Βιοομοειδή σήμερα: Το τοπίο αλλάζει;

ΣΠΥΡΟΣ Ν ΝΙΚΑΣ
ΡΕΥΜΑΤΟΛΟΓΟΣ
ΙΩΑΝΝΙΝΑ
snnikas@yahoo.com

Διευκρινίσεις

- Η παρουσίαση αυτή προορίζεται μόνο για **μη-προωθητικό επιστημονικό** σκοπό και μπορεί να περιέχει πληροφορίες σχετικά με τα προϊόντα ή τις ενδείξεις τους, που επί του παρόντος μπορεί να είναι υπό διερεύνηση ή/και που δεν έχουν εγκριθεί από τις ρυθμιστικές αρχές.

- Η παρουσίαση αυτή εκφράζει αποκλειστικά τις απόψεις του **ομιλητή**.

- Οι πληροφορίες που περιέχονται είναι **ακριβείς** κατά τη δημιουργία της παρουσίασης.

- Τυχόν δεδομένα σχετικά με προϊόντα τα οποία δεν ανήκουν στη Novartis βασίζονται σε **δημόσια** διαθέσιμες πληροφορίες κατά τη δημιουργία της παρουσίασης.

ΣΥΓΚΡΟΥΣΗ ΣΥΜΦΕΡΟΝΤΩΝ (2 ΕΤΗ)

ΕΛΠΕΝ 1/17

MSD (9/17)

BIANEX (4/16)

ΕΕΜΜΟ (11/16)

ΕΠΕΜΥ (12/16)

ΕΠΙΤΡΟΠΗ ΕΡΕΥΝΩΝ (11/16)

PHIZER (11/15)

ΤΙΜΙΤΙΚΗ ΑΜΟΙΒΗ ΓΙΑ ΤΗΝ ΣΗΜΕΡΙΝΗ ΠΑΡΟΥΣΙΑΣΗ

ΕΙΝΑΙ ΓΝΩΣΤΌ

Τι είναι βιο-ομοειδές (biosimilar)

Τρόπος παρασκευής

Απαιτούμενες μελέτες

Λόγος ύπαρξης τους

Νεότερα – σύγχρονα δεδομένα

Τοπίο αλλάζει ?

Το τοπίο αλλάζει (I)


First, published on September 2, 2017 as 10.1136/annrheumdis-2017-211937

Recommendation

Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases

Jonathan Kay,[1] Monika M Schoels,[2] Thomas Dörner,[3] Paul Emery,[4] Tore K Kvien,[5] Josef S Smolen,[2,6] Ferdinand C Breedveld,[7] on behalf of the Task Force on the Use of Biosimilars to Treat Rheumatological Diseases

evidence-based συστάσεις: εξέλιξη & χρήση biosimilars στα ρευματικά νοσήματα

29 full-text άρθρα
&
20 abstracts
από ACR & EULAR abstract databases

Kay J, Schoels MM, Dörner T on behalf of the Task Force on the Use of Biosimilars to Treat Rheumatological Diseases, et al
Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases
Annals of the Rheumatic Diseases ***2018*** *;77:165-174*

Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases

			Level of	Grade of
Overarching principles				
A.	Treatment of rheumatic diseases is based on a shared decision-making process between patients and th rheumatologists.			
B.	The contextual aspects of the healthcare system should be taken into consideration when treatment dec are made.			
C.	A biosimilar, as approved by authorities in a highly regulated area, is neither better nor worse in efficacy and not inferior in safety to its bio-originator.	88	5	D
D.	Patients and healthcare providers should be informed about the nature of biosimilars, their approval process, and their safety and efficacy.	96	5	D
E.	Harmonised methods should be established to obtain reliable pharmacovigilance data, including traceability, about both biosimilars and bio-originators.	100	5	D
Consensus recommendations				
1.	The availability of biosimilars must significantly lower the cost of treating an individual patient and increase access to optimal therapy for all patients with rheumatic diseases.	100	5	D
2.	Approved biosimilars can be used to treat appropriate patients in the same way as their bio-originators.	100	1b	A
3.	As no clinically significant differences in immunogenicity between biosimilars and their bio-originators have been detected, antidrug antibodies to biosimilars need not be measured in clinical practice.	100	2b	B
4.	Relevant preclinical and phase I data on a biosimilar should be available when phase III data are published.	100	5	D
5.	Since the biosimilar is equivalent to the bio-originator in its physicochemical, functional and pharmacokinetic properties, confirmation of efficacy and safety in a single indication is sufficient for extrapolation to other diseases for which the bio-originator has been approved.	100	5	D
6.	Currently available evidence indicates that a single switch from a bio-originator to one of its biosimilars is safe and effective; there is no scientific rationale to expect that switching among biosimilars of the same bio-originator would result in a different clinical outcome but patient perspectives must be considered.	96	1b	A
7.	Multiple switching between biosimilars and their bio-originators or other biosimilars should be assessed in registries.	100	5	D
8.	No switch to or among biosimilars should be initiated without the prior awareness of the patient and the treating healthcare provider.	91	5	D

Kay J, Schoels MM, Dörner, et al Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases Annals of the Rheumatic Diseases 2018;77:165-174

Βασικές αρχές

Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases

- Η απόφαση για τη θεραπεία είναι **κοινή** μεταξύ ρευματολόγου & ασθενούς
- Σχετικά θέματα του **συστήματος υγείας** θα πρέπει να λαμβάνονται υπόψη
- Το εγκεκριμένο **biosimilar** δεν είναι ούτε καλύτερο – ούτε χειρότερο σε αποτελεσματικότητα vs bio-originator, ούτε χειρότερο σε ασφάλεια
- Ασθενείς και συστήματα υγείας θα πρέπει να **ενημερώνονται** για την φύση των biosimilars, την διαδικασία έγκρισης και ασφάλεια & αποτελεσματικότητα
- **Κοινοί** μέθοδοι για την φαρμακο -επαγρύπνηση (& traceability)

Kay J, Schoels MM, Dörner T, et al Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases Annals of the Rheumatic Diseases 2018;77:165-174

Συστάσεις

Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases

biosimilars : σημαντικά χαμηλότερο **κόστος** => αύξηση της πρόσβαση ασθ στην ιδανική θεραπεία

*price discounted only 15% (USA) below that of the bio-originator may **not be sufficient** to motivate use of a biosimilar*

χρήση σε κατάλληλους ασθενείς με **τον ίδιο τρόπο** με το OR (new batch)

αφού δεν υπάρχουν σημαντικές διαφορές στην ανοσογονικότητα => έλεγχος **antidrug antibodies** δεν απαιτείται στην κλ πράξη

Προκλινικά δεδομένα & φάσης I πρέπει να είναι διαθέσιμα όταν δημοσιεύονται φάσης III

Kay J, Schoels MM, Dörner T, et al Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases Annals of the Rheumatic Diseases 2018;77:165-174

Συστάσεις

Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases

Εφόσον το BS είναι ισοδύναμο με OR (φυσιο-χημικά, λειτουργικά, ΦΚ), η επιβεβαίωση της ασφάλειας και την αποτελεσματικότητας **σε μια ένδειξη =>** είναι επαρκής για την επέκταση (extrapolation)

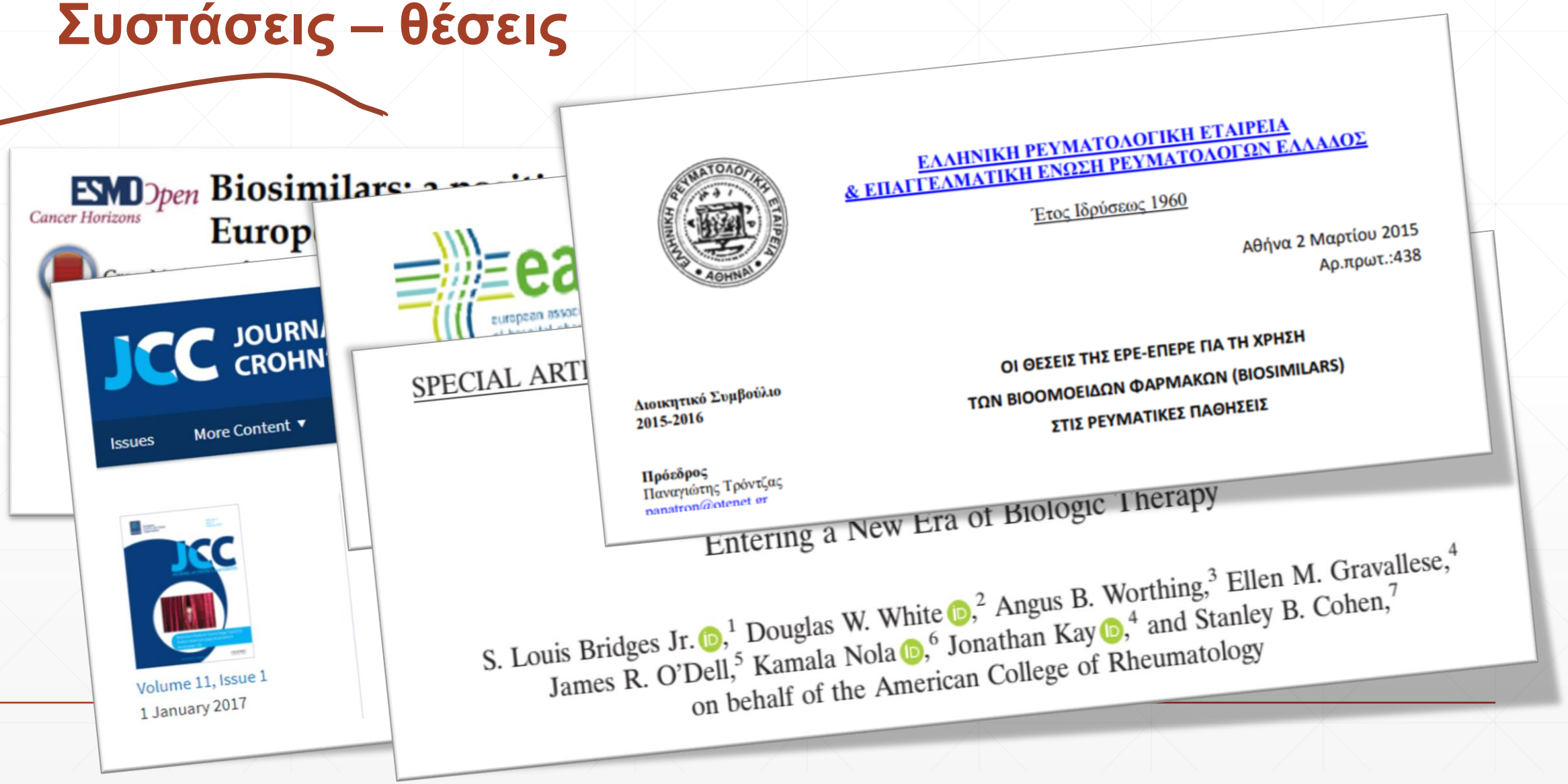
Η **ΜΙΑ αλλαγή** από το bio-originator σε ένα BS είναι **ασφαλής** και **αποτελεσματική** - ΔΕΝ υπάρχουν ενδείξεις ότι το switching μεταξύ biosimilars του ίδιου bio-originator θα έχει διαφορετική έκβαση - ο ασθενής θα πρέπει να λαμβάνεται υπόψη

Πολλαπλά switching μεταξύ biosimilars και bio-originators ή άλλων biosimilars θα πρέπει να εκτιμώνται στα registries

Καμία αλλαγή μεταξύ biosimilars δεν θα πρέπει να γίνεται χωρίς την **ενημέρωση** του ασθενούς και του συστήματος υγείας

Kay J, Schoels MM, Dörner T, et al Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases Annals of the Rheumatic Diseases 2018;77:165-174

Συστάσεις – θέσεις



Το τοπίο αλλάζει (II)

482 ασθ υπο INX τυχαιοποιήθηκαν για 52 εβδ σε

- **241 infliximab originator**
- **241 CT-P13**

- 155 (32%) Crohn's disease
- 93 (19%) ulcerative colitis
- 91 (19%) spondyloarthritis
- 77 (16%) rheumatoid arthritis
- 30 (6%) psoriatic arthritis
- 35 (7%) chronic plaque psoriasis

Επιδείνωση νόσου σε

- 53 (**26**%) infliximab originator
- 61 (**30**%) CT-P13

(per-protocol set; *adjusted treatment difference −4·4%, 95% CI −12·7 to 3·9).*

Συνολικές ΑΕ

- 168 [**70**%] infliximab originator
- 164 [**68**%] CT-P13

Η “δύναμη» της μελέτης δεν είναι επαρκής
για κάθε νόσημα ξεχωριστά

*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*
*Jørgensen, et al.The Lancet , Volume 389 , Issue 10086 , 2304 – 2316. **Jun 2017***

Το τοπίο αλλάζει (II)
η άλλη άποψη…

non-mandatory "μεταφορά" ασθ από originator **etanercept** (ENB) στο biosimilar etanercept (SB4)

99% συμφώνησαν (625 ασθ)

- 433 RA
- 128 PsA
- 64 AS

Σύγκριση : 600 ασθ από μια **historical cohort**

Η ομάδα αλλαγής είχε σημαντικά :

- Υψηλότερο κίνδυνο **διακοπής** (adjusted HR 1.57, 95%CI 1.05-2.36)
- **Μικρότερες μειώσεις σε CRP** (adjusted diff 1.8 (95%CI 0.3-3.2)) και **DAS28-CRP** (adjusted diff 0.15 (95%CI 0.05-0.25))

Στους 6 μήνες VS *historical cohort*.

FDA : no clinically meaningful differences

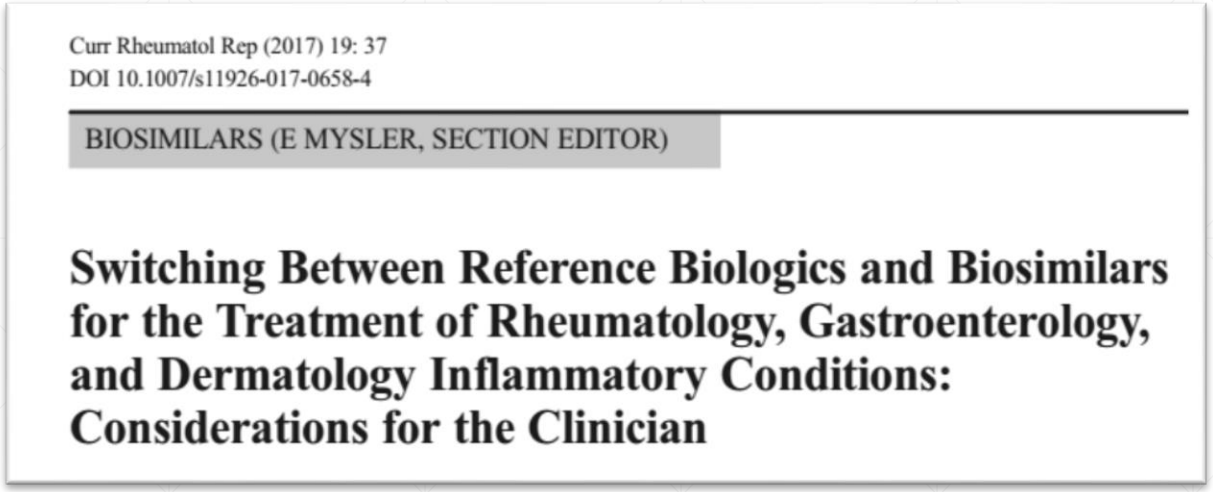
Οι διαφορές αυτές θεωρήθηκαν as **not being clinically** relevant.

Tweehuysen, L. , et al. (2018), Open-Label Non-Mandatory Transitioning From Originator Etanercept to Biosimilar SB4: 6-Month Results From a Controlled Cohort Study. Arthritis Rheumatol. Accepted Author Manuscript.

Το τοπίο αλλάζει (II)

53 μελέτες (switching studies)

- Infliximab publications covered CT-P13 (25 studies), SB2 (1), infliximab NK (1), and unspecified infliximab biosimilars (2)
- Etanercept publications covered SB4 (2) and GP2015 (2)
- Adalimumab publications covered ABP 501 (2) and SB5 (1)
- Rituximab publications covered CT-P10 (1)


Curr Rheumatol Rep (2017) 19: 37
DOI 10.1007/s11926-017-0658-4

BIOSIMILARS (E MYSLER, SECTION EDITOR)

Switching Between Reference Biologics and Biosimilars for the Treatment of Rheumatology, Gastroenterology, and Dermatology Inflammatory Conditions: Considerations for the Clinician

Efficacy and safety data generally showed **no differences** between patients who

- switched treatments versus
- those who did not

No differences were seen pre- and post-switch

Moots R et al Curr Rheumatol Rep. ***2017*** *Jun;19(6):37*

Το τοπίο αλλάζει (II)

Drugs

March 2018, Volume 78, Issue 4, pp 463–478 | Cite as

Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes

Authors | Authors and affiliations

Hillel P. Cohen, Andrew Blauvelt, Robert M. Rifkin, Silvio Danese, Sameer B. Gokhale, Gillian Woollett

Δεδομένα από **90 μελέτες , με 14.225 ασθενείς**

3 large *multiple switch studies with different biosimilars*

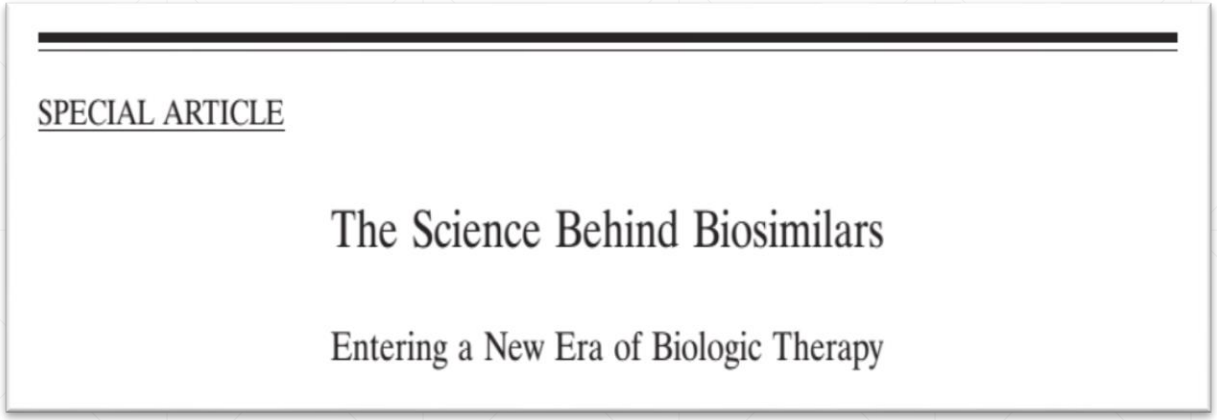
these results provide **reassurance** to healthcare professionals and the public that the risk of

- immunogenicity-related safety concerns or
- diminished efficacy

is **unchanged after switching** from a reference biologic to a biosimilar medicine

Cohen HP et al Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes. Drugs. ***2018*** *Mar;78(4):463-478.*

Το τοπίο αλλάζει (III)



SPECIAL ARTICLE

The Science Behind Biosimilars

Entering a New Era of Biologic Therapy

Όταν ασθενής αναπτύσσει ADA στο φάρμακο αναφοράς → με συνέπεια απώλεια κλινικής απόκρισης → **should not be switched to its biosimilar**

antidrug antibodies to a reference product => **cross react** with its biosimilar

Όπως έχει δειχθεί σε μελέτες με infliximab-dyyb σε ασθ με

RA, AS, και IBD

Bridges SL JrThe Science Behind Biosimilars: Entering a New Era of Biologic Therapy. Arthritis Rheumatol. ***2018*** *Mar;70(3):334-344*

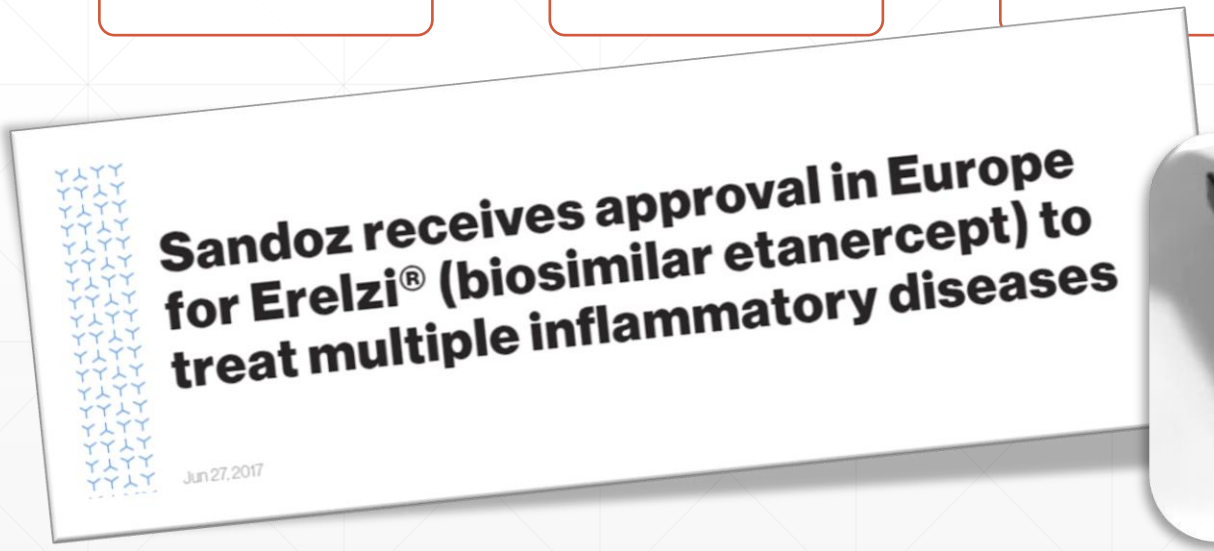
Το τοπίο αλλάζει (IV) - 2018

ΝΕΕΣ ΕΠΙΛΟΓΕΣ

ΝΕΕΣ ΔΥΝΑΤΟΤΗΤΕΣ

GP2015

Etanercept
SANDOZ



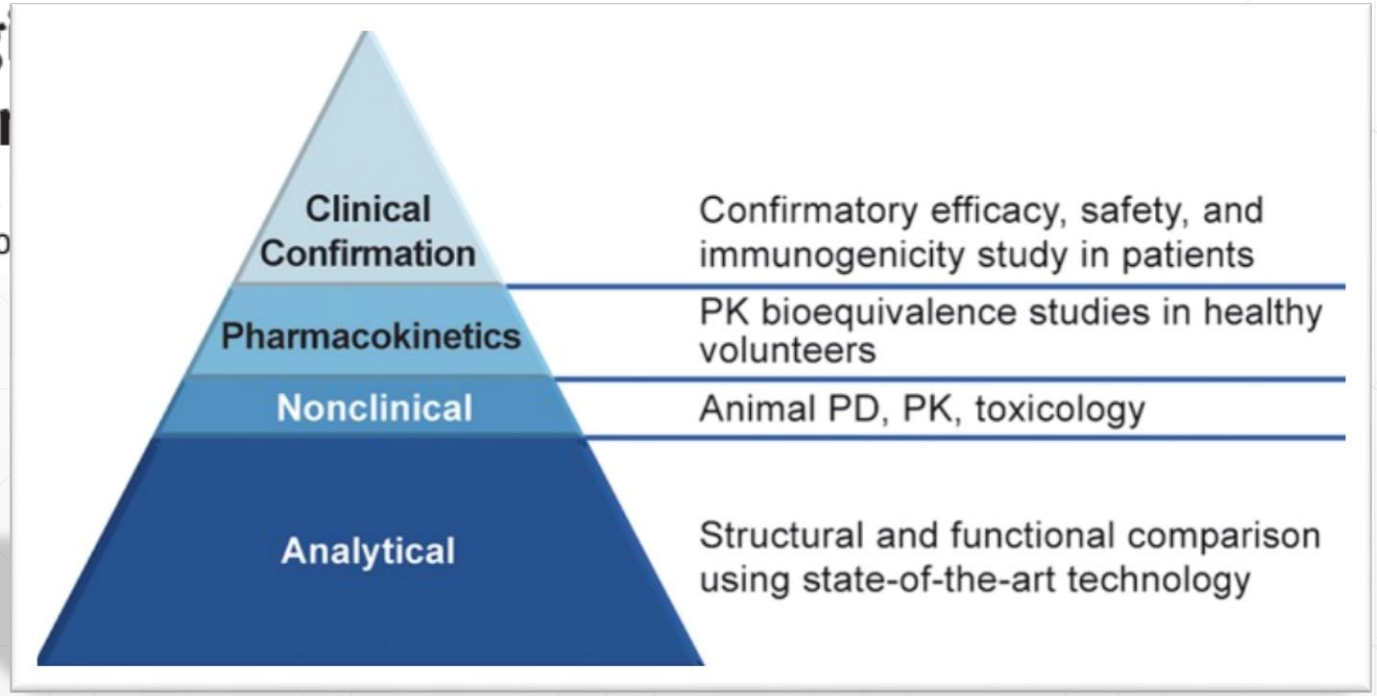
Erelzi was approved by the US Food and Drug Administration (**FDA**) in **August 2016**

CLINICAL TRIALS

BJD
British Journal of Dermatology

The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the orig
moderate-to-severe ch

C.E.M. Griffiths,[1] D. Thaçi,[2] S. Gerdes,[3] P.
EGALITY study group; N. Hattebuhr,[8] J. Po



Journal
Expert Opinion on Biological Therapy ›
Volume 16, 2016 - Issue 10

Original Research

Characterization and non-clinical assessment of the proposed etanercept biosimilar GP2015 with originator etanercept (Enbrel®)

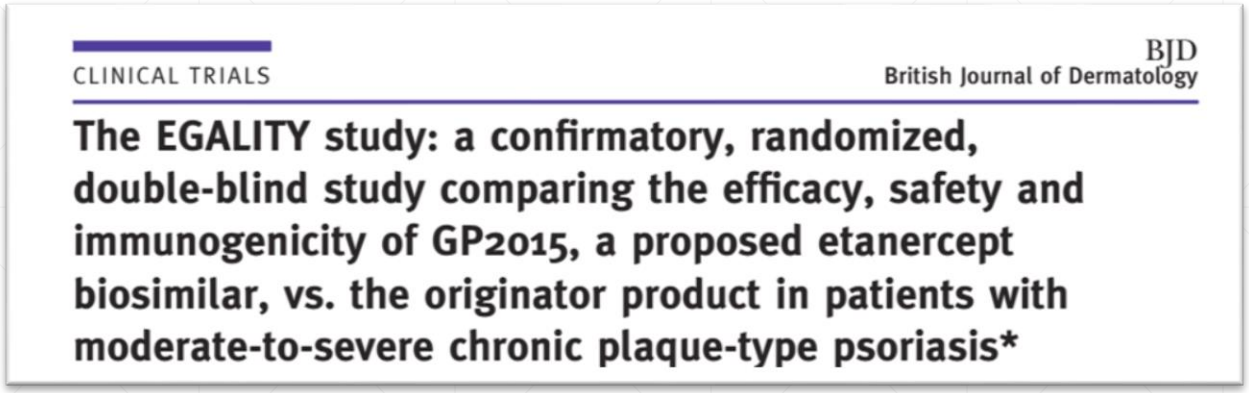
Hans-Peter Hofmann, Ulrich Kronthaler, Cornelius Fritsch, Roger Grau, Stefan O. Müller, Robert Mayer, ...show all

Pages 1185-1195 | Received 24 Jun 2016, Accepted 22 Jul 2016, Accepted author version posted online: 27 Jul 2016, Published online: 16 Aug 2016

Hofmann HP et al Characterization and non-clinical assessment of the proposed etanercept biosimilar GP2015 with originator etanercept (Enbrel(®)). Expert Opin Biol Ther. ***2016*** *Oct;16(10):1185-95*

GP2015 vs ETA(or)

2 καινούργια & ενδιαφέροντα θέματα



531 ασθενείς (μέτρια- σοβαρή κατά πλάκας **ψωρίαση**) τυχαιοποιήθηκαν 1 : 1 to (self-administer) **GP2015 ή ETN** (50 mg x2 / εβδ SC)

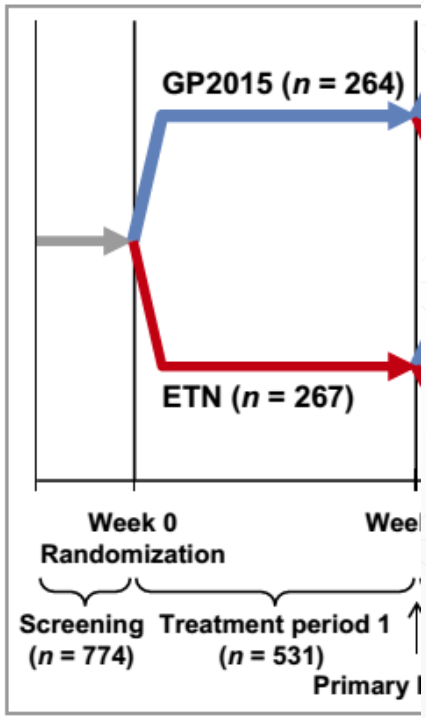
Ασθενείς με ≥ 50% βελτίωση στο PASI 50 την εβδ 12 =>

- Συνέχιση της ίδιας θεραπείας (50mg/w)
- Σχήμα **3 switches** μεταξύ GP2015 και ETN μέχρι εβδ 30

Σύνολο παρακολούθησης 52 εβδ

Griffiths CEM et al. 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. ***2017*** *Apr;176(4):928-938*

GP2015 vs ETA(or)



CLINICAL TRIALS

BJD
British Journal of Dermatology

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*

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GP2015 vs ETA(or)

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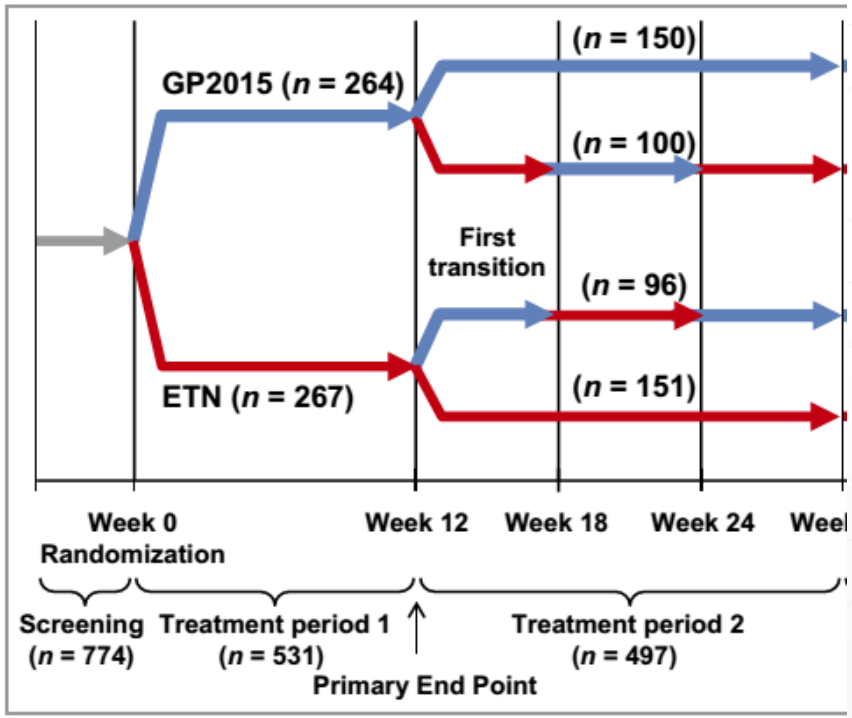

Griffiths CEM et al. The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. Br J Dermatol. ***2017*** *Apr;176(4):928-938*

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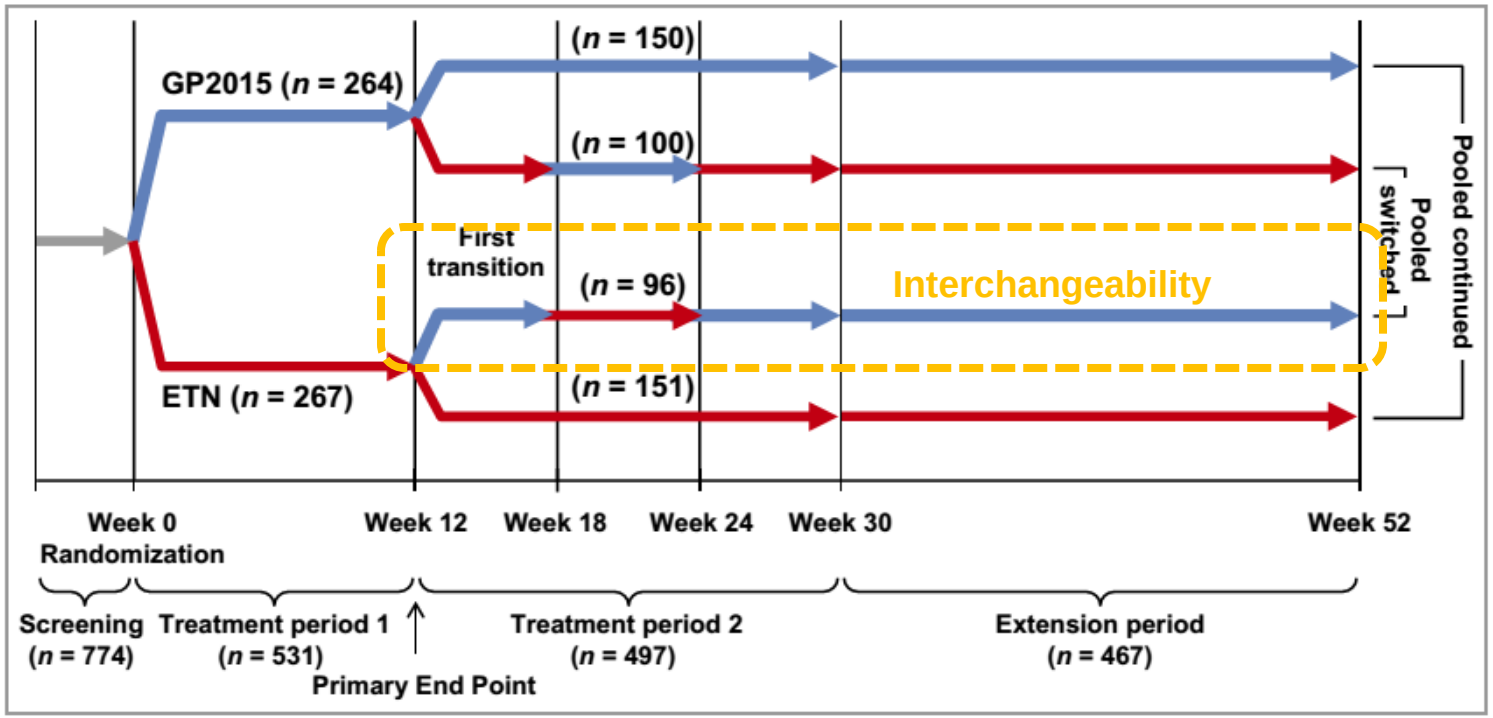
1η μελέτη



eahp
european association of hospital pharmacists

EAHP Position Paper on Biosimilar Medicines

Supports that a biosimilar product and other biosimilar(s) to the same reference product are **interchangeable** and therefore **can be switched**

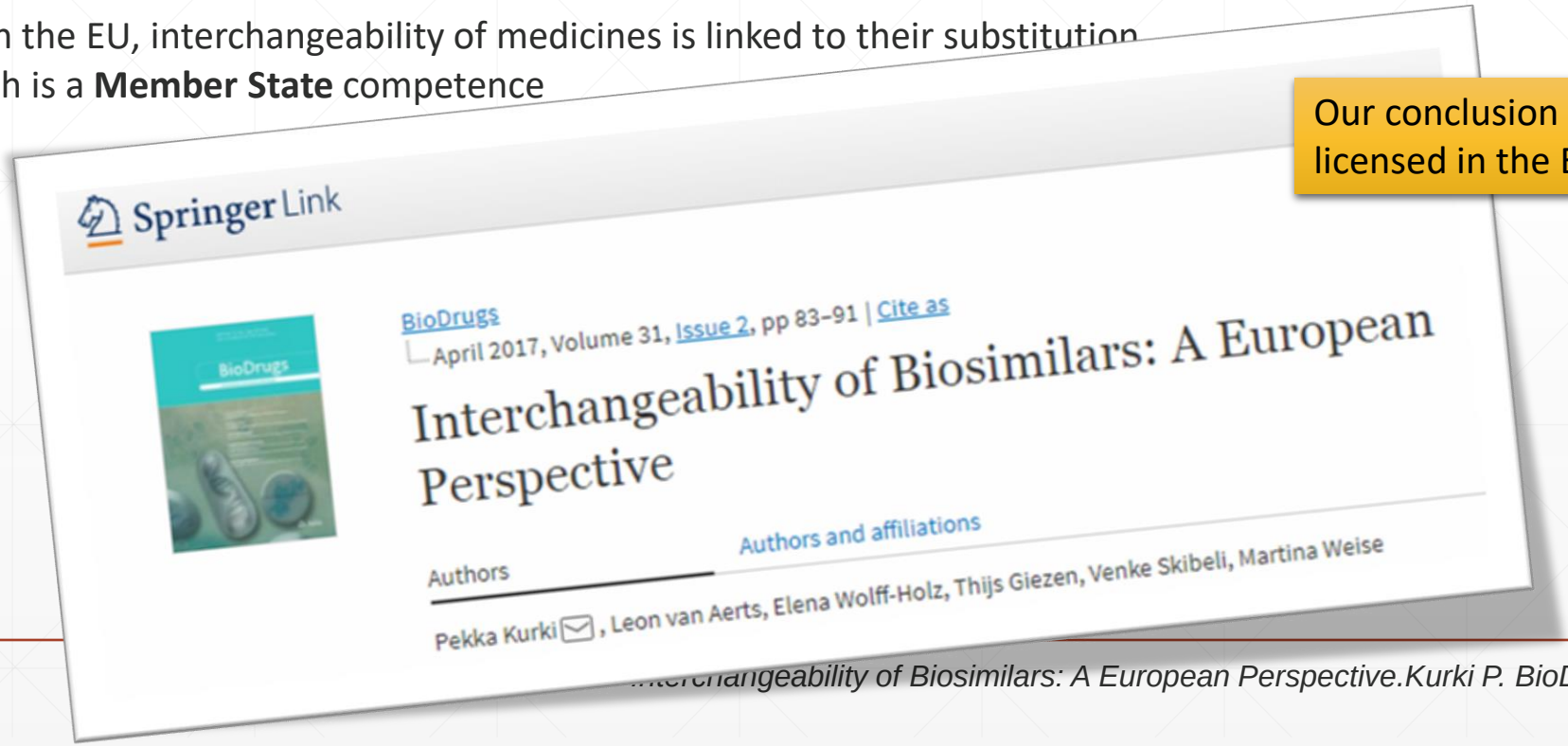
Griffiths CEM et al. The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. Br J Dermatol. ***2017*** *Apr;176(4):928-938*

Interchangeability ?

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

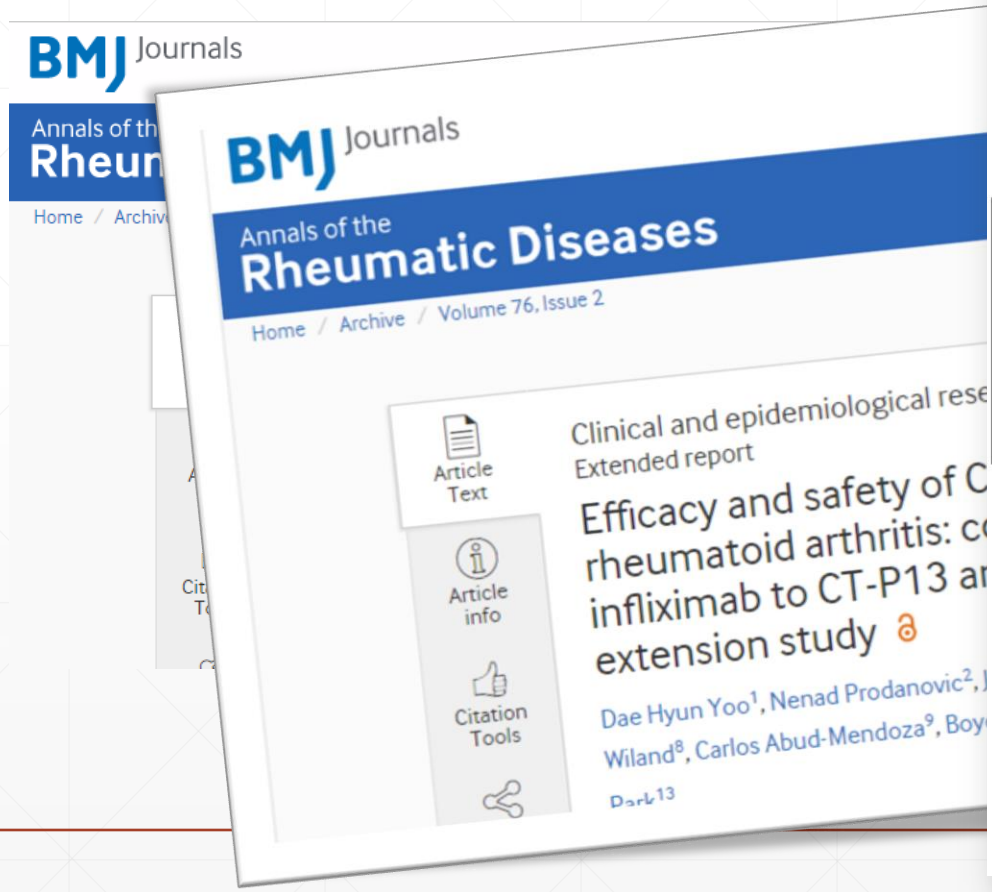
- EMA cannot have an opinion on interchangeability
- In the EU, interchangeability of medicines is linked to their substitution which is a **Member State** competence

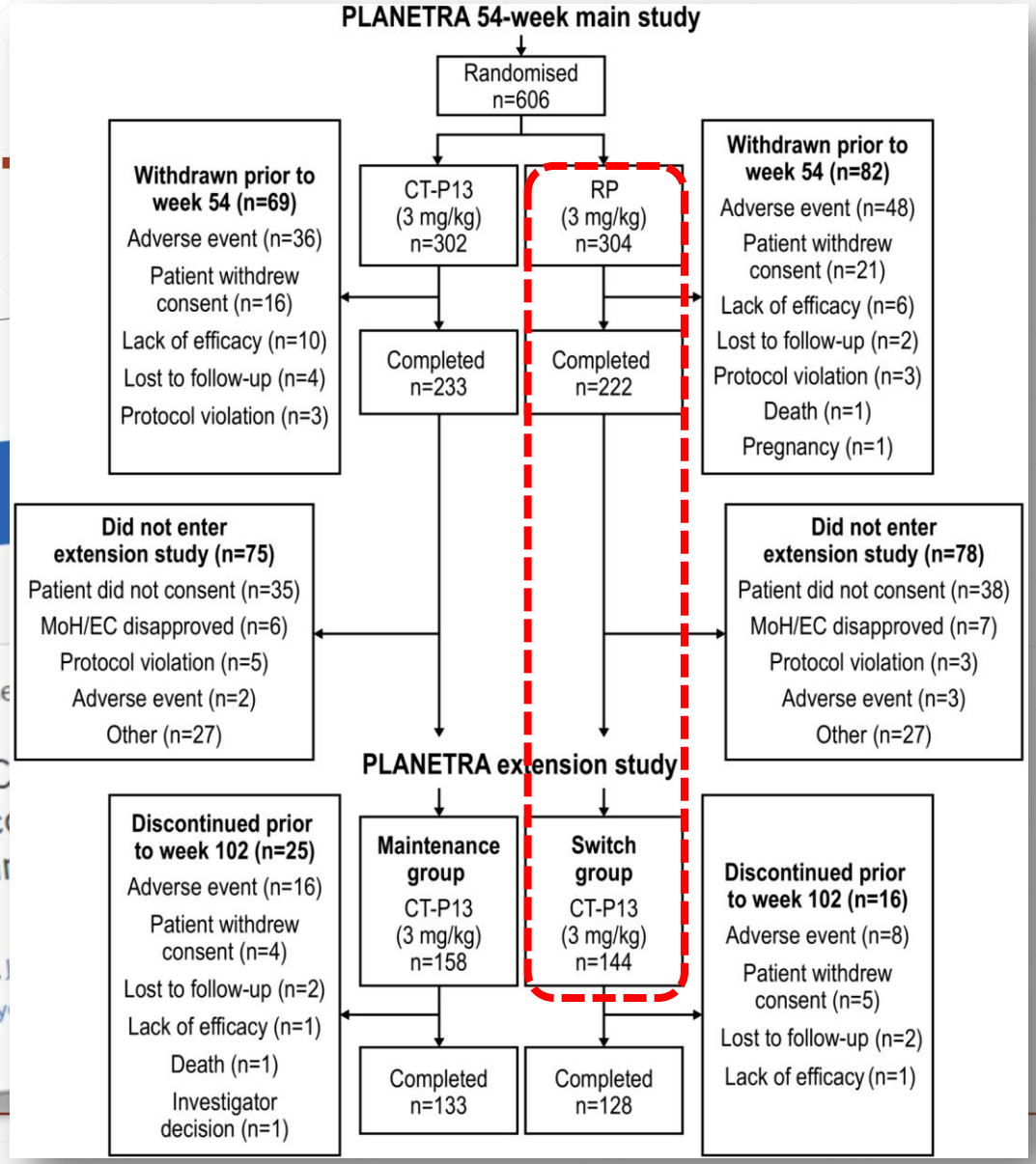
Our conclusion is that biosimilars licensed in the EU **are interchangeable**.



...nterchangeability of Biosimilars: A European Perspective.Kurki P. BioDrugs. ***2017*** *Apr;31(2):83-91*

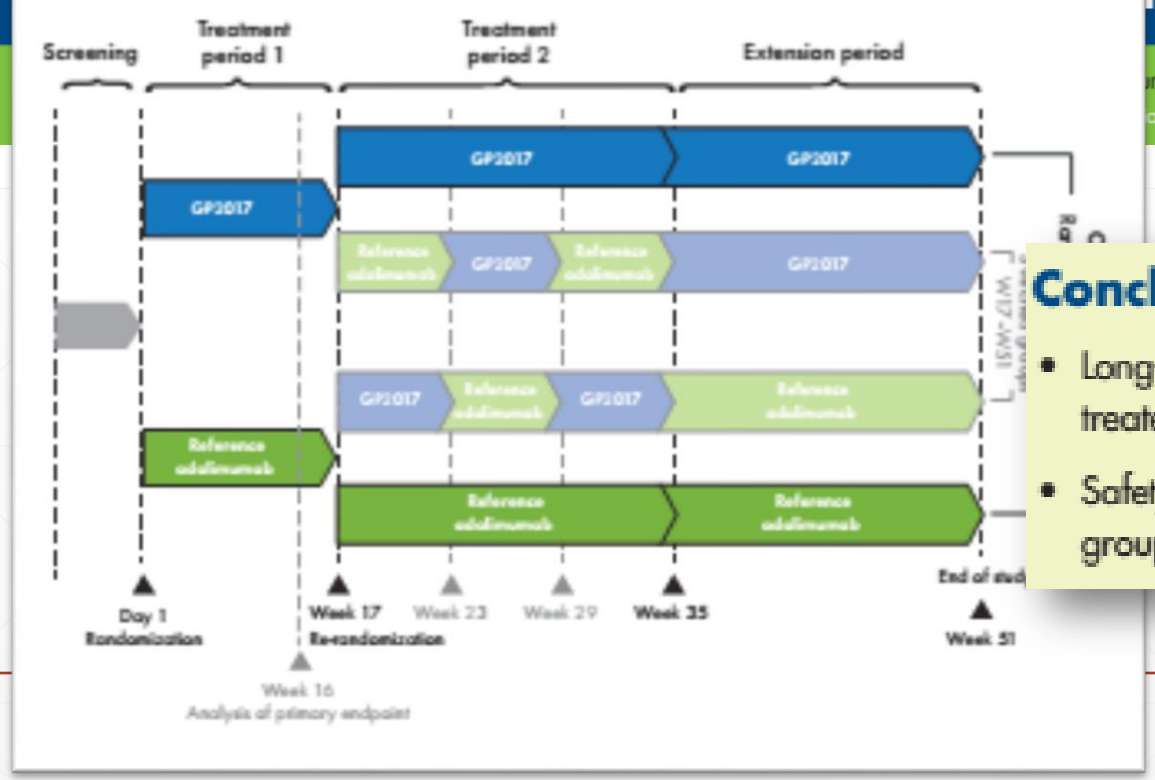
Είναι λίγο διαφορετικό …





Η πρώτη αλλά όχι η μοναδική…

Figure 1. Study design



data from a Phase III confirmatory
r, with reference adalimumab

r,[4] and Craig L Leonardi[5]

alists, Louisville, Kentucky; [4]Hexal AG, Holzkirchen, Germany; [5]Central Dermatology, St Louis, Missouri

Conclusions

- Long-term efficacy was similar and sustained in patients continuously treated with GP2017 and reference adalimumab up to 51 weeks.
- Safety profiles and immunogenicity were similar among patients in both groups, with no new safety concerns.

Poster presented at the 25th UEG Week 2017, October 28 to November 1 2017, Barcelona, Spain

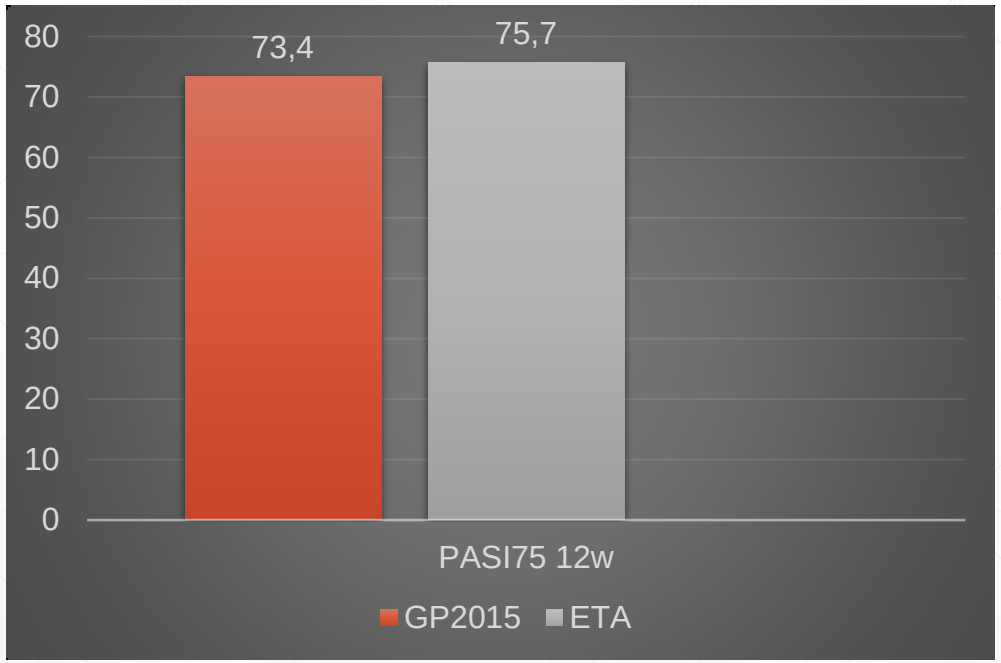
GP2015 vs ETA(or)
αποτελεσματικότητα

CLINICAL TRIALS

BJD
British Journal of Dermatology

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*

-2,3%



Η διαφορά στο PASI 75 (*75% βελτίωση στο PASI score)* την εβδ 12 μεταξύ GP2015 και ETN (primary end point) ήταν **-2,3%** (73,4 vs 75.7)

*The 95% confidence interval (-**9,85 to 5, 30**) was well contained within the prespecified margin range of -18 to 18*

*Griffiths CEM et al. 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. **2017** Apr;176(4):928-938*

GP2015 vs ETA(or)
αποτελεσματικότητα

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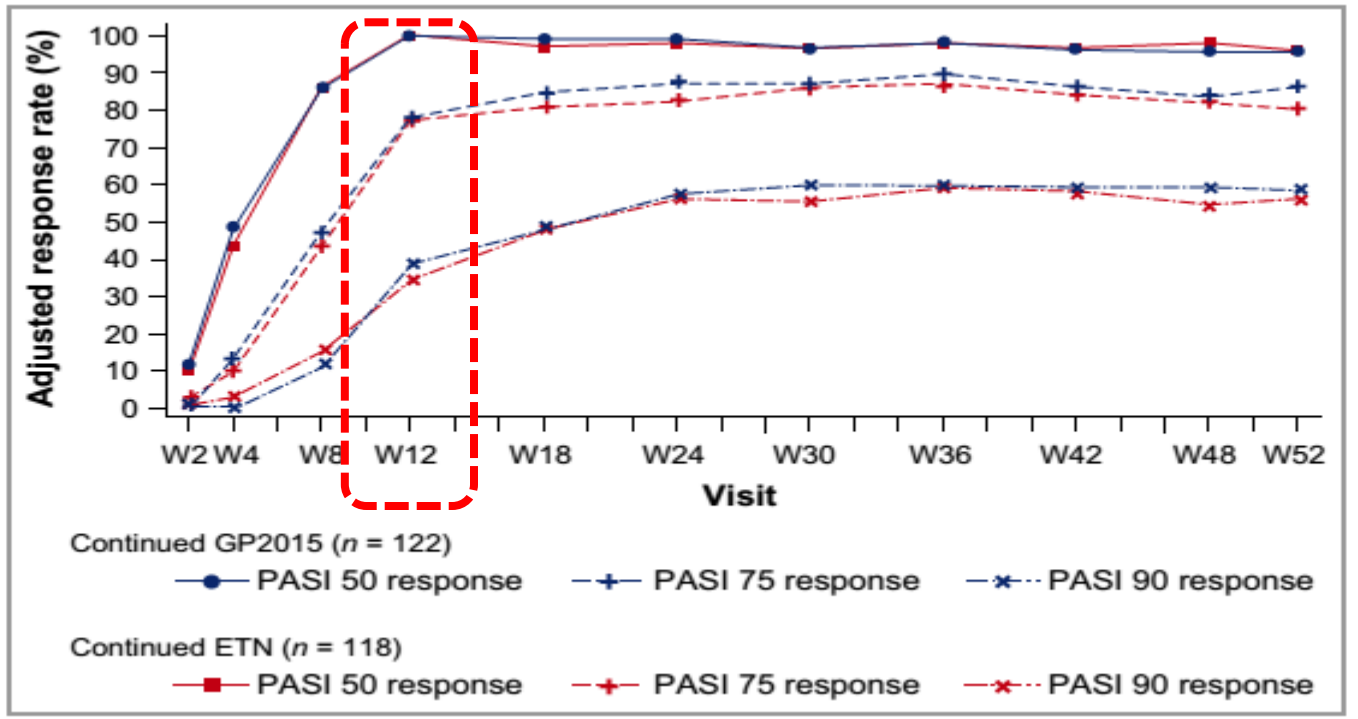
BJD
British Journal of Dermatology

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*



PASI 50
PASI 75
PASI 90

Υπό ΣΥΝΕΧΗ Χορήγηση

Griffiths CEM et al. 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. ***2017*** *Apr;176(4):928-938*

GP2015 vs ETA(or)
φαρμακοκινητική

CLINICAL TRIALS

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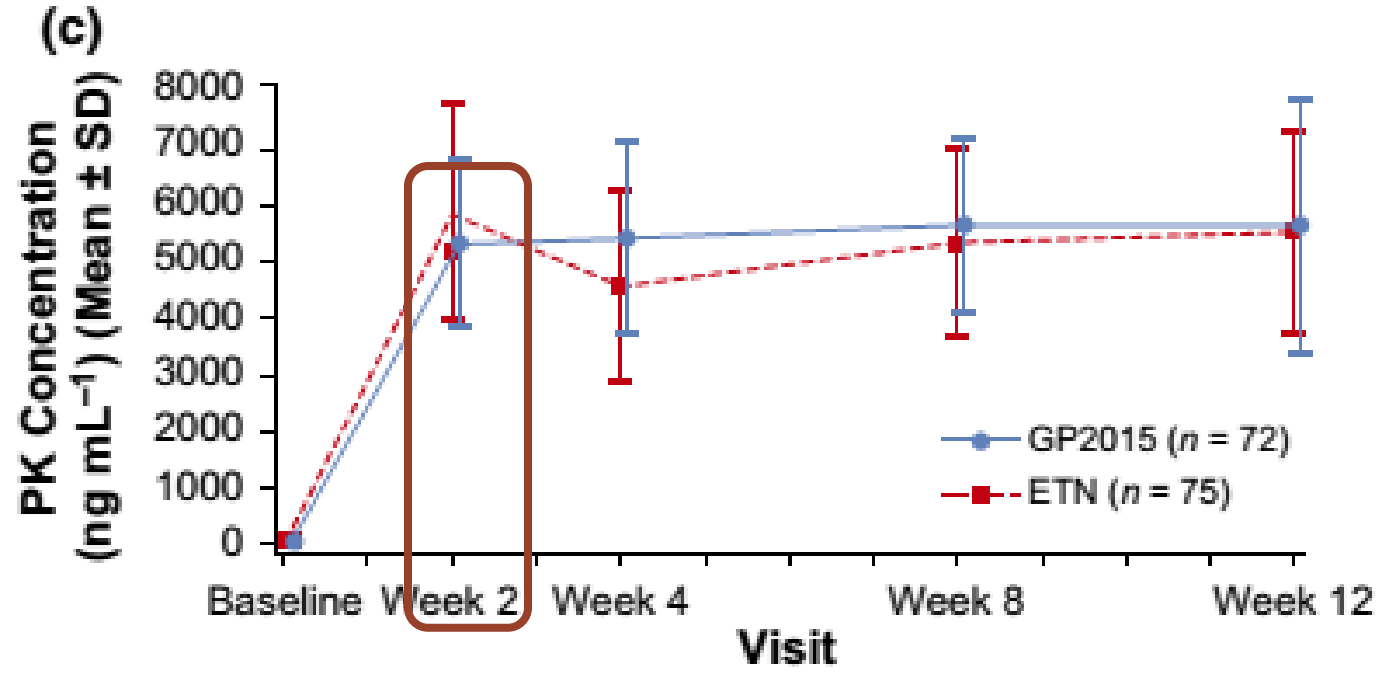
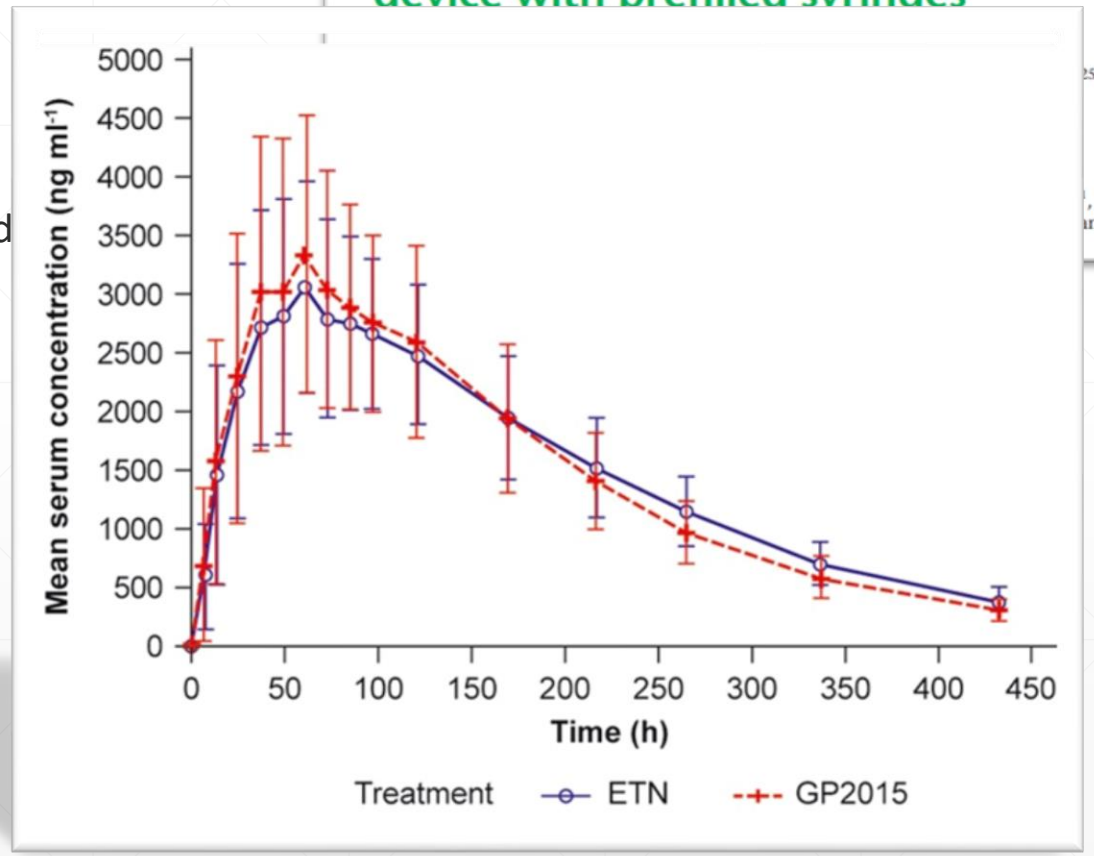


Griffiths CEM et al. The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. Br J Dermatol. ***2017*** *Apr;176(4):928-938*

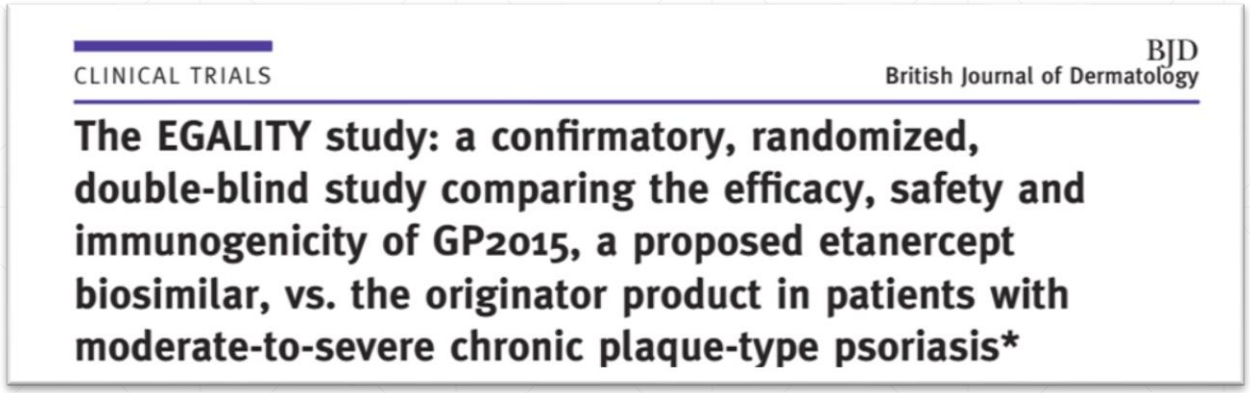
GP2015 vs ETA(or)
φαρμακοκινητική (φάση Ι)

Σύγκριση με
- etanercept originator (ETN, bioequivalence study)
- GP2015 χορηγούμενο με autoinjector (AI) ή prefilled
  delivery study).



Von Richter O,, et al. GP2015, a proposed etanercept biosimilar: Pharmacokinetic similarity to its reference product and comparison of its autoinjector device with prefilled syringes. British Journal of Clinical Pharmacology. 2017;83(4):732-741

GP2015 vs ETA(or)
ασφάλεια



Οι ασθενείς με τουλάχιστον μια treatment-emergent adverse event (TEAE) μέχρι την εβδ 52 ήταν **παρόμοια** μεταξύ αυτών που **συνέχισαν** (continued)

- GP2015 (n = 98, 59.8%)
- ETN (n = 98, 57.3%)

Αλλά και αυτών που άλλαξαν **switched**

- GP2015 (n = 61, 61%)
- ETN (n = 57, 59%)

Griffiths CEM et al. 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. ***2017*** *Apr;176(4):928-938*

GP2015 vs ETA(or)
ασφάλεια

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Η επίπτωση των

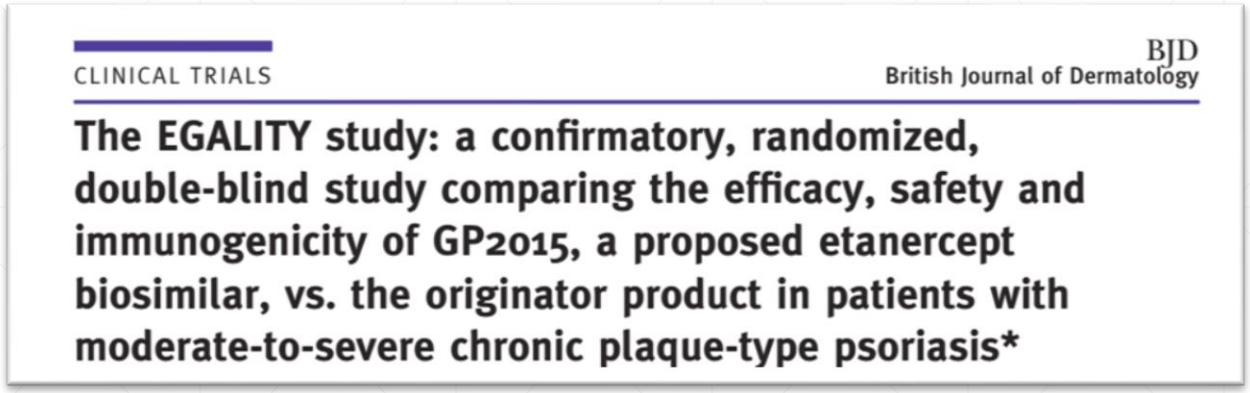
- **Σοβαρών ΑΕ**
- TEAEs => διακοπή από τη μελέτη
- treatment-related TEAEs

Ήταν **παρόμοιες** μεταξύ

- Των 2 συνεχιζόμενων ομάδων
- 2 ομάδων αλλαγής (switched treatment groups)

Griffiths CEM et al. 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. ***2017*** *Apr;176(4):928-938*

GP2015 vs ETA(or)
ασφάλεια



Antidrug antibodies, (όλα non-neutralizing) :

- 5 ασθ στο **ETN** κατά τη διάρκεια period 1
- 1 ασθ στην ομάδα «αλλαγή σε ETN» (αρχικά **GP2015** για 12 εβδ)

Griffiths CEM et al. 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. ***2017*** *Apr;176(4):928-938*

ΑΝΟΣΟΓΟΝΙΚΟΤΗΤΑ TNFi

BioDrugs
August 2015, Volume 29, Issue 4, pp 241–258 | Cite as

Comparative Immunogenicity of TNF Inhibitors: Impact on Clinical Efficacy and Tolerability in the Management of Autoimmune Diseases. A Systematic Review and Meta-Analysis

Authors | Authors and affiliations

Sarah S. Thomas, Nabeel Borazan, Nashla Barroso, Lewei Duan, Sara Taroumian, Benjamin Kretzmann, Ricardo Bardales, David Elashoff, Sitaram Vangala, Daniel E. Furst

RA, SpA, IBD

Ανάπτυξη ADABs

- 25.3 % (95 % CI 19.5–32.3) infliximab
- 14.1 % (95 % CI 8.6–22.3) adalimumab
- 6.9 % (95 % CI 3.4–13.5) certolizumab
- 3.8 % (95 % CI 2.1–6.6) golimumab
- **1.2** % (95 % CI 0.4–3.8) etanercept

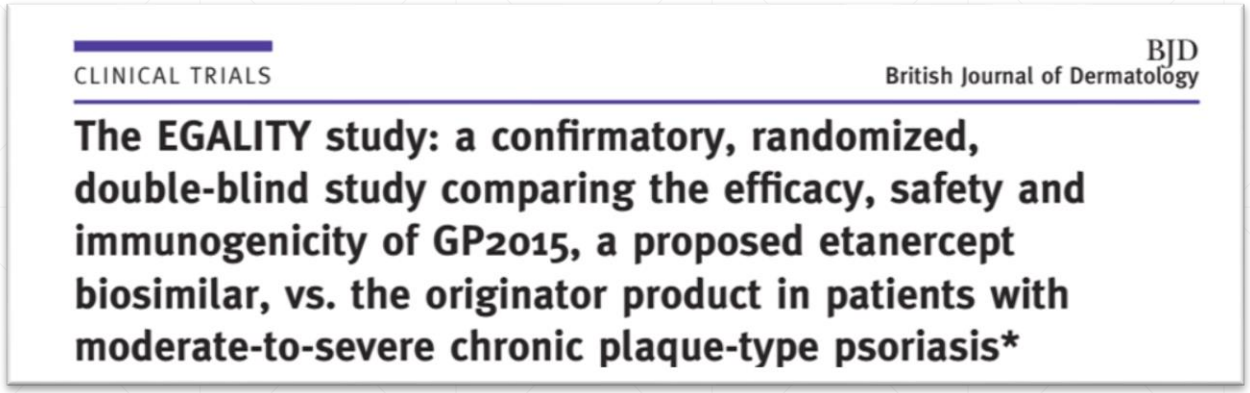
ADABS **μείωση αποτελεσματικότητας** κατά

- 27 % στην RA
- 18 % στις SpA

both of which were statistically significant

*Thomas, S.S., Borazan, N., Barroso, N. et al. BioDrugs (**2015**) 29: 241*

GP2015 vs ETA(or)
ΤΟ ΤΟΠΙΟ ΑΛΛΑΖΕΙ


CLINICAL TRIALS

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Αντιδράσεις στο σημείο της έγχυσης

- 13 (**4.9%**) GP2015 group
- 38 (**14**.%) ETN group

Την εβδ 12

- 14 **(8.5%)** continued GP2015
- 27 (**15. 8%)** continued ETN groups

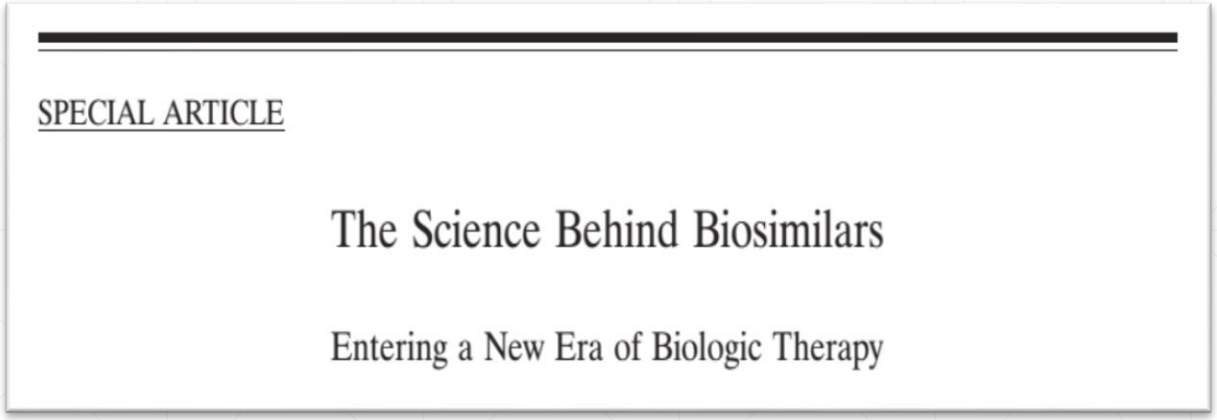
Την εβδ 52

difference in formulation between the two products ?

Ένα βήμα «παραπέρα» ?

Griffiths CEM et al. 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. ***2017*** *Apr;176(4):928-938*

ΤΟ ΤΟΠΙΟ ΑΛΛΑΖΕΙ


SPECIAL ARTICLE

The Science Behind Biosimilars

Entering a New Era of Biologic Therapy

difference in formulation between the two products ?

Although the **primary structures** of biosimilars must be **identical** to those of their reference products, there **may** be **differences** in

- secondary (e.g., a-helix and b-sheet)
- tertiary (e.g., disulfide and salt bridges)
- quaternary (e.g., protein subunit interactions) structure
- differences in glycosylation and other posttranslational modifications.

ΚΑΙ ΑΥΤΟ ΔΕΝ ΕΙΝΑΙ ΑΠΑΡΑΙΤΗΤΑ ΚΑΚΟ!

Bridges SL JrThe Science Behind Biosimilars: Entering a New Era of Biologic Therapy. . Arthritis Rheumatol. ***2018*** *Mar;70(3):334-344*

Δεν είναι απαραίτητα κακό …

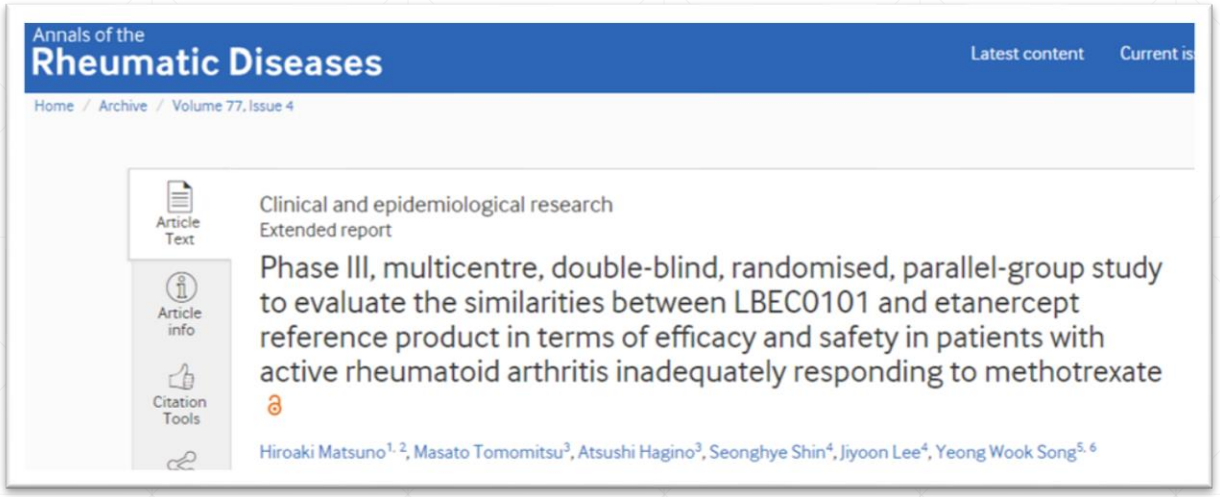
Η επίπτωση των AE (**treatment-emergent adverse events)** ήταν παρόμοια (55.2% vs 58.2%)

Η επίπτωση των **antidrug antibody** την εβδ 24 ήταν **χαμηλότερη** στο **SB4** vs ETN (0.7% vs 13.1%)

ΕΝΑ ΒΗΜΑ «ΠΑΡΑΠΕΡΑ» ?

*Emery P, Vencovský J, Sylwestrzak A, et al A phase III randomised, double-blind, parallel-group study comparing SB4 with etanercept reference product in patients with active rheumatoid arthritis despite methotrexate therapy Annals of the Rheumatic Diseases **2017**; 76:51-57.*

ΚΑΙ ΔΕΝ ΕΙΝΑΙ ΤΟ ΜΟΝΑΔΙΚΟ



AEs μέχρι την εβδ 54 ήταν παρόμοιες μεταξύ των 2 ομάδων (**LBEC0101** 92.0% vs **ETN-RP** 92.5%)

Λιγότεροι ασθενείς υπό LBEC0101 (**1.6%**) Vs ETN-RP group (**9.6%**) ανάπτυξαν **ADAs**

ΕΝΑ ΒΗΜΑ «ΠΑΡΑΠΕΡΑ» ?

*Matsuno H, Tomomitsu M, Hagino A, et al . Annals of the Rheumatic Diseases **2018** ;77:488-494..*

EGALITY …κα

CLINICAL TRIALS

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GP2015
ETAor
Μέτρια-σοβαρή Ψ

Βιο-παρομοιότητα

ΠΟΛΛΑΠΛΟ Switching δεν επηρεάζει την αποτελεσματικότητα – ασφάλεια - ανοσογονικότητα

Αποτελεσματικότητα

Ασφάλεια (!)

Ανοσογονικότητα

Interchangeability ?

Griffiths CEM et al. 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. ***2017*** *Apr;176(4):928-938*

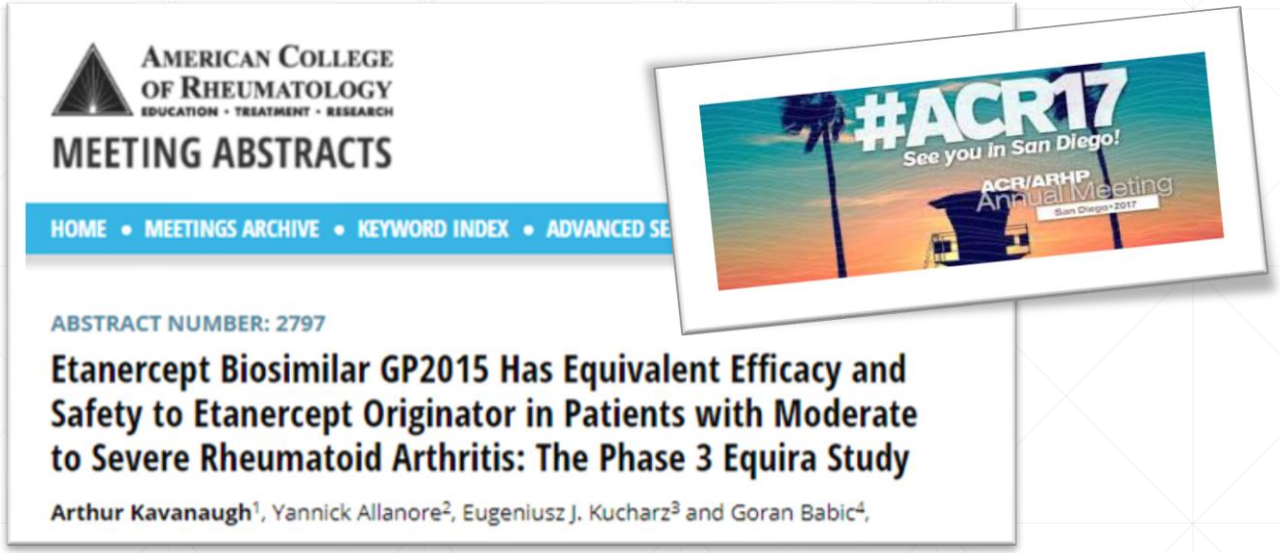
GP2015 στην PA

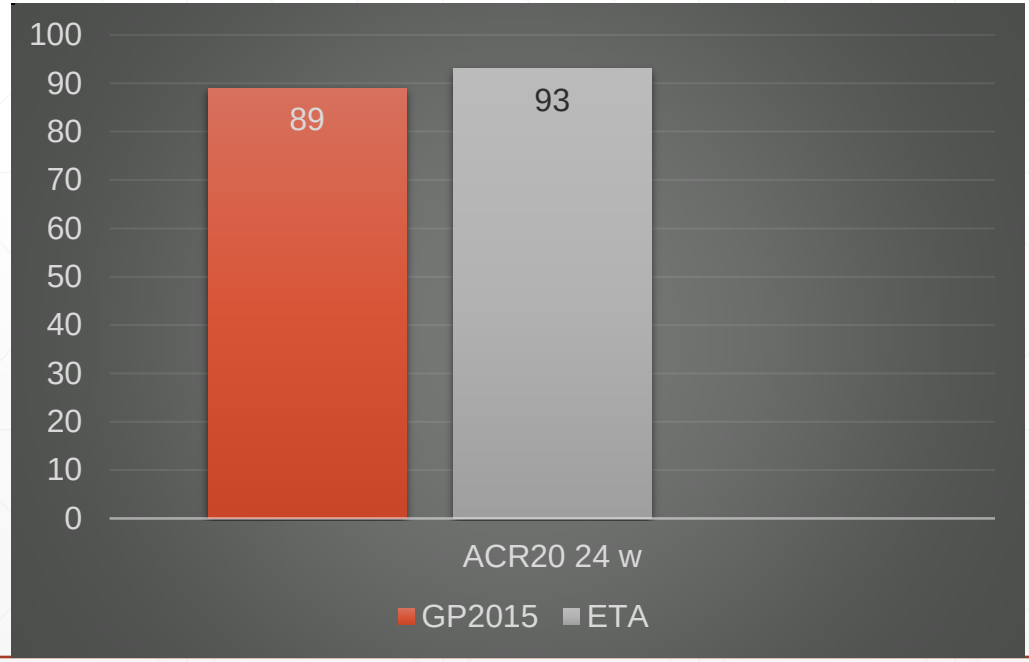
GP2015 (n=170) - ETN (n=156)

113 κέντρα / 16 χώρες

GP2015 **ισοδύναμο** με το ETN στην μείωση μέχρι την εβδ 24 στο **DAS28-CRP**

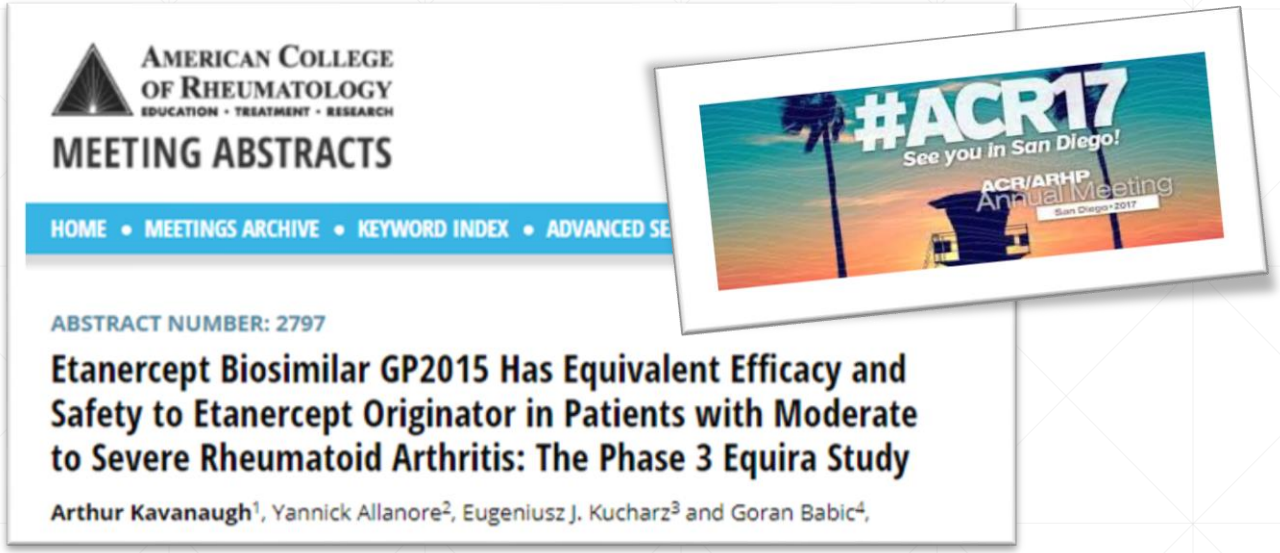
95% CI was within the pre-specified equivalence margin of -0.6; 0.6 (LS means difference between GP2015 vs ETN: -0.04, 95% CI: -0.24, 0.15).





Kavanaugh A, Allanore Y, Kucharz EJ, Babic G. Etanercept Biosimilar GP2015 Has Equivalent Efficacy and Safety to Etanercept Originator in Patients with Moderate to Severe Rheumatoid Arthritis: The Phase 3 Equira Study [abstract]. Arthritis Rheumatol. 2017; 69 (suppl 10)

GP2015 στην PA



- AE (treatment-emergent adverse events) => 43.5% (GP2015) vs 49.5% (ETA) ασθ
- **SAEs** : **0.5%** (GP2015) vs **3.2%** (ETA)/ *1 ασθ πέθανε στην ομάδα ETN*
- *Αντιδράσεις στο σημείο έγχυσης :* **7.0**% υπό GP2015 και **17.9%** υπό ETN

difference in formulation between the two products => ΕΝΑ ΒΗΜΑ «ΠΑΡΑΠΕΡΑ» ?

- Πολύ χαμηλοί τίτλοι ADAs περιοδικά ανιχνεύθηκαν – την εβδ **24 κανένας από τους ασθενείς δεν είχε** (very sensitive assay)

Kavanaugh A, Allanore Y, Kucharz EJ, Babic G. Etanercept Biosimilar GP2015 Has Equivalent Efficacy and Safety to Etanercept Originator in Patients with Moderate to Severe Rheumatoid Arthritis: The Phase 3 Equira Study [abstract]. Arthritis Rheumatol. 2017; 69 (suppl 10)

ΤΙ ΛΕΙΠΕΙ ?

ΑΛΛΑΓΕΣ , ΠΟΛΛΑΠΛΕΣ Ή ΟΧΙ

ΜΕΤΑΞΥ BIOSIMILARS

ΤΟΥ ΙΔΙΟΥ OR

ΠΡΕΠΕΙ ΝΑ ΕΚΤΙΜΗΘΕΙ ΣΤΑ REGISTRIES

ΤΟ ΤΟΠΙΟ ΑΛΛΑΖΕΙ !!!

Monoclonal Antibodies

Amgevita/Solymbic (8)	Amgen	adalimumab	Humira
Cyltezo (9)	Boehringer Ingelheim	adalimumab	Humira
Imraldi	Samsung Bioepis	adalimumab	Humira
Flixabi (10)	Samsung Bioepis	infliximab	Remicad
Inflectra (11)	Hospira	infliximab	Remicad
Remsima (11)	Celltrion	infliximab	Remicad
Rixathon/Riximyo (12)	Sandoz	rituximab	MabTher
Truxima/Blitzima/ Ritemvia/Rituzena (13)	Celltrion	rituximab	MabTher
Ontruzant (14)	Samsung Bioepis	trastuzumab	Hercepti

BIOSIMILARS APPROVED AS OF DECEMBER 2017

Drug Name	Approval Date	More Information
Zarxio (Filgrastim-sndz)	March 2015	Zarxio information Press Release: FDA approves first biosimilar
Inflectra (Infliximab-dyyb)	April 2016	Inflectra information Press Release: FDA approves Inflectra
Erelzi (Etanercept-szzs)	August 2016	Erelzi information Press Release: FDA approves Erelzi
Amjevita (Adalimumab - atta)	September 2016	Amjevita information Press Release: FDA approves Amjevita
Renflexis (Infliximab-abda)	May 2017	Renflexis information
Cyltezo (Adalimumab-adbm)	August 2017	Cyltezo information
Mvasi (Bevacizumab-awwb)	September 2017	Mvasi information Press Release: FDA approves first biosimilar for the treatment of cancer
Ogivri (trastuzumab-dkst)	December 2017	Ogivri information Press Release: FDA approves first biosimilar for the treatment of certain breast and stomach cancers
Ixifi (infliximab-qbtx)	December 2017	Ixifi information

Το τοπίο αλλάζει ?
Ονοματολογία

biosimilars of infliximab [Remicade]
infliximab-dyyb (Inflectra)
infliximab-abda (Renflexis)
infliximab-qbtx (Ixifi)

biosimilar of etanercept [Enbrel]
etanercept-szzs (Erelzi)

biosimilars of adalimumab [Humira]
adalimumab-adbm (Cyltezo)
adalimumab-atto (Amjevita)

Μέχρι τον 12/2017
ο **FDA** έχει εγκρίνει 9 biosimilars

Προστασία από interchangeability

Member States of the EU
and the European Economic Area =>
brand names for postmarketing surveillance

Το τοπίο αλλάζει !

- Τα biosimilars είναι **παρόμοια** των φαρμάκων αναφοράς
- Είναι ισοδύναμα σε θέματα **αποτελεσματικότητας ή ασφάλειας (& ανοσογονικότητας)**
- **Switching => δεν επηρεάζει** (Interchangeability ?)
- Αποτελούν μια ευκαιρία (αγορά) για τη Φ-βιομηχανία

  αλλά και για τα συστήματα υγείας

  Και τους ασθενείς

ΠΡΟΣΒΑΣΗ

difference in formulation between the two products ?

ΕΝΑ ΒΗΜΑ «ΠΑΡΑΠΕΡΑ» ?

Και όχι μονο σε θέματα ασφάλειας …

Ενα βημα «παραπερα» ?

biobetters


Open Access Review

ESMO Open Cancer Horizons

CrossMark

Biosimilars: a position paper of the European Society for Medical Oncology, with particular reference to oncology prescribers

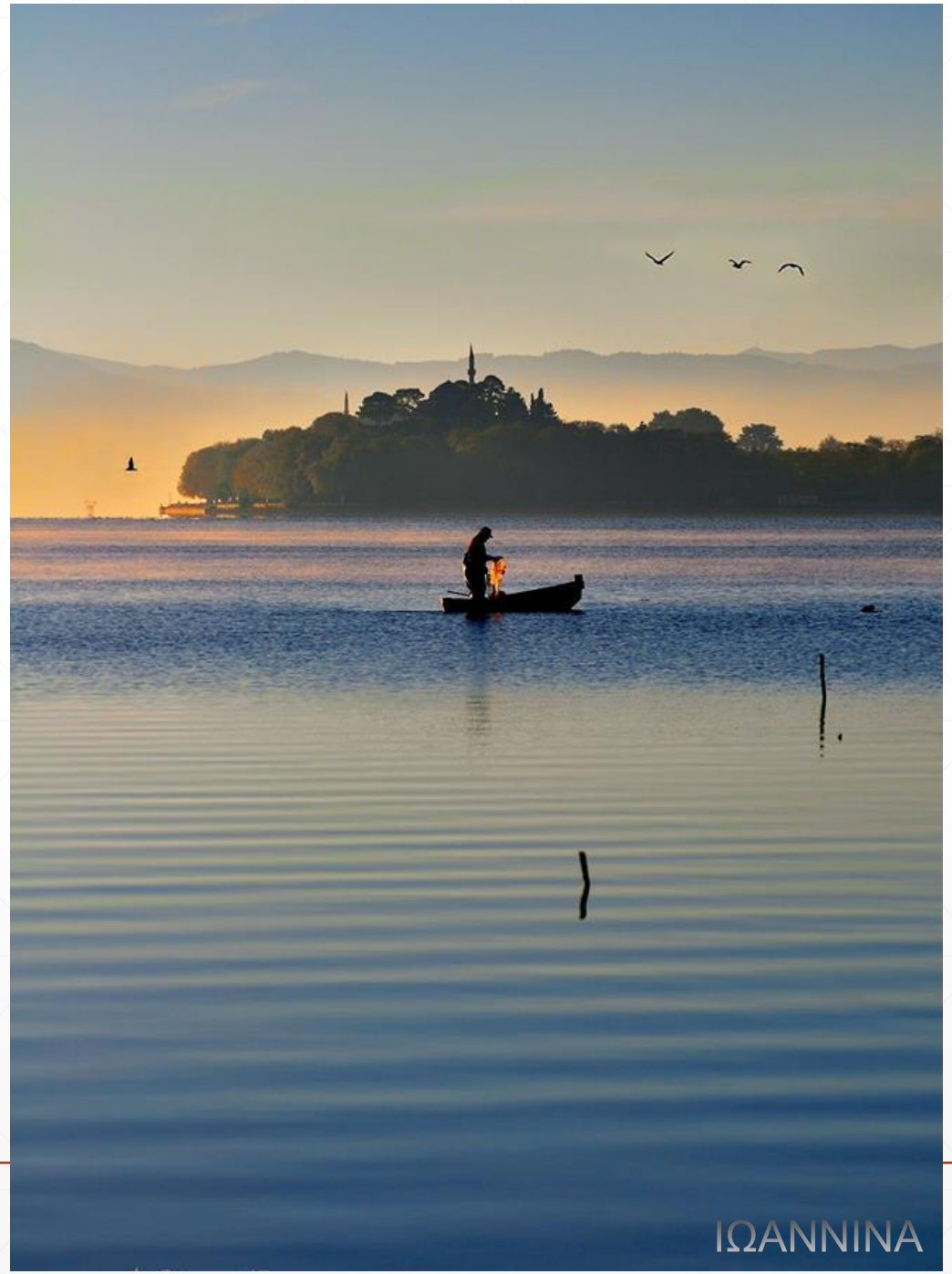
creation
of **improved versions**
of existing biologics (biobetters)

Are Biosimilars Actually "Bio-Betters"?

- "Bio-betters" is a term applied to biosimilar copies of originator biologics. In observational and clinical trials, these "bio-betters" would appear to have greater efficacy than the originator biologics
- The differences between bio-originators and so-called biosimilar "bio-betters" typically do not reach significance
- Small differences in, for example, ACR20 response, could be an artifact of trial design. In the head-to-head trials between biosimilars and bio-originators there isn't a placebo arm. Both cohorts know they are receiving active treatment. Expectation of benefit may explain slight differences between bio-originators and so-called "bio-betters"
- The important consideration is that equivalency is demonstrated

Mysler E, et al. *Rheumatol Int*. 2016;36:613-625.

Το τοπίο αλλάζει !



ΕΥΧΑΡΙΣΤΩ ΘΕΡΜΑ
ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ