioning of fistula**
  - Seton(s) removed if present
  - Closure of internal opening(s) (IO) done using polyglactin absorbable 2/0 stitches and confirmed by pressured injection of 10 mL physiological saline solution through the external opening

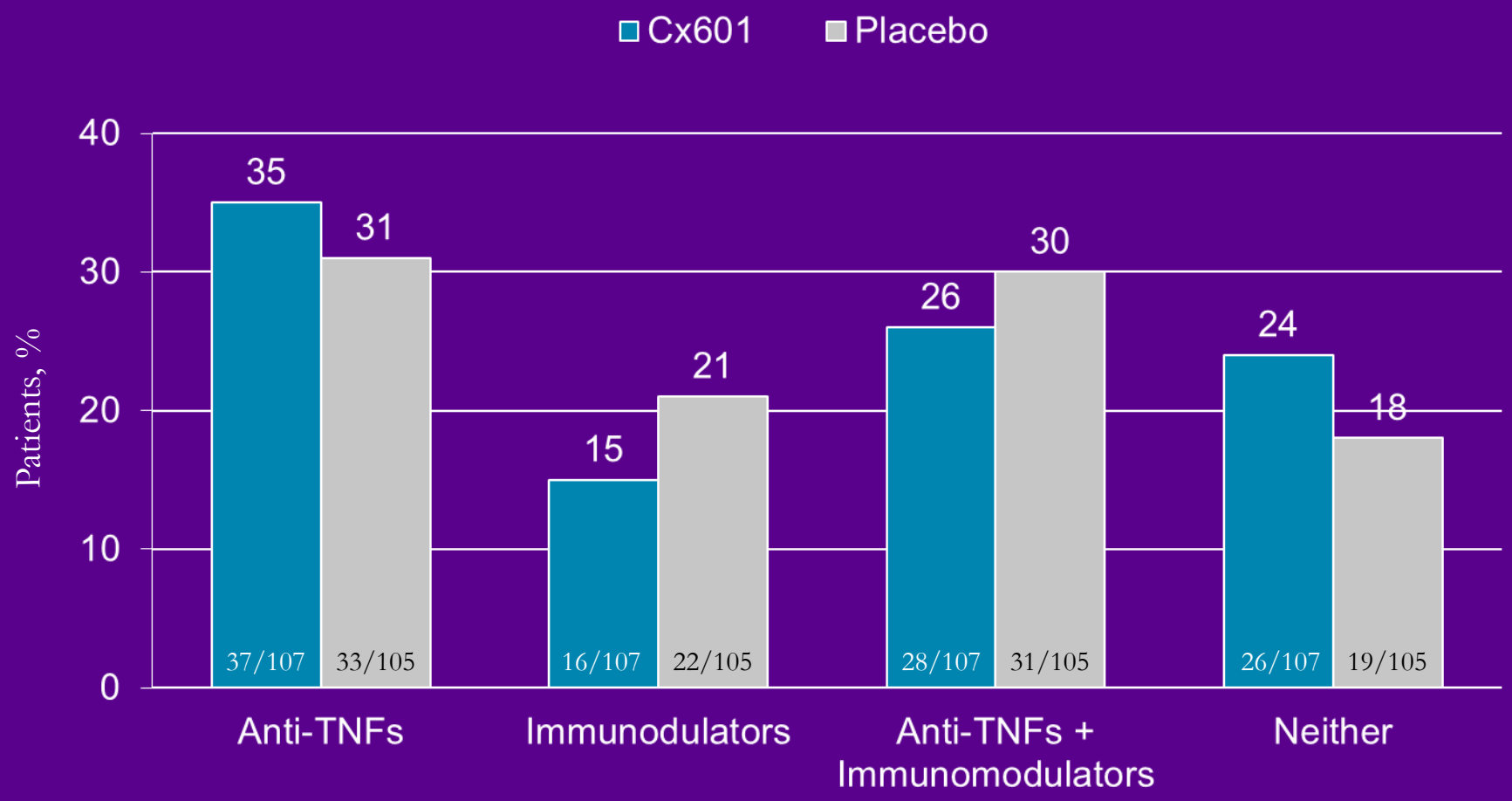
- **Cx601 administration (Figure)**
  - Re-suspend Cx601 vials
  - Inject the contents of 2 vials ($60x10^6$ cells) into tissue surrounding IO(s)
  - Inject the contents of the other 2 vials ($60x10^6$ cells) into the fistula walls along the length of the fistula tract(s)
  - Placebo administration: 24 mL of saline solution



- **Post-injection care**
  - Massage softly EO(s) area
  - Patient discharged according to outpatient surgery

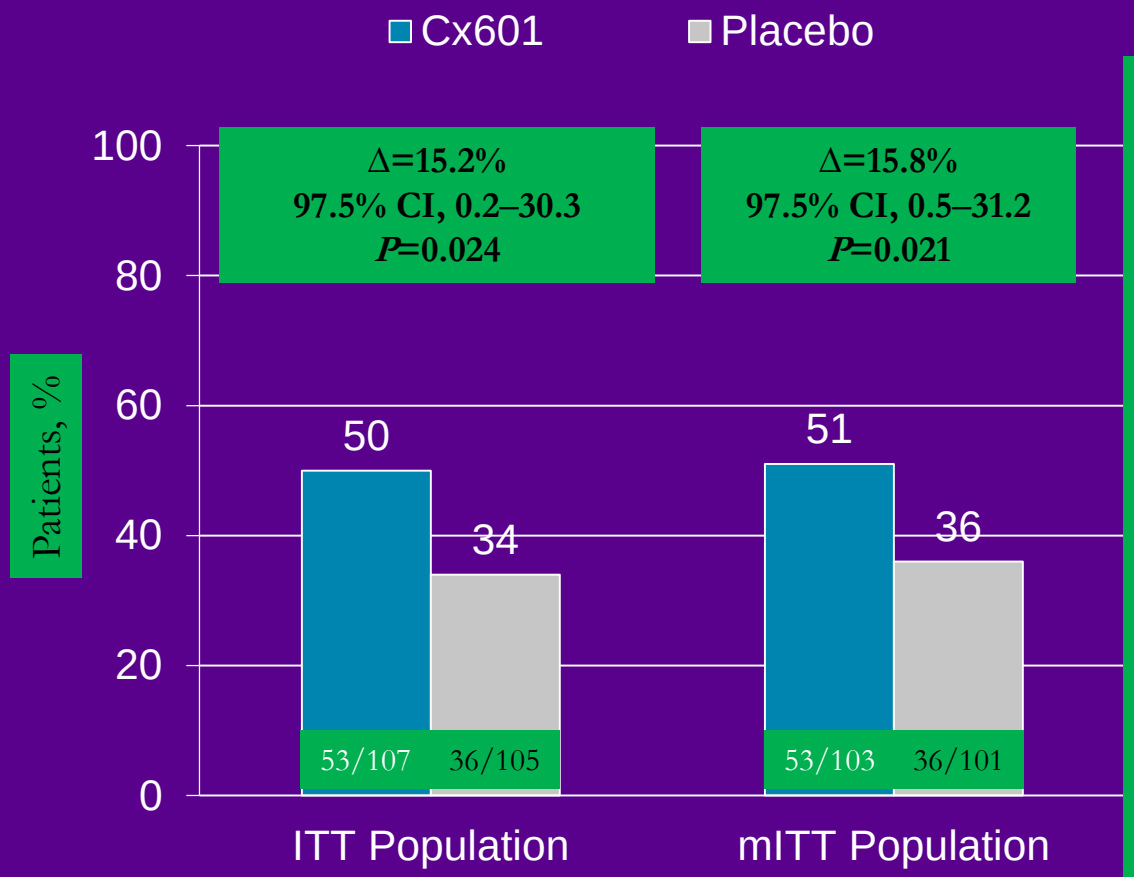
Baseline Characteristics: Concomitant CD Treatment

ITT Population, N=212



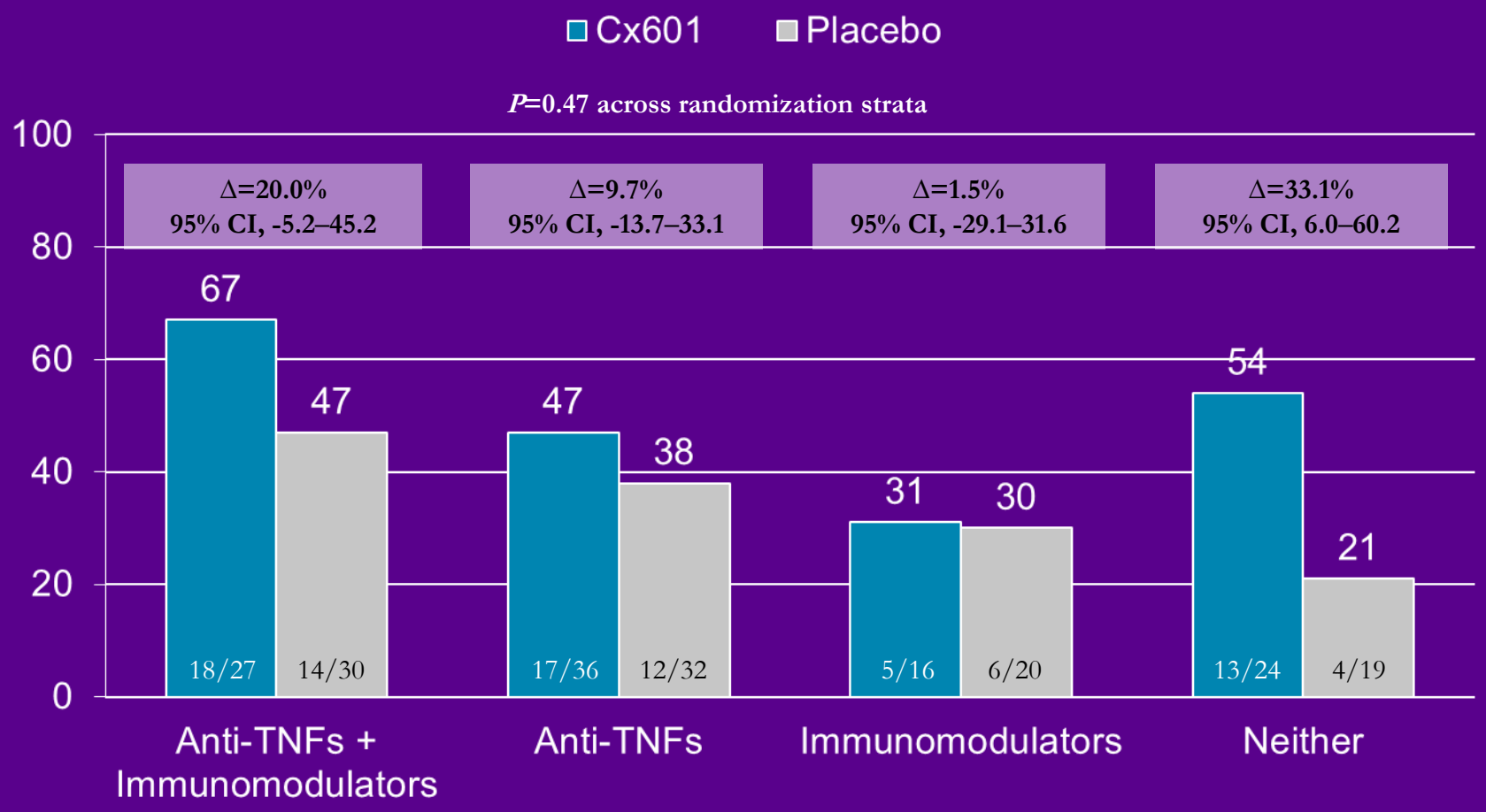
Primary Endpoint: Combined Remission at Week 24

ITT, mITT, and primary PP Populations



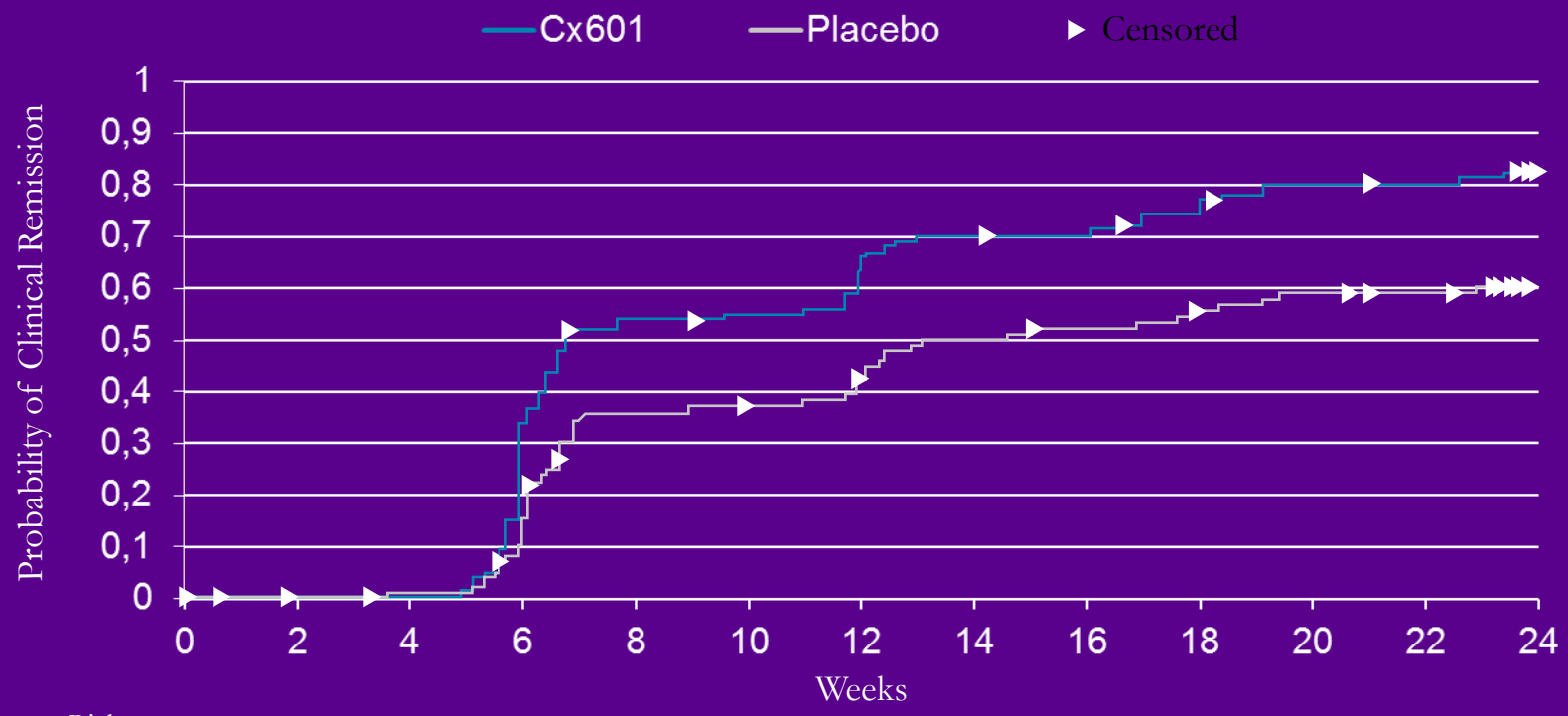
- A significantly greater proportion of patients in Cx601 group than placebo group achieved primary endpoint of combined remission at week 24 in ITT and mITT populations
  - These results were confirmed in the PP population (Δ=20.1%; 97.5% CI, 3.3–36.9; *P*=0.010)

Primary Endpoint: Combined Remission at Week 24
mITT Population, N=204



[a]Defined as clinical assessment of closure of all treated external openings that were draining at baseline, despite gentle finger compression, and absence of collections >2 cm of treated perianal fistulas in ≥2 of 3 dimensions, confirmed by masked central MRI.
mITT, modified intention-to-treat; MRI, magnetic resonance imaging.
Panés J, et al. *Lancet.* 2016;388:1281-90.

Time to Clinical Remission
ITT Population, n=212



Number at Risk

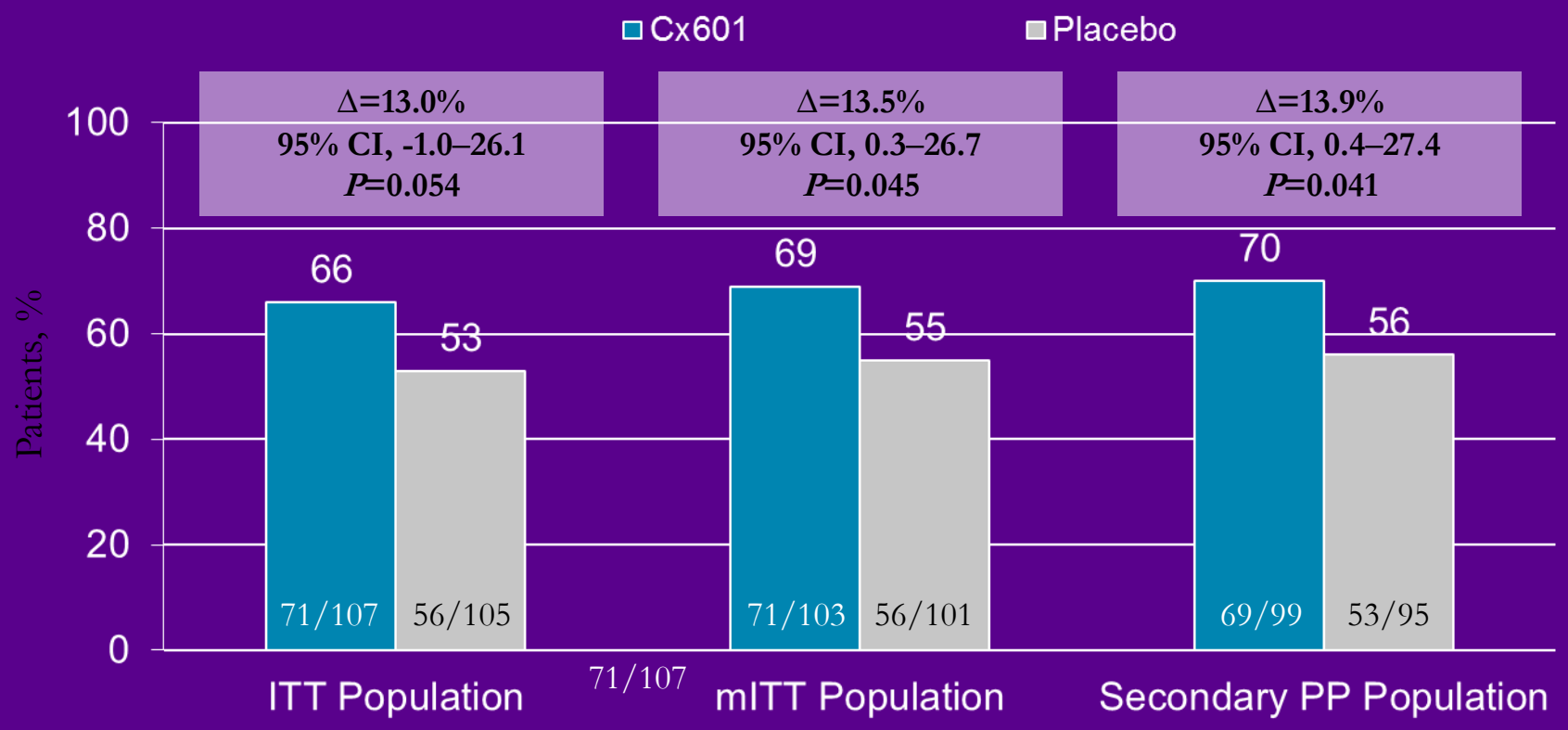
Cx601	107	101	101	79	46	44	36	29	28	23	17	16	10
Placebo	105	100	98	88	61	60	55	46	43	40	36	34	22

- Median time to clinical remission was shorter with Cx601 (6.7 weeks, 95% CI, 6.4–11.9) compared with placebo (14.6 weeks, 95% CI, 11.9–22.9; HR 0.57, 95% CI 0.41–0.79)

HR, hazard ratio; ITT, intention-to-treat.

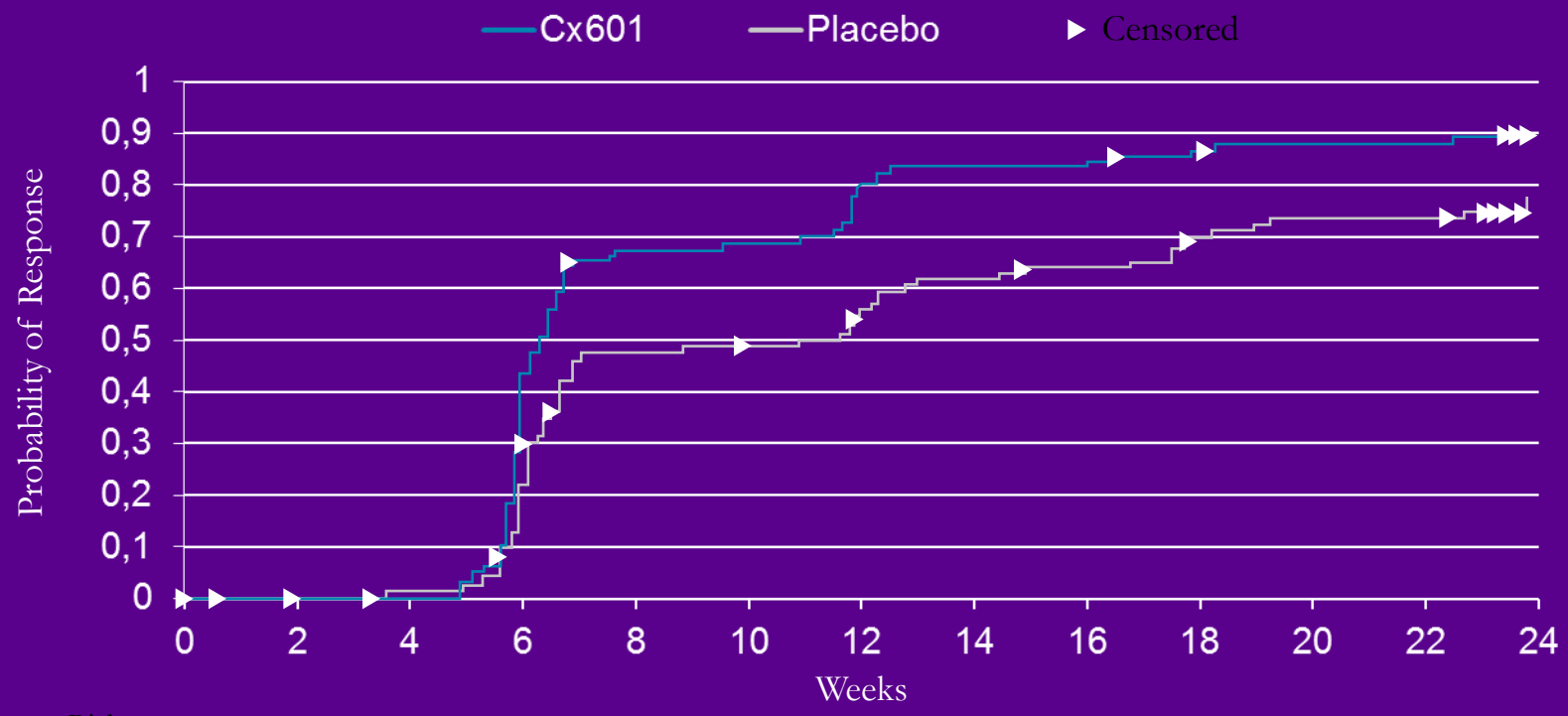
Panés J, et al. *Lancet.* 2016;388:1281-90 Suppl.

Key Secondary Endpoint: Response at Week 24
ITT, mITT, and secondary PP Populations



[a]Closure of ≥50% of all treated external openings were draining at baseline.
mITT, modified intention-to-treat; PP, per protocol.
Panés J, et al. *Lancet*. 2016;388:1281-90.

Time to Response
ITT Population, n=212



Number at Risk

Cx601	107	101	101	73	32	31	23	17	17	14	11	11	7
Placebo	105	100	98	86	50	49	44	35	32	28	23	23	15

- Median time to response was shorter with Cx601 (6.3 weeks, 95% CI, 6.0–6.6) compared with placebo (11.7 weeks, 95% CI, 6.7–12.9; HR 0.59, 95% CI 0.43–0.81)

HR, hazard ratio; ITT, intention-to-treat.
Panés J, et al. *Lancet.* 2016;388:1281-90 Suppl..

Treatment-Emergent Adverse Events to Week 24

Safety Population, n=205

	Cx601 n=103	Placebo n=102
Overall, n (%)	68 (66)	66 (65)
TEAS leading to study withdrawal, n (%)	5 (5)	6 (6)
TEAS in ≥5% of patients[a], n (%)		
Proctalgia	13 (13)	11 (11)
Anal abscess	12 (12)	13 (13)
Nasopharyngitis	10 (10)	5 (5)
Diarrhea	7 (7)	3 (3)
Abdominal pain	4 (4)	6 (6)
Fistula[b]	3 (3)	6 (6)
Treatment-related AEs, n (%)	18 (17)	30 (29)
Treatment-related AES in ≥2% of patients[a], n (%)		
Anal abscess	6 (6)	9 (9)
Proctalgia	5 (5)	9 (9)
Procedural pain	1 (1)	2 (2)
Fistula discharge[c]	1 (1)	2 (2)
Induration	0	2 (2)

- Most TEAEs were mild or moderate in intensity

[a]In either treatment group; [b]New fistula, reopening of closed fistula; [c]Fistula discharge in a closed fistula. AEs, adverse events; TEAEs, treatment-emergent adverse events. Panés J, et al. *Lancet*. 2016;388:1281-90.

Infliximab Reduces Endoscopic, but Not Clinical, Recurrence of Crohn's Disease After Ileocolonic Resection

Miguel Regueiro,[1] Brian G. Feagan, Bin Zou,[3] Jewel Johanns, Marion A. Blank, Marc Chevrier, Scott Plevy, John Popp, Freddy J. Cornillie, Milan Lukas, Silvio Danese, Paolo Gionchetti, Stephen B. Hanauer, Walter Reinisch, William J. Sandborn, Dario Sorrentino, and Paul Rutgeerts, for the PREVENT Study Group

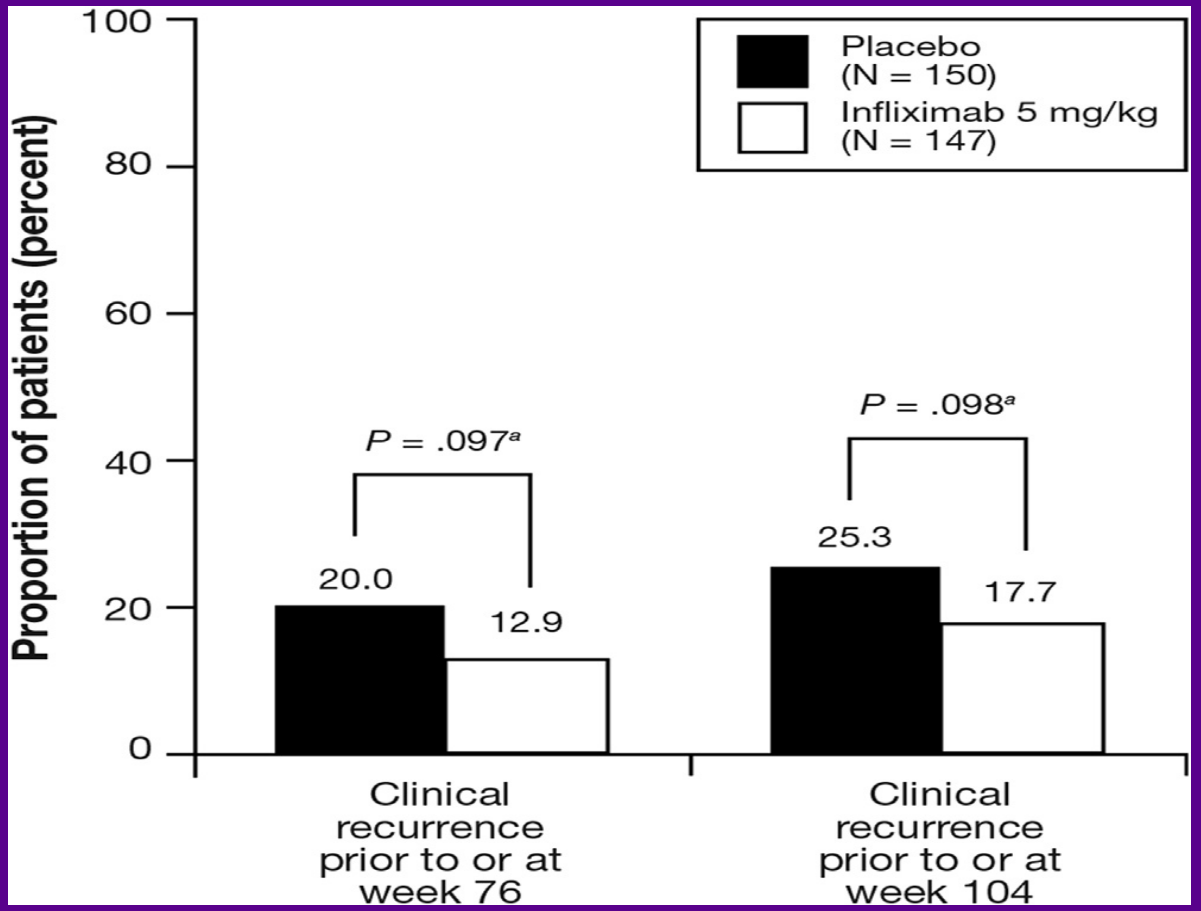
Gastroenterology 2016;150:1568–1578

Σχεδιασμός μελέτης

- 297pts από 104 κέντρα ανά τον κόσμο
- Χειρουργική επέμβαση (ειλεοκολική εκτομή) εντός 45 ημερών από την τυχαιοποίηση στην μελέτη
- Infliximab 5mg/Kg ΒΣ ανά 8 εβδομάδες ή placebo
- **Κλινική υποτροπή** (CDAI>200 και ⇑ >70) και **ενδοσκοπική υποτροπή** (Rutgeert's score > i2) ή εμφάνιση συριγγίου ή/και αποστήματος)

Gastroenterology 2016;150:1568–1578

Μετεγχειρητική κλινική υποτροπή



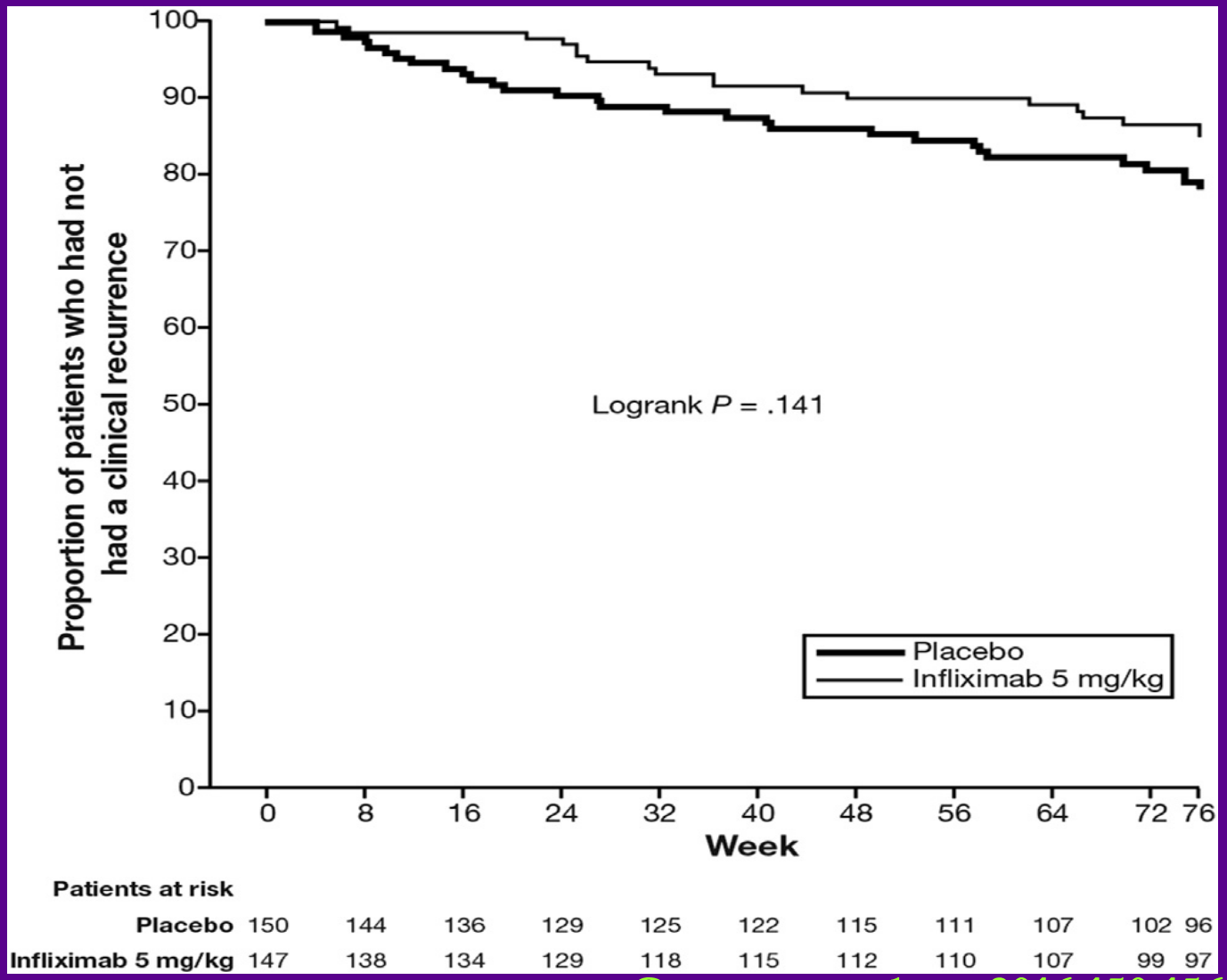
⇧ πιθανότητα υποτροπής

- χορήγηση αντι-TNF
- > 1 χειρουργική επέμβαση

Κλινική και ενδοσκοπική υποτροπή 4 % (IFX) vs 9% placebo, p= 0.056

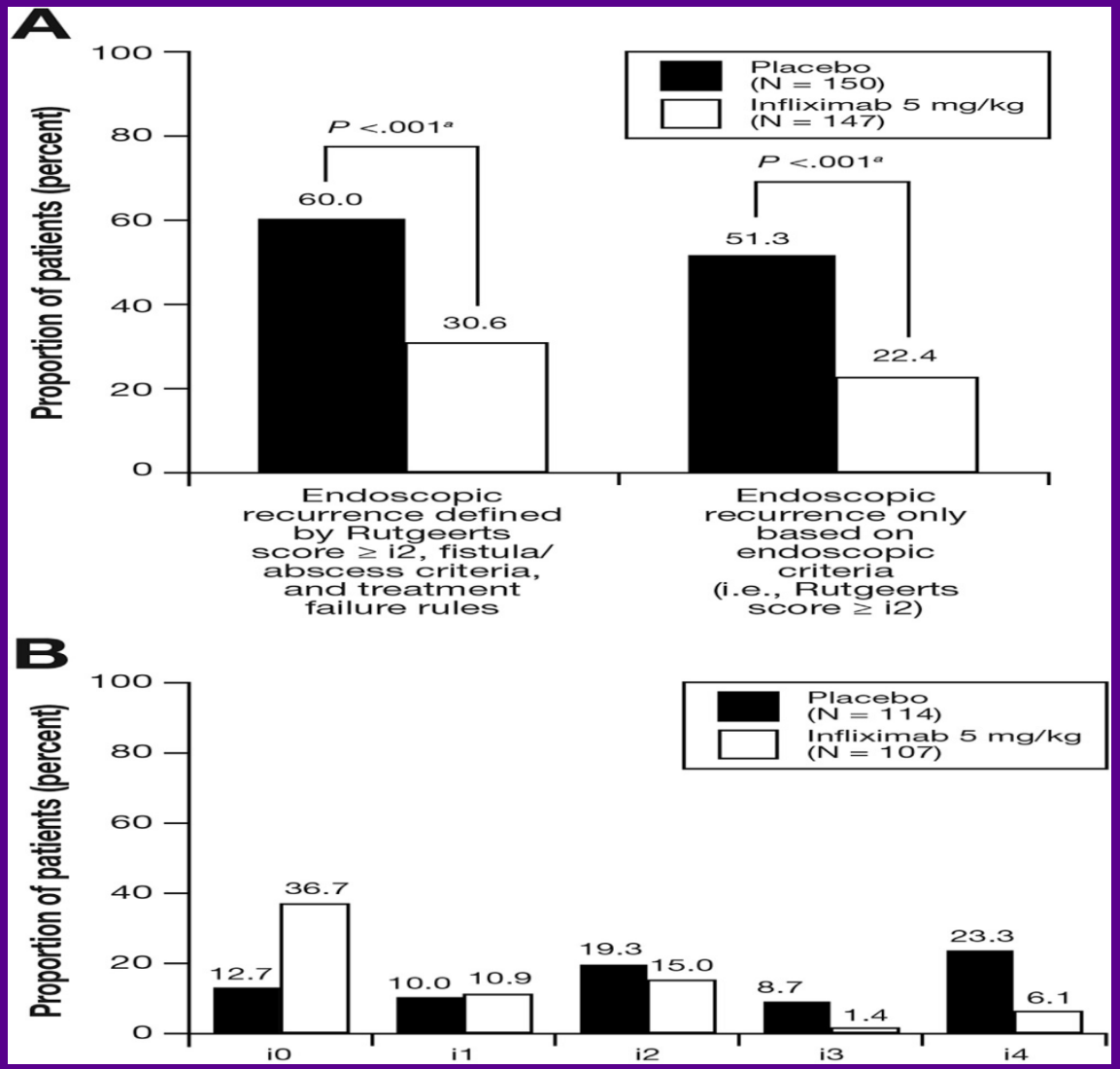
Gastroenterology 2016;150:1568–1578

Χρόνος εμφάνισης της υποτροπής



Gastroenterology 2016;150:1568–1578

Ενδοσκοπική υποτροπή



Gastroenterology 2016;150:1568–1578

Συμπέρασμα

- Η χορήγηση του IFX μετά την θεραπεία με ειλεοκολική εκτομή δεν υπερέχει σημαντικά στην πρόληψη της κλινικής υποτροπής αλλά φαίνεται να περιορίζει την ενδοσκοπική υποτροπή.