Professor Tore Kristian Kvien, MD, PhD, Norway

- Professor of Medicine and Rheumatology, Head of Department of Rheumatology, Diakonhjemmet Hospital, Norway

GaBI Scientific Meetings

2nd MENA Stakeholder Meeting on **Regulatory Approval, Clinical Settings, Interchangeability and Pharmacovigilance of Biosimilars**

10 October 2018, Le Meridien Dubai, United Arab Emirates

An update on biosimilars – the clinical perspective

Professor Tore Kristian Kvien, MD, PhD, Norway

10 October 2018

GaBi
GENERICS AND BIOSIMILARS INITIATIVE
Building trust in cost-effective treatments

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MINISTRY OF HEALTH & PREVENTION

An up-date on biosimilars – the clinical perspective

Tore K Kvien

Dept of Rheumatology
Diakonhjemmet Hospital
Oslo, Norway

Tore K. Kvien – disclosures

	Honorarium		Institutional support NOR-DMARD	
	Presentation	Advice	Previous	Current
AbbVie	X	X	X	
BMS	X	X	X	X
MSD	X	X	X	
Pfizer/Wyeth	X	X	X	
Roche	X	X	X	
UCB	X	X	X	
Hospira/Pfizer	X	X		
Epirus		X		
Orion	X	X		
Merck Serono		X		
Mundi Pharma	X			
Celltrion	X	X		
Sandoz	X			
Samsung	X			
Biogen	X	X		
Amgen	X			

Why Biosimilars?

- Similar to the originator product
  - Not better
  - Not worse
  - But less expensive!

Could improve accessibility to good therapies for more people with RMDs

EXTENDED REPORT

Inequities in access to biologic and synthetic DMARDs across 46 European countries

Polina Putrik,[1] Sofia Ramiro,[2] Tore K Kvien,[3] Tuulikki Sokka,[4] Milena Pavlova,[5] Till Uhlig,[6] Annelies Boonen,[7] Working Group 'Equity in access to treatment of rheumatoid arthritis in Europe'

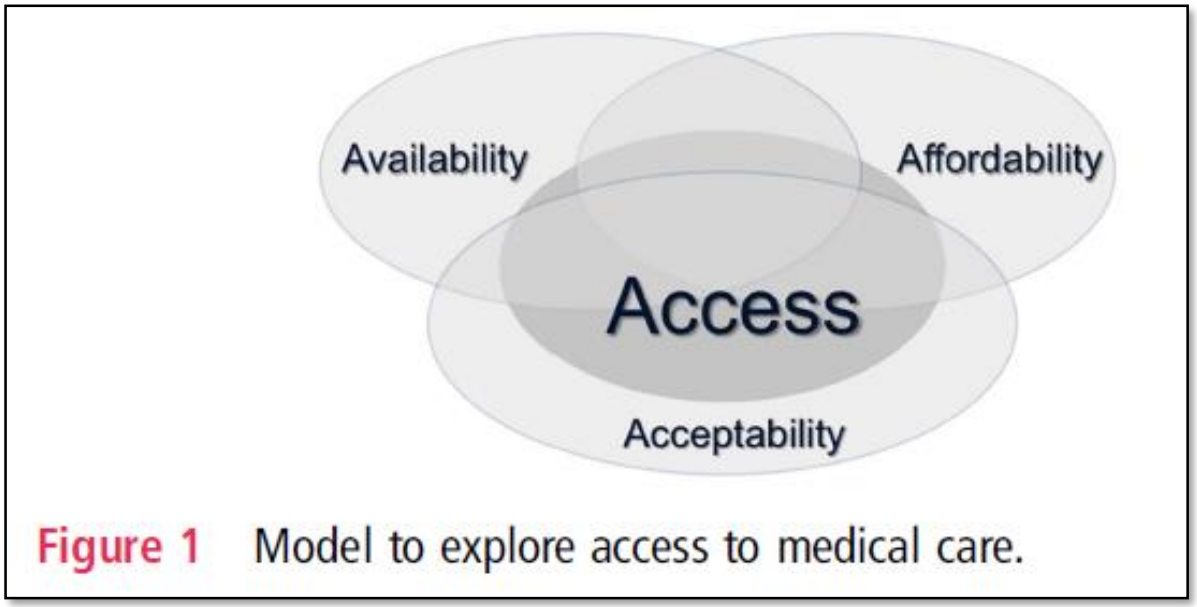


Figure 1 Model to explore access to medical care.

Putrik P, et al. Ann Rheum Dis 2014;73:198-206.

Inequities in Access to Biologic and Synthetic DMARDs Across 46 European Countries

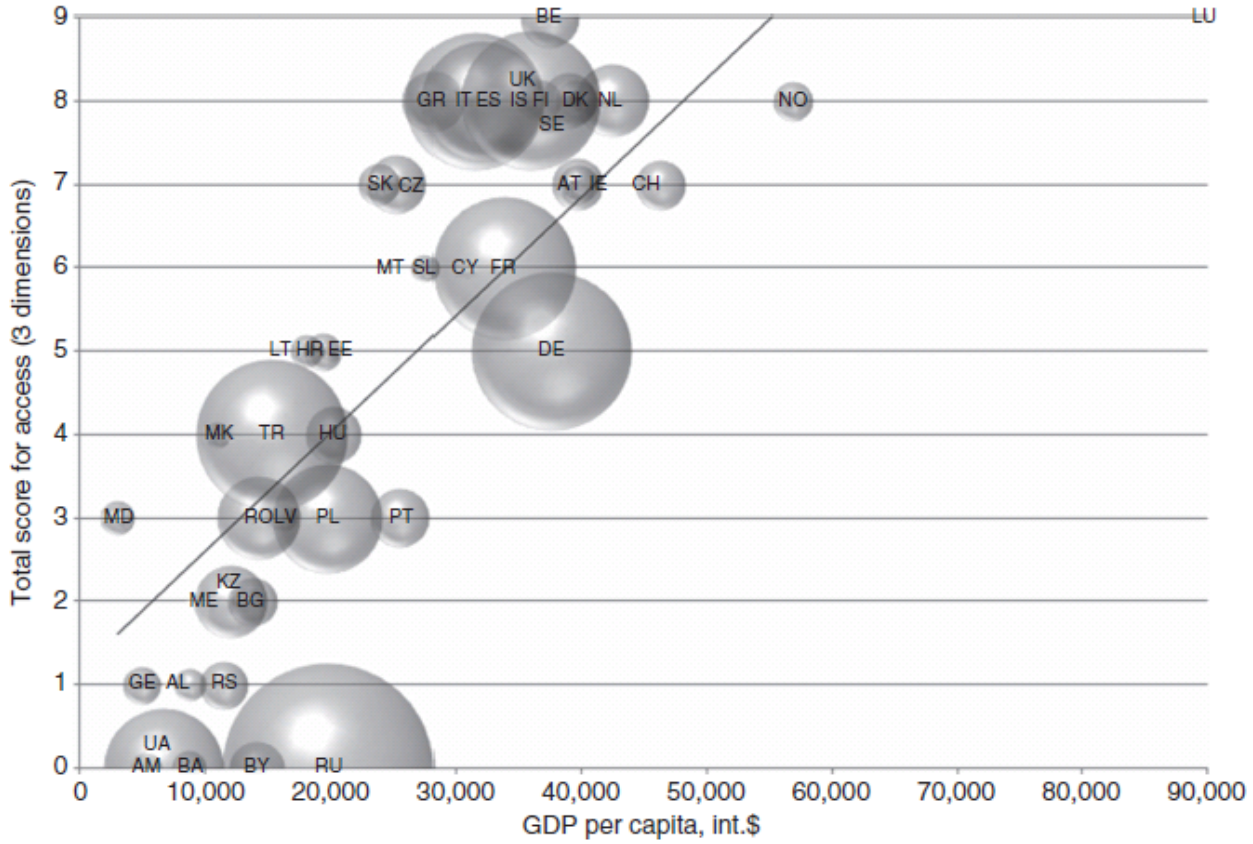


Figure 3 Access to biologic disease modifying antirheumatic drugs and gross domestic product per capita, international dollars (n=44). Size of the bubbles is proportional to the population size of the country. AL, Albania; AM, Armenia; AT, Austria; BA, Bosnia and Herzegovina; BE, Belgium; BG, Bulgaria; BY, Belarus; CH, Switzerland; CY, Cyprus; CZ, Czech Republic; DE, Germany; DK, Denmark; EE, Estonia; ES, Spain; FI, Finland; FR, France; GE, Georgia; GR, Greece; HR, Croatia; HU, Hungary; IE, Ireland; IS, Iceland; IT, Italy; KZ, Kazakhstan; LT, Lithuania; LU, Luxemburg; LV, Latvia; MD, Moldova; ME, Montenegro; MK, Macedonia; MT, Malta; NL, Netherlands; NO, Norway; PL, Poland; PT, Portugal; RO, Romania; RS, Serbia; RU, Russia; SE, Sweden; SK, Slovakia; SL, Slovenia; TR, Turkey; UA, Ukraine; UK, United Kingdom.

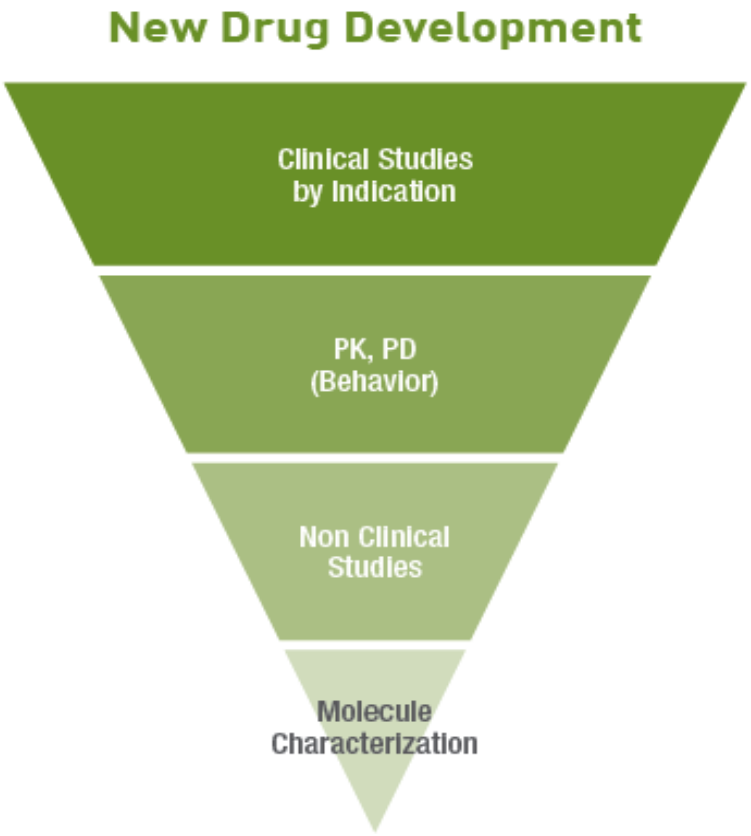
Putrik P, et al. Ann Rheum Dis 2014;73:198-206.

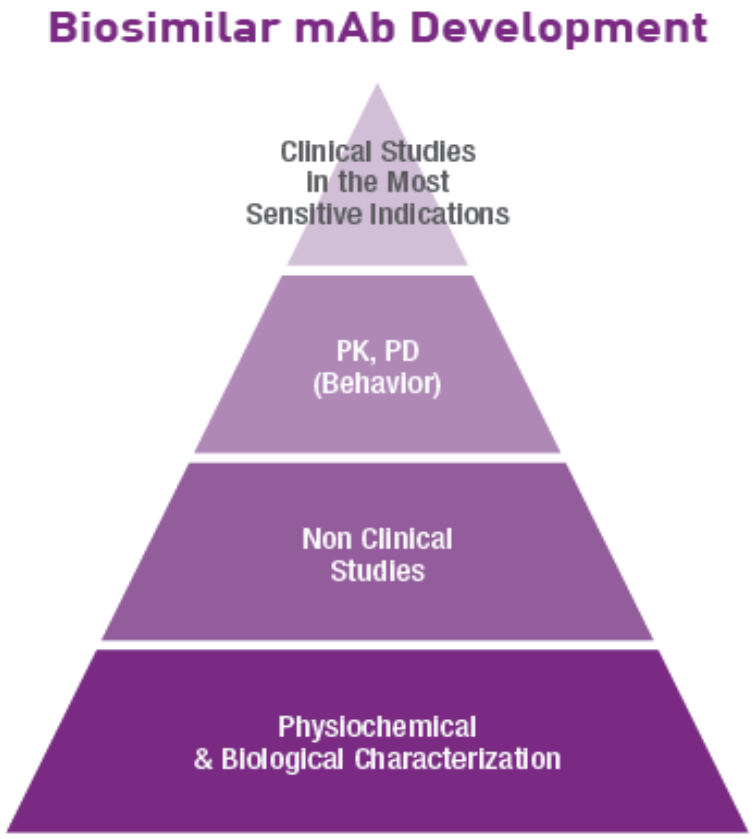
Two Main Questions

- Prescription of biosimilar when to start new therapy or to change therapy for medical reasons?
  - Not controversial (?)

Comparison of Regulatory Requirements

- The aim of a biosimilar development program is to establish ***"biosimilarity"*** based upon totality of evidence.





1. Guideline on similar biological medicinal products. European Medicines Agency 23rd October 2014.
2. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/10/WC500176768.pdf (Accessed October 2016).

Clinical and epidemiological research

OPEN ACCESS

EXTENDED REPORT

A randomised, double-blind, parallel-group study to demonstrate equivalence in efficacy and safety of CT-P13 compared with innovator infliximab when coadministered with methotrexate in patients with active rheumatoid arthritis: the PLANETRA study

Dae Hyun Yoo,[1] Pawel Hrycaj,[2] Pedro Miranda,[3] Edgar Ramiterre,[4] Mariusz Piotrowski,[5] Sergii Shevchuk,[6] Volodymyr Kovalenko,[7] Nenad Prodanovic,[8] Mauricio Abello-Banfi,[9] Sergio Gutierrez-Ureña,[10] Luis Morales-Olazabal,[11] Michael Tee,[12] Renato Jimenez,[13] Omid Zamani,[14] Sang Joon Lee,[15] HoUng Kim,[16] Won Park,[17] Ulf Müller-Ladner[18]

Clinical and epidemiological research

OPEN ACCESS

EXTENDED REPORT

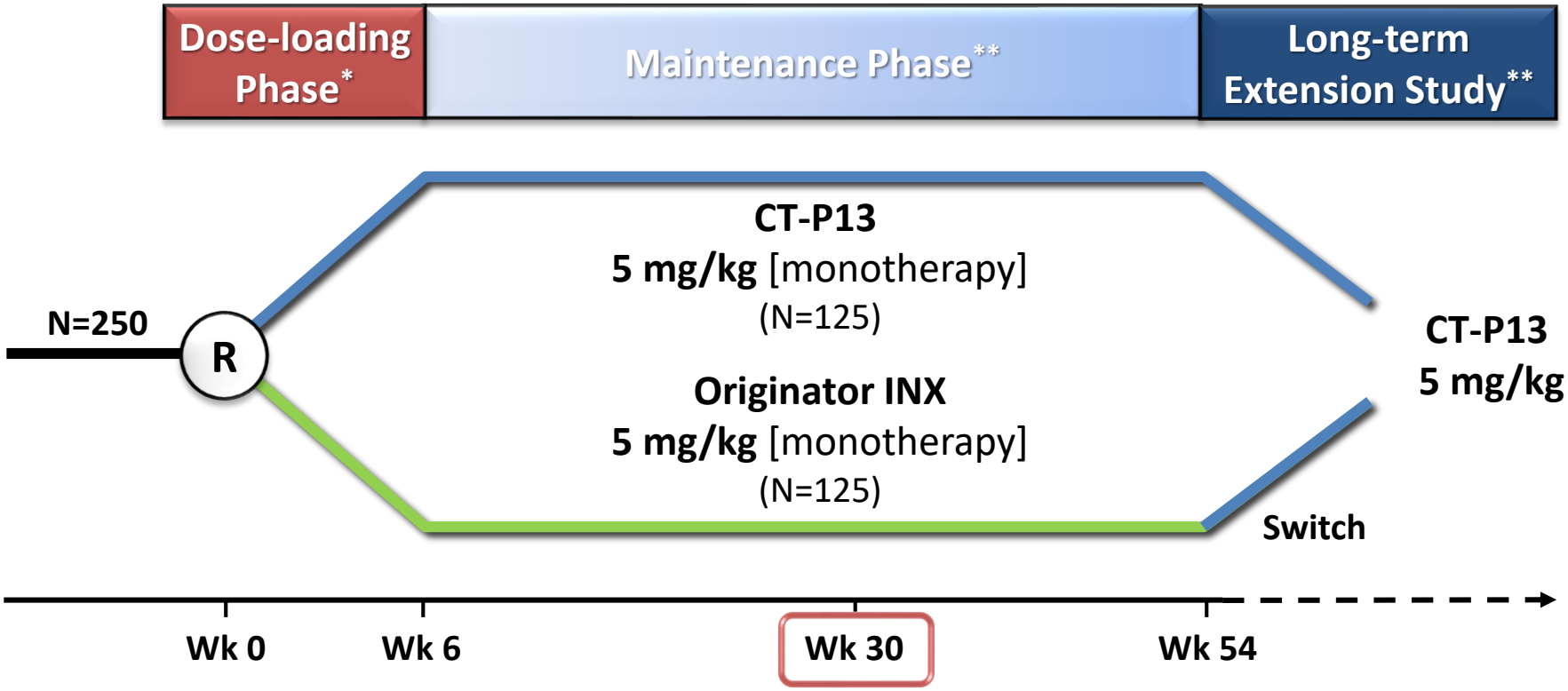
A randomised, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy of CT-P13 and innovator infliximab in patients with ankylosing spondylitis: the PLANETAS study

Won Park,[1] Pawel Hrycaj,[2] Slawomir Jeka,[3] Volodymyr Kovalenko,[4] Grygorii Lysenko,[5] Pedro Miranda,[6] Helena Mikazane,[7] Sergio Gutierrez-Ureña,[8] MieJin Lim,[1] Yeon-Ah Lee,[9] Sang Joon Lee,[10] HoUng Kim,[11] Dae Hyun Yoo,[12] Jürgen Braun[13]

Yoo DH, et al. *Ann Rheum Dis* 2013;72:1613-1620.
Park W, et al. *Ann Rheum Dis* 2013;72:1605-1612.

CT-P13 Phase 1 Pharmacokinetic Equivalence Trial in AS: Study Schematic

Randomised double-blind study in patients with AS



*Doses at weeks 0, 2 and 6 by 2-hr IV infusion.
**Doses every 8 weeks up to 54 weeks by 2-hr IV infusion.

EMA/CHMP/589422/2013; CT-P13 Assessment Report.

CT-P13 PK Study in AS: PK Analysis

The PK profiles of CT-P13 and the originator INX are equivalent in terms of AUC_T and $C_{max, ss}$

Dose 5 (Week 22)

Parameter	Treatment	N	Geometric Mean	Ratio (%) of Geometric Means	90% CI of Ratio (%)
AUC_τ (µg*h/mL)	**CT-P13** (5 mg/kg) **Originator INX** (5 mg/kg)	**111** **110**	**32,765.51** **31,475.68**	**104.10**	(93.93–115.36)
$C_{max,ss}$ (µg/mL)	**CT-P13** (5 mg/kg) **Originator INX** (5 mg/kg)	**112** **110**	**146.94** **144.81**	**101.47**	(94.57–108.86)

Pre-defined bioequivalence acceptance range:
80% – 125%

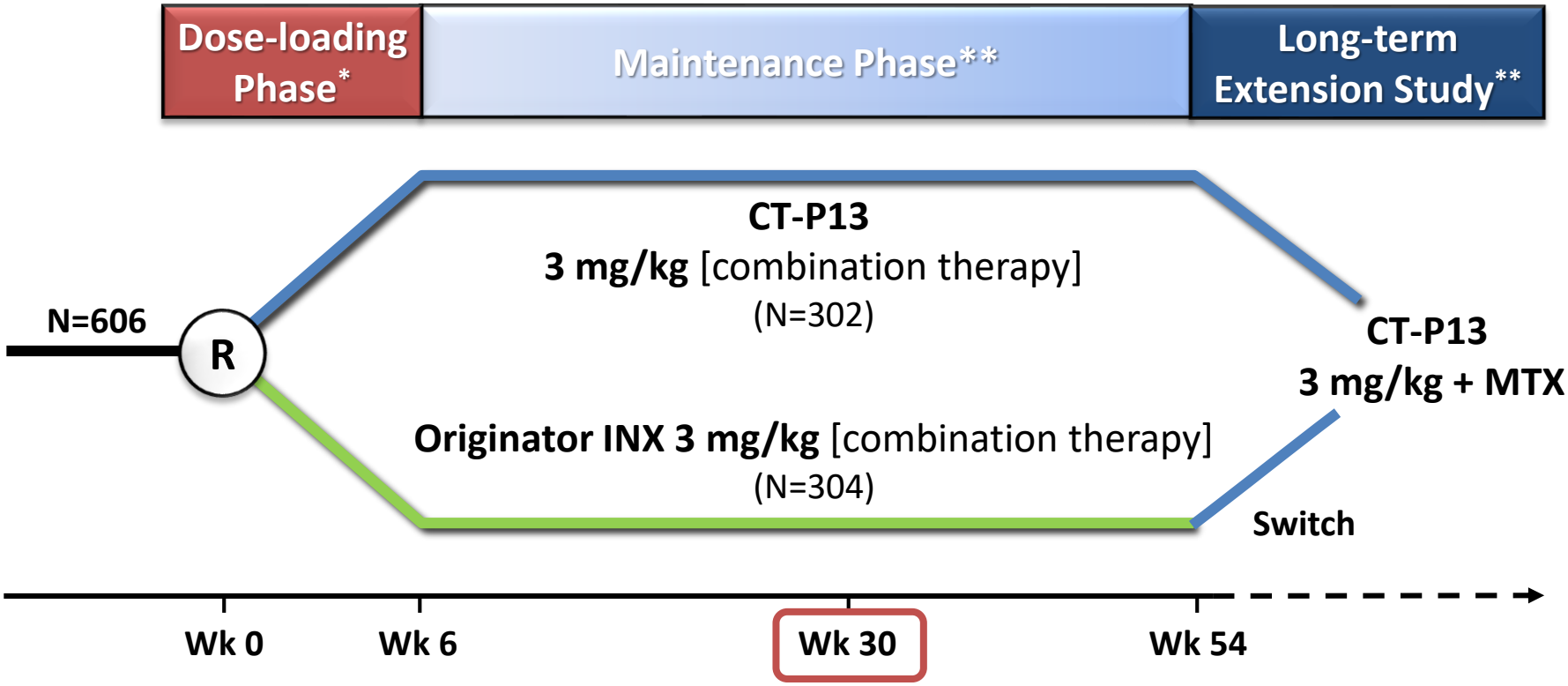
Source: EMA Inflectra EPAR, June 2013.

PLANETRA

- Standard design and inclusion criteria for phase 3 trial in pts being IA responders to MTX
- Primary endpoint ACR20 week 30
- Equivalence of efficacy if the 95% CI for treatment difference was within + 15%

Phase 3 Therapeutic Equivalence Trial in RA: Study Schematic

Randomised double-blind study in patients with RA

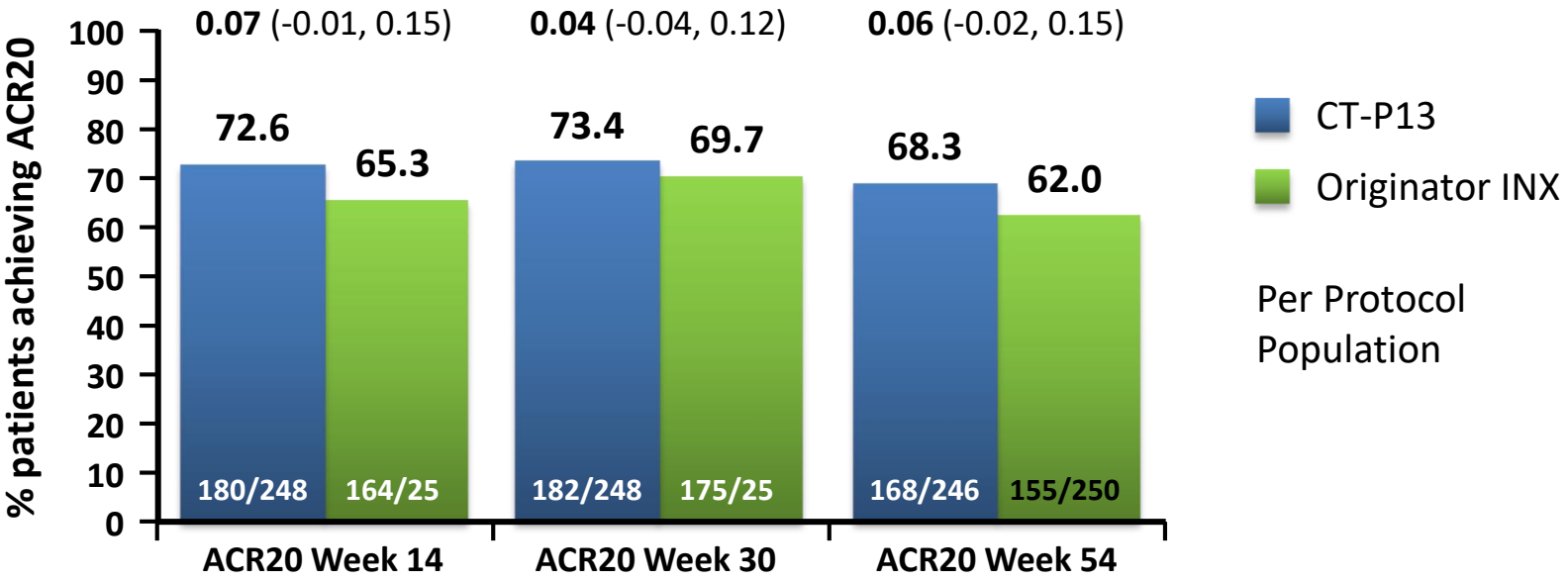


*Doses at weeks 0, 2 and 6 by 2-hr IV infusion.
**Doses every 8 weeks up to 54 weeks by 2-hr IV infusion.

EMA/CHMP/589422/2013; CT-P13 Assessment Report

CT-P13 Study in RA: ACR20 Response

ACR response at Weeks 14, 30 and 54
Estimate of treatment difference (95% CI)



Primary endpoint:	**-15**	**Equivalence margin**		**+15**
ACR at Week 30:		**-4**	**CT-P13 result**	**+12**
ACR at Week 54:		**-2**	**CT-P13 result**	**+15**

Source: EMA Inflectra EPAR, June 2013

ARD Online First, published on September 22, 2015 as 10.1136/annrheumdis-2015-207588

OPEN ACCESS

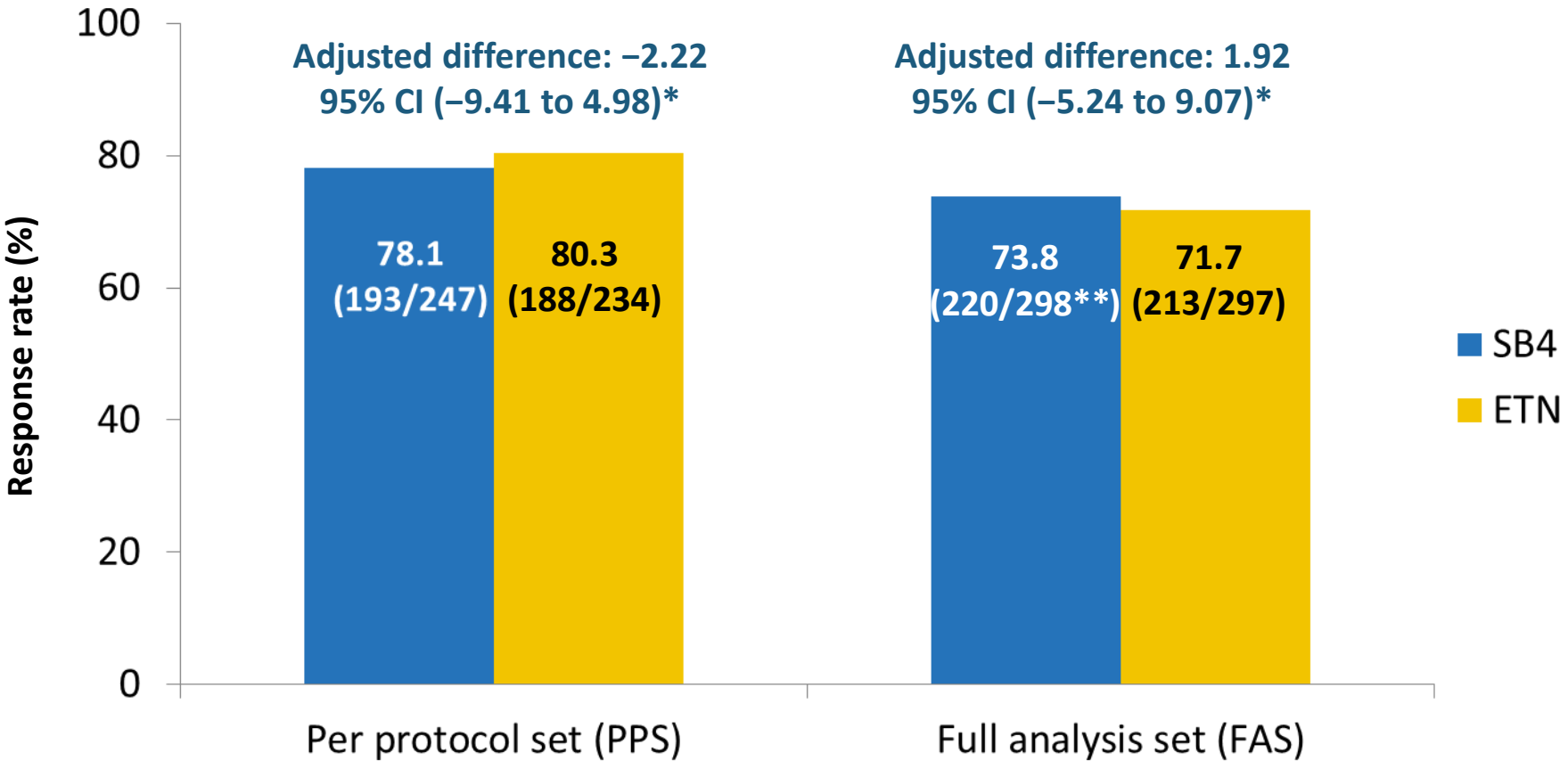
EXTENDED REPORT

A phase III randomised, double-blind, parallel-group study comparing SB4 with etanercept reference product in patients with active rheumatoid arthritis despite methotrexate therapy

Paul Emery,[1] Jiří Vencovský,[2] Anna Sylwestrzak,[3] Piotr Leszczyński,[4] Wieslawa Porawska,[5] Asta Baranauskaite,[6] Vira Tseluyko,[7] Vyacheslav M Zhdan,[8] Barbara Stasiuk,[9] Roma Milasiene,[10] Aaron Alejandro Barrera Rodriguez,[11] Soo Yeon Cheong,[12] Jeehoon Ghil[12]

To cite: Emery P, Vencovský J, Sylwestrzak A, *et al. Ann Rheum Dis* 2017;**76**:51–57.

ACR20 Response Rate at Week 24 Equivalent between SB4 and ETN



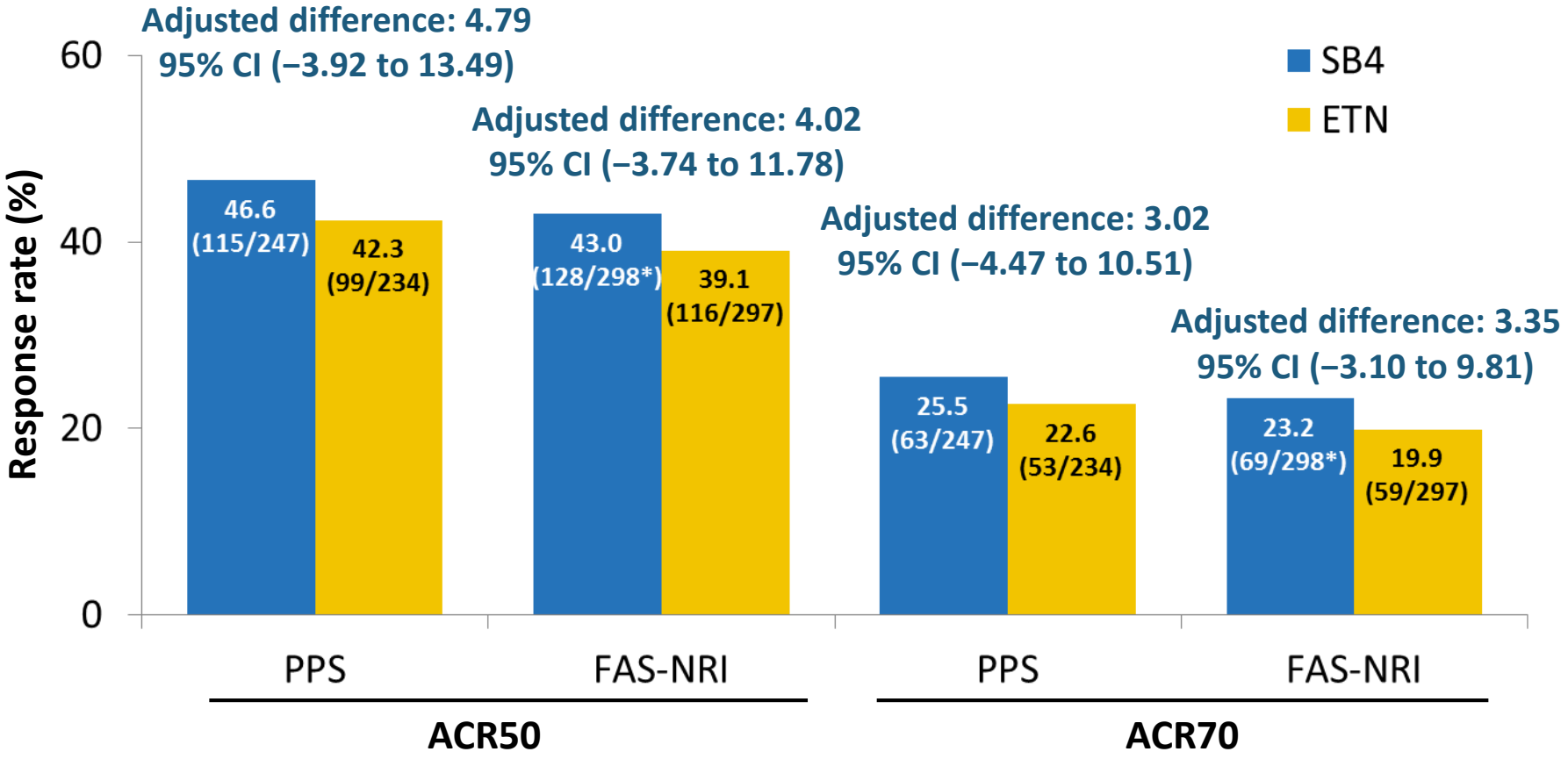
* Predefined equivalence margin -15% to 15%

**One patient from the SB4 group was excluded from the FAS due to missing efficacy data at baseline.

ACR20, American College of Rheumatology 20% response;
ETN, etanercept.

Emery P, et al. Ann Rheum Dis. Jul 6. pii: annrheumdis-2015-207588.

ACR50, ACR70 Response Rates at Week 24 Comparable between SB4 and ETN



*One patient from the SB4 group was excluded from the FAS due to missing efficacy data at baseline.

ACR50/70, American College of Rheumatology 50%/70% response; ETN, etanercept; FAS: full analysis set; NRI: non-responder imputation; PPS, per-protocol set.

Emery P, et al. Ann Rheum Dis. Jul 6. pii: annrheumdis-2015-207588.

Two main questions

- Prescription of biosimilar when to start new therapy or to change therapy for medical reasons?
  - Not controversial (?)

- **Can patients on stable treatment with an originator drug be switched to a cheaper biosimilar of this drug?**
  - **More controversial (concerning efficacy, safety and immunogenicity)**

Evidence to support switching from reference product to biosimilar for non-medical reasons

- Extension of phase 3 RCTs
- Switching within RCTs
- Real life data
- Randomizing patients on stable long-term treatment

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EXTENDED REPORT

Efficacy and safety of switching from reference infliximab to CT-P13 compared with maintenance of CT-P13 in ankylosing spondylitis: 102-week data from the PLANETAS extension study

Won Park,[1] Dae Hyun Yoo,[2] Pedro Miranda,[3] Marek Brzosko,[4] Piotr Wiland,[5] Sergio Gutierrez-Ureña,[6] Helena Mikazane,[7] Yeon-Ah Lee,[8] Svitlana Smiyan,[9] Mie-Jin Lim,[1] Vladimir Kadinov,[10] Carlos Abud-Mendoza,[11] HoUng Kim,[12] Sang Joon Lee,[12] YunJu Bae,[12] SuYeon Kim,[12] Jürgen Braun[13]

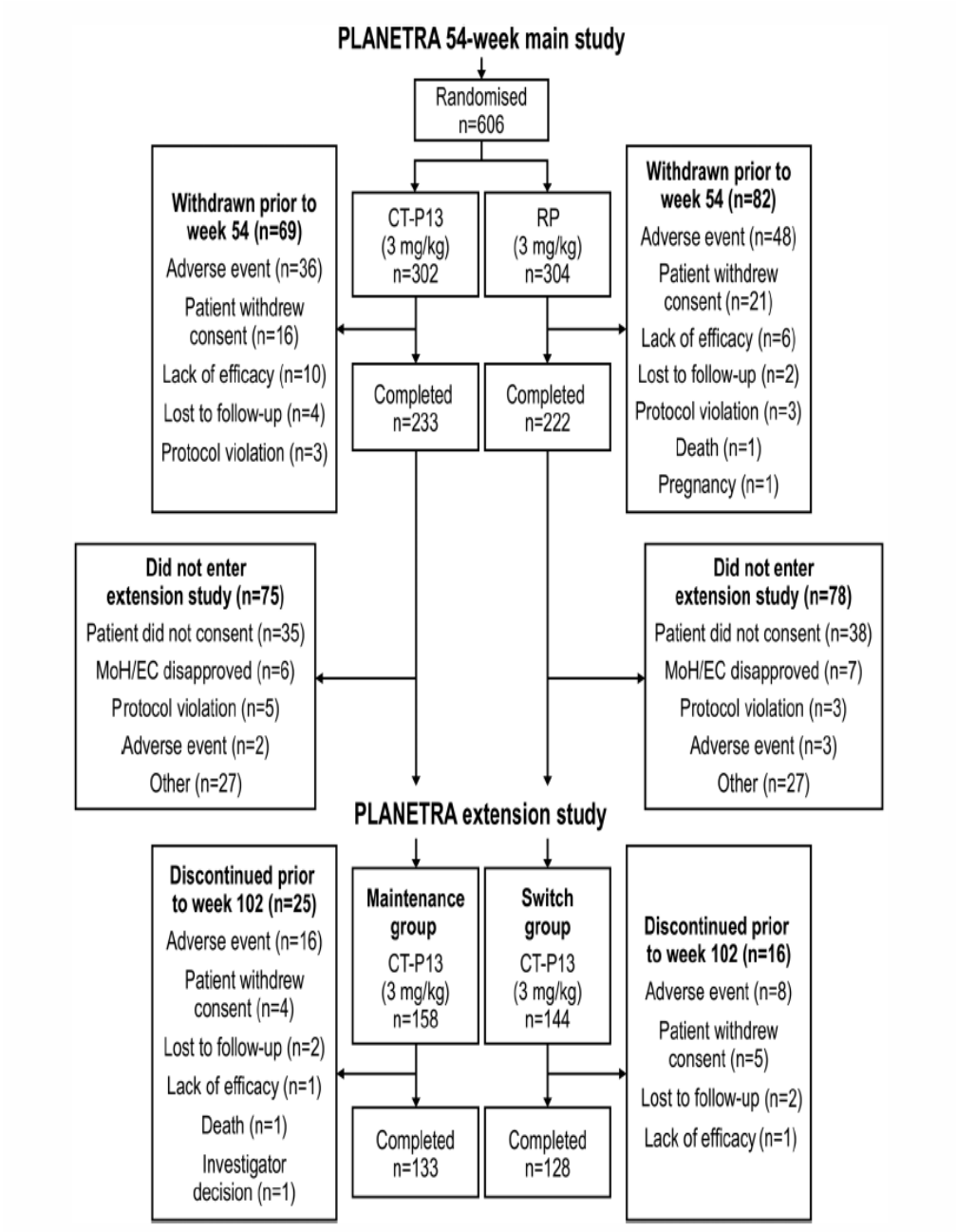
OPEN ACCESS

EXTENDED REPORT

Efficacy and safety of CT-P13 (biosimilar infliximab) in patients with rheumatoid arthritis: comparison between switching from reference infliximab to CT-P13 and continuing CT-P13 in the PLANETRA extension study

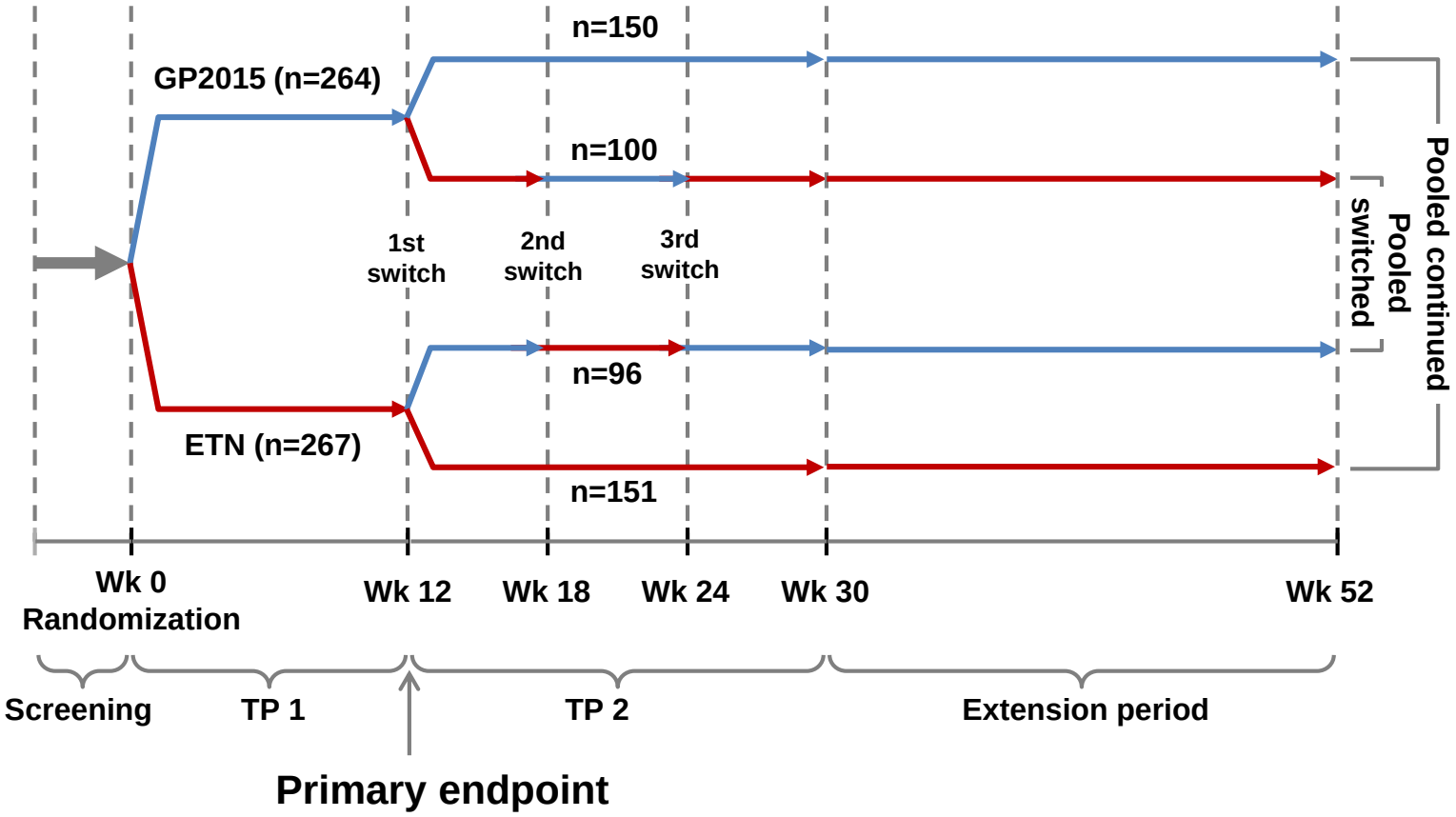
Dae Hyun Yoo,[1] Nenad Prodanovic,[2] Janusz Jaworski,[3] Pedro Miranda,[4] Edgar Ramiterre,[5] Allan Lanzon,[6] Asta Baranauskaite,[7] Piotr Wiland,[8] Carlos Abud-Mendoza,[9] Boycho Oparanov,[10] Svitlana Smiyan,[11] HoUng Kim,[12] Sang Joon Lee,[12] SuYeon Kim,[12] Won Park[13]

Park W, et al. Ann Rheum Dis. 2017;76:346–354;
Yoo DH, et al. Ann Rheum Dis. 2017;76:355–363.



Yoo DH, et al. Ann Rheum Dis. 2017;76:355–363.

Study design – EGALITY study

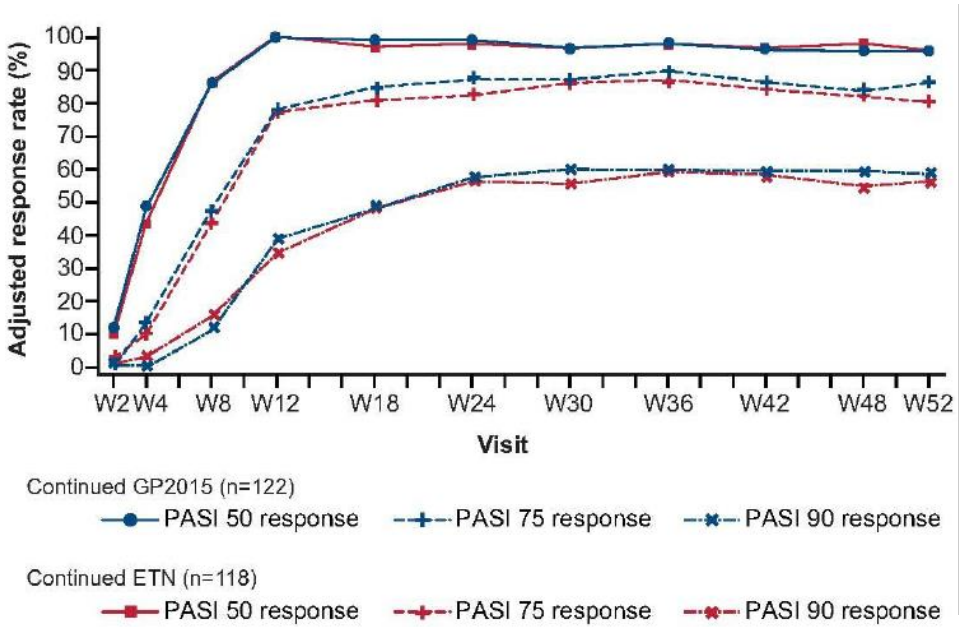


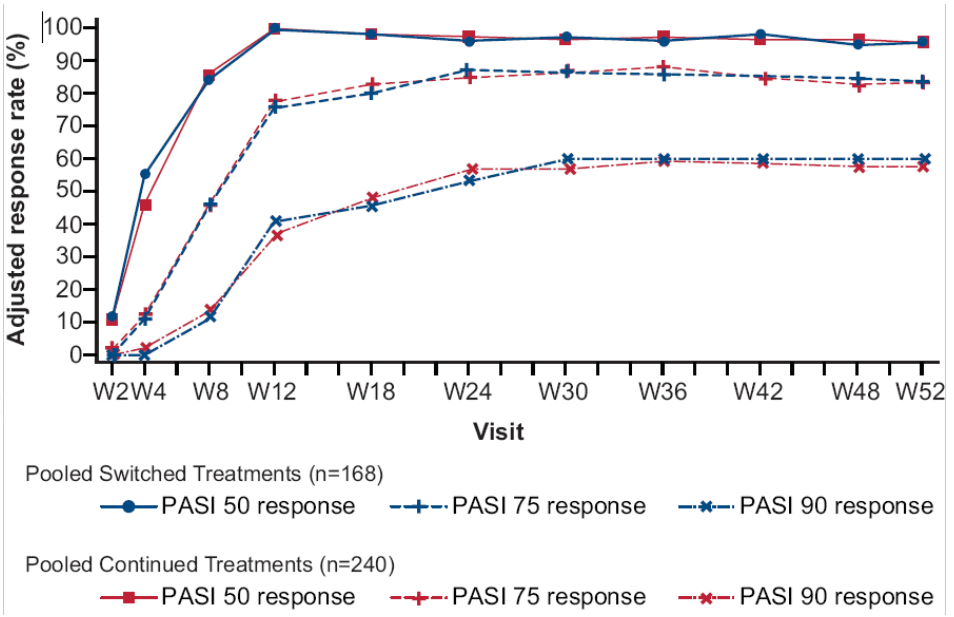
ETN, reference etanercept; TP, treatment period; Wk, week

Griffiths CE et al. Br J Dermatol. 2016 Oct 27. doi: 10.1111/bjd.15152. [Epub ahead of print]

Biosimilar Switch Study

GP2015 in PsO [a]





[a] Griffiths, C.E.M., Thaçi, D., Gerdes, S., Arenberger, P., Pulka, G., Kingo, K., Weglowska, J., the EGALITY study group, Hattebuhr, N., Poetzl, J., Woehling, H., Wuerth, G. and Afonso, M. (2017), The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. Br J Dermatol, 176: 928–938. doi:10.1111/bjd.15152

CONCISE REPORT

A nationwide non-medical switch from originator infliximab to biosimilar CT-P13 in 802 patients with inflammatory arthritis: 1-year clinical outcomes from the DANBIO registry

Bente Glintborg,[1,2] Inge Juul Sørensen,[3,4] Anne Gitte Loft,[5] Hanne Lindegaard,[6] Asta Linauskas,[7] Oliver Hendricks,[8] Inger Marie Jensen Hansen,[9] Dorte Vendelbo Jensen,[2,3] Natalia Manilo,[10] Jakob Espesen,[11] Mette Klarlund,[12] Jolanta Grydehøj,[13] Sabine Sparre Dieperink,[3] Salome Kristensen,[14] Jimmi Sloth Olsen,[15] Henrik Nordin,[16] Stavros Chrysidis,[17] Dorte Dalsgaard Pedersen,[18] Michael Veedfald Sørensen,[19] Lis Smedegaard Andersen,[20] Kathrine Lederballe Grøn,[3] Niels Steen Krogh,[21] Lars Pedersen,[22] Merete Lund Hetland, [1,4]On behalf of all departments of rheumatology in Denmark

To cite: Glintborg B, Sørensen IJ, Loft AG, *et al*. *Ann Rheum Dis* Published Online First: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2016-210742

Non-medical switches

- Switch from originator bDMARD to biosimilar for non medical reasons
- Non-medical switch, DK:

May 2015:	originator infliximab	→	biosimilar CT-P13
April 2016:	originator etanercept	→	biosimilar SB4

- All Danish patients with inflammatory diseases (rheumatology, dermatology, gastroenterology)

Disease activity and flares

	Disease activity			Changes over time		P*
	3 months pre-switch	Switch	3 months post-switch	Δpre-switch	Δpost-switch	
RA, n=403						
Patients with available data, n	319	310	309	276	265	-
DAS28	2.2	2.2	2.2	0.1	0.0	0.8
HAQ (0-3)	0.6	0.6	0.6	0.0	0.1	0.3
CRP, mg/l (<10mg/L)	4	4.5	5	0	0	0.4
Patient's global score, mm	26	25	26	0.0	0.0	0.5
PsA, n=120						
Patients with available data, n	94	92	94	78	81	-
DAS28	2.5	2.3	2.4	0.0	0.1	0.10
HAQ (0-3)	0.5	0.6	0.5	0.0	0.0	0.5
CRP, mg/l (<10mg/L)	4	4	3	0	0	0.046
Patient's global score, mm	32	34	35	-3	0	0.01
AxSpA, n=279						
Patients with available data, n	202	199	204	160	169	-
BASDAI, mm	23	24	25	0	0	0.3
CRP, mg/l	3	4	4	0	0	0.2
Patient's global score, mm	26	31	27	1	-1	0.7
ASDAS	1.8	2.0	2.0	0.0	0.0	0.8
Flare rates pre-switch vs. post-switch						
RA and PsA (ΔDAS28≥0.6), %				22	22	
RA and PsA (ΔDAS28≥1.2), %				10	10	
AxSpA (ΔASDAS>1.1), %				3	4	

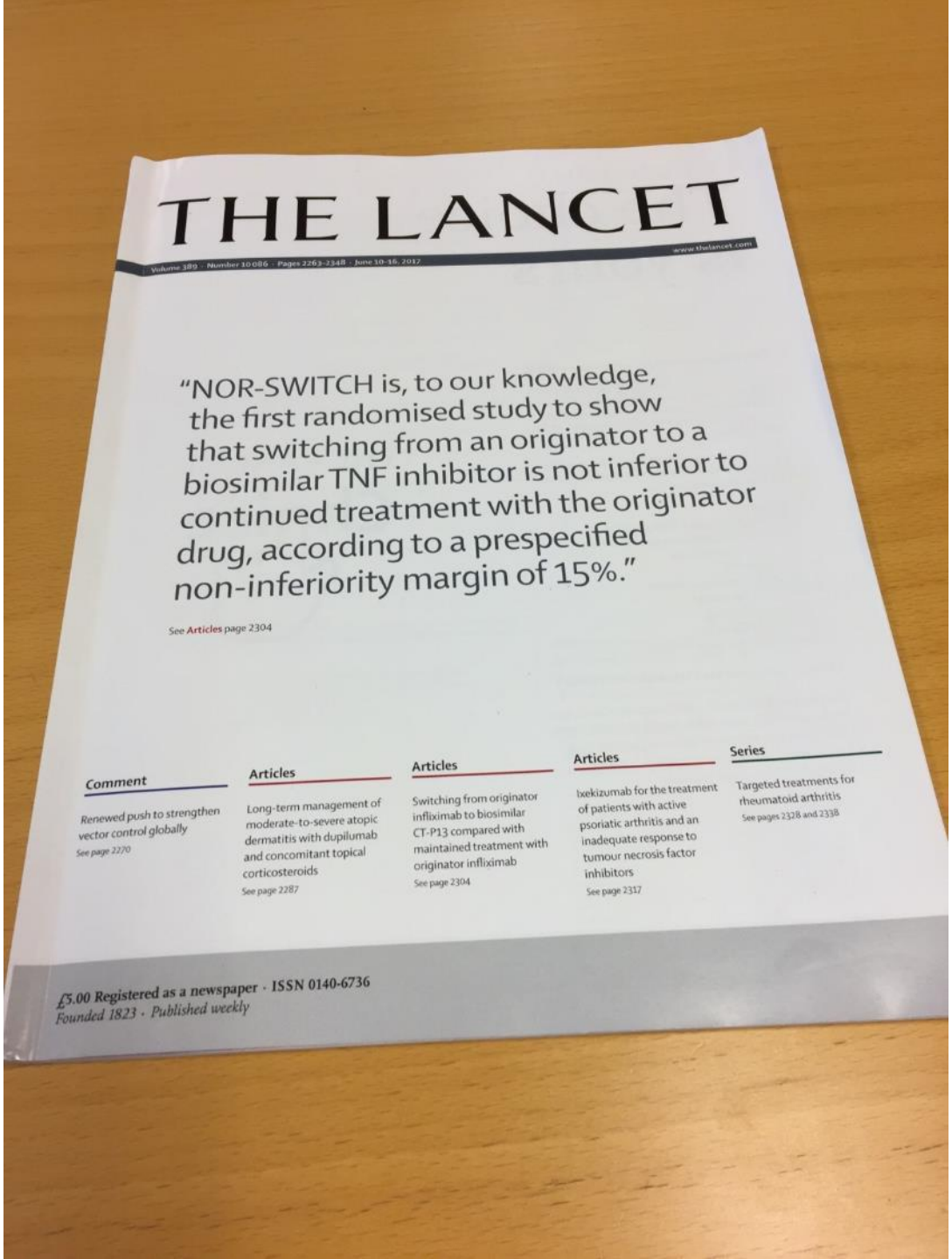
Numbers are medians unless otherwise stated

Glintborg B, Sørensen IJ, Loft AG, et al.
Ann Rheum Dis, Online First May 8th 2017
doi:10.1136/annrheumdis-2016-210742

Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial

Kristin K Jørgensen, Inge C Olsen*, Guro L Goll*, Merete Lorentzen*, Nils Bolstad, Espen A Haavardsholm, Knut E A Lundin, Cato Mørk†, Jørgen Jahnsen†, Tore K Kvien†, on behalf of the NOR-SWITCH study group*

Published Online
May 11, 2017
http://dx.doi.org/10.1016/S0140-6736(17)30068-5



THE LANCET

Volume 389 · Number 10086 · Pages 2263–2348 · June 10–16, 2017

www.thelancet.com

"NOR-SWITCH is, to our knowledge, the first randomised study to show that switching from an originator to a biosimilar TNF inhibitor is not inferior to continued treatment with the originator drug, according to a prespecified non-inferiority margin of 15%."

See **Articles** page 2304

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Founded 1823 · Published weekly

Study objectives

Primary:

•To assess if CT-P13 is **non-inferior** to innovator infliximab (INX) with regard to **disease worsening** in patients who have been on stable INX treatment for at least 6 months

Secondary:

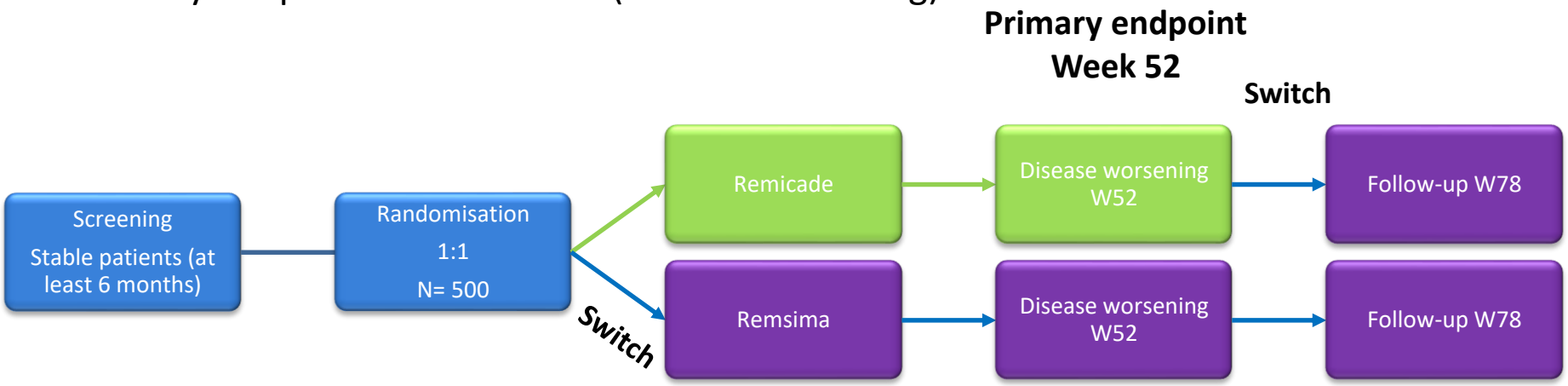
•To assess the **safety** and **immunogenicity** of CT-P13 compared to INX in patients who have been on stable INX treatment for at least 6 months

•To compare the **efficacy** of CT-P13 to INX in patients who have been on stable INX treatment for at least 6 months applying generic and disease-specific outcome measures

NOR SWITCH

NOR- SWITCH Study design

- Exploring switching for non-medical reasons
- Primary endpoint: Effectiveness (disease worsening)



A randomized, double-blind, parallel-group study to evaluate the safety and efficacy of switching from innovator infliximab to biosimilar infliximab compared with continued treatment with innovator infliximab in patients with rheumatoid arthritis, spondylarthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease and chronic plaque psoriasis

Assumption : 30% worsening in 52 weeks
Non-inferiority margin:15%

Open Label Follow-up

NOR SWITCH

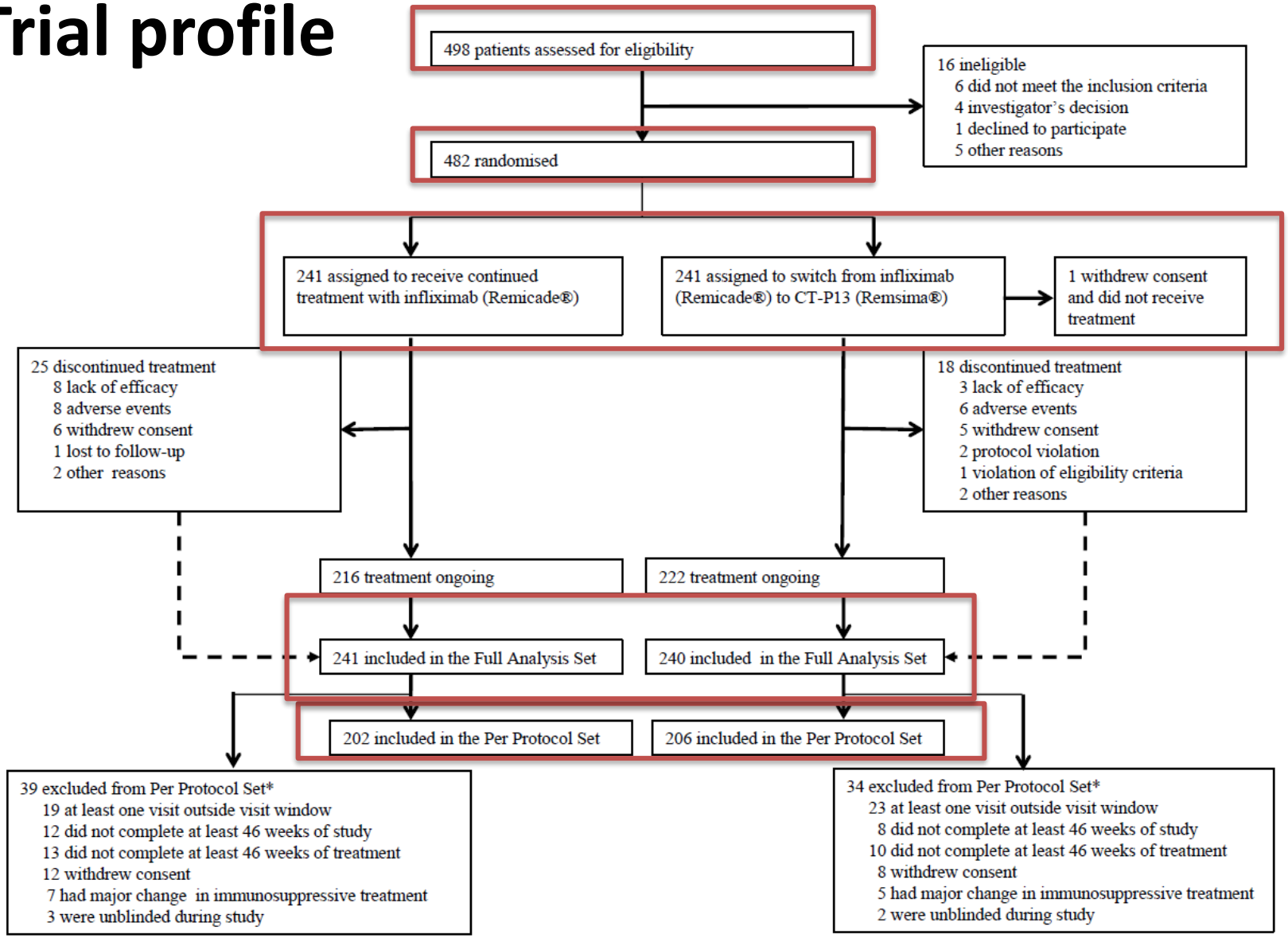
Table 1: The numbers in the cells represent the total number of patients needed in total. All calculations are based on a power of 80% and alpha 2.5%

Non-inferiority Margin	*10% disease worsening at 52 w*	*20% disease worsening at 52 w*	*30% disease worsening at 52 w*
10%	248	504	660
15 %	126	224	294
20 %	72	126	166

Table 2: The numbers in the cells represent the total number of patients needed in total. All calculations are based on a power of 90% and alpha 2.5%.

Non-inferiority Margin	*10% disease worsening at 52 w*	*20% disease worsening at 52 w*	*30% disease worsening at 52w*
10%	380	674	884
15 %	170	300	394
20 %	96	170	222

Trial profile



NOR SWITCH

Kvien T. NOR-SWITCH Principal Investigator. Unpublished data.

Primary endpoint

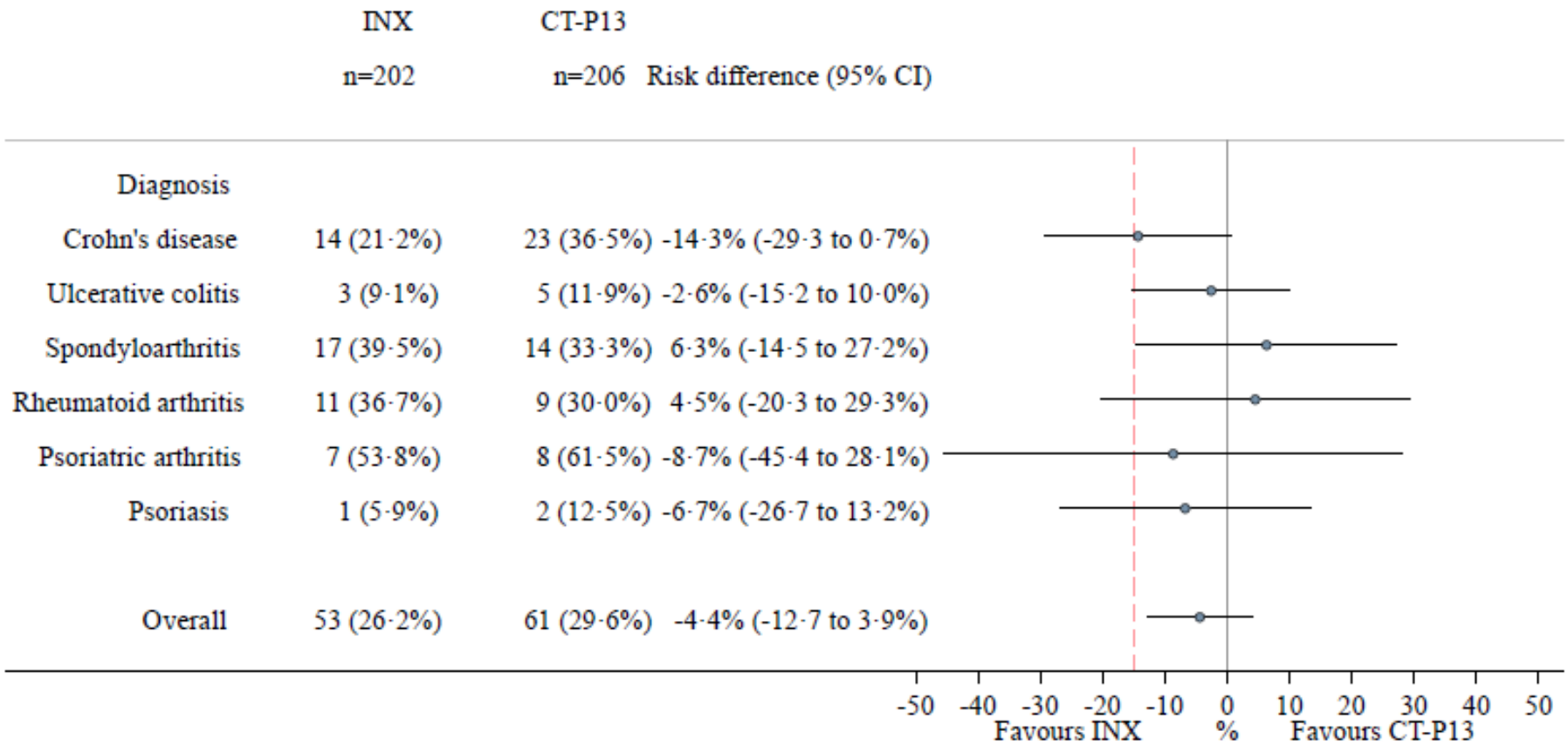
	INX (n= 202)	CT-P13 (n=206)	Rate difference (95% CI)
Disease worsening*	53 (26.2%)	61 (29.6%)	-4.4 (-12.7 – 3.9)

* UC: increase in p-Mayo score of ≥ 3 points and a p-Mayo score of ≥ 5 points,
CD: increase in HBI of ≥ 4 points and a HBI score of ≥7 points
RA/PsA: increase in DAS28 of ≥ 1.2 from randomization and a DAS score of ≥ 3.2
AS/SpA: increase in ASDAS of ≥1.1 and ASDAS of ≥ 2.1
Psoriasis: increase in PASI of ≥ 3 points from randomization and a minimum PASI score of ≥ 5

If a patient does not fulfill the formal definition, but experiences a clinically significant worsening according to both the investigator and patient and which leads to a major change in treatment this should be considered as a disease worsening but recorded separately in the CRF

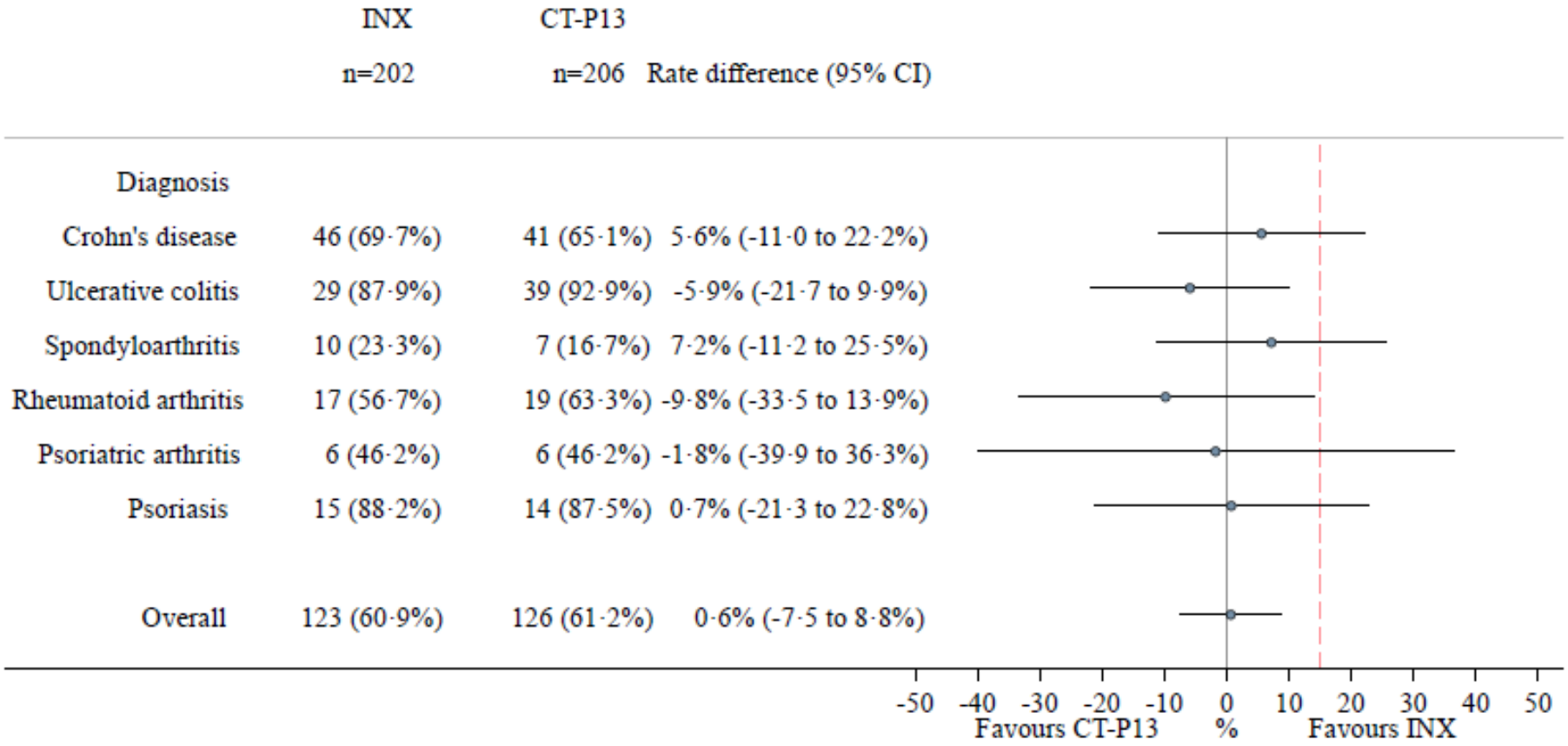
NOR SWITCH

Disease Worsening



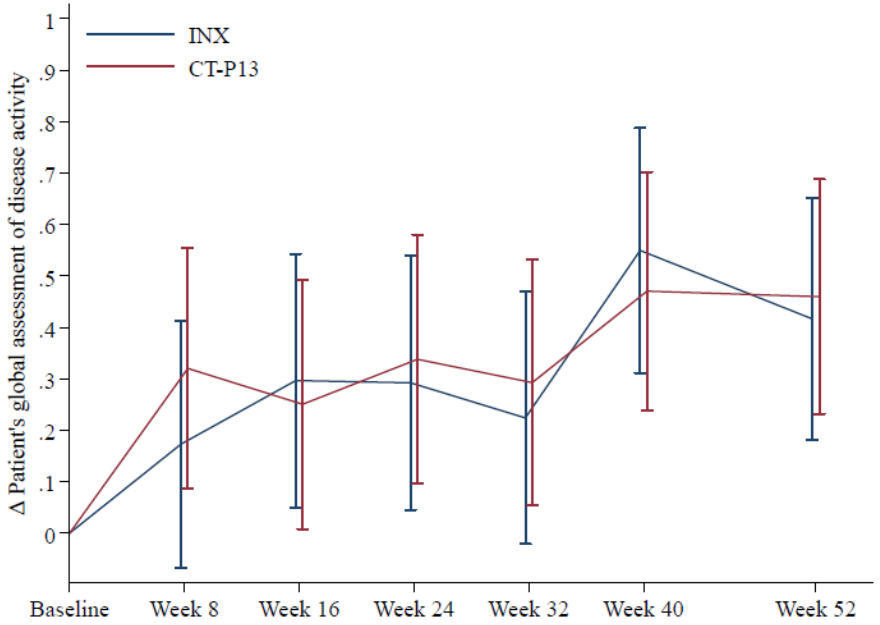
NOR SWITCH

Remission

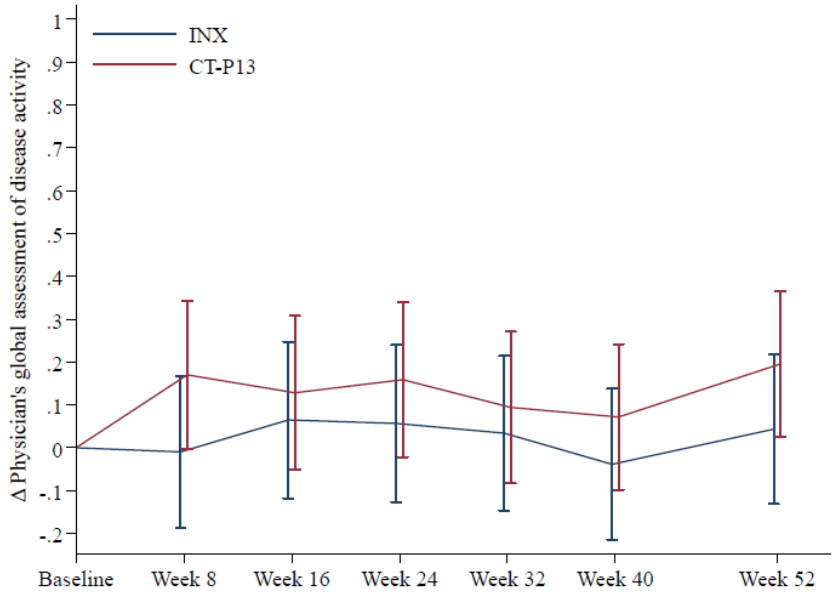


NOR SWITCH

Global Assessment of Disease Activity



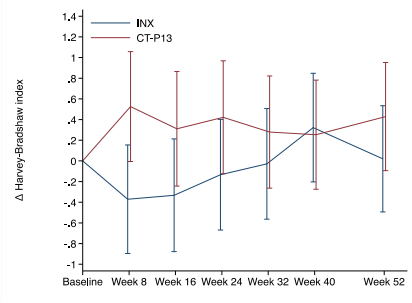
Patient



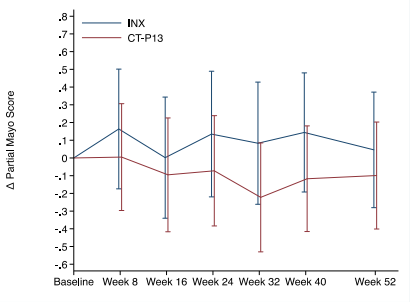
Physician

NOR SWITCH

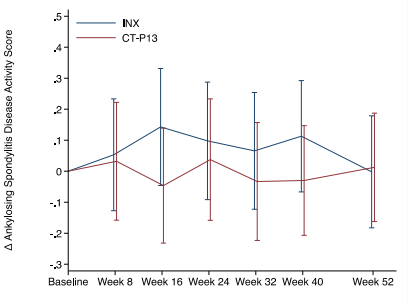
Disease Activity



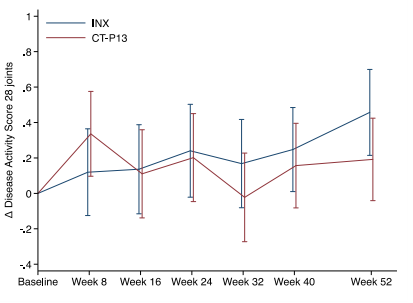
HBI



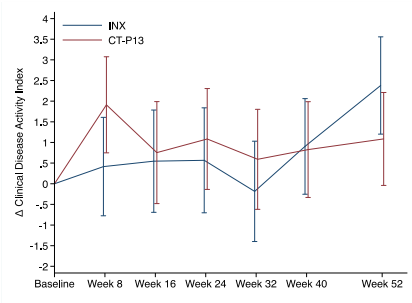
p-Mayo score



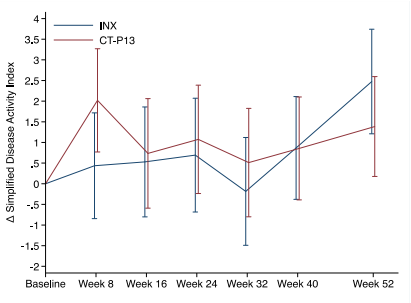
ASDAS



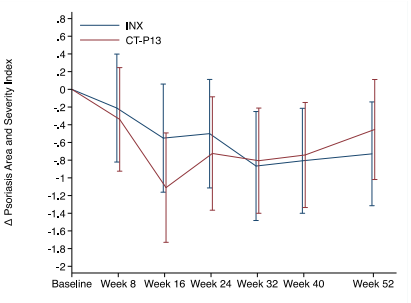
DAS28



CDAI



SDAI

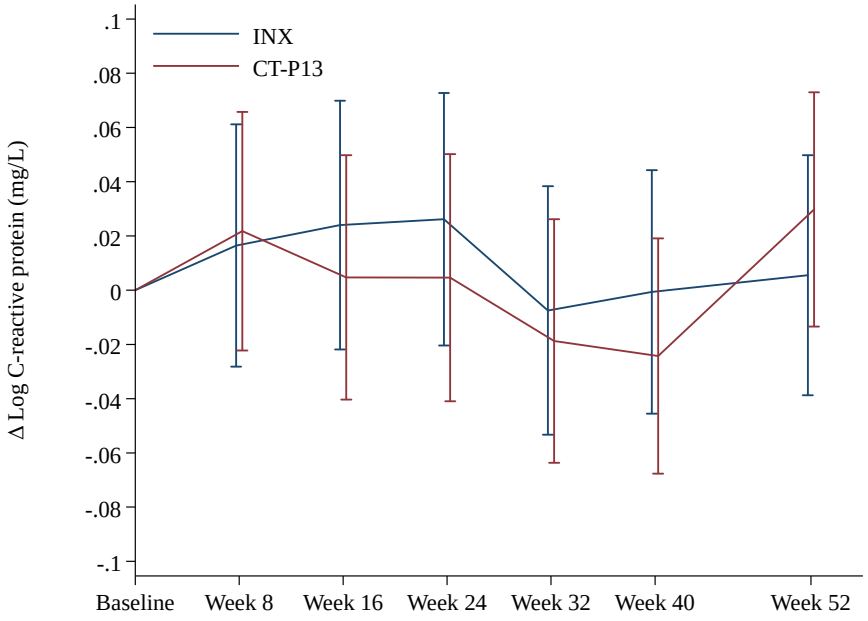


PASI

NOR SWITCH

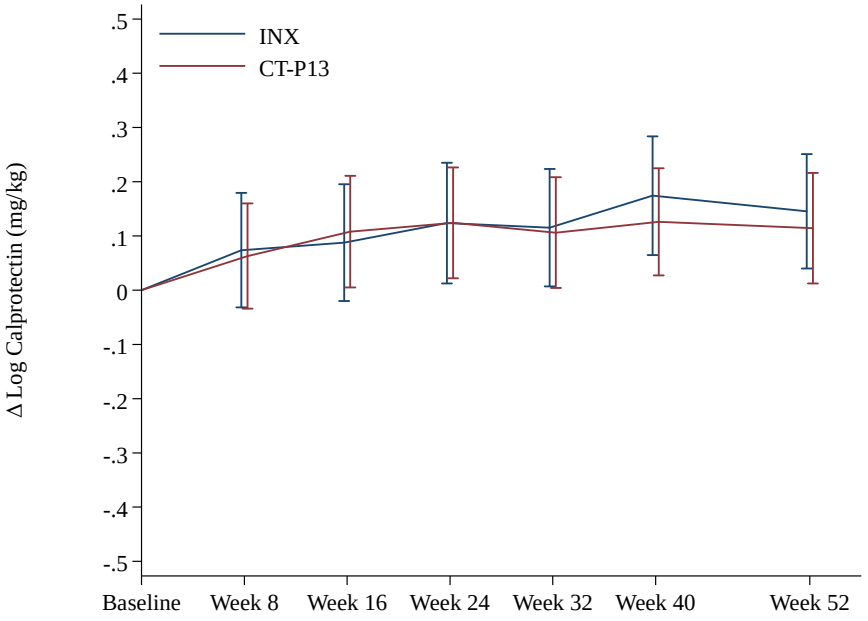
CRP and Calprotectin

Over all



CRP

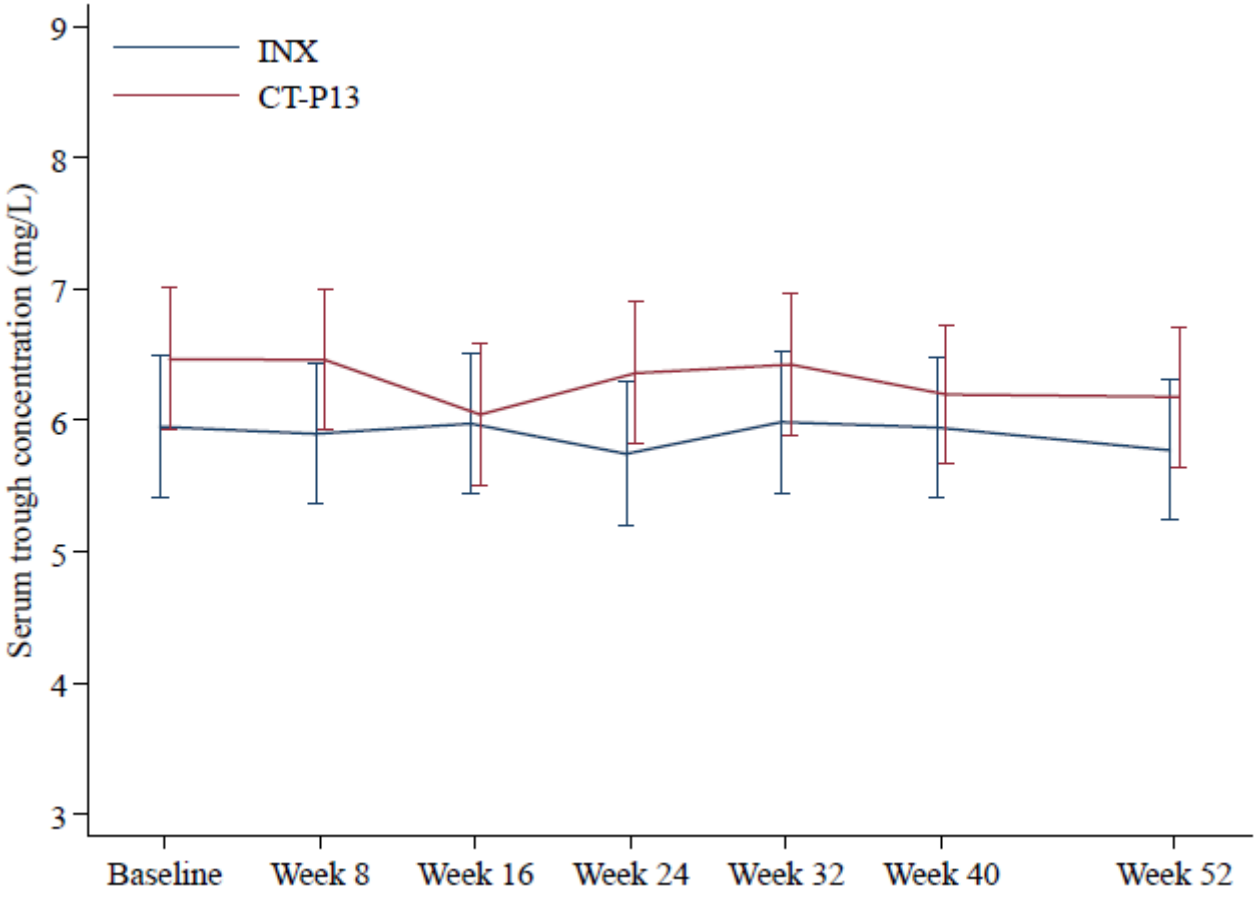
IBD



Calprotectin

NOR SWITCH

Drug trough levels



Over all

NOR SWITCH

Anti-drug antibodies (ADAb)

	INX (n= 241)	CT-P13 (n=240)
ADAb observed at any time point	26 (10.8%)	30 (12.5%)
Incidence of ADAb	17 (7.1%)	19 (7.9%)

NOR SWITCH

Adverse events – safety population

Overview *	INX (n=241)	CT-P13 (n=240)
SUSAR	0	0
Serious adverse events (SAE)	[32] 24 (10·0%)	[27] 21 (8·8%)
Adverse events (AE)	[422] 168 (69·7%)	[401] 164 (68·3%)
Adverse event leading to study drug discontinuation	[18] 9 (3·7%)	[9] 8 (3·3%)

*[number of events] n (%)

NOR SWITCH

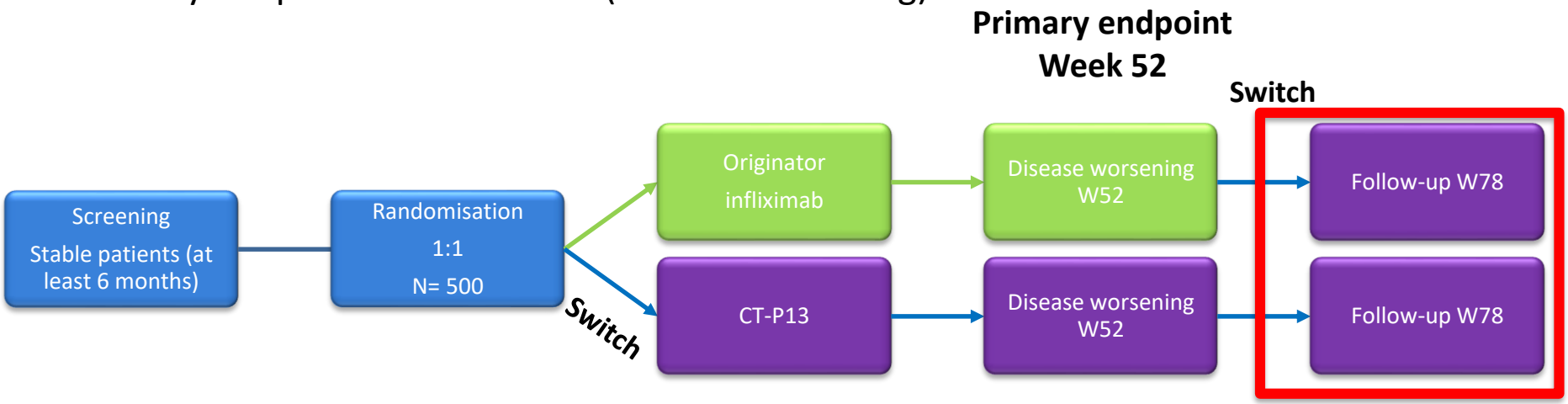
Interpretation

- The NOR-SWITCH trial demonstrated that switch from INX to CT-P13 was not inferior to continued treatment with INX
- The results support switching from INX to CT-P13 for non-medical reasons

NOR SWITCH

NOR- SWITCH Study design

- Exploring switching for non-medical reasons
- Primary endpoint: Effectiveness (disease worsening)

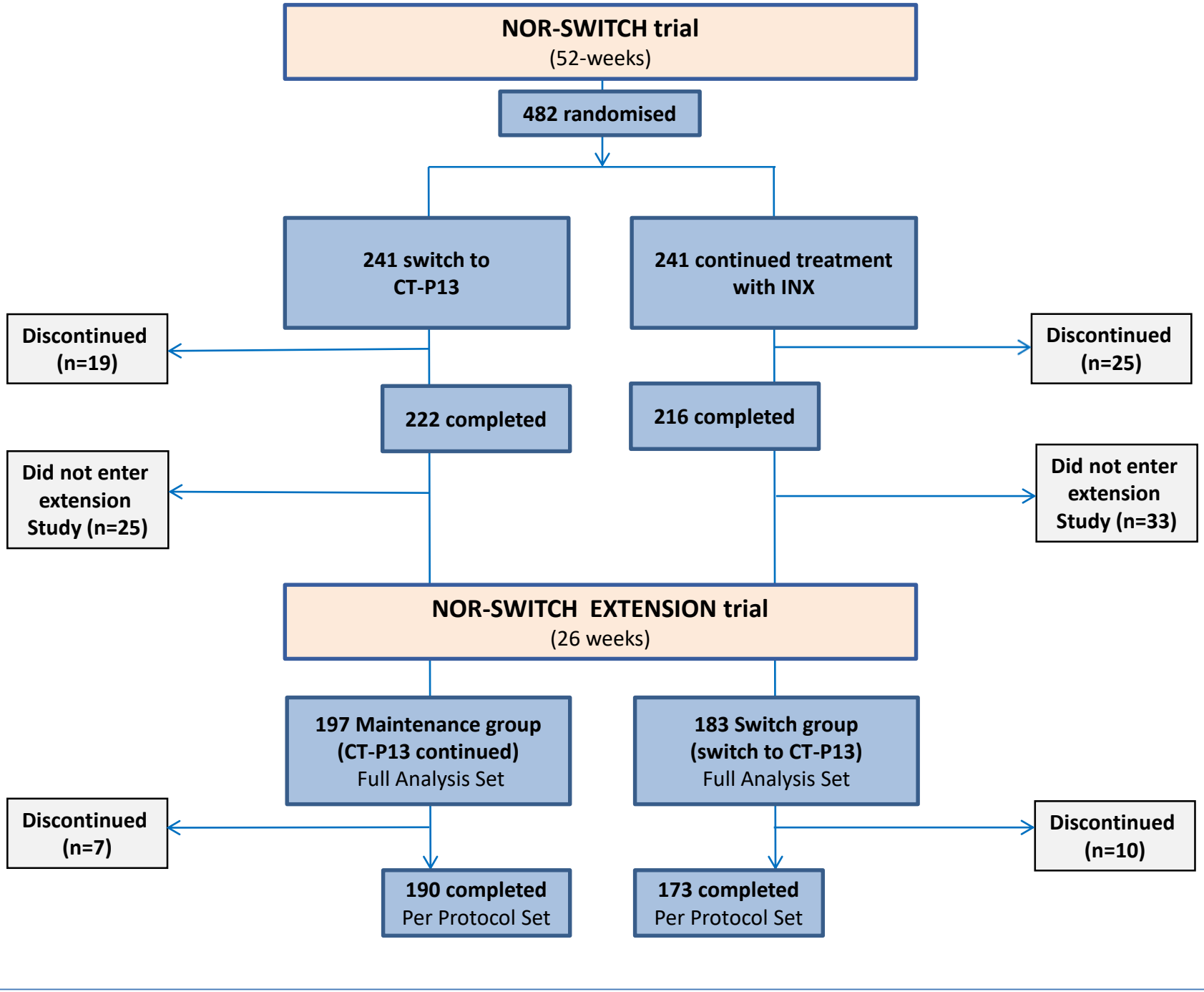


A randomized, double-blind, parallel-group study to evaluate the safety and efficacy of switching from innovator infliximab to biosimilar infliximab compared with continued treatment with innovator infliximab in patients with rheumatoid arthritis, spondylarthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease and chronic plaque psoriasis

Assumption : 30% worsening in 52 weeks
Non-inferiority margin:15%

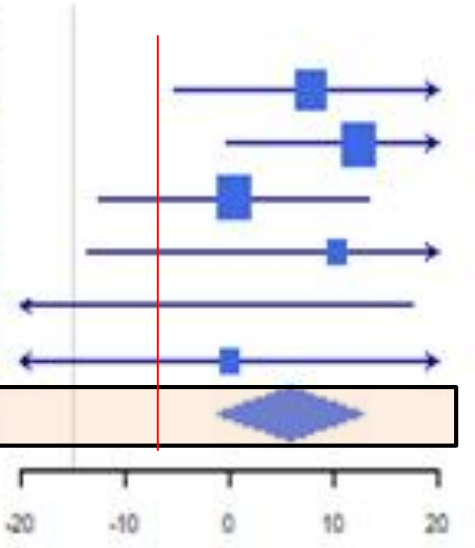
Open Label Follow-up

NOR SWITCH


NOR-SWITCH trial
(52-weeks)
482 randomised
241 switch to CT-P13
241 continued treatment with INX
Discontinued (n=19)
Discontinued (n=25)
222 completed
216 completed
Did not enter extension Study (n=25)
Did not enter extension Study (n=33)
NOR-SWITCH EXTENSION trial
(26 weeks)
197 Maintenance group (CT-P13 continued)
Full Analysis Set
183 Switch group (switch to CT-P13)
Full Analysis Set
Discontinued (n=7)
Discontinued (n=10)
190 completed
Per Protocol Set
173 completed
Per Protocol Set

Nor-Switch extension: disease worsening

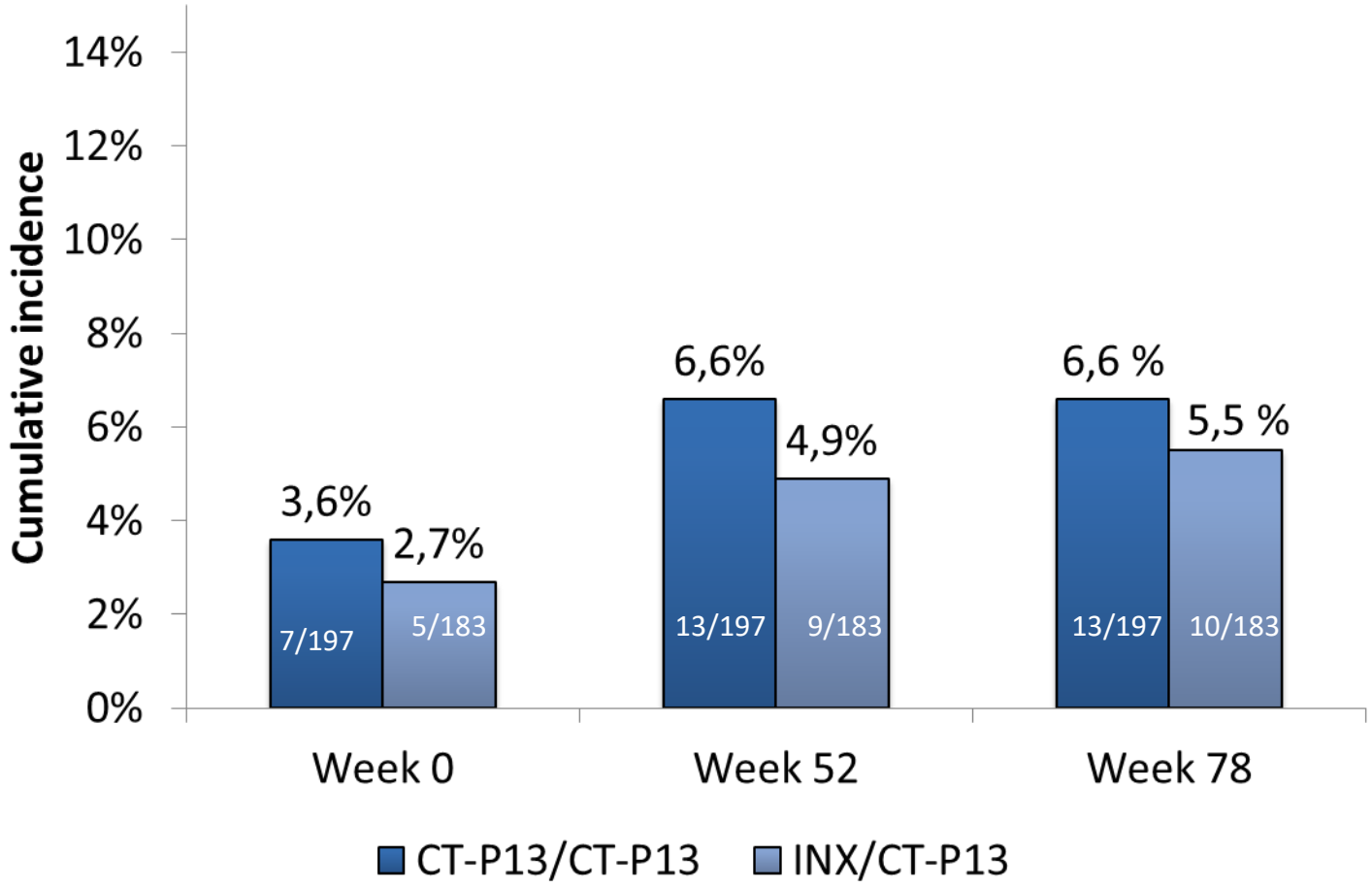
Diagnosis	Maintenance	Switch	Risk difference (95% CI)
Crohn's disease	13/63 (20.6%)	8/61 (13.1%)	7.9% (-5.2 to 21)
Ulcerative colitis	6/39 (15.4%)	1/35 (2.9%)	12.4% (-0.1 to 25)
Spondyloarthritis	3/38 (7.9%)	2/28 (7.1%)	0.6% (-12.2 to 13.5)
Rheumatoid arthritis	9/26 (34.6%)	6/27 (22.2%)	10.5% (-13.6 to 34.6)
Psoriatic arthritis	1/8 (12.5%)	3/9 (33.3%)	-20.8% (-59.1 to 17.6)
Psoriasis	0/16 (0%)	0/13 (0%)	0% (-20.6,24.7)
Overall	32/190 (16.8%)	20/173 (11.6%)	5.9% (-1.1 to 12.9)



Maintenance group: **CT-P13 throughout study period**
Switch group: **INX main study period, switched to CT-P13**

NOR SWITCH

Anti-drug antibodies



*neutralising antibodies, measured only in patients with drug trough level ≤ 5 mg/L

NOR SWITCH

Interpretation

- The NOR-SWITCH extension trial confirms results from main trial:
  - a switch from INX to CT-P13 did not lead to an increased rate of disease worsening, adverse events or immunogenicity concerns in overall study population

NOR SWITCH

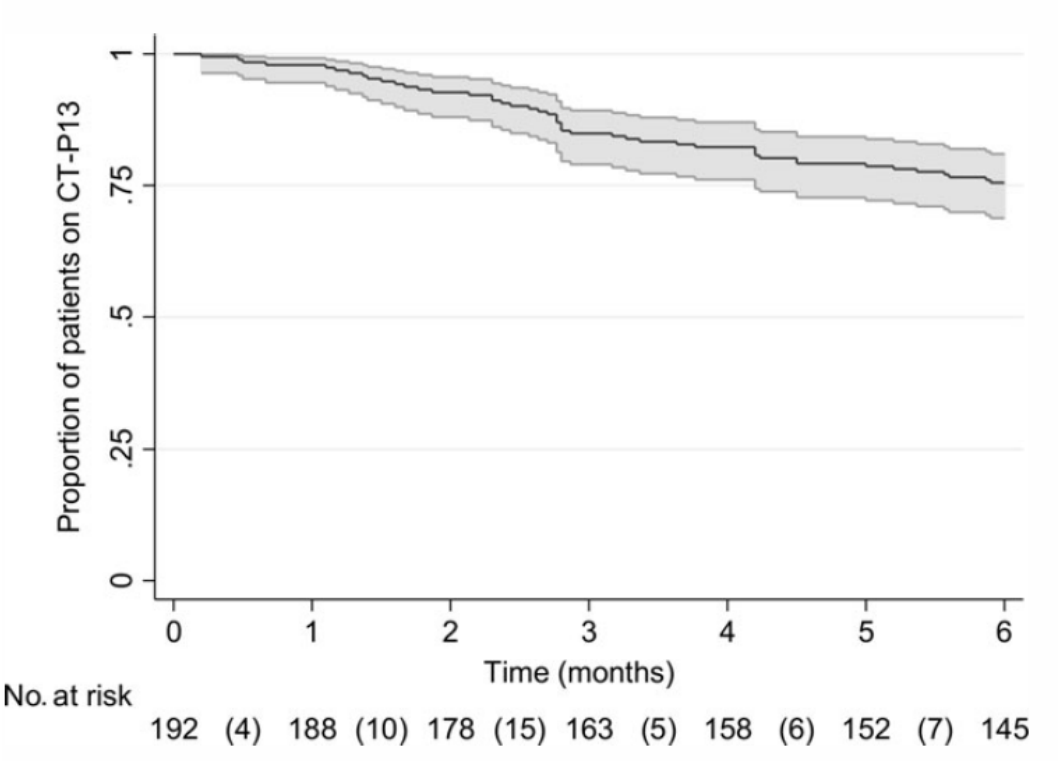
NOCEBO effect and importance of information

NOR SWITCH

Subjective Complaints as the Main Reason for Biosimilar Discontinuation After Open-Label Transition From Reference Infliximab to Biosimilar Infliximab

Lieke Tweehuysen,[1] Bart J. F. van den Bemt,[2] Iris L. van Ingen,[3] Alphons J. L. de Jong,[4] Willemijn H. van der Laan,[5] Frank H. J. van den Hoogen,[2] and Alfons A. den Broeder[2]

BIO-SWITCH study



ARTHRITIS & RHEUMATOLOGY
Vol. 0, No. 0, Month 2018, pp 1–11
DOI 10.1002/art.40516

BIO-SPAN

Open-Label, Non-Mandatory Transitioning From Originator Etanercept to Biosimilar SB4

Six-Month Results From a Controlled Cohort Study

Lieke Tweehuysen,[1] Victor J. B. Huiskes,[1] Bart J. F van den Bemt,[2] Johanna E. Vriezekolk,[1] Steven Teerenstra,[3] Frank H. J. van den Hoogen,[4] Cornelia H. van den Ende,[4] and Alfons A. den Broeder[4]

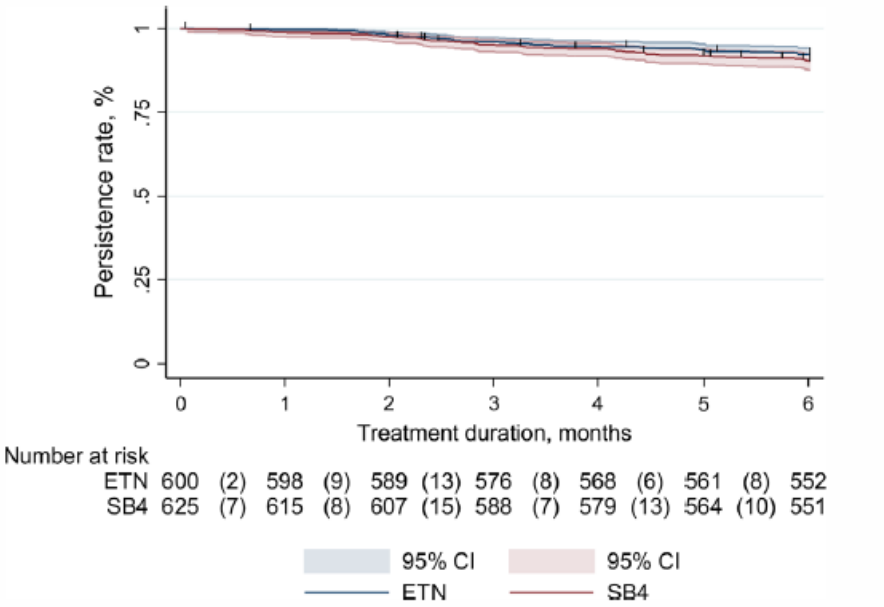


Table 1 Biosimilars for rheumatic diseases for which data have been published in peer-reviewed journals or presented at international scientific meetings

Reference product	Biosimilar molecules
Adalimumab	ABP501
	BI 695501
	CHS-1420
	GP-2017
	M923
	SB5
	ZRC-3197
Etanercept	CHS-0214
	GP2015
	HD203
	SB4*
Infliximab	BOW015†
	CT-P13*‡
	PF-06438179
	SB2
Rituximab	CT-P10
	GP2013
	PF-05280586

*Approved by EMA and multiple other countries.
†Approved in India.
‡Recommended for approval by FDA.
EMA, European Medicines Agency; FDA, Food and Drug Administration.

Dörner T et al
Ann Rheum Dis 2016

Conclusions

- Most data support that switching/ transitioning from originator bDMARD to bsDMARD is safe
- Cost-saving is the major (only?) motivation combined with better access to good therapies for more people
- Nocebo-effect may be an issue and more data are needed on how information may improve acceptability and drug retention