



Ταχύτητα Δράσης των βιολογικών παραγόντων

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Ναυτικού Νοσοκομείου Αθηνών**

Σύγκρουση συμφερόντων

Αμοιβή για την παρουσίαση από τη UCB

Εκπαιδευτικές-ερευνητικές-συμβουλευτικές επιχορηγήσεις
την τελευταία διετία:

MSD, Abbvie, Novartis, BMS, UCB, Roche

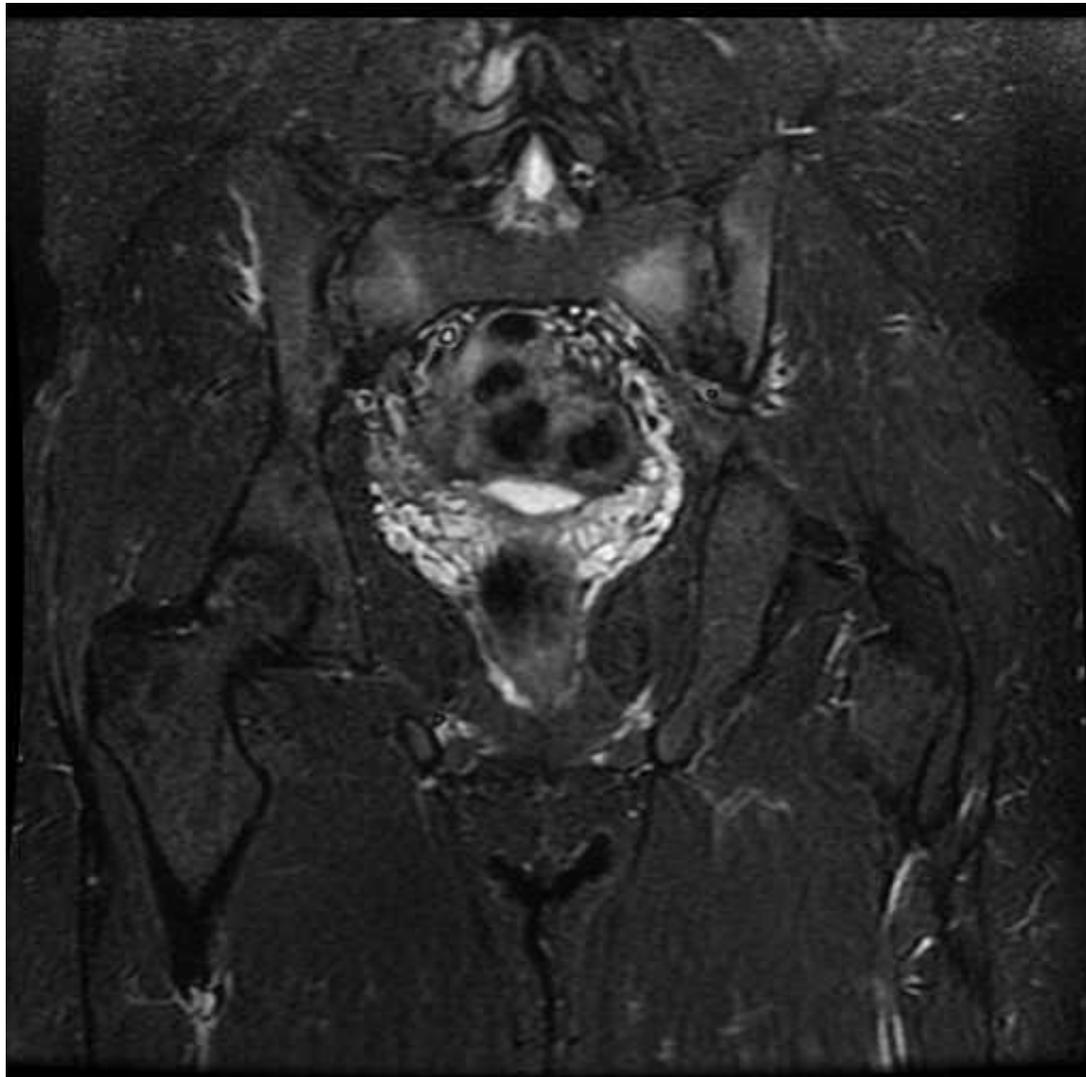
1^ο Περιστατικό

- Πλήρωμα ελικοπτήρου (αεροναυτίλος), ετών 32
- Ψωριασικό εξάνθημα τριχωτού κεφαλής και άκρων
- Πρωϊνή δυσκαμψία
- Σύγκραση ΔΕ αγκώνα
- Αρθρίτιδα ΜΚΦ άμφω
- Δακτυλίτιδα ΔΕ δείκτη
- Μερική ανταπόκριση σε MTX

2^ο Περιστατικό

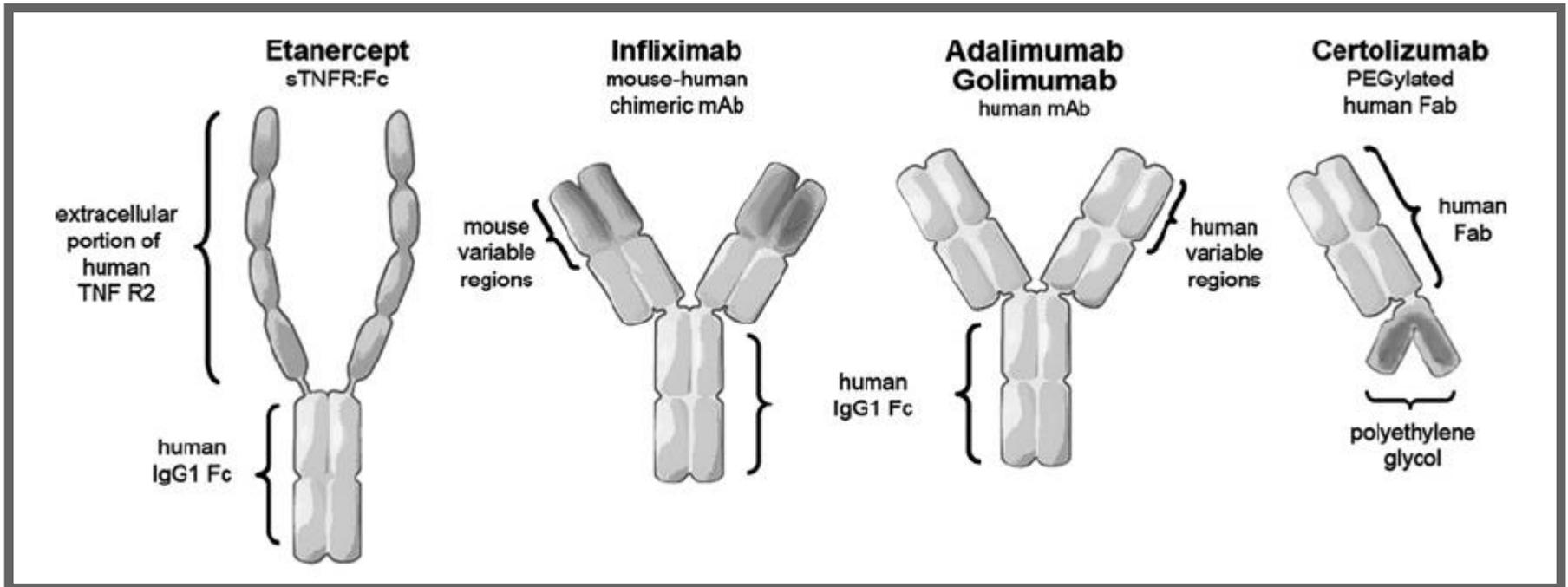
- Μέλος ΟΥΚ, 28 ετών
- Έντονη πρωϊνή δυσκαμψία
- Άλγος ιερολαγονίων άμφω
- Στερνοπλευρική χονδρίτιδα
- Αρθρίτιδα ΔΕ ΠΧΚ
- Μερική ανταπόκριση σε NSAIDs

2° Περιστατικό



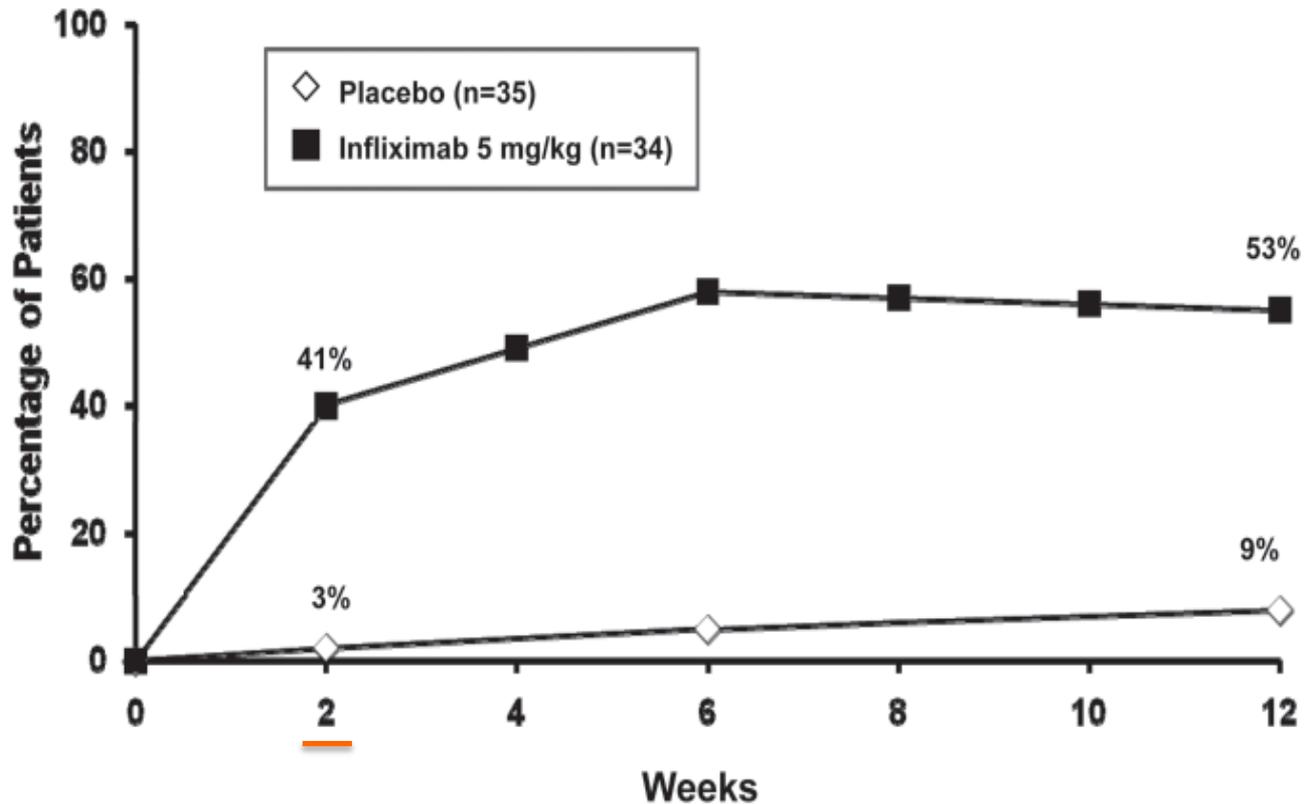
**Θεραπεία
και
Γρήγορα αποτελέσματα**

Anti-TNF α



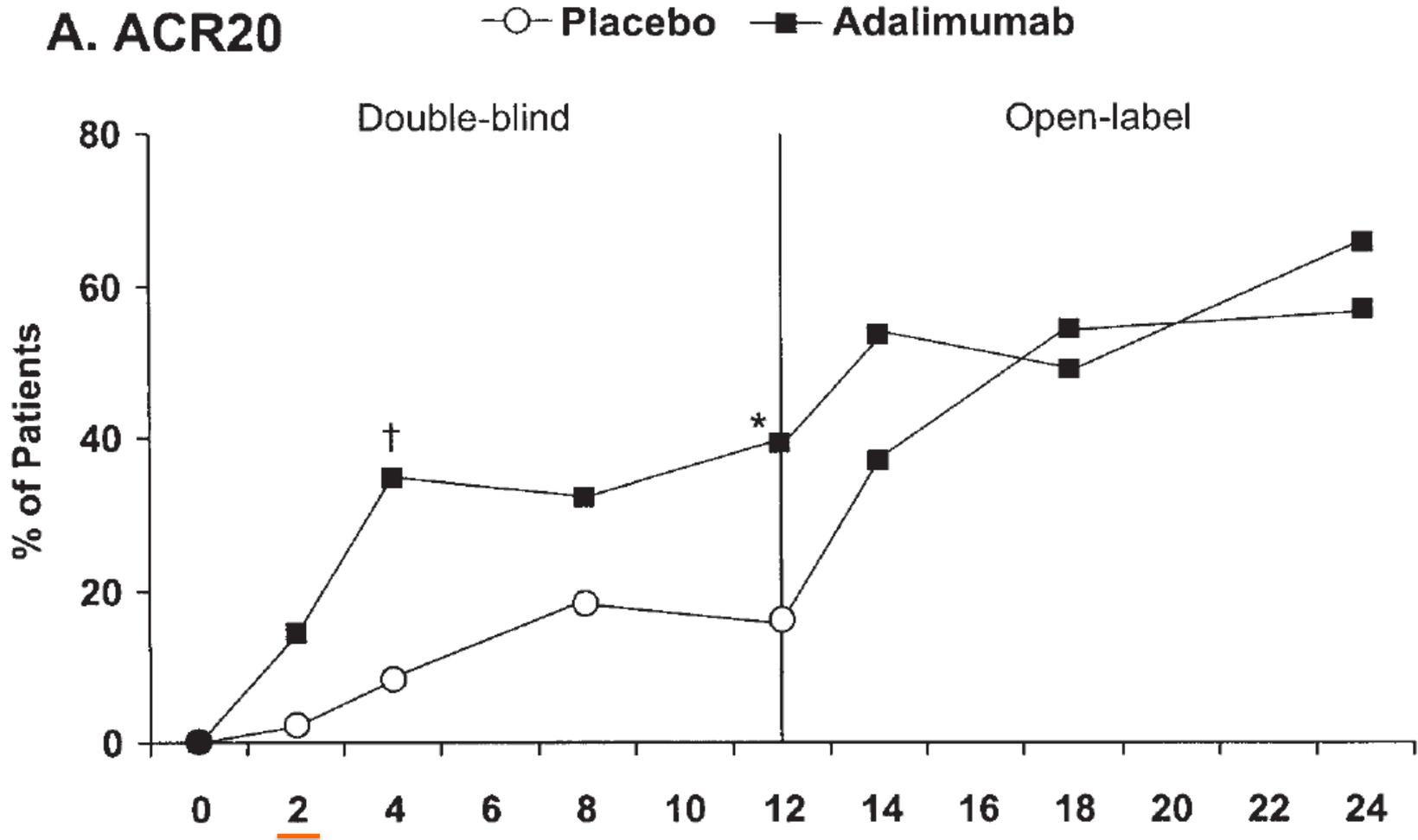
Infliximab in the treatment of AS

Improvement >50% in BASDAI



Adalimumab in PsA

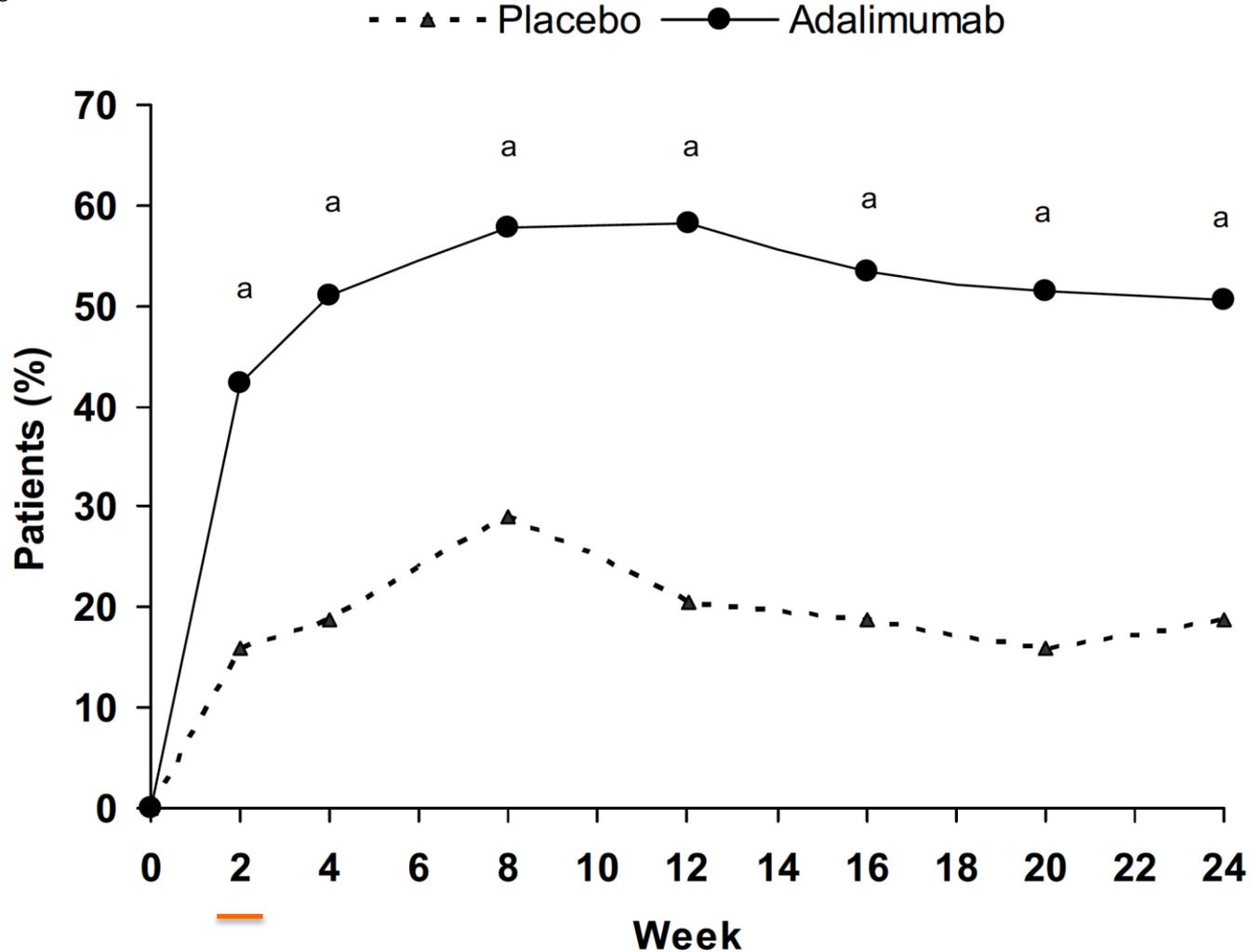
A. ACR20



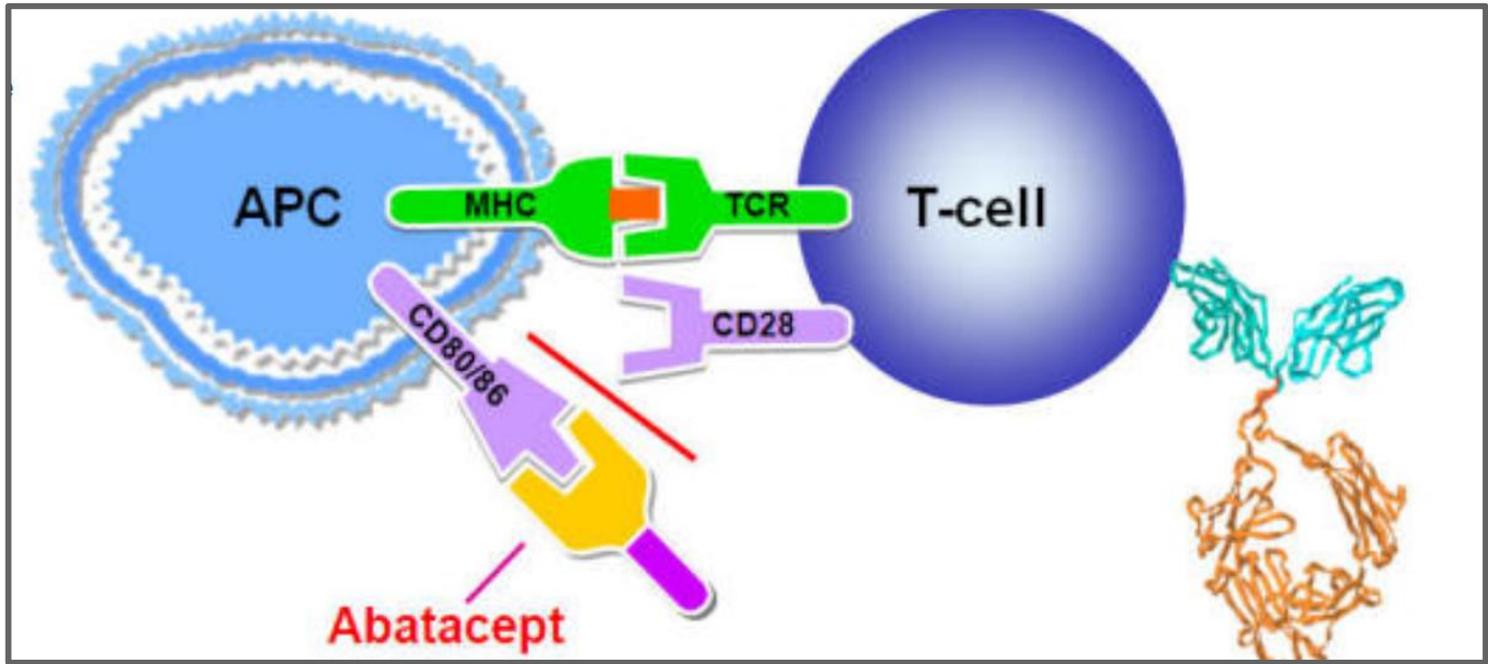
ATLAS

(Adalimumab Trial for Long-Term Efficacy and Safety in AS)

ASAS 20



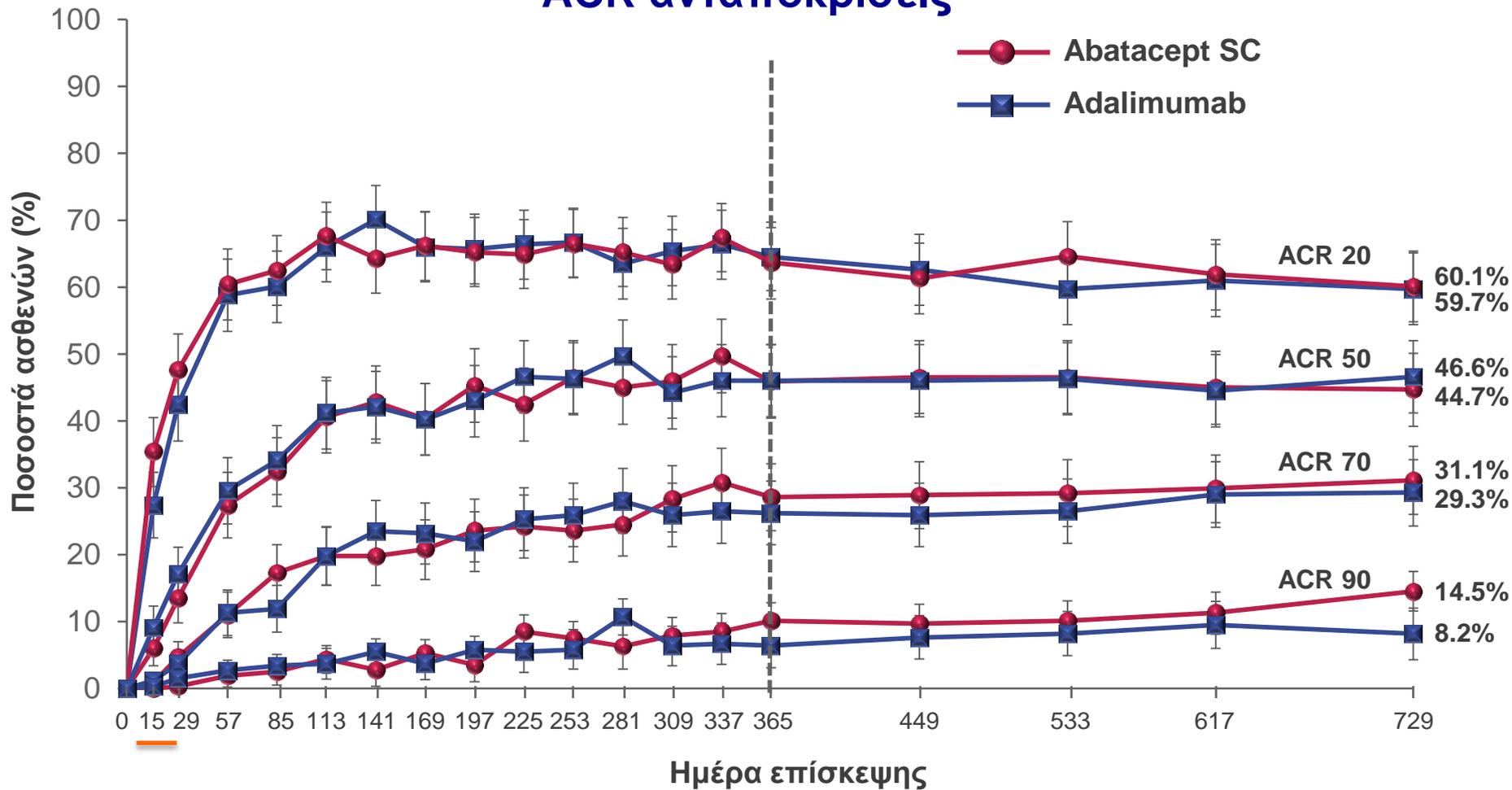
Abatacept (prevents costimulatory binding)



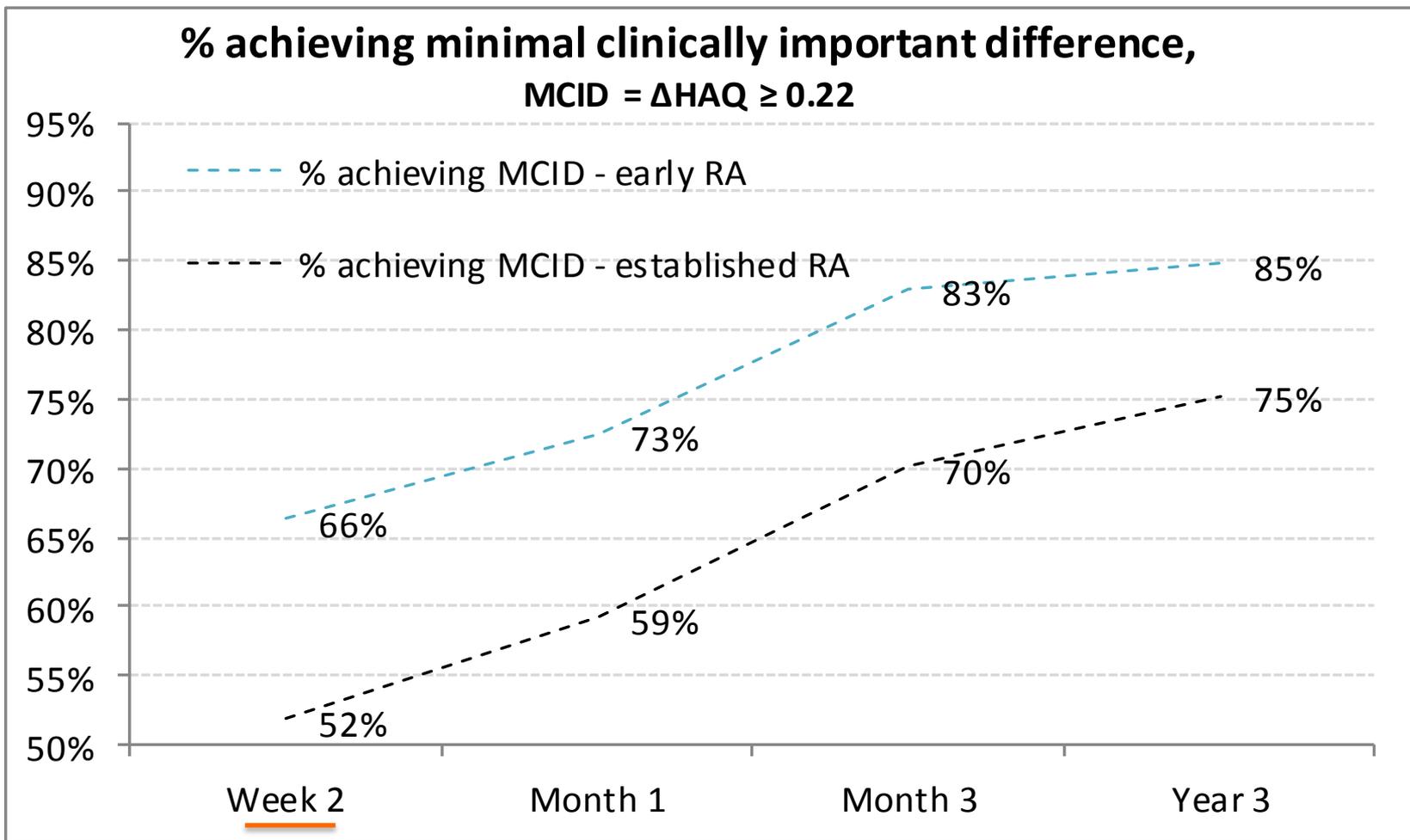
AMPLE - RA

MTX-IR, SC abatacept vs. adalimumab

ACR ανταποκρίσεις

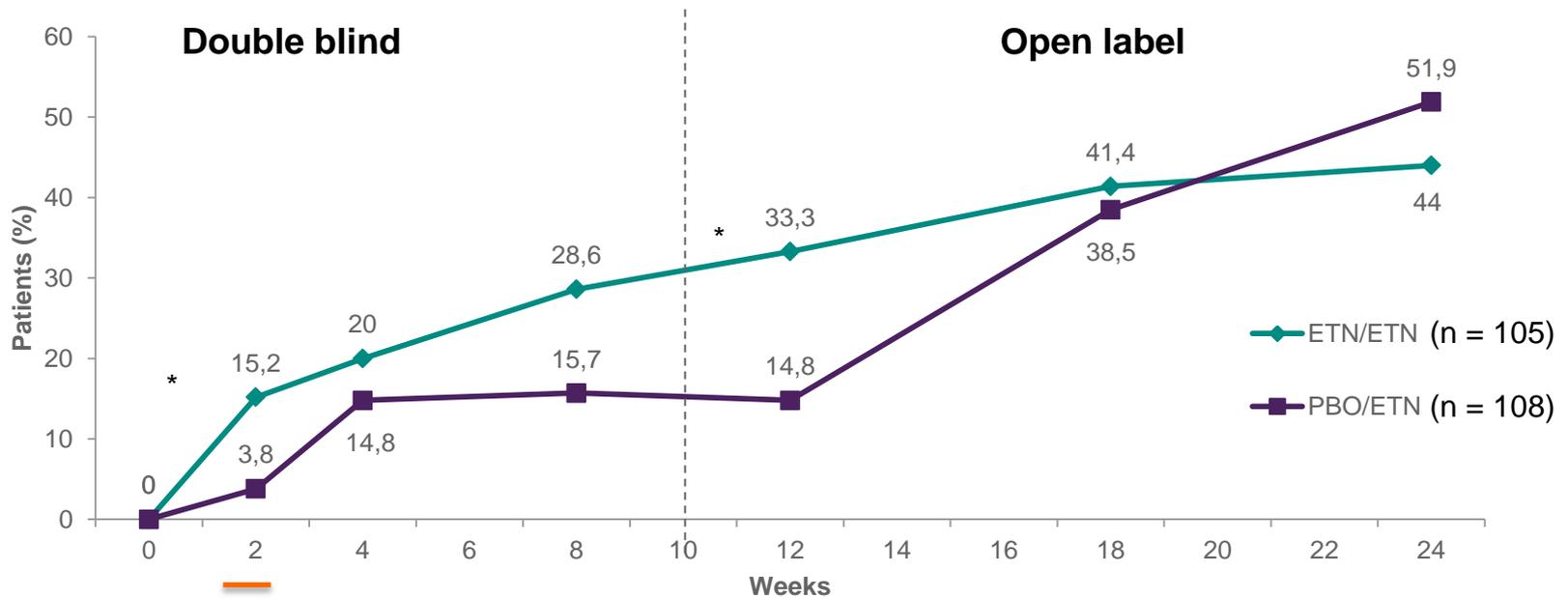


Etanercept - Improvement in disability of RA pts



Etanercept (EMBARC study) proportion of nr-axSpA patients achieving ASAS40

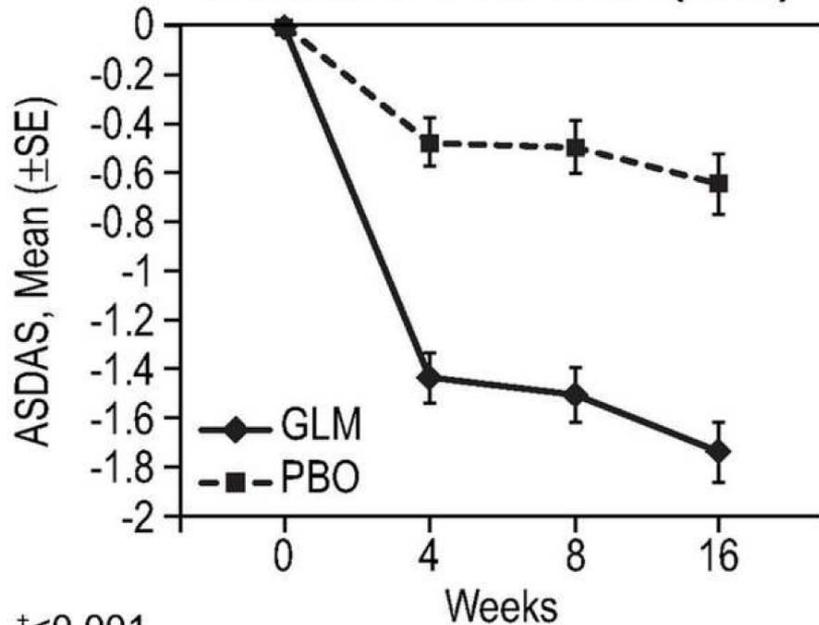
ASAS40 response at week 12 and 24



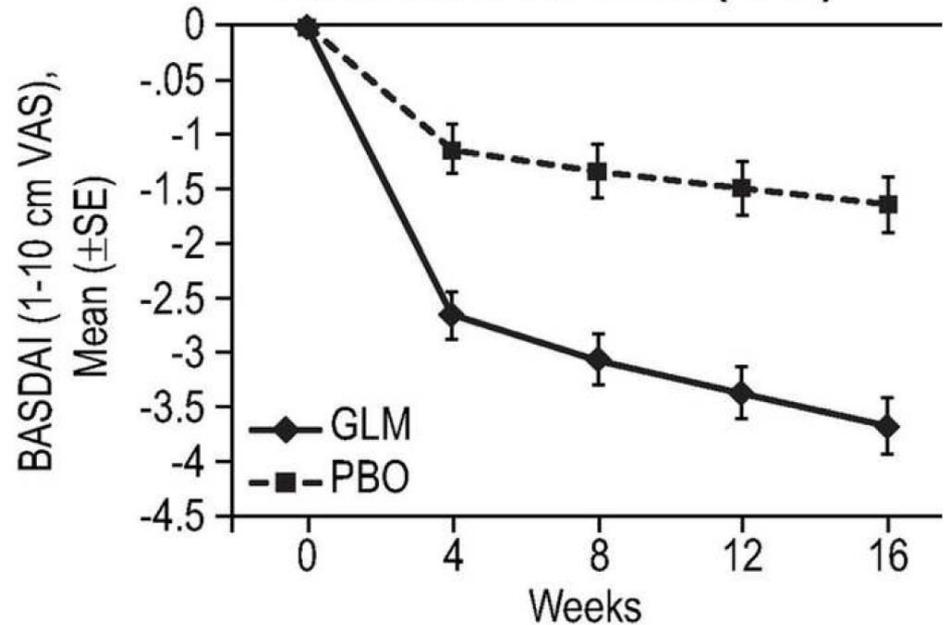
Golimumab σε nr-axSpA GO-AHEAD

C

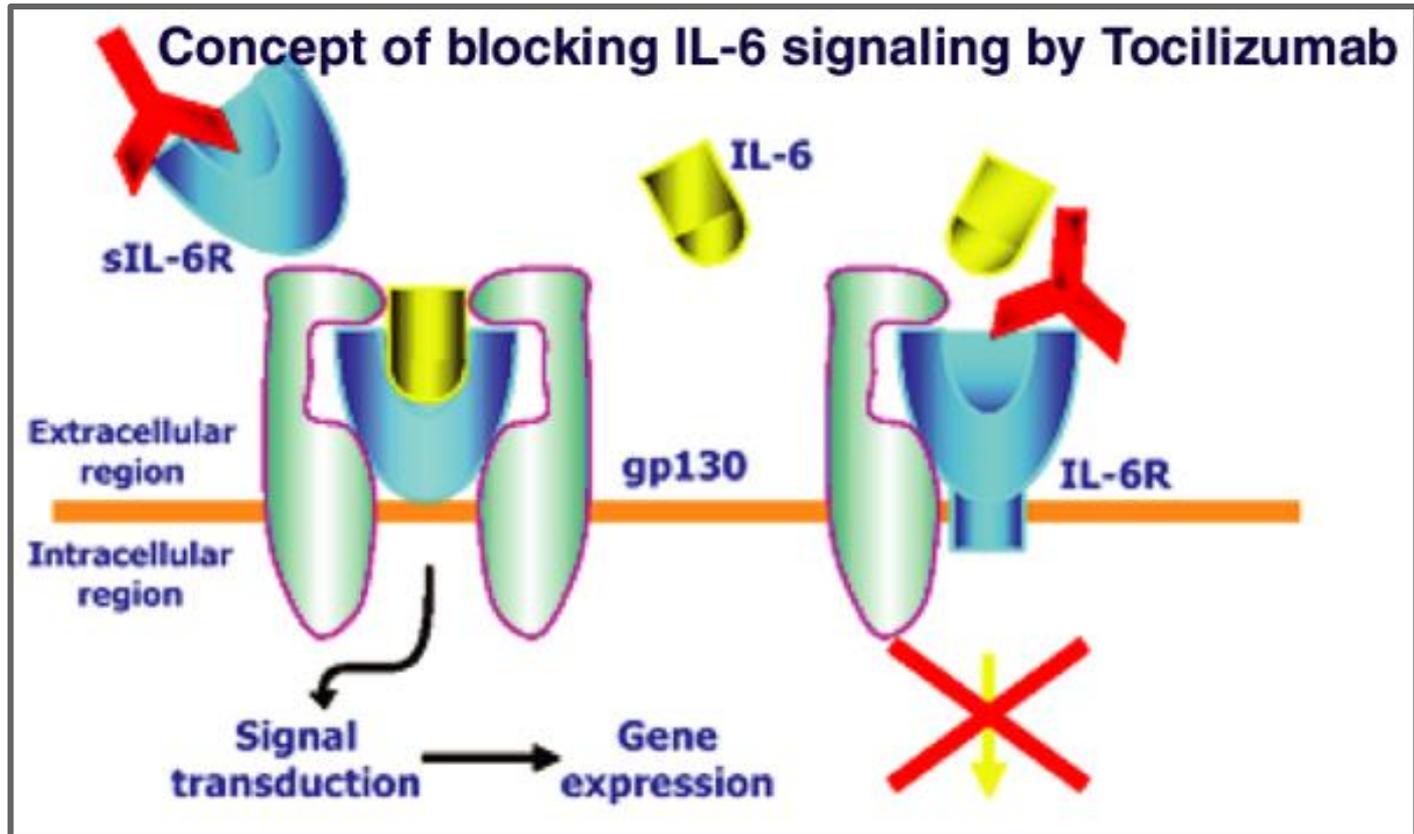
Change From Baseline in ASDAS-C Over Time (FAS)



Patients Achieving BASDAI Over Time (FAS)



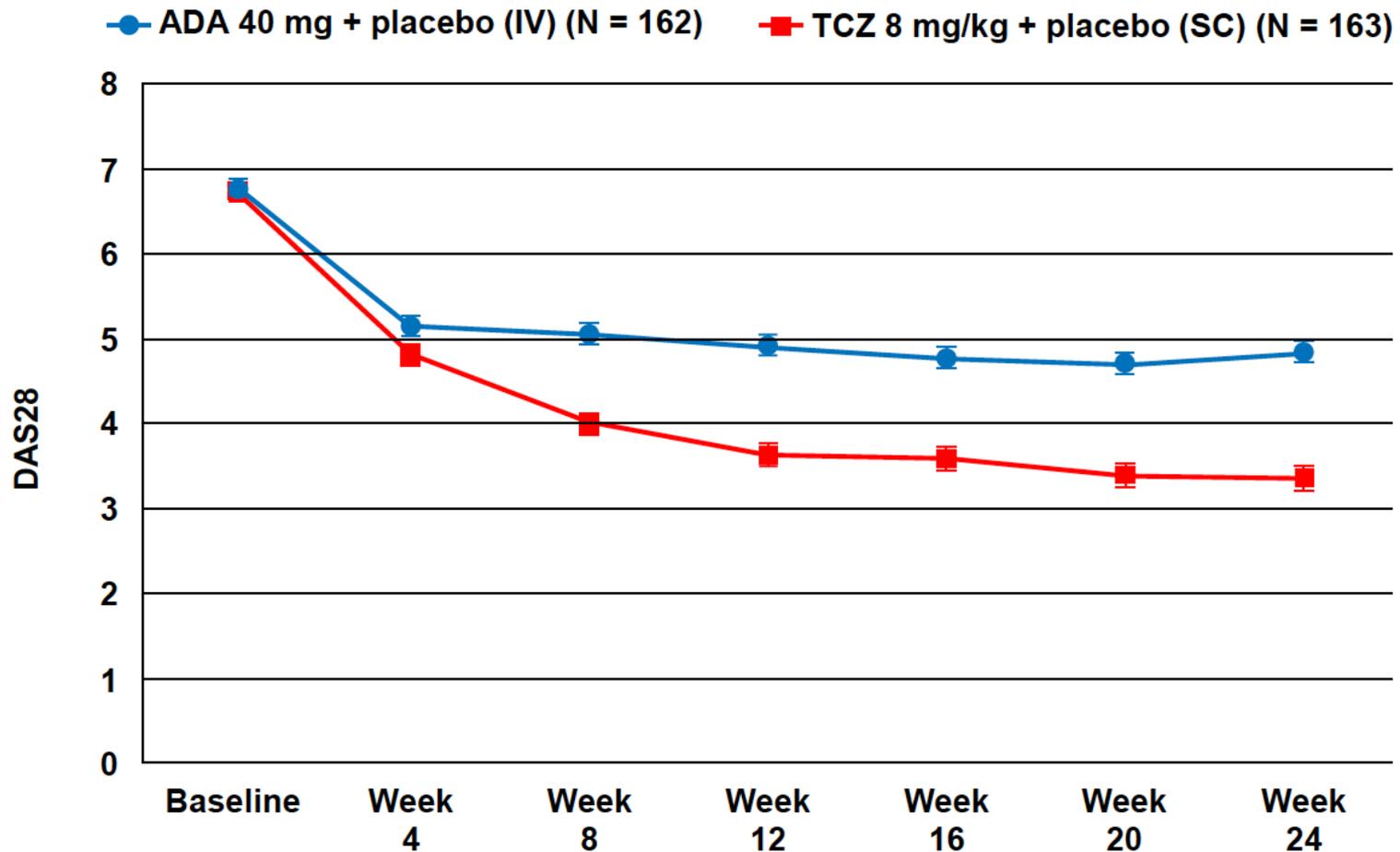
Tocilizumab (anti IL-6R)



ADACTA:

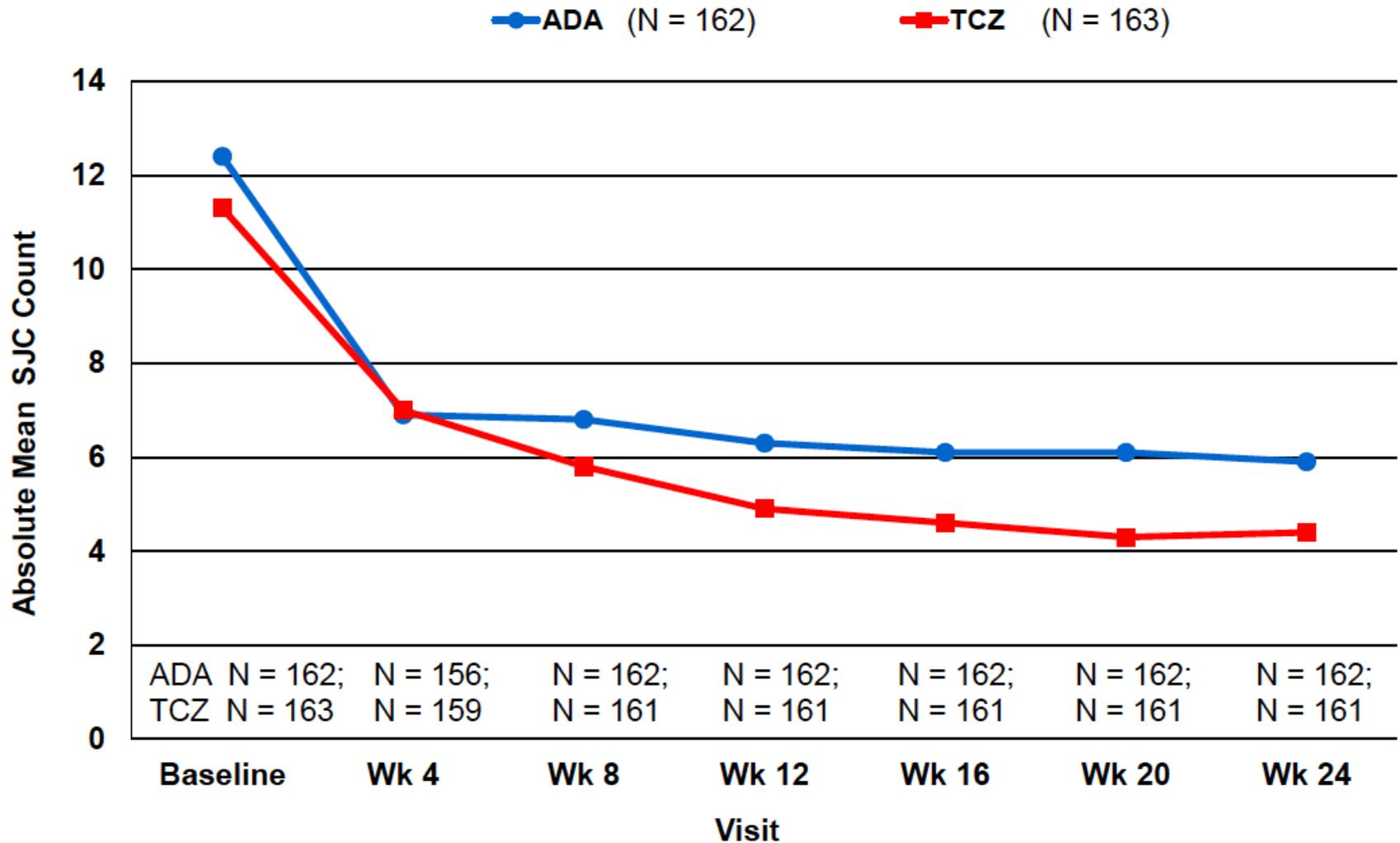
Monotherapy treatment with either tocilizumab or adalimumab

DAS28 Mean (\pm SE*) over time

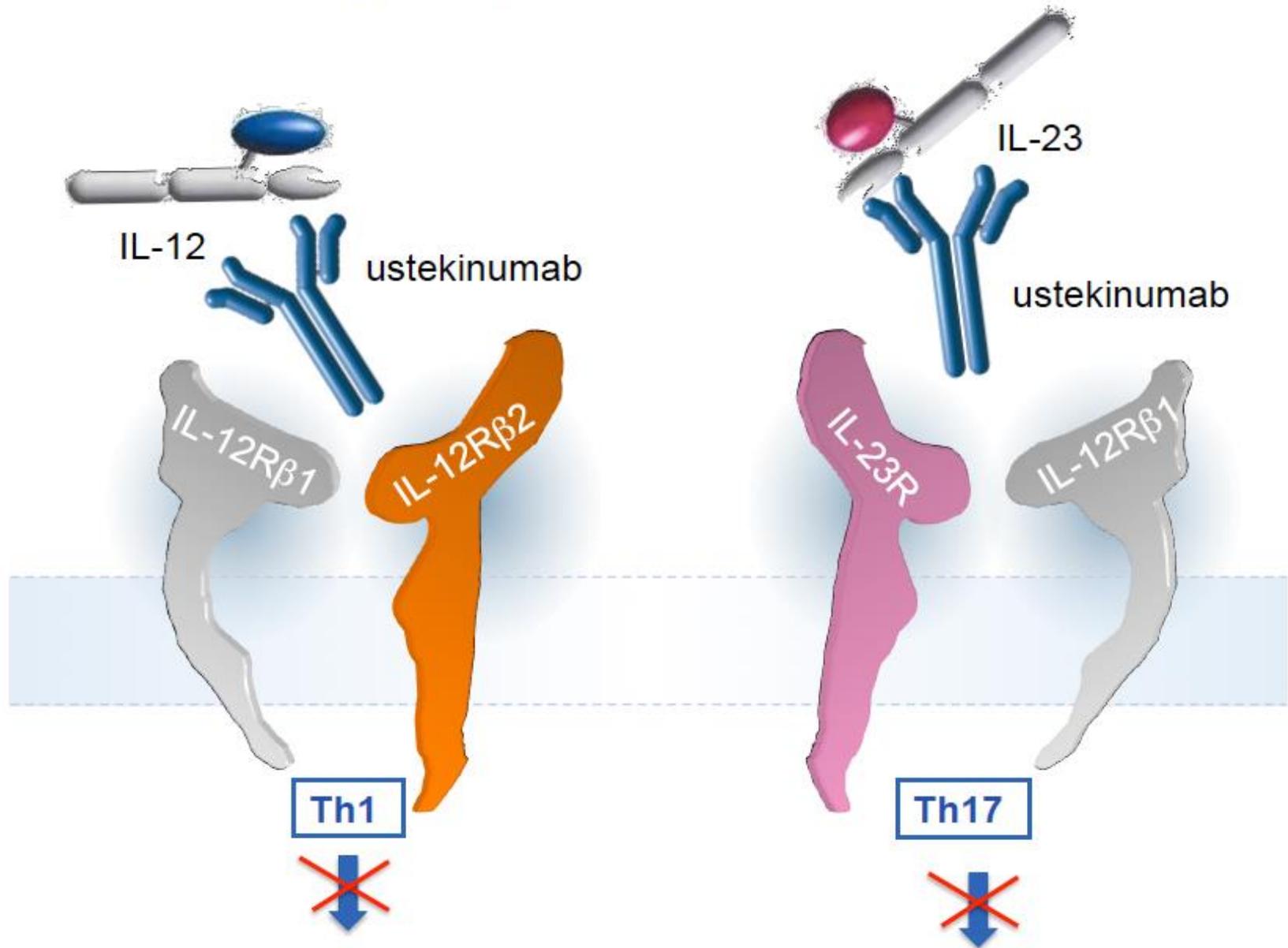


ADACTA

Swollen Joint Counts 28 (intent-to-treat population)

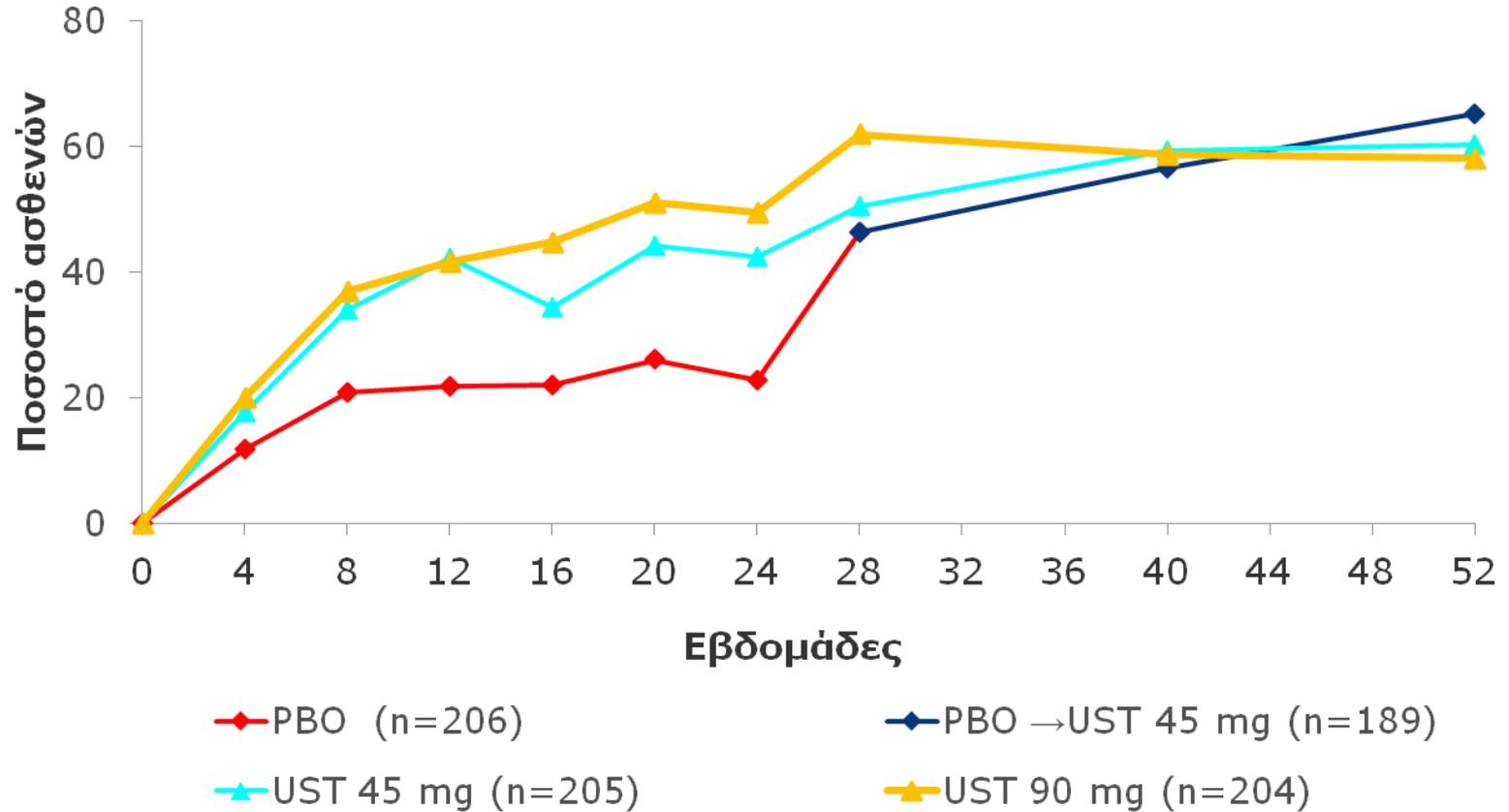


Δέσμευση των IL-12 και IL-23

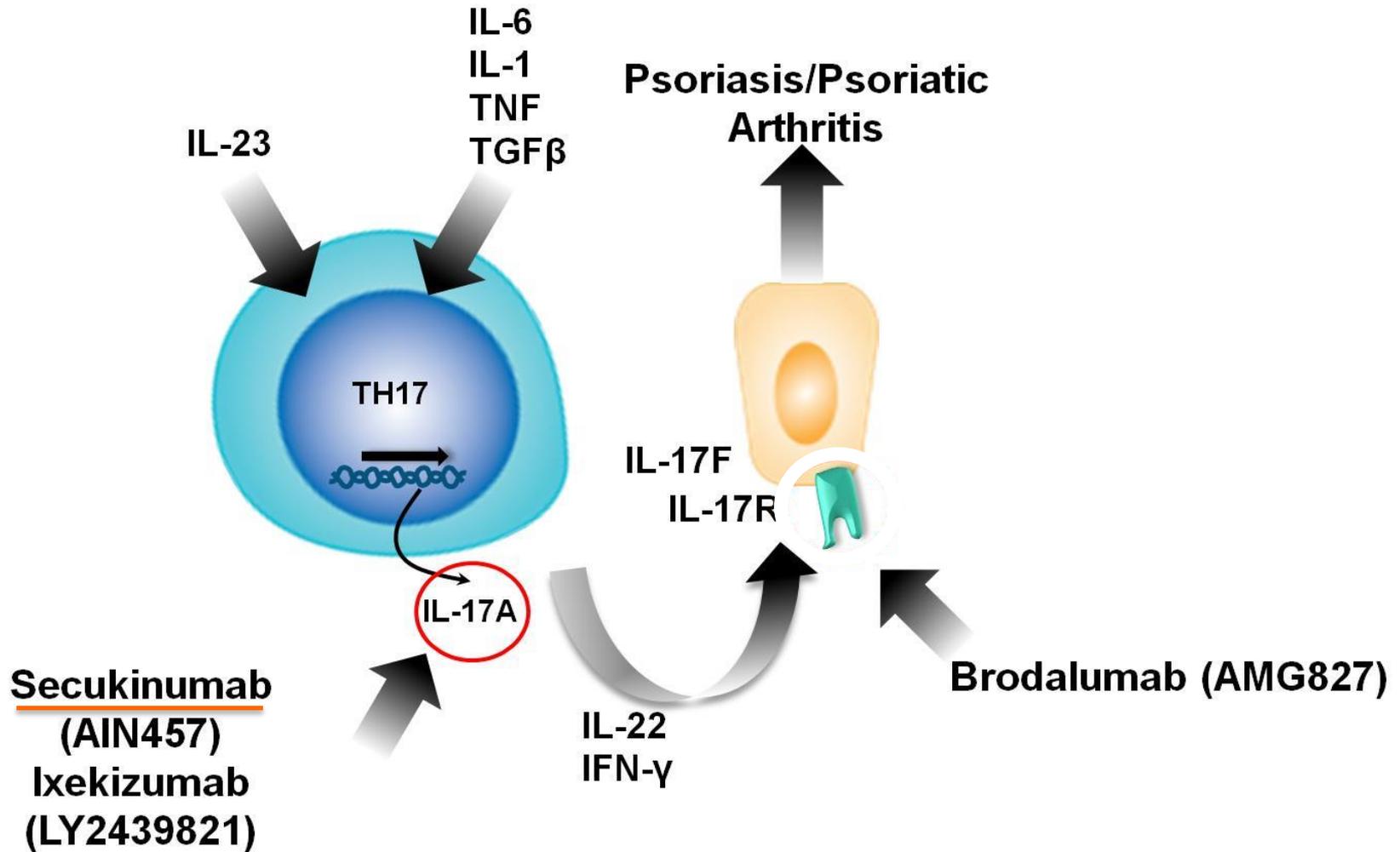


Ustekinumab in PsA, PSUMMIT I

ACR20

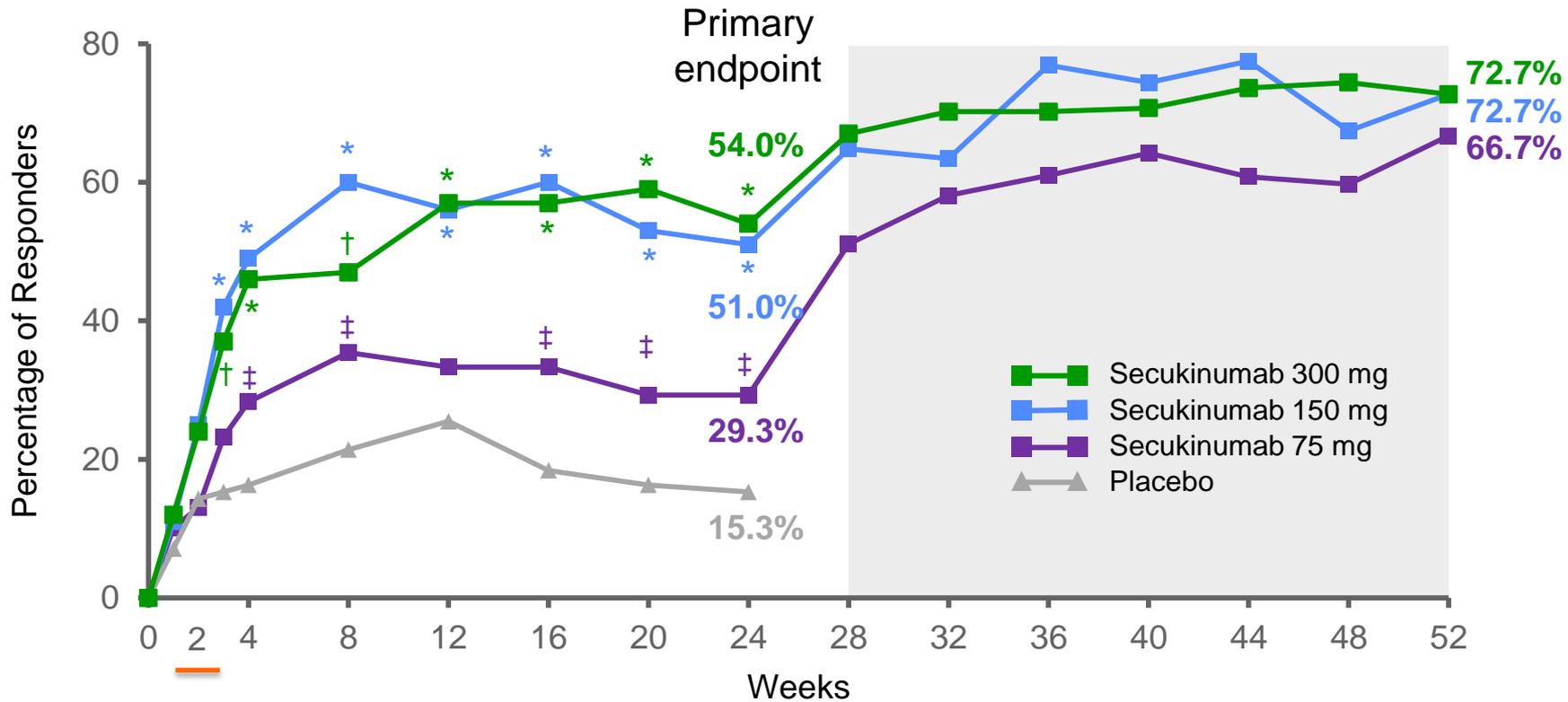


Αναστολείς IL-17 στη θεραπεία της ΑΣ, ΨΑ



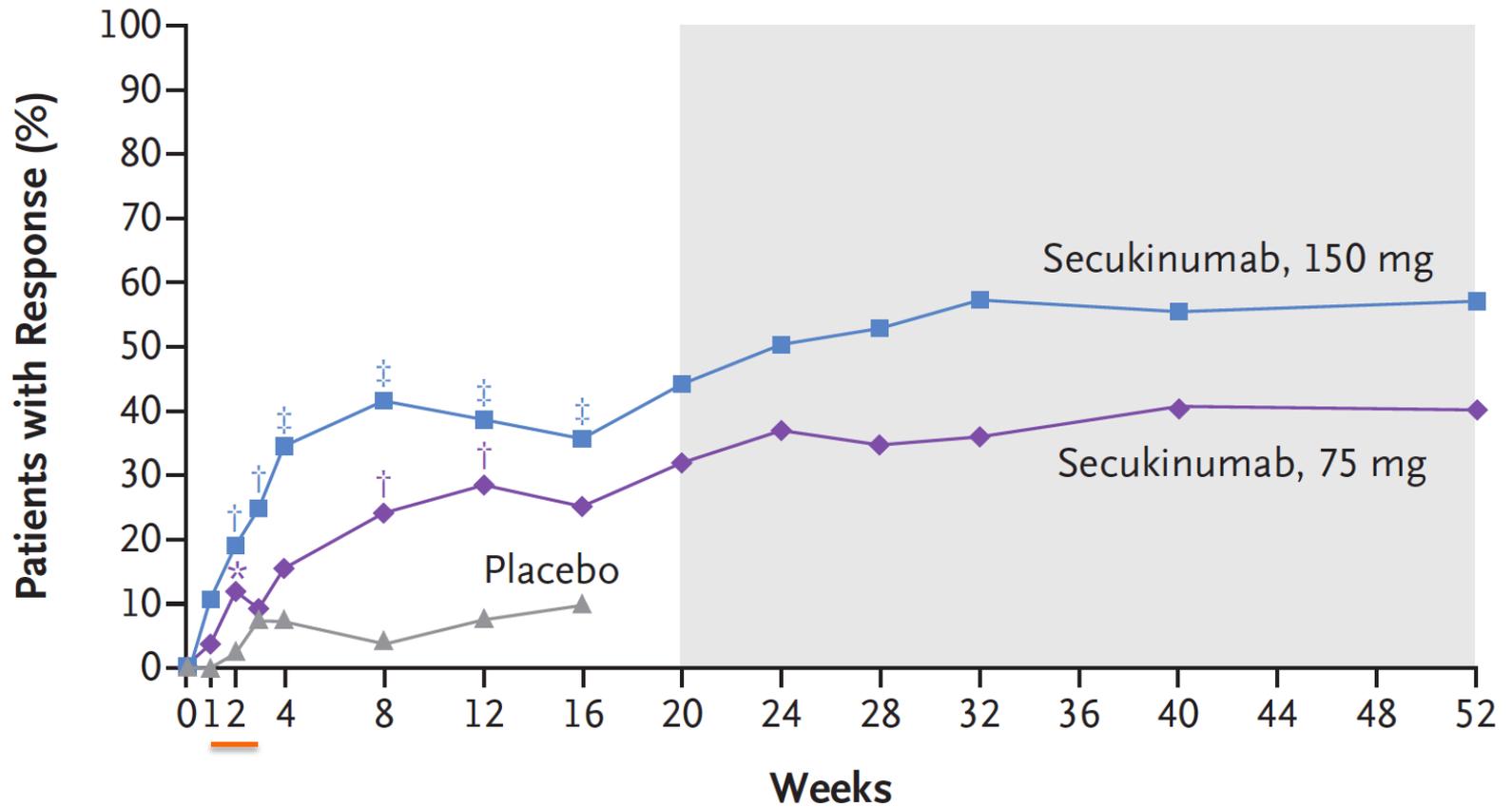
Secukinumab in PsA, FUTURE 2

ACR 20

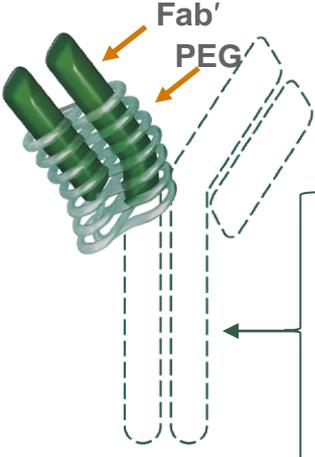
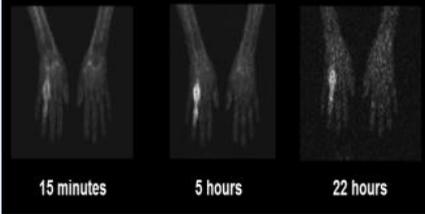


Secukinumab in AS

MEASURE 2, ASAS40 Response



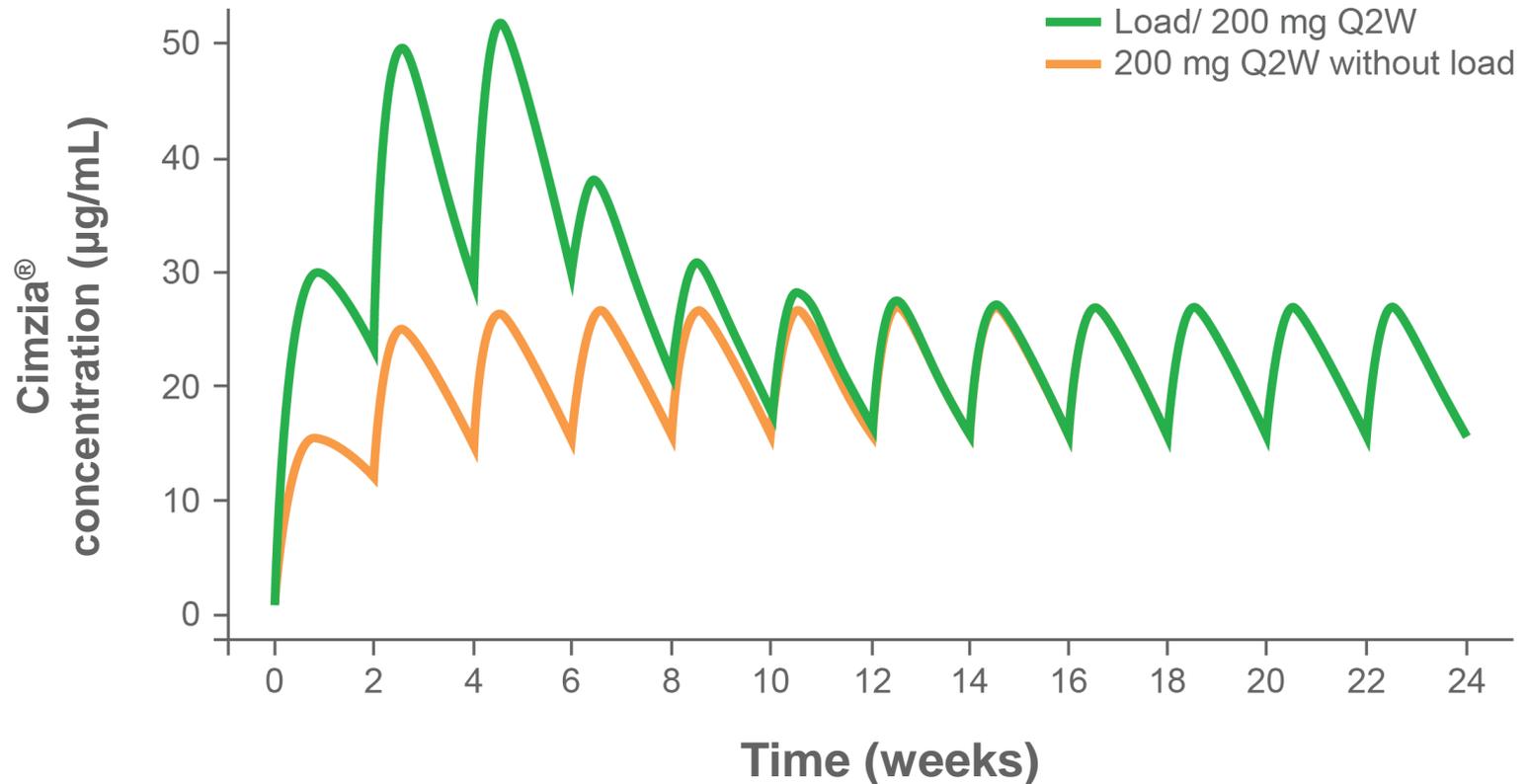
Certolizumab, Fc-free, PEGylated Anti-TNF

| Cimzia® Structure | Cimzia® Feature | Observed effects | Clinical Hypothesis | Ongoing research |
|--|---|--|--|--------------------------|
|  | <p>Only PEGylated anti-TNF</p> | <ul style="list-style-type: none"> Increased half life (14 days) and hydrosolubility with reduced mast cell degranulation (<i>in vitro</i>), compared to the non-PEGylated protein May explain observed enhanced penetration of Cimzia, as compared to Humira and Remicade, into inflamed tissues in animal models A clinical study with radiolabelled Cimzia demonstrated rapid uptake into inflamed joints; in 4 case studies, Cimzia treatment of TNF-resistant patients resulted in fast clinical resolution of oligoarthritis¹⁸ | <p>Enhanced tissue penetration⁵</p>  <p>Distribution of Tc99m radiolabelled Cimzia® in the hands of a patient with dactylitis of the 4th digit of the left hand</p> | |
| | <p>Only anti-TNF with no Fc region</p> | <ul style="list-style-type: none"> Avoidance of Fc-mediated effects such as complement- or antibody-dependent cytotoxicity Longer residency in inflamed tissues | | |
| | <p>Only univalent anti-TNF</p> | <ul style="list-style-type: none"> Cimzia does not cross-link antigens to form large immune complexes, which can cause neutrophil degranulation, superoxide production (<i>in vitro</i>), and increased clearance | <p>Small immune complexes mount less significant immune responses than larger complexes and prolong sustainability</p> | <p>Exxelerate</p> |

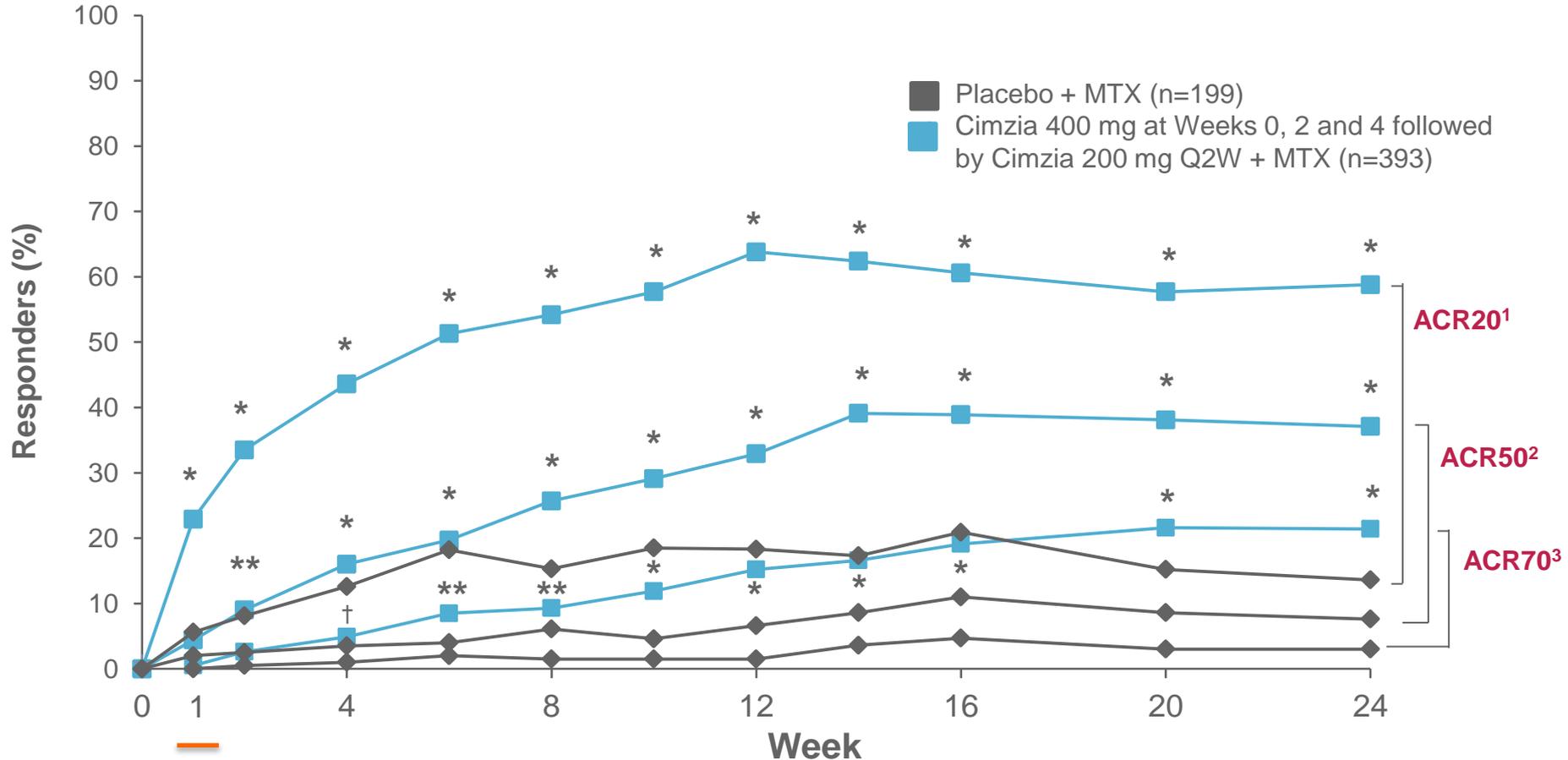
Pasut G. Biodrugs. 2014
 Palframan R et al. J Immunol Methods. 2009.
 Shim H. Exp Mol Med. 2011
 Carron P et al. Arthritis Rheum. 2013
 Schouwenburg P et al. Nat Rev Rheum. 2013

Rapid Induction of Response for Patients with a Loading Dose

PK Profile of a Typical 70 kg RA Subject Derived from the Population PK Model



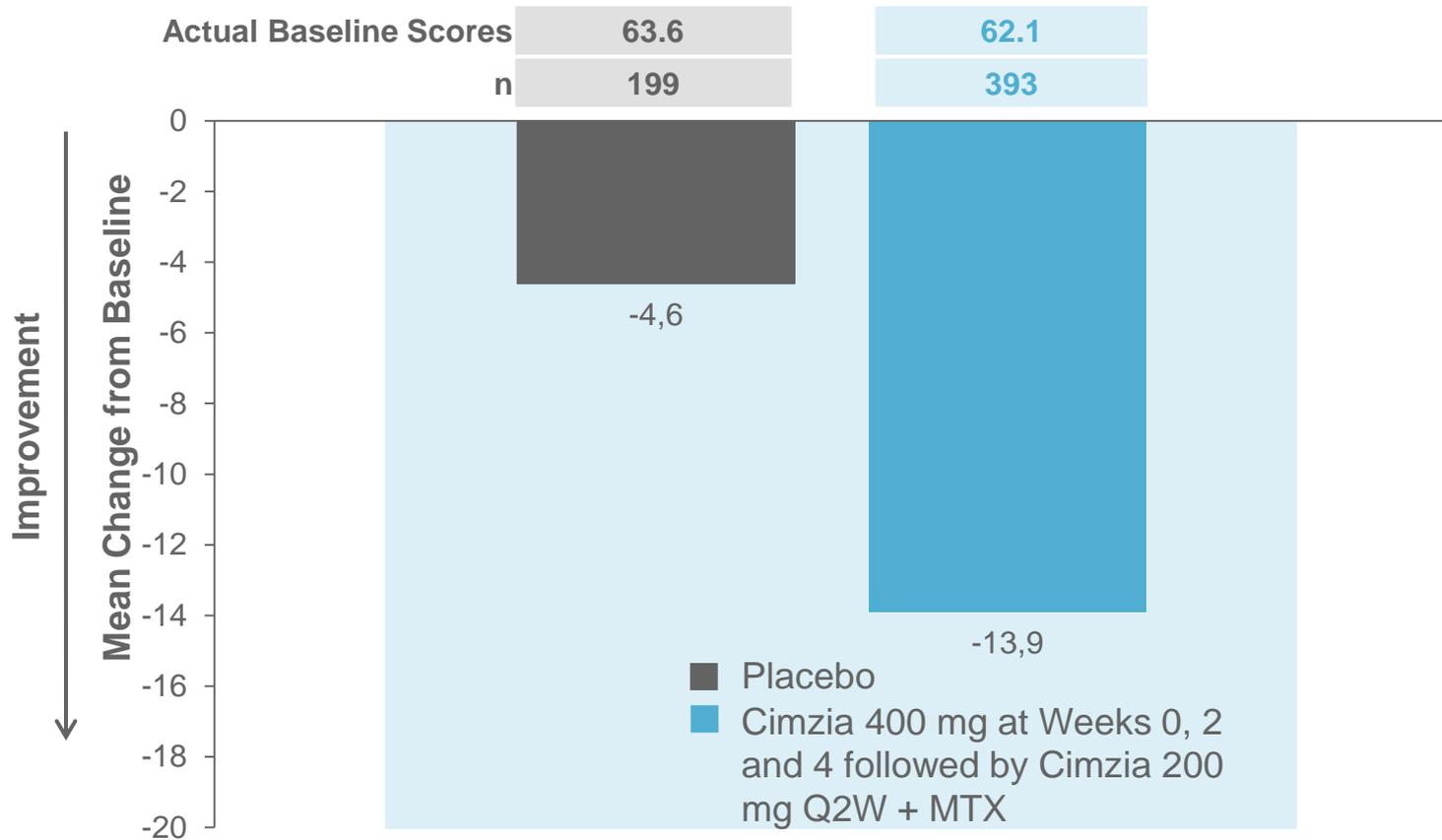
Rapid ACR Responses in Certolizumab pegol-treated RA Patients by Week 1 – RAPID 1



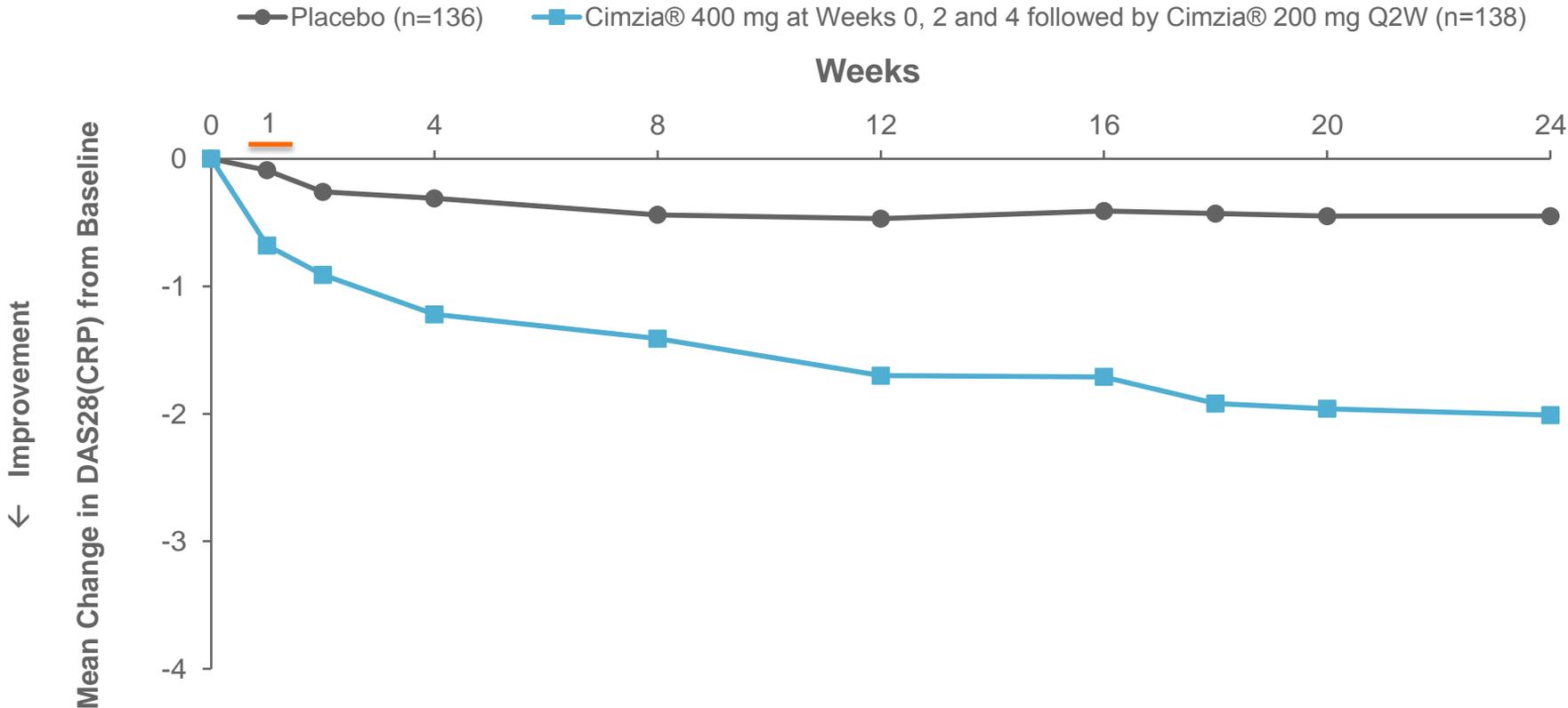
Rapid Improvements in Pain from Week 1

1

Mean change from Baseline in pain (PtAAP-VAS) at Week 1 in certolizumab pegol-treated RA patients (RAPID 1)

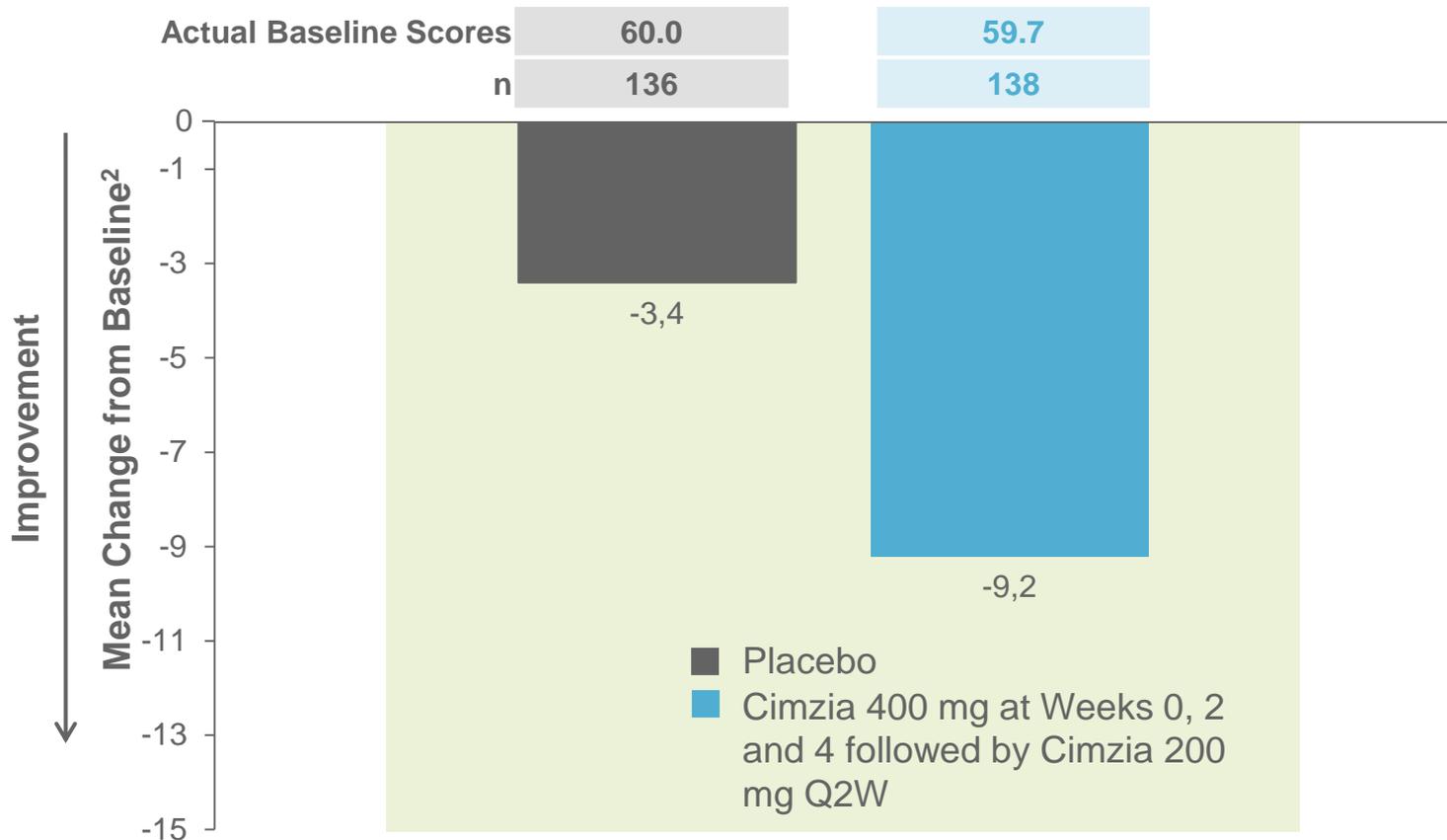


Rapid Improvements in Disease Activity in Certolizumab-pegol-treated PsA Patients by Week 1



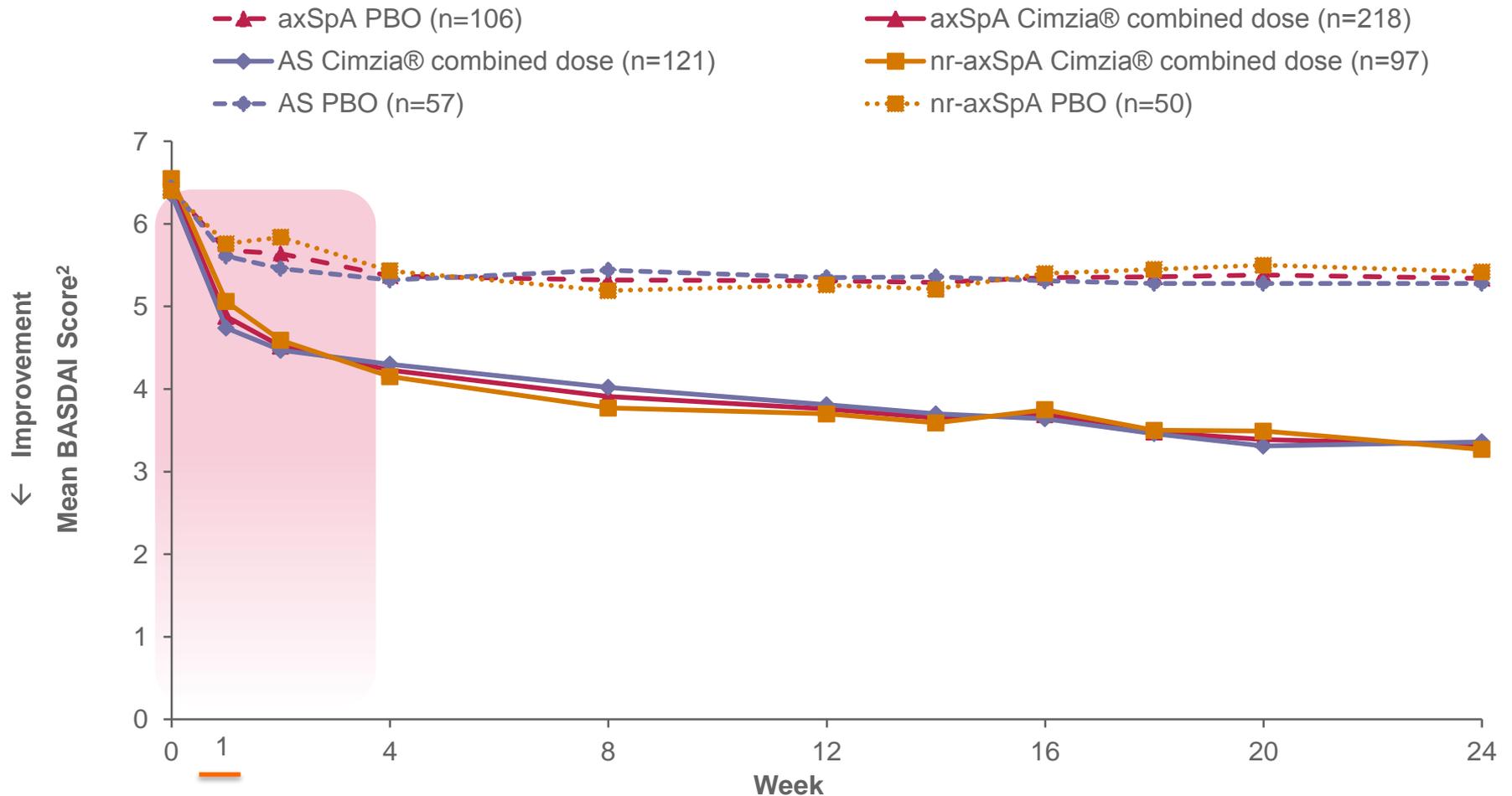
Rapid Improvements in Pain from Week 1

Mean change from Baseline in pain (PtAAP-VAS) at Week 1
in PsA patients (RAPID-PsA)



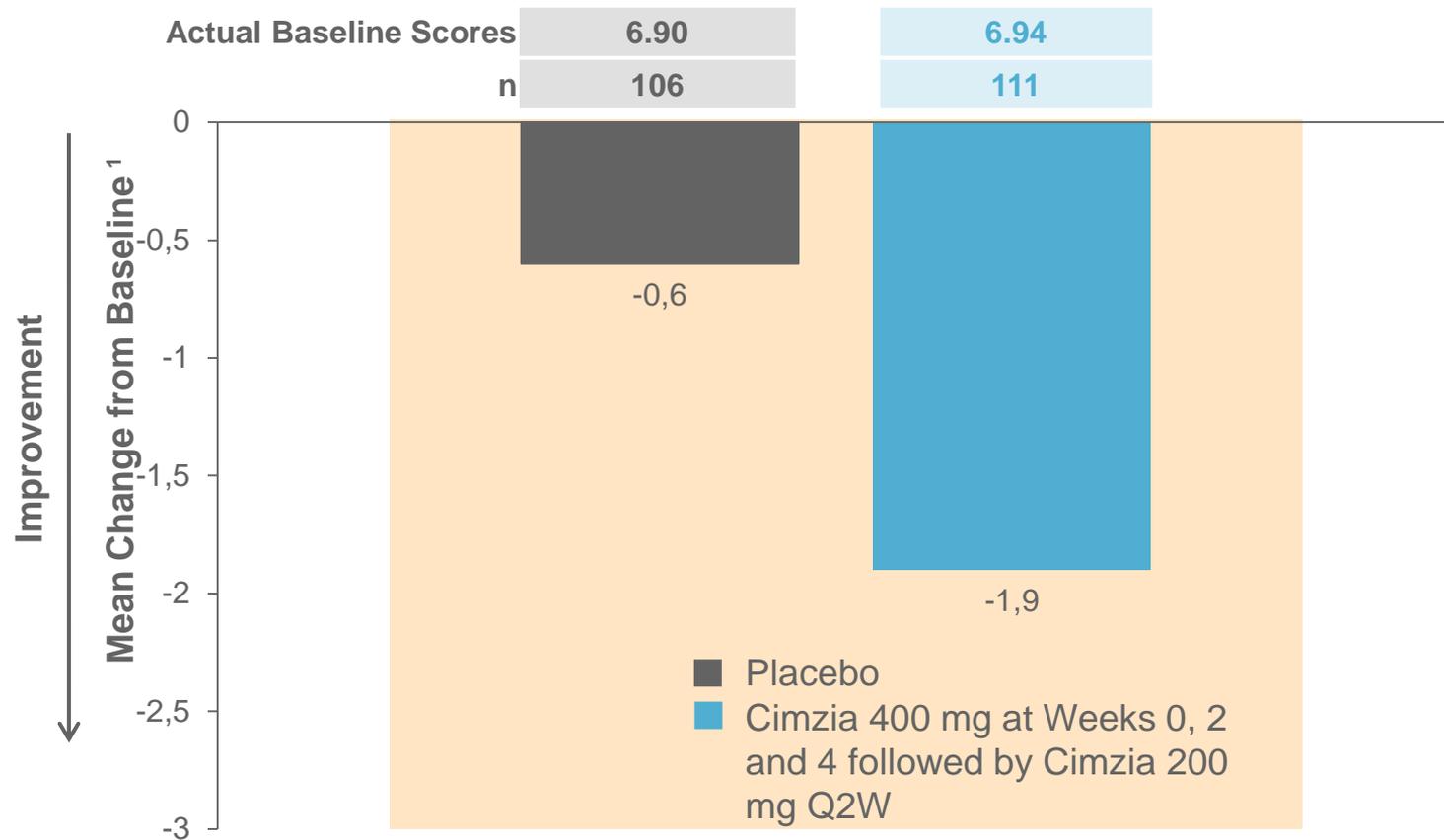
Rapid Improvements in Disease Activity in axSpA with certolizumab pegol by Week 1

Mean BASDAI score in overall axSpA, AS and nr-axSpA subpopulations



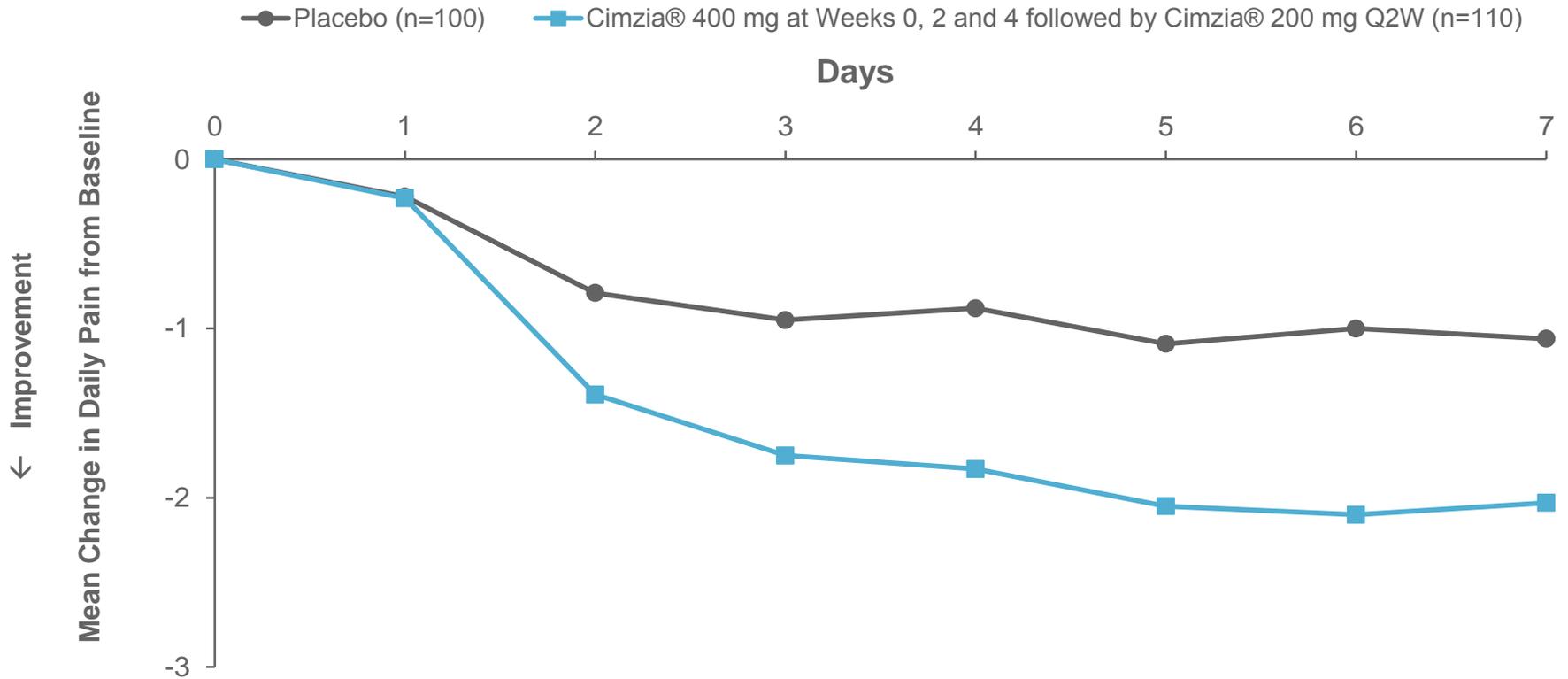
Rapid Improvements in nocturnal pain from Week 1

Mean change from Baseline in nocturnal back pain at Week 1
in certolizumab pegol-treated axSpA patients (RAPID-axSpA)



Rapid Improvements in daily pain from Day 2

Mean change from Baseline in daily pain to day 7 in certolizumab pegol-treated axSpA patients (RAPID-axSpA)



Exxelerate: First Blinded Randomised Head-to-Head Superiority Study Within the Anti-TNF Class

Objective

To evaluate the short- and long-term efficacy of Cimzia® compared with Humira, both in combination with MTX, in the treatment of moderate to severe RA that is not responding adequately to MTX

Inclusion Criteria:

- RA patients with an inadequate response to MTX
- Biologic-naïve
- Positive RF and/or anti-CCP
- Moderate to severe RA:
 - ≥4 swollen joints
 - DAS28(ESR) >3.2
 - CRP ≥10 mg/L or ESR ≥28 mm/hr

Cimzia® LD followed by Cimzia® 200 mg Q2W + MTX²

n=916 1:1 randomisation (no stratification)

Humira 40 mg Q2W + MTX³

Week 12 responders*
Cimzia® 200 mg Q2W + MTX

‘Cimzia® completers’

Week 12 non-responders**
Humira 40 mg Q2W + MTX

‘Cimzia® → Humira switchers’

Week 12 responders*
Humira 40 mg Q2W + MTX

‘Humira completers’

Week 12 non-responders**
Cimzia® LD (at Weeks 12, 14, 16) followed by Cimzia® 200mg Q2W + MTX

‘Humira → Cimzia® switchers’

Primary Endpoints

% with ACR20 response at Week 12

% with DAS28(ESR) ≤3.2 at Week 104

Week

0

12

24

52

78

104

Συμπερασματικά

- Οι βιολογικοί παράγοντες εμφανίζουν ταχεία έναρξη δράσης και αποτελεσματικότητας στη Ρευματοειδή αθρίτιδα και τις Σπονδυλοαρθρίτιδες – ήδη από τη 2^η εβδομάδα.
- Το certolizumab pegol εμφανίζει δεδομένα αποτελεσματικότητας από την 1^η εβδομάδα.
- Ανάγκη ύπαρξης περισσότερων δεδομένων από άμεση σύγκριση (Head-to-head comparison).



ΕΠΙΣΤΗΜΟΝΙΚΗ ΕΤΑΙΡΕΙΑ ΓΙΑ
ΤΗ ΜΥΟΣΚΕΛΕΤΙΚΗ ΥΓΕΙΑ
(ΕΠΕΜΥ)

8^ο Ετήσιο Επιστημονικό
Συμπόσιο **ΕΠΕΜΥ**

Ολοκληρωμένη διαχείριση των Αυτοάνοσων Φλεγμονωδών
Νοσημάτων και των άβηλων Μυοσκελετικών Παθήσεων

21-24
Απριλίου
2016

Avra
Imperial
Χανιά

