Biosimilars…

- Κατώτερα ?
- Ανώτερα ?
- Ανοσογονικό(τερα) ?

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]

ABSTRACT

Objectives To compare the pharmacokinetics (PK), safety and efficacy of innovator infliximab (INX) and CT-P13, a biosimilar to INX, in patients with active ankylosing spondylitis (AS).

Methods Phase 1 randomised, double-blind, multicentre, multinational, parallel-group study. Patients

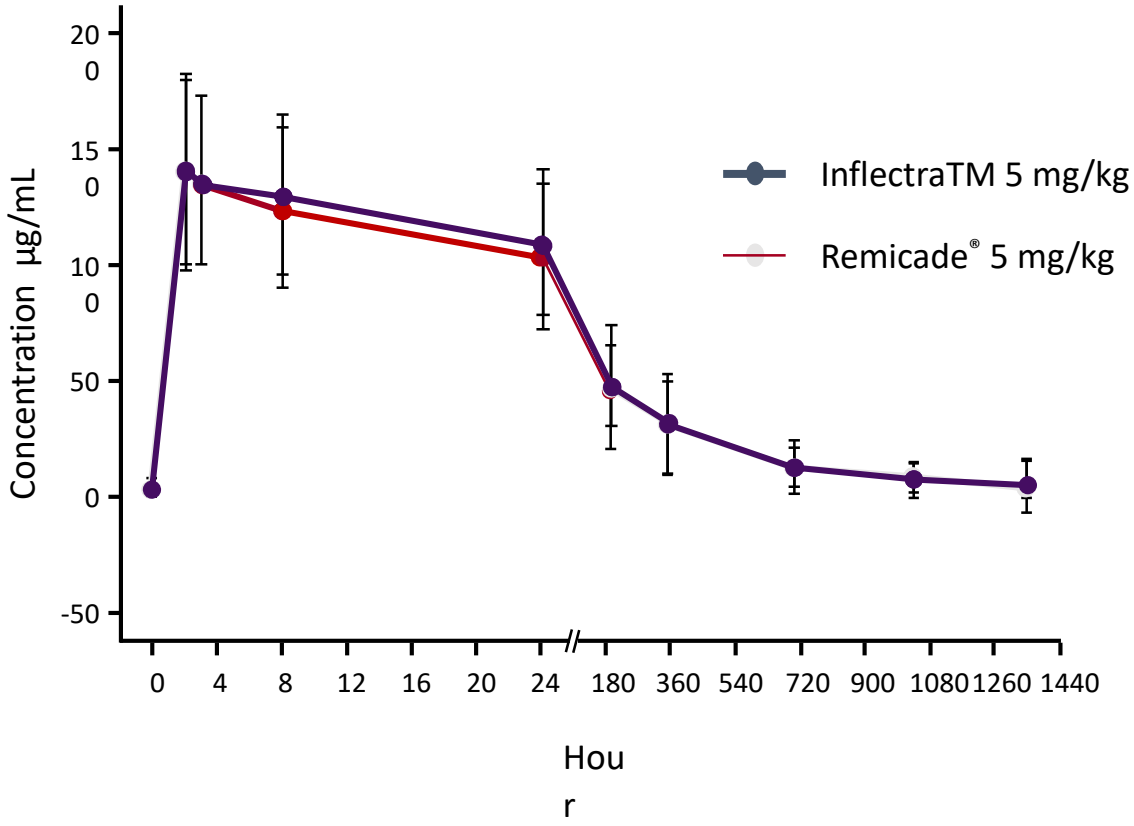
seen as early as 2 weeks after initiation of therapy and an acceptable safety profile.[2–4] In the Ankylosing Spondylitis Study for the Evaluation of Recombinant Infliximab Therapy (ASSERT) trial, patients receiving INX also showed significant improvement versus placebo in 20% and 40% improvement response according to Assessment in

in the CT-P13 and INX groups more than one adverse event occurred in 64.8% and 63.9% of patients, infusion reactions occurred in 3.9% and 4.9%, active tuberculosis occurred in 1.6% and 0.8%, and 27.4% and 22.5% of patients tested positive for anti-drug antibodies, respectively.

Conclusions The PK profiles of CT-P13 and INX were equivalent in patients with active AS. CT-P13 was well tolerated, with an efficacy and safety profile comparable to that of INX up to week 30.

INTRODUCTION

Innovator infliximab (INX), a chimeric monoclonal



Source: EMA Inflectra EPAR, June 2013

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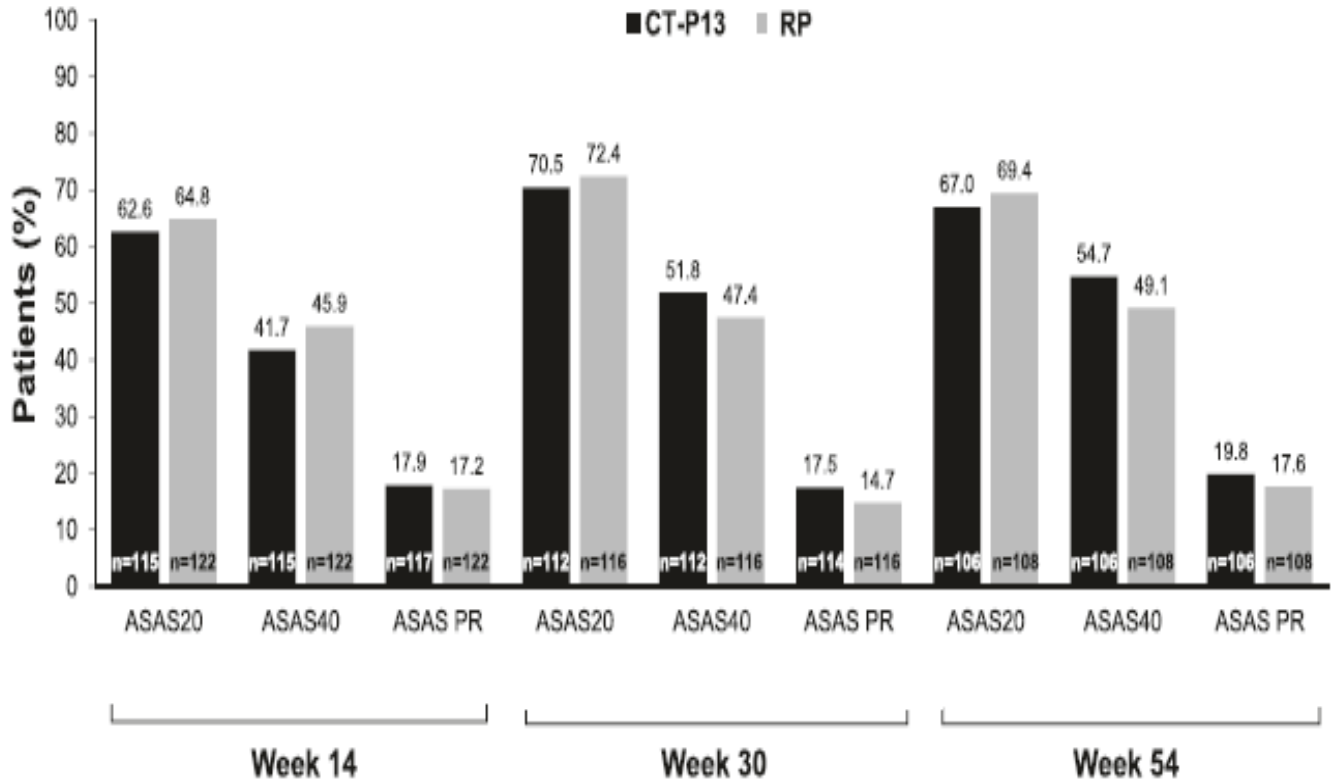

Park et al. Arthritis Research & Therapy 2016 :18, 25

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]

ABSTRACT

Objectives To compare the efficacy and safety of innovator infliximab (INX) and CT-P13, an INX biosimilar, in active rheumatoid arthritis patients with inadequate response to methotrexate (MTX) treatment.

demonstrated beneficial effects in rheumatoid arthritis (RA) patients, was approved in 1999. The approval of INX was based on data from the ATTRACT study.[1]

The availability of targeted biological therapies

rates, ACR50/ACR70 responses and all other PK and PD endpoints were highly similar at week 30. Incidence of drug-related adverse events (35.2% vs 35.9%) and detection of antidrug antibodies (48.4% vs 48.2%) were highly similar for CT-P13 and INX, respectively.

Conclusions CT-P13 demonstrated equivalent efficacy to INX at week 30, with a comparable PK profile and immunogenicity. CT-P13 was well tolerated, with a safety profile comparable with that of INX.

ClinicalTrials.gov Identifier NCT01217086

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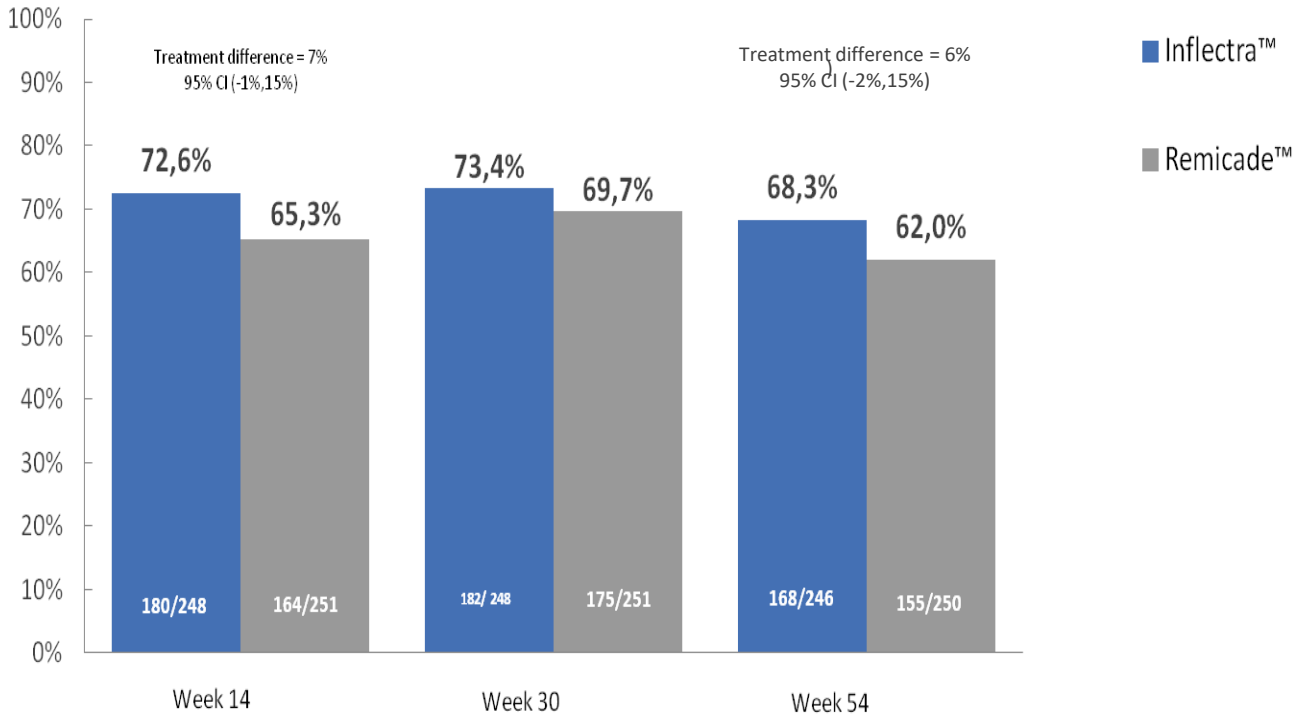
ACR20 Efficacy - per protocol population

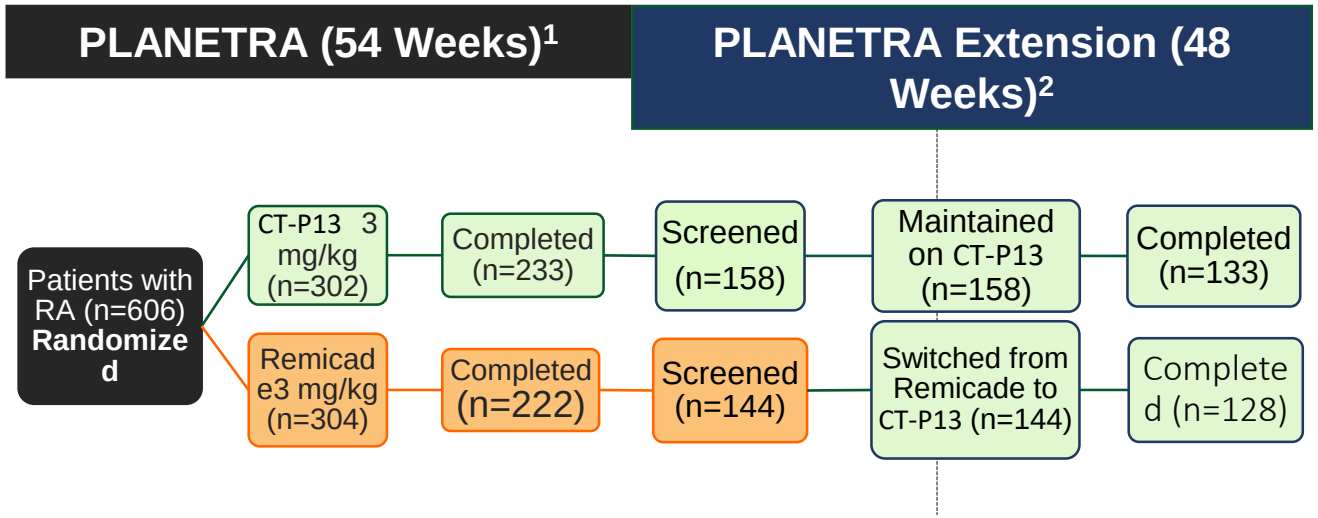


Equivalence demonstrated

Inflectra EPAR. 2013

PLANETRA Extension Trial Design

PLANETRA Extension

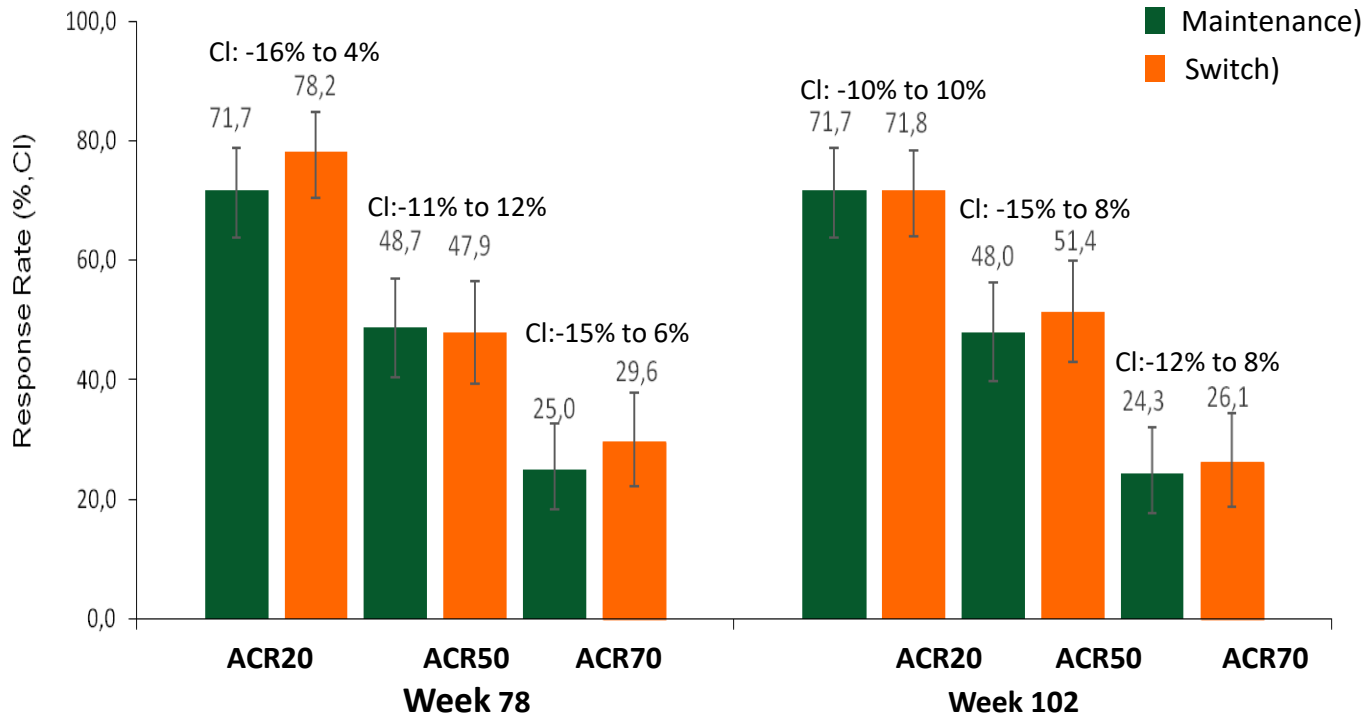


- Eligible patients with RA from PLANETRA were enrolled in a 48-week extension study to assess the efficacy and safety of switching from Remicade to CT-P13 (**switch** group) relative to maintenance on CT-P13 (**maintenance** group)[2]
- The objective of the study was to confirm long-term efficacy and safety of CT-P13 and to investigate switching from Remicade to CT-P13 in patients with RA[2]

1. Yoo DH, et al. *Arthritis Res Ther.* 2016l18(1):82. **2.** Yoo DH, et al. *Ann Rheum Dis.* 2016;Apr 29 [Epub ahead of print].

Clinical Response Rates (ACR Criteria) at Weeks 78 and 102 (Efficacy Population)

PLANETRA Extension

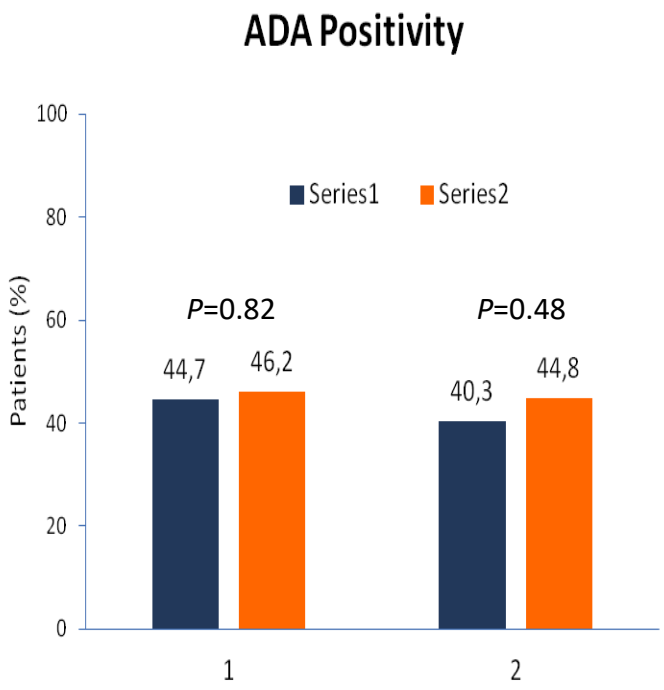


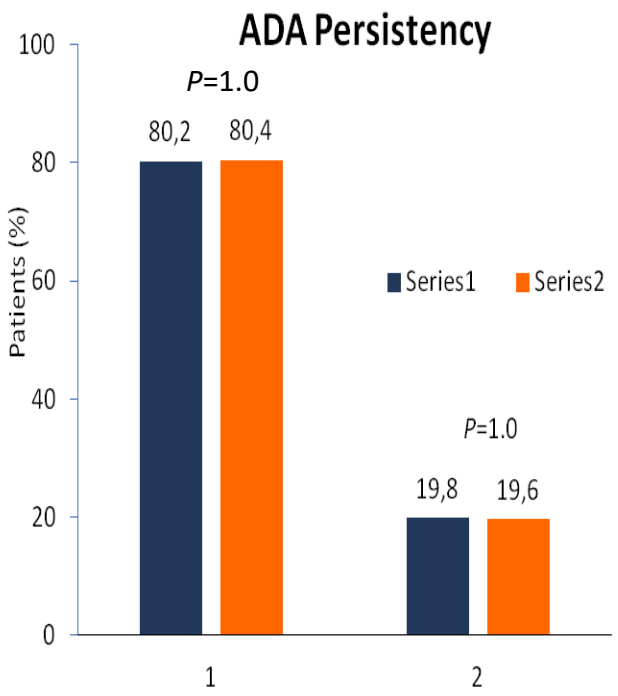
ACR20/ACR50/ACR70, American College of Rheumatology definition of a 20%/50%/70% improvement; CI, 95% confidence interval.

Yoo DH, et al. *Ann Rheum Dis.* 2016;Apr 29 [Epub ahead of print].

Antidrug Antibody (ADA) Detection at Weeks 78 and 102 (Safety Population)

PLANETRA Extension

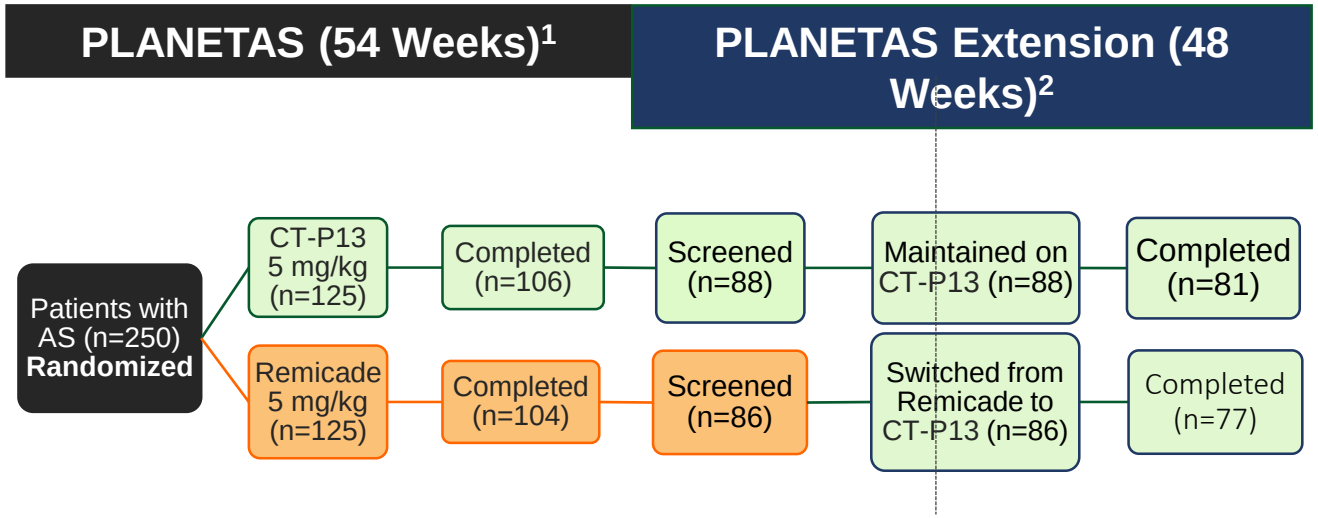




Yoo DH, et al. *Ann Rheum Dis.* 2016;Apr 29 [Epub ahead of print].

PLANETAS Extension Trial Design

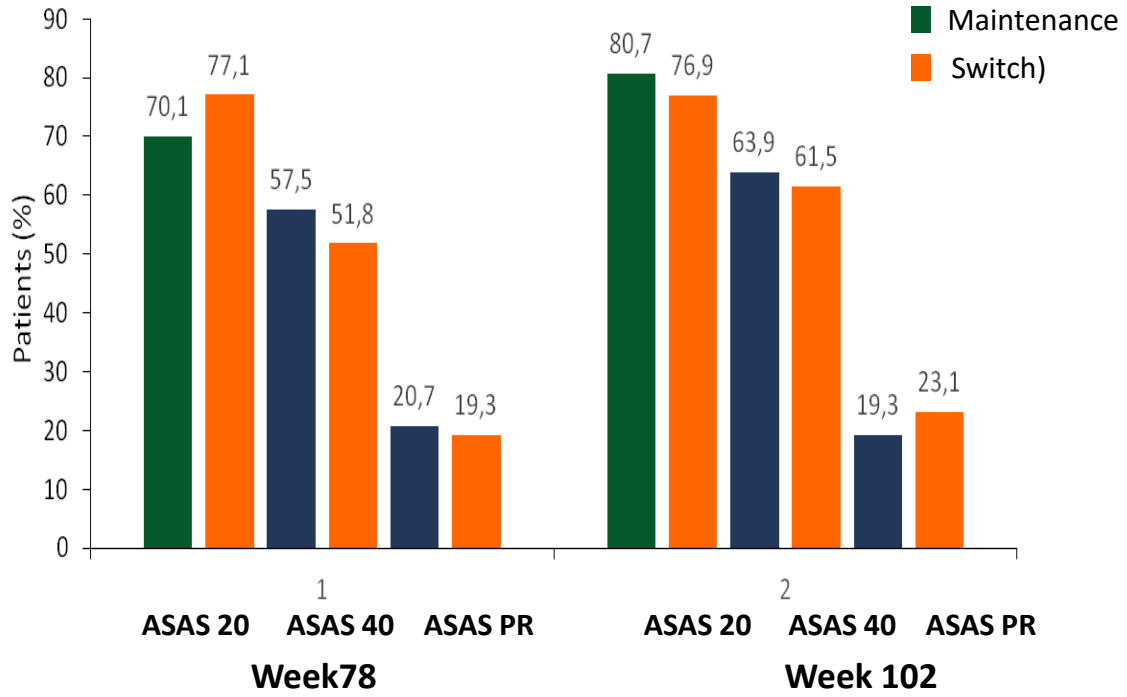
PLANETAS Extension



- Eligible patients with AS from PLANETAS were enrolled in a 48-week extension study to assess the efficacy and safety of switching from Remicade to CT-P13 (**switch** group) relative to maintenance on CT-P13 (**maintenance** group)[2]
- The objective of the study was to confirm long-term efficacy and safety of CT-P13 and to investigate switching from Remicade to CT-P13 in patients with AS[2]

1. Park W, et al. *Arthritis Res Ther.* 2016;18(1):25. **2.** Park W, et al. *Ann Rheum Dis.* 2016;Apr 29 [Epub ahead of print].

PLANETAS Extension



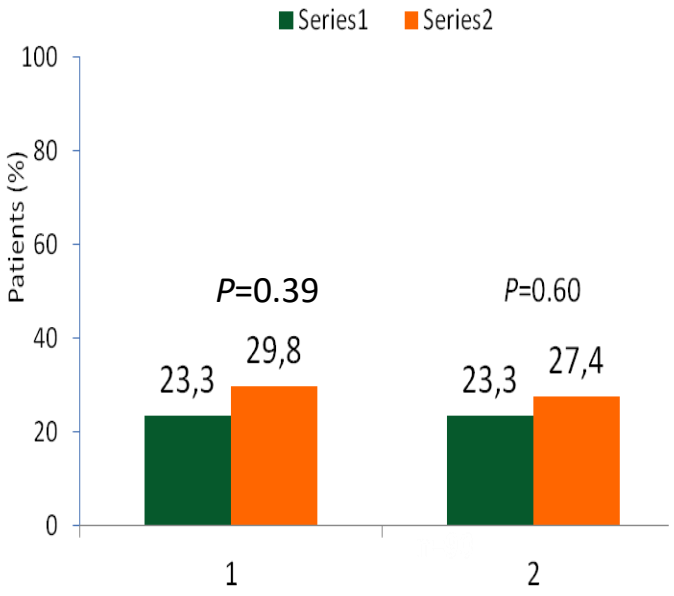
- ASAS 20, ASAS 40, and ASAS PR responses were similar between the maintenance and switch groups at weeks 78 and 102

•ASAS 20/ASAS 40/ASAS PR, Assessment of SpondyloArthritis international Society 20%/40% improvement criteria/partial remission.

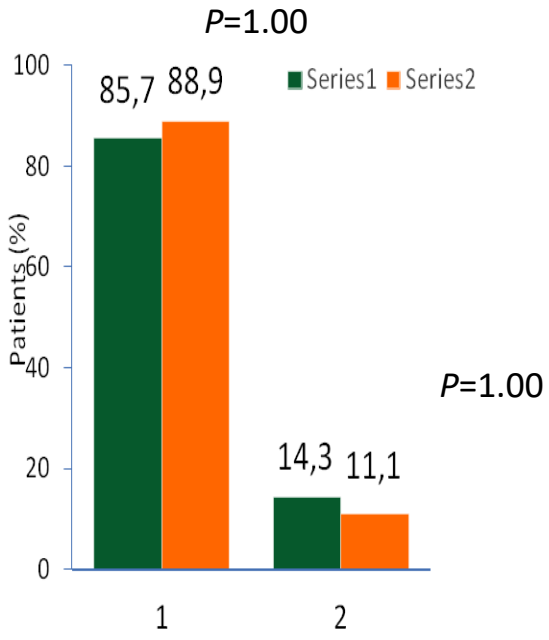
•Park W, et al. *Ann Rheum Dis.* 2016;Apr 29 [Epub ahead of print].

PLANETAS Extension

ADA Positivity



ADA Persistency



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•Park W, et al. *Ann Rheum Dis.* 2016;Apr 29 [Epub ahead of print].

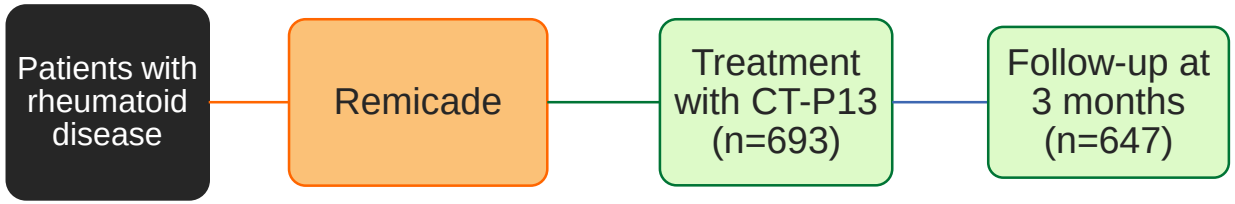
CONCISE REPORT

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

DANBIO Study Design

DANBIO



- Clinical efficacy and safety of switching from Remicade to CT-P13 were assessed in patients with rheumatoid disease (n=647)
- Patient diagnoses: RA (n=300), AS (n=219), PsA (n=96), other (n=32)
- Disease activity was measured and reasons for withdrawal were registered

Glintborg B, et al. Presented at: EULAR 2016. Abstract OP0225.

Results and Conclusions: DANBIO

DANBIO

	Disease Activity, Mean (IQR)			Delta Value, Median (IQR)		
	3 Months Before Switch	Switch	3 Months After Switch	Before Switch	After Switch	*P* Value
DAS28	**2.3 (1.8 to 3.0)**	**2.3 (1.8 to 3.2)**	**2.3 (1.9 to 3.2)**	**0.0 (-0.3 to 0.5)**	**0.1 (-0.2 to 0.5)**	**0.07**
BASDAI, mm	**26 (12 to 47)**	**23 (7 to 41)**	**23 (7 to 41)**	**0 (-4 to 5)**	**0 (-3 to 3)**	**0.5**

- Mean time on Remicade was 6.7 years (range, 4.1-9.4 years)

•Disease activity was largely unchanged after switching from Remicade to CT-P13 compared to the 3-month period prior to switching

•During the follow-up period, 45 patients (7%) discontinued treatment with CT-P13:
- 6% due to loss of efficacy (20) or AEs (16: 3 allergic reactions, 2 infections, 2 rashes, 9 unspecified)
- 3 were in clinical remission
- 2 due to cancer
- 4 due to other reasons

- In 647 patients with inflammatory rheumatic diseases treated with Remicade for >4 years, disease activity was largely unaffected in the majority of patients 3 months after nonmedical switch to CT-P13 and comparable to the fluctuations observed in the 3 months prior to the switch. However, several patients (~6%) stopped treatment due to LOE or AE. This warrants further investigation before such a non-medical switch can be recommended

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*

Summary

Background TNF inhibitors have improved treatment of Crohn's disease, ulcerative colitis, spondyloarthritis, rheumatoid arthritis, psoriatic arthritis, and chronic plaque psoriasis, but are expensive therapies. The aim of NOR-SWITCH was to examine switching from originator infliximab to the less expensive biosimilar CT-P13 regarding efficacy, safety, and immunogenicity.

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

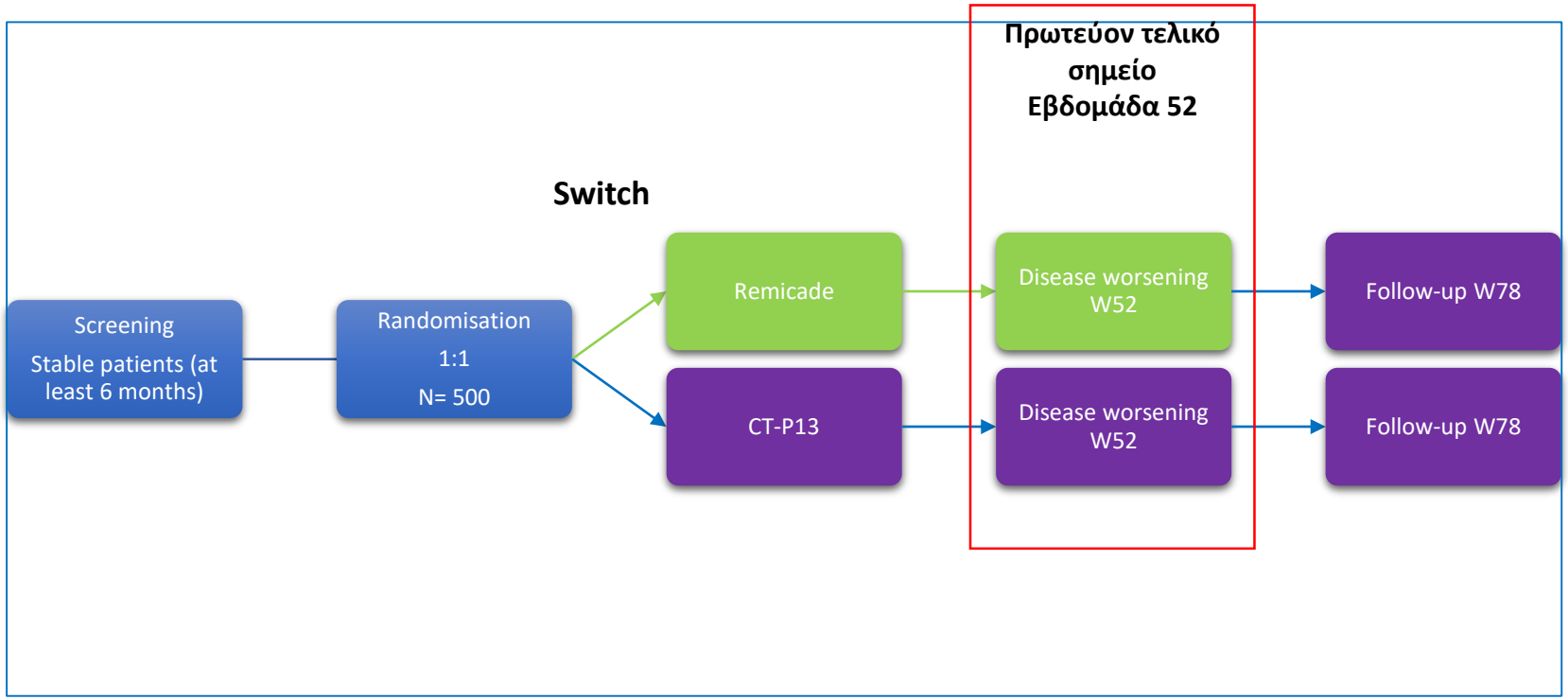
NOR-SWITCH

- CT-P13 ήταν διαθέσιμο στη Νορβηγία από τον Ιαν 2014

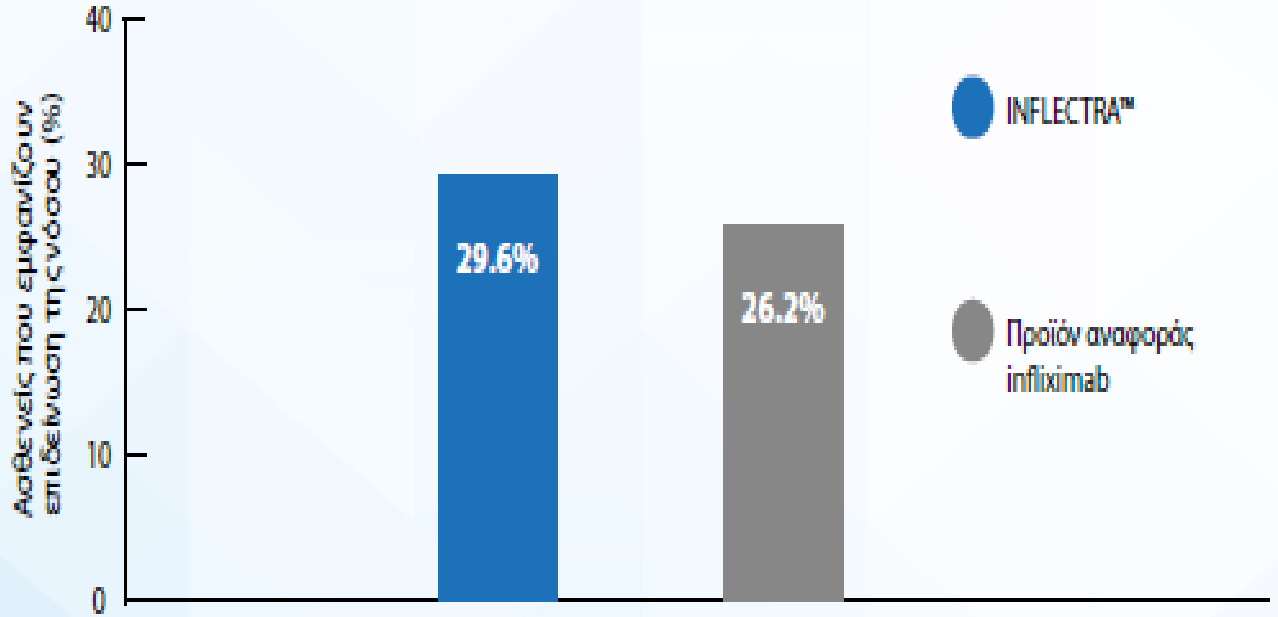
- Η **νορβηγική κυβέρνηση** χρηματοδότησε τη μελέτη, NOR-Switch για να ελέγξει την ανταλλαξιμότητα από το προϊόν αναφοράς σε βιο-ομοειδές infliximab
- Τυχαιοποιημένη, διπλή-τυφλή, παράλληλων ομάδων μελέτη
- 500 ασθενείς για όλες τις ενδείξεις [ρευματοειδούς αρθρίτιδας, σπονδυλοαρθρίτιδας, ψωριασική αρθρίτιδα, ελκώδης κολίτιδα, νόσος του Crohn και η χρόνια ψωρίαση κατά πλάκας]
- Πρωτεύον καταληκτικό σημείο ήταν η επιδείνωση της νόσου
- Τυχαιοποίηση ξεκίνησε το Νοέμβριο 2014

NOR- SWITCH Σχεδιασμός μελέτης

- **Πρωτεύον τελικό σημείο: Αποτελεσματικότητα (επιδείνωση της νόσου)**

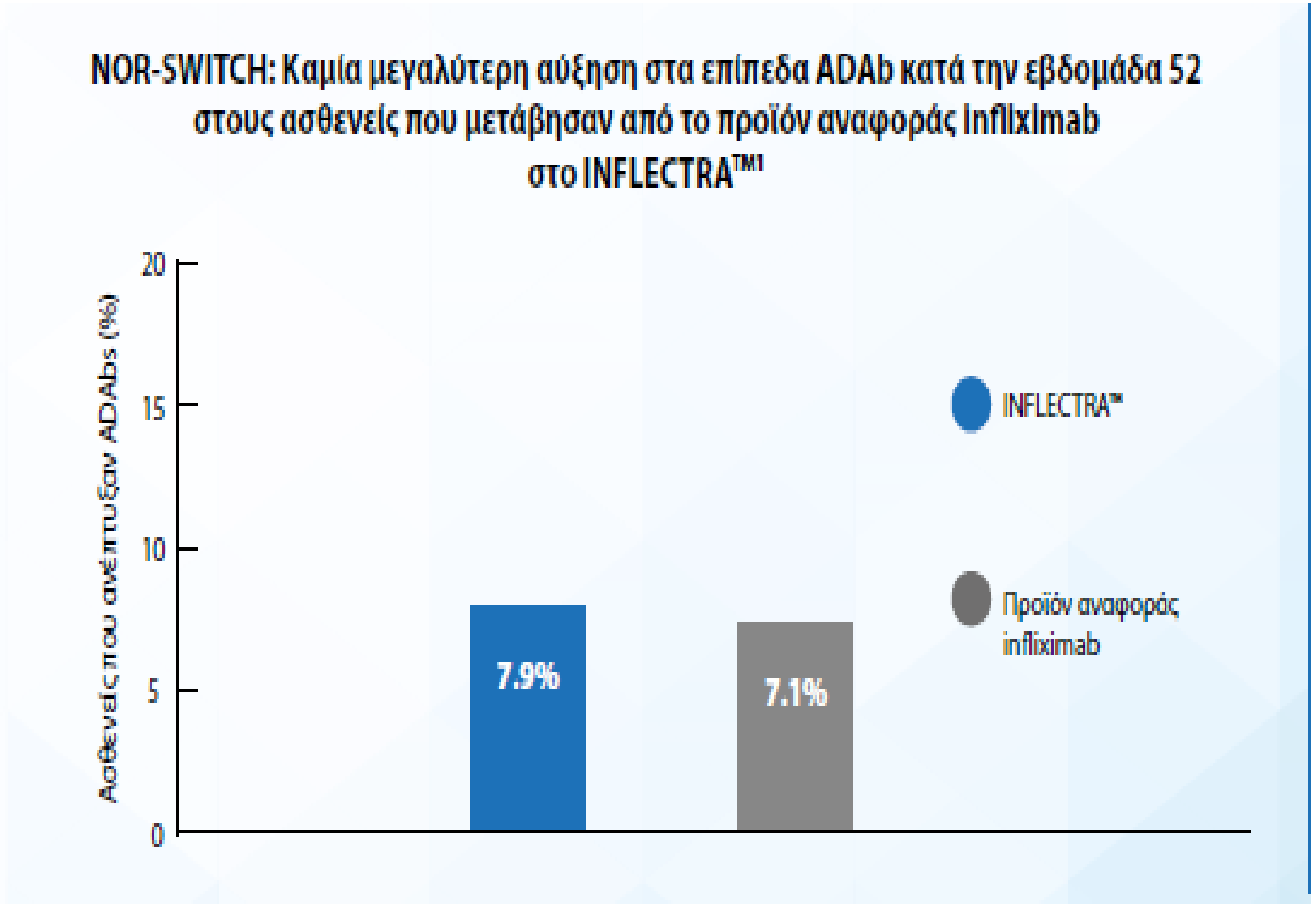


NOR-SWITCH: Καμία μεγαλύτερη επιδείνωση της νόσου κατά την εβδομάδα 52 σε ασθενείς που μετέβησαν από το προϊόν αναφοράς Infliximab στο INFLECTRA™[1]



Kvien T, et al. Abstract LB15. UEGW 2016

Ανοσογονικότητα



Kvien T, et al. Abstract LB15. UEGW 2016

Ongoing registries and post marketing studies for evaluation of CT-P13.

Study	Country	Patients number	Indication	Study type (ClinicalTrials.gov identifier)
NOR-SWITCH study	Norway	500	RA, SpA, PsA, UC, CD, and PsO	RCT (NCT02148640)
CD switching study	19 countries	214	CD	RCT (NCT02096861)
RA switching study	Japan	~100	RA	RCT
RA registry in Korea, EU	7 countries	2450	RA	Registry
IBD registry in Korea, EU	9 countries		IBD (CD,UC)	Registry
AS registry in Korea, EU	5 countries		AS	Registry
Post-marketing study in Korea	Korea	1600	RA, AS, IBD, PsA, PsO	Post-marketing Study
BSRBR	UK	500	RA	Registry
RABBIT	Germany	500	RA	Registry

RCT: Randomized clinical trial.
BSRBR: The British Society for Rheumatology Biologics Registers.
RABBIT: Rheumatoid Arthritis oBservation of BIologic Therapy.

CT-P13: clinical evidence base

CT-P13
Phase I PK, safety and efficacy in ankylosing spondylitis (PLANETAS)[1]
Phase III RA (PLANETRA)[2]
Extension studies in AS & RA containing switch data[3,4]
Real World Evidence in IBD (>2000 patients)[5-29]
Over 2 years' in-market experience and >20,000 patient years[30]

1. Park *et al. Ann Rheum Dis* 2013;72(10):1605–1612
2. Yoo *et al. Ann Rheum Dis* 2013; 72:1613–1620
3. Park et al. *Ann Rheum Dis* 2016;0:1–9 epub
4. Yoo et al. *Ann Rheum Dis* 2016;0:1–9 epub

5-29. References can be found on the following slide

30. Data on file; Pfizer PSUR submission