«Πώς η αναστολή της IL-17 με το ixekizumab μεταφράζεται σε κλινικά σημαντικό όφελος για τον ασθενή με ψωρίαση».

Μαρίνα Παπουτσάκη MD, PhD
Δερματολόγος-Αφροδισιολόγος
Διευθύντρια ΕΣΥ
Α’ Πανεπιστημιακή Κλινική Αφροδισίων και Δερματικών Νόσων Ιατρικής Σχολής Ε.Κ.Π.Α
Νοσοκομείο Αφροδισίων και Δερματικών Παθήσεων, «Ανδρέας Συγγρός»

Σύγκρουση συμφερόντων

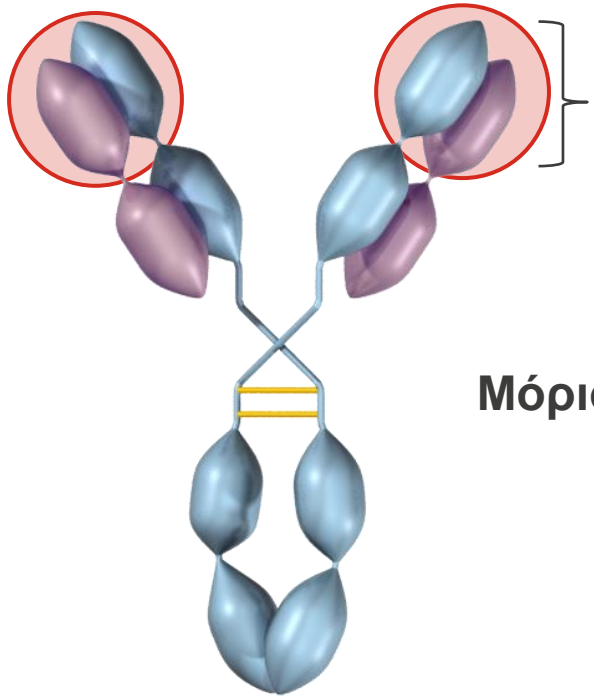
- **Έχω λάβει αμοιβή για ομιλίες και συμβουλευτικές δραστηριότητες από :**
  Janssen, LEO, MSD, Genesis pharma, Pfizer, Novartis, Abbvie, UCB, Lilly, Menarini

- **Ερευνήτρια σε κλινικές μελέτες για:**
  Janssen, Pfizer, Novartis, Abbvie, LEO

- **Έχω λάβει αμοιβή για την συγκεκριμένη ομιλία**

Βασικά Χαρακτηριστικά του Ixekizumab

- Το ixekizumab είναι ένα μονοκλωνικό αντίσωμα IgG4 που στοχεύει την IL-17A με υψηλή συγγένεια πρόσδεσης[1]
- Η αναστολή της IL-17A μειώνει το ρυθμό πολλαπλασιαμού των κερατινοκυττάρων και εμποδίζει την έκφραση φλεγμονωδών κυτοκινών.



Μόριο Ixekizumab

Χρόνος ημίσειας ζωής = 13 ημέρες[2]
Συγγένεια πρόσδεσης = 1,8 pM (<3 pM)[2,3,α]

Ελαφρά αλυσίδα
Βαριά αλυσίδα

Προσαρμογή της εικόνας από The Immune System. 3rd ed. Garland Science 2009.

IgG=Immunoglobulin G; IL=Interleukin; IXE Q2W=80 mg of Ixekizumab Every 2 Weeks; IXE Q4W=80 mg of Ixekizumab Every 4 Weeks; PsO=Psoriasis.

1. Liu L, et al. *J Inflamm Res.* 2016:9:39-50. 2. Krueger JG, et al. *J Allergy Clin Immunol*. 2012;130:145-154. 3. Taltz USPI. 2021. 4. Taltz SmPC. 2021.

Ιξεκιζουμάμπη - Θεραπευτικές ενδείξεις

Ψωρίαση κατά πλάκας

- ✓ Θεραπεία της **μέτριας έως σοβαρής ψωρίασης** κατά πλάκας σε **ενήλικες**, οι οποίοι είναι υποψήφιοι για συστηματική θεραπεία
- ✓ Θεραπεία της μέτριας έως σοβαρής ψωρίασης κατά πλάκας **σε παιδιά από την ηλικία των 6 ετών και άνω** και με σωματικό βάρος τουλάχιστον 25 kg και σε εφήβους που είναι υποψήφιοι για συστηματική θεραπεία

Ψωριασική Αρθρίτιδα

- ✓ Θεραπεία της ενεργού ψωριασικής αρθρίτιδας, ως **μονοθεραπεία ή σε συνδυασμό με μεθοτρεξάτη**, **σε ενήλικες** ασθενείς που έχουν εμφανίσει ανεπαρκή ανταπόκριση ή δυσανεξία σε μία ή περισσότερες θεραπείες με τροποποιητικό της νόσου αντιρρευματικό φάρμακο (DMARD)

Αξονική σπονδυλαρθρίτιδα

- ✓ ***Αγκυλοποιητική σπονδυλίτιδα*** *(ακτινογραφικά επιβεβαιωμένη αξονική σπονδυλαρθρίτιδα)* Θεραπεία ενηλίκων ασθενών με ενεργό αγκυλοποιητική σπονδυλίτιδα που έχουν εμφανίσει ανεπαρκή ανταπόκριση σε συμβατική θεραπεία.
- ✓ *Μη ακτινογραφικά επιβεβαιωμένη αξονική σπονδυλαρθρίτιδα* Η ιξεκιζουμάμη ενδείκνυται για τη θεραπεία ενηλίκων ασθενών με ενεργό, μη ακτινογραφικά επιβεβαιωμένη, αξονική σπονδυλαρθρίτιδα με αντικειμενικά σημεία φλεγμονής, όπως υποδεικνύεται από αυξημένα επίπεδα C-αντιδρώσας πρωτεΐνης (CRP) ή/και από ευρήματα σε τομογραφία μαγνητικού συντονισμού (MRI), οι οποίοι έχουν εμφανίσει ανεπαρκή ανταπόκριση σε μη στεροειδή αντιφλεγμονώδη φάρμακα (ΜΣΑΦ)

Πώς προσεγγίζω θεραπευτικά τον ασθενή με Ψωρίαση σήμερα;

- Η Ψωρίαση είναι ένα χρόνιο, συστηματικό νόσημα με σημαντική επιβάρυνση της υγείας αλλά και της Ποιότητας Ζωής των ασθενών
- Υψηλό ποσοστό ασθενών με Ψωρίαση συνεχίζουν να μην είναι ικανοποιημένοι από τη θεραπεία τους.

IXE

H2H=Head-to-Head; IL=Interleukin; IXE=Ixekizumab; PASI 100=100% Improvement in Psoriasis Area and Severity Index; PsA=Psoriatic Arthritis. References listed in slide notes.

Συλλογή δεδομένων από όλες τις πηγές της βιβλιογραφίας.

RCTs + **NMA** + **RWE**

Πώς διαφέρουν τα δεδομένα από τις τυχαιοποιημένες κλινικές μελέτες και τα δεδομένα από τον πραγματικό κόσμο και ποια η σημασία τους;

	Randomized Controlled Trial	vs.	Real-World Evidence
Purpose	Είναι αποτελεσματικό;[1]		Θα είναι αποτελεσματικό στην πράξη για τον ασθενή μου;[1]
Setting	Ελεγχόμενες συνθήκες[2]		Αντανακλά την πραγματική κλινική πρακτική[3]
Population	Πληθυσμός αποκλειστικά σύμφωνος μ την ένδειξη του φαρμάκου		Χρήση σε ετερογενείς πληθυσμούς[4] • Συννοσηρότητες[5] • Συγχορήγηση με άλλα φάρμακα[5]
Comparator	Προκαθορισμένος από την αρχή[1]		Επιτρέπουν σύγκριση με πολλαπλά φάρμακα[3,5]

Randomized Controlled Trials[4]

Real-World Evidence[4]

Gap

Need

1. Nazha B, et al. *Future Oncol*. 2021;17(8):965-977. 2. Monti S, et al. *Rheumatology (Oxford)*. 2018;57(57 Suppl 7):vii54-vii58. 3. Blonde L, et al. *Adv Ther*. 2018;35(11):1763-1774.
4. Katkade VB, et al. *J Multidiscip Healthc*. 2018;11:295-304. 5. Naidoo P, et al. *Wien Klin Wochenschr*. 2021:1-7.

Συλλογή δεδομένων από όλες τις πηγές της βιβλιογραφίας.

RCTs + +

Εγκριτικό Πρόγραμμα Κλινικών Μελετών: UNCOVER Trials

	UNCOVER-1[1]	UNCOVER-2[1,2]	UNCOVER-3[1-3]	UNCOVER-A[3,4]	UNCOVER-J[3,5]
Objective	PBO-controlled efficacy and safety study	PBO- and active-controlled (ETN) efficacy and safety study	PBO- and active-controlled (ETN) efficacy and safety study	Effect of drug delivery device (autoinjector) on PK	Efficacy and safety of IXE in Japanese patients
N	1296	1224	1346	204	91
Population	♦ **Chronic moderate-to-severe plaque psoriasis** ♦ BSA ≥10%; PASI ≥12; sPGA ≥3 ♦ Candidate for phototherapy and/or systemic therapy				♦ **Moderate-to-severe plaque psoriasis[a], erythrodermic psoriasis[b], or generalized pustular psoriasis[c]** ♦ Candidates for phototherapy and/or systemic therapy
Primary endpoint	sPGA (0,1) and PASI 75 response rates at 12 weeks			PK data	PASI 75 at 12 weeks
Study duration	♦ Induction period: Weeks 0-12 ♦ RWP: Weeks 12-60 ♦ LTE: Weeks 60-264	♦ Induction period: Weeks 0-12 ♦ RWP: Weeks 12-60 ♦ LTE: Weeks 60-264	♦ Induction period: Weeks 0-12 ♦ OLE: Weeks 12-264	♦ 52 weeks, open label	192 weeks, open label
Geography	Global			USA, Puerto Rico	Japan

[a]Patients were eligible if they had a PASI ≥12; sPGA ≥3; and BSA ≥10%. [b]Patients were eligible if they had BSA ≥80% (with inflammatory erythema). [c]Patients were eligible if they met Japanese Ministry of Health, Labour and Welfare (MHLW) criteria. Note: Other IXE trials in adult PsO include I1F-MC-RHAJ.[6] BSA=Body Surface Area; ETN=Etanercept; LTE=Long-Term Extension; OLE=Open-Label Extension; PASI=Psoriasis Area and Severity Index; PBO=Placebo; RWP=Randomized Withdrawal Period; sPGA=Static Physician's Global Assessment.

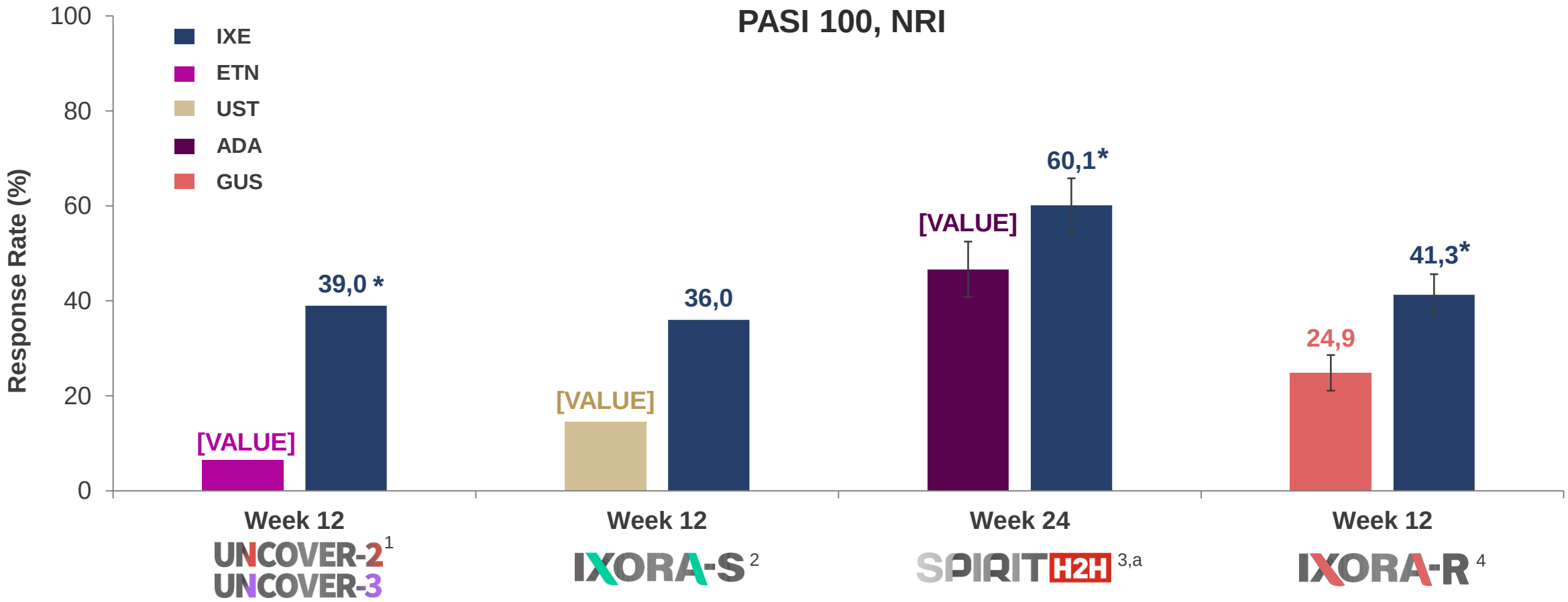
1. Gordon KB, et al. *N Engl J Med*. 2016;375:345-356. 2. Griffiths CE, et al. *Lancet*. 2015;386:541-551. 3. Gottlieb AB, et al. Poster presented at: *Psoriasis: From Gene to Clinic 2017*. Poster P014. 4. Callis Duffin K, et al. *J Eur Acad Dermatol Venereol*. 2017;31:107-113. 5. Saeki H, et al. *J Eur Acad Dermatol Venereol*. 2015;29:1148-1155. 6. Armstrong A, et al. *Dermatol Ther (Heidelb)*. 2020;10:133-150.

Πρόγραμμα Κλινικών Δοκιμών: IXORA Trials

	IXORA-P [1]	IXORA-S [2]	IXORA-Q [3]	IXORA-Z [4,5]	IXORA-R [6,7]
Objective	Efficacy of IXE continuous Q2W dosing	Efficacy and safety of IXE vs. UST	Genital psoriasis, PBO-controlled efficacy and safety	Efficacy and safety of IXE vs. FAEs and MTX	Efficacy and safety of IXE vs. GUS
N	1467	302	149	162	1027
Population	♦ **Chronic moderate-to-severe plaque psoriasis** ♦ BSA ≥10%; PASI ≥12; sPGA ≥3	♦ **Chronic plaque psoriasis** ♦ PASI ≥10 ♦ Failed/intolerant of ≥1 systemic therapy	♦ **Chronic plaque psoriasis** ♦ sPGA ≥3; BSA ≥1%; sPGA of genitalia ≥3 ♦ Failed/intolerant of ≥1 topical therapy for genital psoriasis	♦ **Chronic moderate-to-severe plaque psoriasis** ♦ PASI >10 and DLQI >10 **OR** BSA >10% and DLQI >10	♦ **Chronic moderate-to-severe plaque psoriasis** ♦ BSA ≥10%; PASI ≥12; sPGA ≥3
Primary endpoint	sPGA (0,1) and PASI 75 at Week 52	PASI 90 at 12 weeks	sPGA of genitalia (0,1) at 12 weeks	PASI 75 at 24 weeks	PASI 100 at 12 weeks
Study duration	52 weeks			60 weeks	24 weeks
Geography	Global			Germany	US and Canada

1. Langley RG, et al. *Br J Dermatol.* 2018;178:1315-1323. 2. Reich K, et al. *Br J Dermatol.* 2017;177:1014-1023. 3. Ryan C, at al. *Br J Dermatol.* 2018;179:844-852. 4. Reich K, Presented at*: EADV 2017*, Geneva, Switzerland. Poster P1938. 5. https://clinicaltrials.gov/ct2/show/NCT02634801 (Accessed March 2020). 6. Blauvelt A, et al. *Br J Dermatol.* 2020;182:1348-1358. 7. https://clinicaltrials.gov/ct2/show/NCT03573323 (Accessed March 2020).

Το Ixekizumab απέδειξε στατιστικώς σημαντική ανωτερότητα στην ταχύτητα έναρξης δράσης αλλά και στην επίτευξη του απόλυτα **καθαρού** δέρματος σε 5 Head-to-Head Μελέτες.



*p≤.001 vs. comparator. [a]SPIRIT H2H study participants received label doses of assigned treatments. All patients randomized to ixekizumab (IXE) received a 160 mg starting dose. Patients then received 80 mg Q4W from Week 4 onwards unless meeting criteria for moderate-to-severe PsO, in which case they received 80 mg Q2W from Weeks 2-12, followed by Q4W. Patients randomized to adalimumab (ADA) received a 40 mg starting dose followed by 40 mg Q2W starting at Week 2, or if meeting criteria for moderate-to-severe PsO an 80 mg starting dose followed by 40 mg Q2W starting at Week 1. Note: Error bars represent 95% confidence intervals. ETN=50 mg Etanercept Twice Weekly; GUS=100 mg Guselkumab at Weeks 0, 4, then Q8W thereafter; IXE=160 mg starting dose, then IXE Q2W up to and including Week 12, followed by IXE Q4W thereafter (UNCOVER-2 and -3, IXORA-S and -R studies); PASI=Psoriasis Area and Severity Index; UST=45 mg UST for patients ≤100 kg and 90 mg UST for patients >100 kg at Weeks 0 and 4, and every 12 weeks thereafter per label.

1. Gordon KB, et al. *N Engl J Med*. 2016;375:345-356 . 2. Reich K, et al. *Br J Dermatol*. 2017;177:1014-1023. 3. Mease PJ, et al. *Ann Rheum Dis*. 2020;79:123-131. 4. Blauvelt A, et al. *Br J Dermatol*. 2020;182:1348-1358.

AAD 2022

Simultaneous Nail and Skin Clearance in Five Ixekizumab Head-to-Head Trials for Moderate-to-Severe Psoriasis and Psoriatic Arthritis

Boni E. Elewski,[1] Andrew Blauvelt,[2] Gaia Gallo,[3] Eric Wolf,[3] Missy McKean-Matthews,[4] Russel Burge,[3] Joseph F. Merola,[5] Alice B. Gottlieb,[6] Lyn C. Guenther[7,8]

[1]University of Alabama at Birmingham, Birmingham, USA; [2]Oregon Medical Research Center, Portland, USA; [3]Eli Lilly and Company, Indianapolis, USA; [4]Syneos Health, Raleigh, USA; [5]Harvard Medical School, Brigham and Women's Hospital, Boston, USA; [6]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, USA; [7]Guenther Dermatology Research Center, London, Canada; [8]Western University, London, Canada

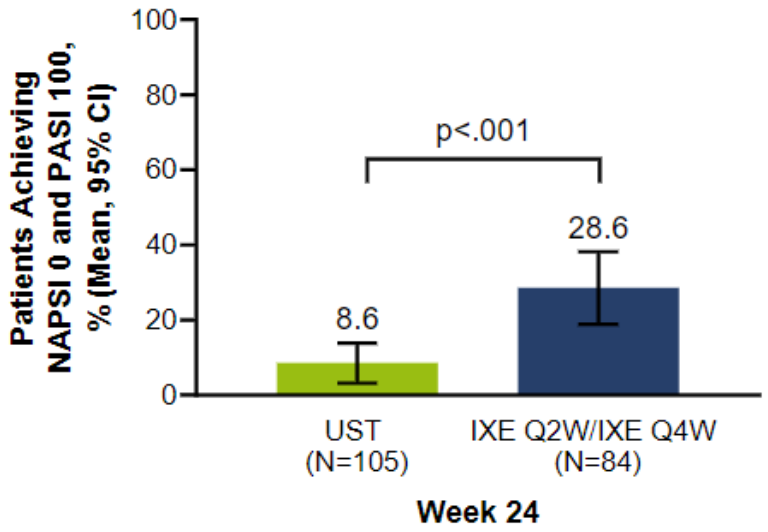
DISCLOSURES: B. E. Elewski has received honoraria, grant, and/or research support from: AbbVie, AnaptysBio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Incyte Corporation, LEO Pharma, Menlo Therapeutics, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Sun Pharma, UCB Pharma, Valeant Pharmaceuticals, and Vanda Pharmaceuticals; **A. Blauvelt** has served as a scientific advisor and/or clinical study investigator for: AbbVie, Abcentra, Aligos Therapeutics, Almirall, Amgen, Arcutis, Arena Pharmaceuticals, ASLAN Pharmaceuticals, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant Sciences, EcoR1 Capital, Eli Lilly and Company, Evommune, Forté Pharma, Galderma, Incyte Corporation, Janssen, Landos Biopharma, LEO Pharma, Novartis, Pfizer, RAPT Therapeutics, Regeneron, Sanofi Genzyme, Sun Pharma, UCB Pharma, and Vibliome Therapeutics; **G. Gallo**, **E. Wolf**, and **R. Burge** are employees and shareholders of: Eli Lilly and Company; **M. McKean-Matthews** is an employee of: Syneos Health; **J. F. Merola** is a consultant and/or investigator for: AbbVie, Arena Pharmaceuticals, Avotres, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, EMD Serono, Janssen, LEO Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB Pharma; **A. B. Gottlieb** has received honoraria as an advisory board member and/or consultant for: AnaptsysBio, Avotres, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sun Pharma, UCB Pharma, and XBiotech; and has received research and/or educational grants from: Boehringer Ingelheim, Incyte Corporation, Janssen, Novartis, Sun Pharma, UCB Pharma, and XBiotech; **L. C. Guenther** is on the speakers bureau of, is a consultant for, and/or has received grant and/or research support from: AbbVie, Amgen, Bausch Health, Celgene, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Novartis, Pfizer, and Sun Pharma; and has received grant and/or research support from: Boehringer Ingelheim, Bristol Myers Squibb, Merck Frosst, and UCB Pharma

This study was sponsored by Eli Lilly and Company. Medical writing assistance was provided by Linda Donnini, PhD, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company

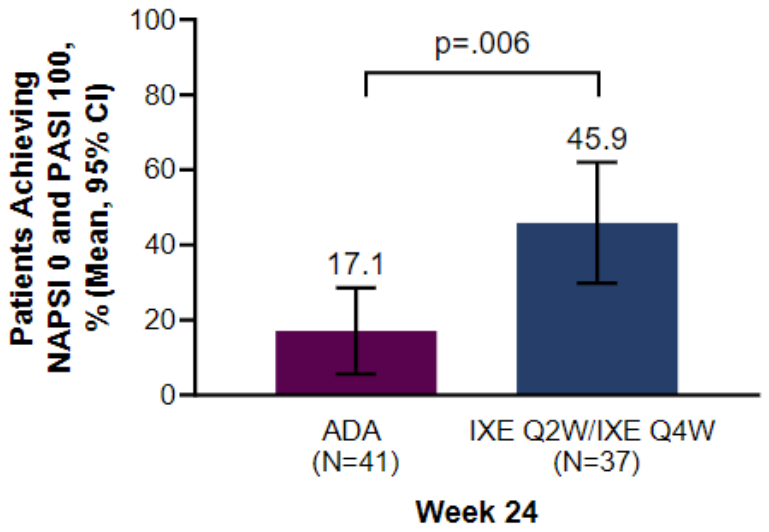
RESULTS

At Week 24, IXE Achieved Significantly Greater Simultaneous Nail and Skin Clearance vs. UST and ADA and Numerically Greater Clearance vs. GUS

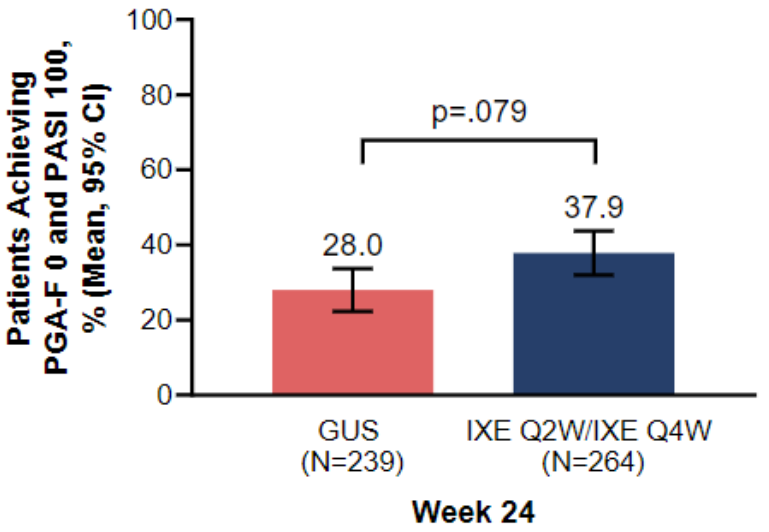
IXORA-S



SPIRIT-H2H



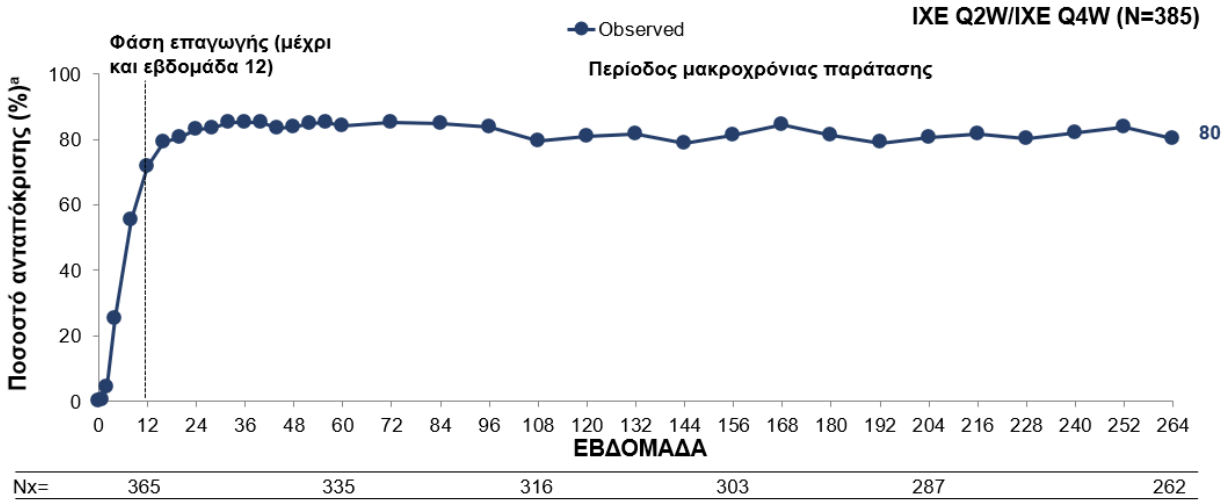
IXORA-R



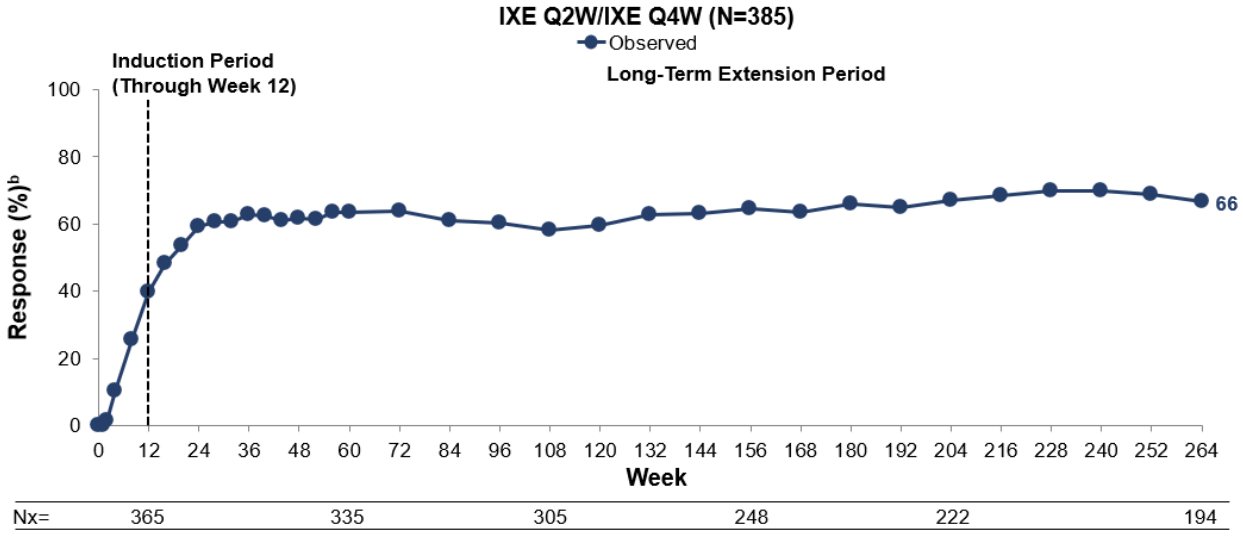
ADA=adalimumab; CI=confidence interval; GUS=guselkumab; IXE=ixekizumab; IXE Q2W/IXE Q4W=80 mg IXE every 2 weeks to Week 12 then 80 mg IXE every 4 weeks thereafter; NAPSI=Nail Psoriasis Severity Index; PASI=Psoriasis Area and Severity Index; PGA-F=Physician's Global Assessment of Fingernail Psoriasis; UST=ustekinumab

Επίτευξη PASI90,100 ανά Εβδομάδα - Observed Φάση επαγωγής και μακροχρόνια περίοδος παράτασης, ITT Population (UNCOVER-3)

PASI90



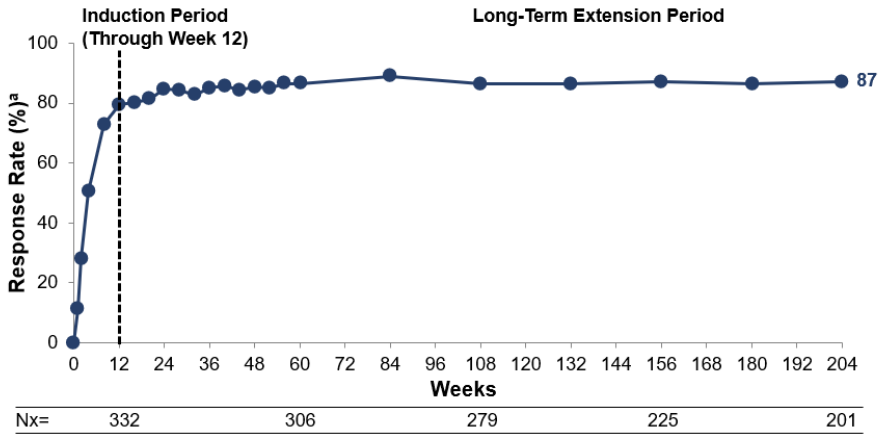
PASI100



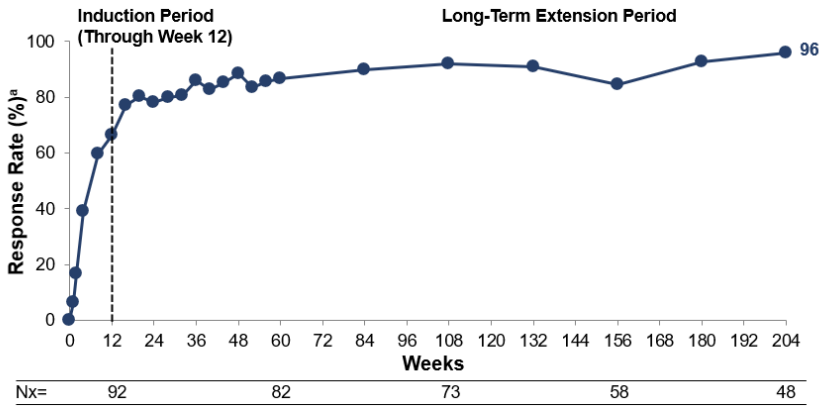
[a]Patients were allowed to increase dose to IXE Q2W after Week 60. [b]For observed, percentages based on the number of observed patients with non-missing data (Nx). The MI and mNRI results are based on the average response values across multiple imputed datasets from the corresponding ITT population. 1. Long-term efficacy and safety ofixekizumab: A 5-year analysis of theUNCOVER-3 randomized controlled trialAndrew Blauvelt,et al,JAAD 2021.

Διατήρηση αποτελεσμάτων σε βάθος 5ετίας στις δύσκολες ειδικές εντοπίσεις.

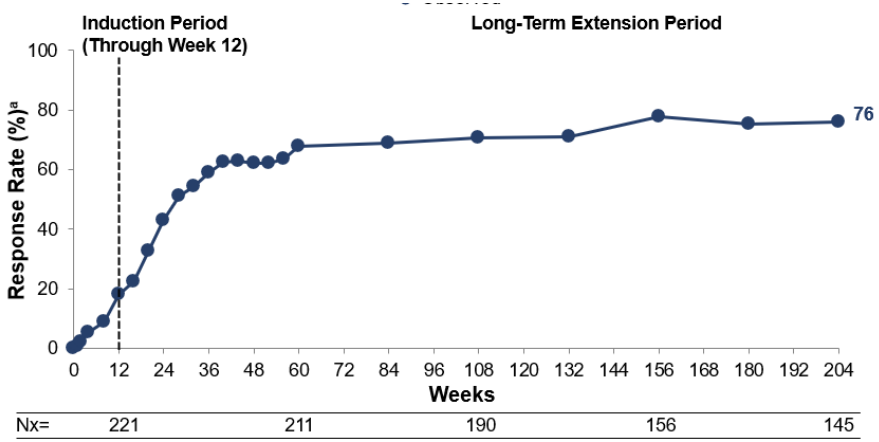
PSSI



PPASI



NAPSI



[a]For observed, percentages based on the number of observed patients with non-missing data (Nx). The MI and mNRI results are based on the average response values across multiple imputed datasets from the corresponding ITT population.
MI=Multiple Imputation; mNRI=Modified Nonresponder Imputation; PSSI=Psoriasis Scalp Severity Index.
Lebwohl MG, et al. *J Eur Acad Dermatol Venereol*. 2019; doi: 10.1111/jdv.15921 (Ahead of print).

Overall and Common Adverse Events

	Induction Period (UNCOVER-1, -2, and -3) Weeks 0 to 12									Total UNCOVER IXE-Treated Population Weeks 0 to 60		
	Placebo (N=791, PY=180.0)			IXE Q4W (N=1161, PY=265.9)			IXE Q2W (N=1167, PY=268.6)			All IXE Exposure (N=3736, PY=3458.4)		
	n	%	IR per 100 PY	n	%	IR per 100 PY	n	%	IR per 100 PY	n	%	IR per 100 PY
Any Adverse Event	370	46.8	205.5	683	58.8	256.8	681	58.4	253.6	3021	80.9	87.4
Serious adverse event	12	1.5	6.7	26	2.2	9.8	20	1.7	7.4	250	6.7	7.2
D/C due to AE	9	1.1	5.0	24	2.1	9.0	25	2.1	9.3	165	4.4	4.8
Death	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	3	0.1	0.1
Common Adverse Events[a]												
Nasopharyngitis	69	8.7	38.3	104	9.0	39.1	111	9.5	41.3	733	19.6	21.2
Upper respiratory tract infection	28	3.5	15.6	45	3.9	16.9	51	4.4	19.0	372	10.0	10.8
Injection site reaction	9	1.1	5.0	89	7.7	33.5	117	10.0	43.6	387	10.4	11.2
Arthralgia	17	2.1	9.4	22	1.9	8.3	29	2.5	10.8	196	5.2	5.7
Headache	23	2.9	12.8	50	4.3	18.8	51	4.4	19.0	243	6.5	7.0

[a] Common treatment-emergent adverse events were defined as those that had an incidence rate of at least 5% of patients for the All Ixekizumab Exposure group and were numerically higher in ixekizumab-treated patients vs. patients on placebo during the induction periods.

Click to edit Master text styles

IR=incidence rate per 100 patient-years; IXE=ixekizumab; IXEQ2W=ixekizumab every 2 weeks after 160-mg starting dose; IXEQ4W= ixekizumab every 4 weeks after 160-mg starting dose; PY=patient-years.

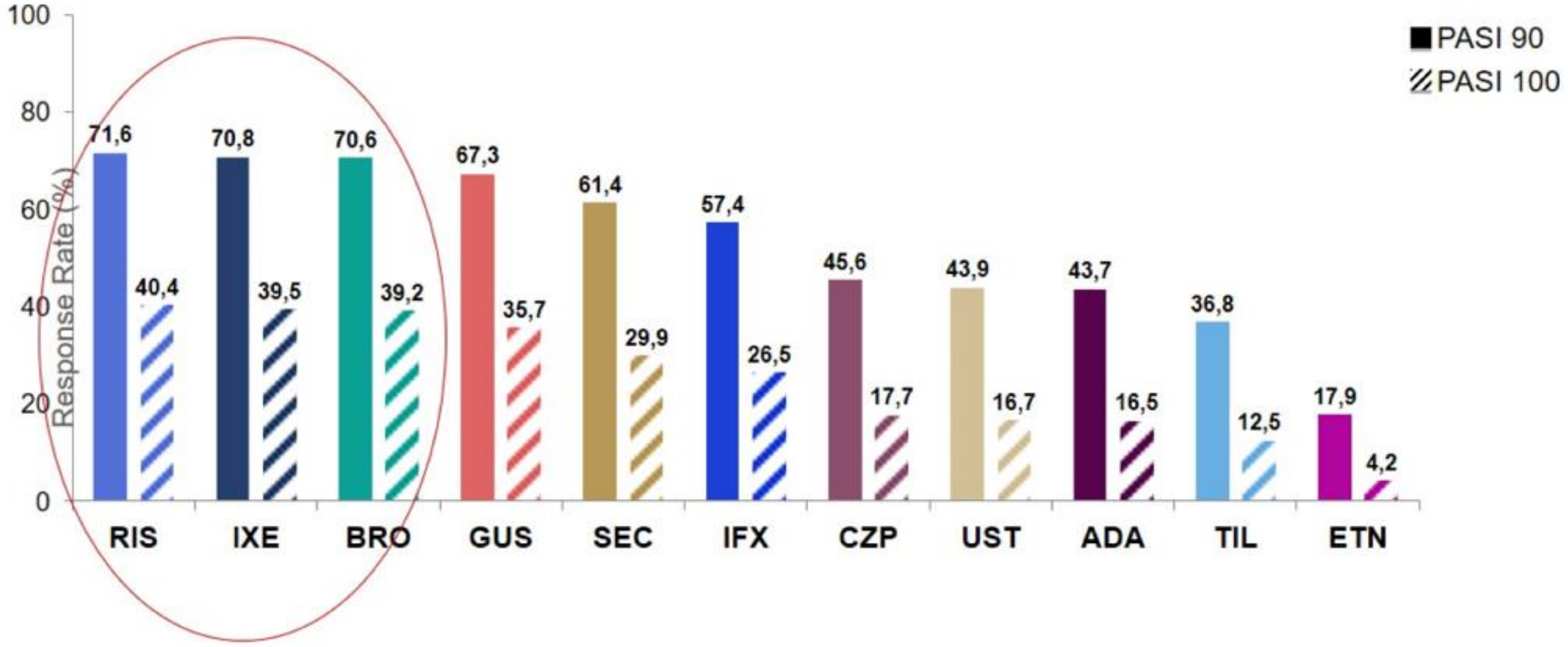
Gordon et al. *New Engl J Med*. 2016; 375:345-356.

Συλλογή δεδομένων από όλες τις πηγές της βιβλιογραφίας.

RCTs + **NMA** +

Ανταπόκριση στις συστηματικές θεραπείες στη μέτρια έως σοβαρή ψωρίαση

Network Meta-analysis[a] (Armstrong AW, et al): PASI 90/100 Responses at Week 10-16



Armstrong AW, et JAMA Dermatol.2020;156(3):258-269

Στατιστικώς σημαντική υπεροχή **ixe,ris,bro** στο PASI 100 και **ris,ixe,bro** στο PASI 90 στις 52 ΕΒδομάδες θεραπείας.

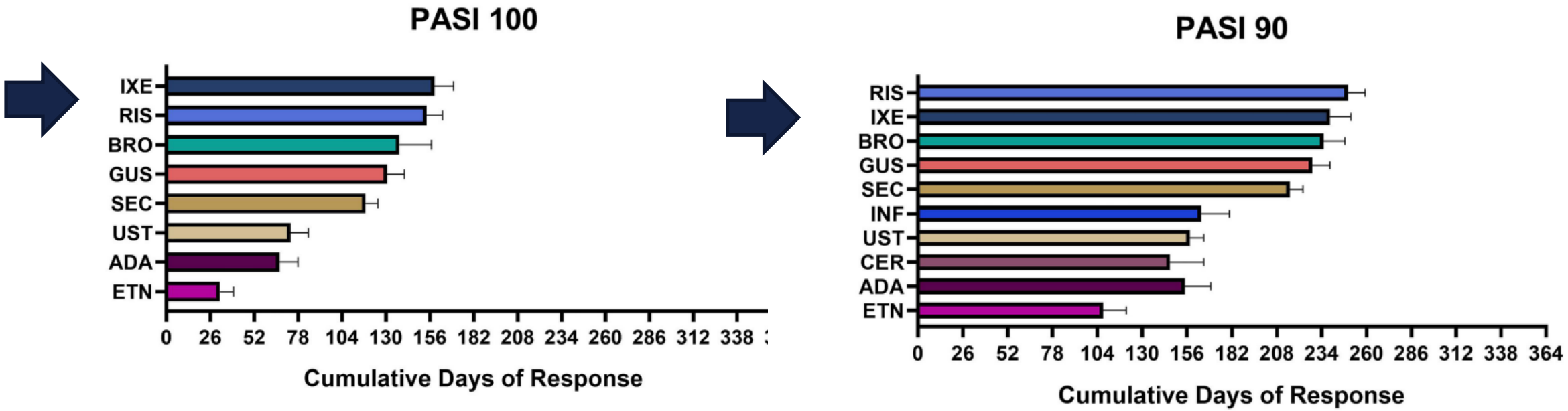
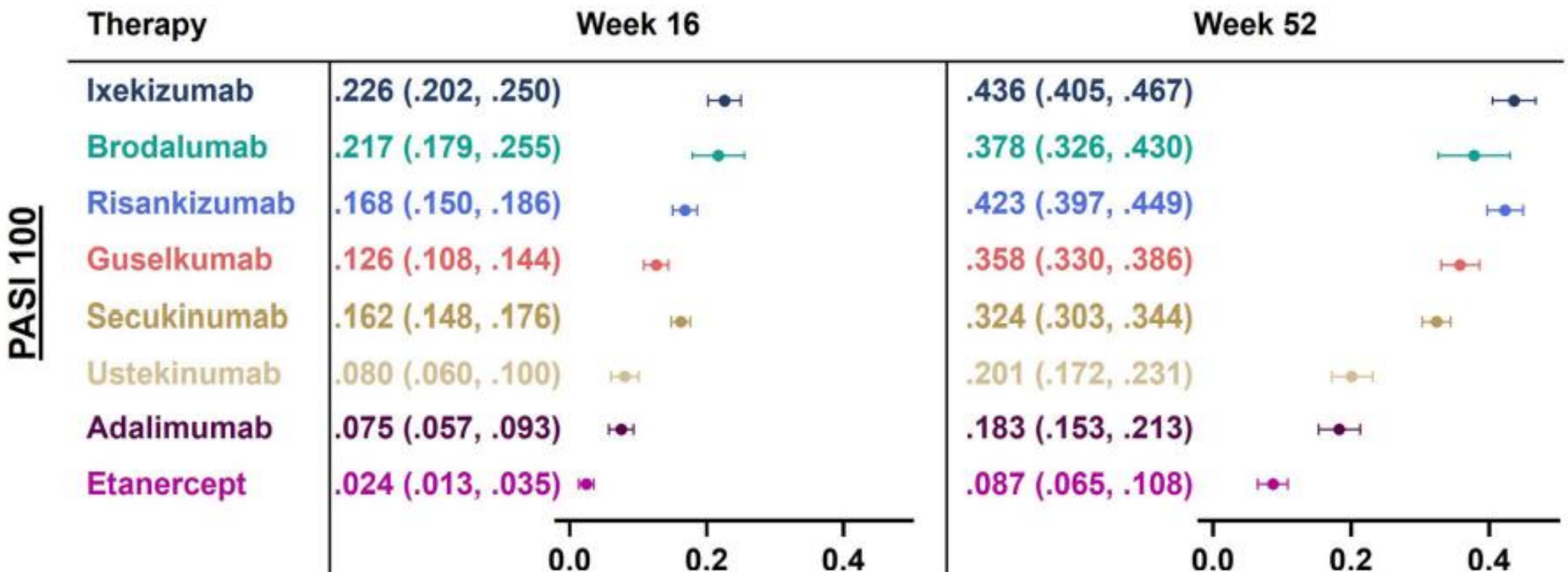


Fig. 2 Cumulative days of response at PASI 100 and PASI 90 over 52 weeks. Data displayed as 100% maximum possible area under the curve and 95% credible interval. ADA adalimumab, BRO brodalumab, CER certolizumab, ETN etanercept, GUS guselkumab, INF infliximab, IXE ixekizumab, PASI 100/90, 100% or C 90% improvement in Psoriasis Area and Severity Index, RIS risankizumab, SEC secukinumab, UST ustekinumab

Cumulative Clinical Benefits of Biologics in the Treatment of Patients with Moderate-to-Severe Psoriasis over 1 Year: a Network Meta-Analysis
Andrew Blauvelt et al, Dermatol Ther (Heidelb),February 2022

Αθροιστικό όφελος

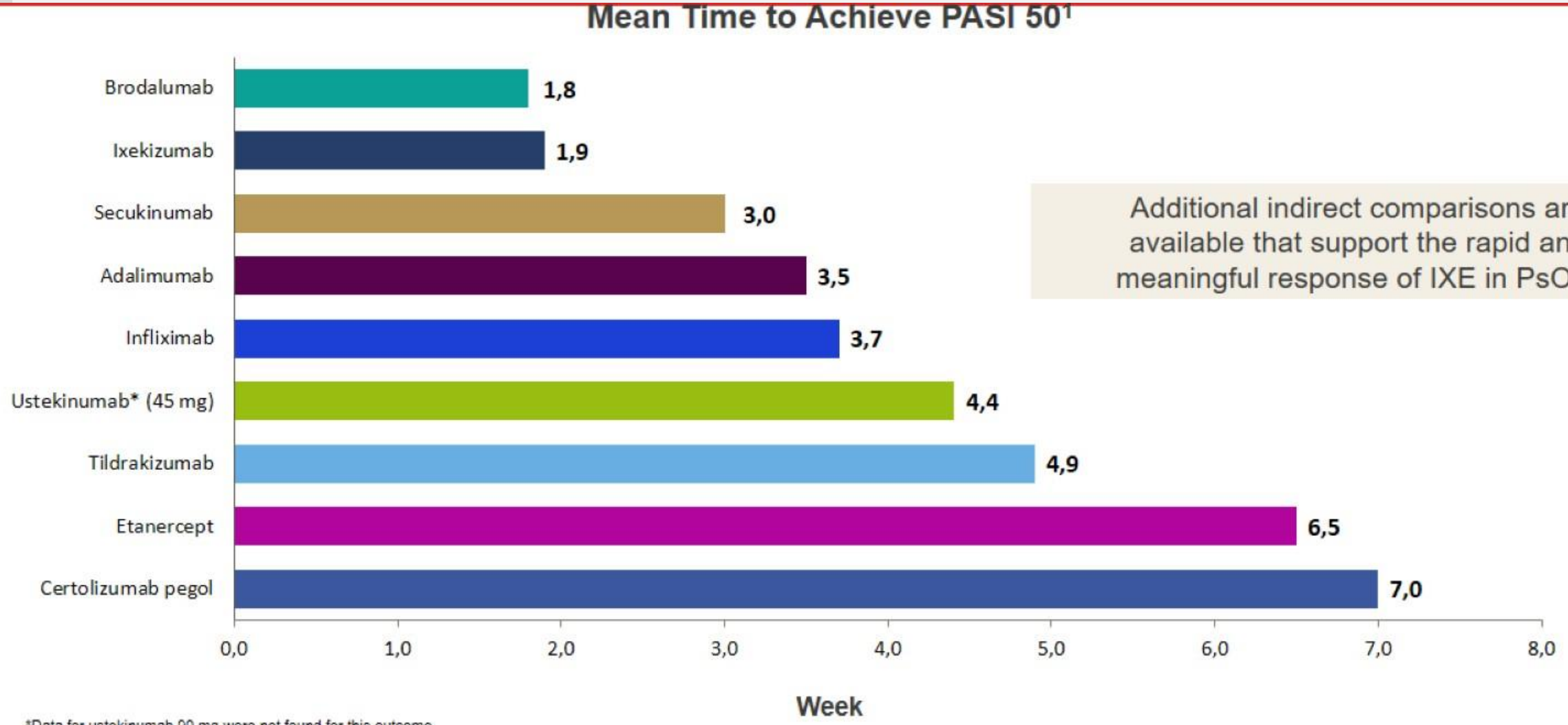


Placebo-adjusted normalized maximum AUC for PASI 100 at 16 and 52 Weeks. Data displayed as median (95% credible interval). AUC area under the curve, PASI 100/90 100% or C 90% improvement in Psoriasis

Cumulative Clinical Benefits of Biologics in the Treatment of Patients with Moderate-to-Severe Psoriasis over 1 Year: a Network Meta-Analysis
Andrew Blauvelt et al, Dermatol Ther (Heidelb),February 2022

Ταχύτητα έναρξης δράσης

Οι αναστολείς της IL-17 πετυχαίνουν γρήγορα & υψηλά ποσοστά καθαρού δέρματος (PASI ≤1) στις πρώτες 12 Εβδομάδες θεραπείας.



*Data for ustekinumab 90 mg were not found for this outcome.

Note: 95% CI values are 1.8-1.9 (brodalumab), 2.8-3.2 (secukinumab), and 4.2-4.7 (ustekinumab 45 mg); no other 95% CI data are available.

1. Yao CJ, et al. *J Drugs Dermatol.* 2019;18:229-233. 2. Armstrong AW, et al. *JAMA Dermatol.* 2020;156:258-269. 3. Sawyer LM, et al. *PLoS One.* 2019;14:e0220868. 4. Warren RB, et al. *Derrmatol Ther (Heidelb).* 2020;10:73-86.

Προφίλ ασφάλειας - Μετανάλυση Network

Dermatol Ther (Heidelb)
https://doi.org/10.1007/s13555-019-00340-3

ORIGINAL RESEARCH

Safety of Ixekizumab Treatment for up to 5 Years in Adult Patients with Moderate-to-Severe Psoriasis: Results from Greater Than 17,000 Patient-Years of Exposure

April Armstrong · Carle Paul · Luis Puig · Wolf Henning Boehncke · Michael Freeman · Hideshi Torii · Kim Papp · Christopher E. M. Griffiths · Andrew Blauvelt · Kristian Reich · Melinda Gooderham · Tadashi Terui · Lisa Renda · Noah Agada · Wen Xu · Gaia Gallo · Mark G. Lebwohl

Received: August 8, 2019

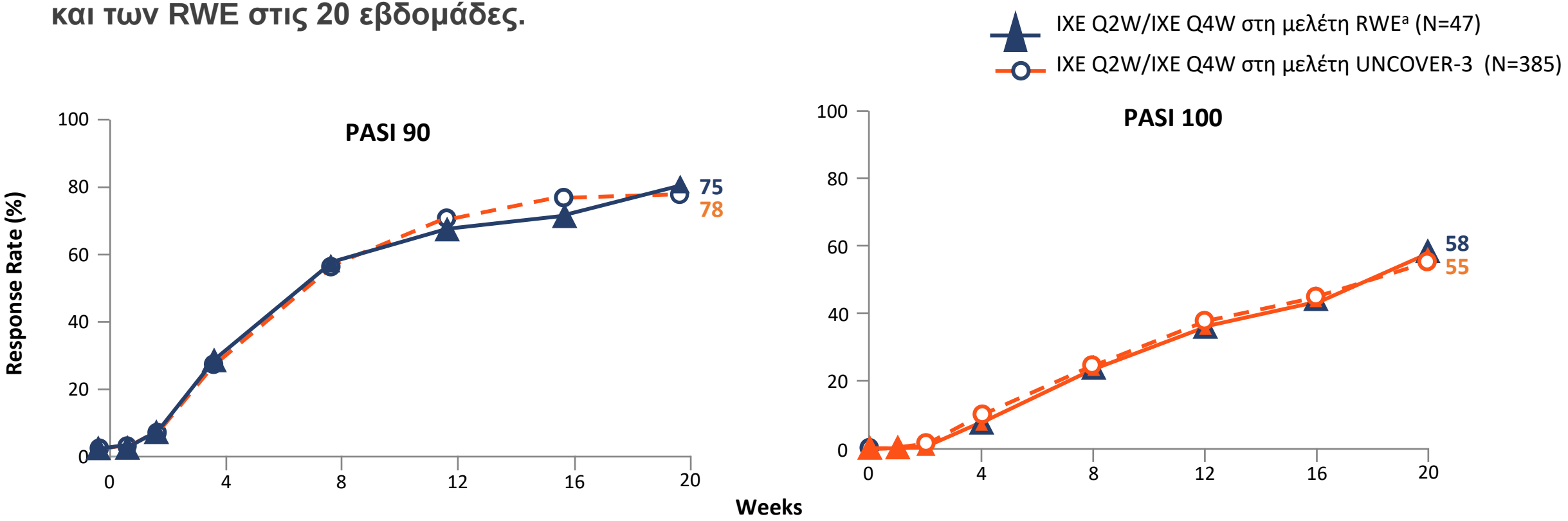
- **Δεν προέκυψε καμία νέα ανησυχία για το προφίλ ασφαλείας του ixekizumab στη μακροχρόνια χορήγηση.**

Συλλογή δεδομένων από όλες τις πηγές της βιβλιογραφίας.

RCTs + **NMA** + **RWE**

From randomized clinical trials to real life data.
Η κλινική εμπειρία από την Ιταλία με το ixekizumab.

Τα ποσοστά ανταπόκρισης στη θεραπεία είναι παρόμοια μεταξύ του πληθυσμού των RCTs και των RWE στις 20 εβδομάδες.



[a]Single-center study from Italy.
Damiani G, et al. *Dermatol Ther.* 2019;32:e12886.

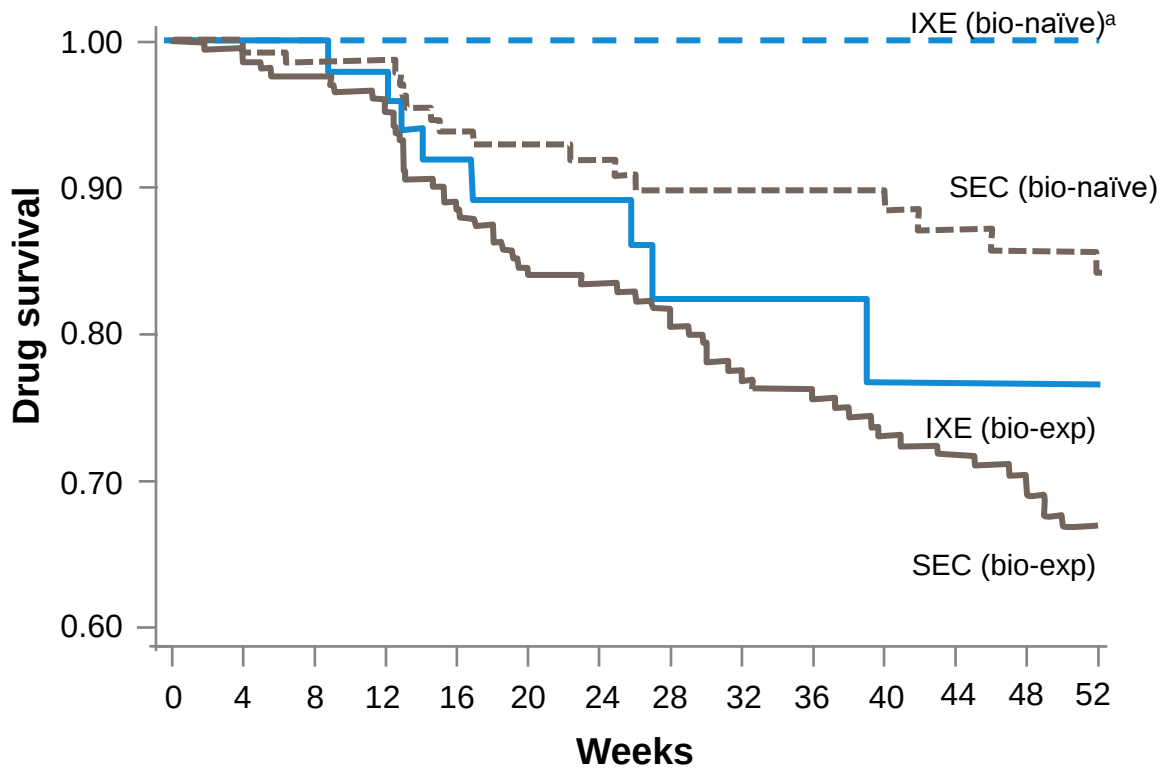
Drug Survival των αναστολέων της IL-17
DERMBIO Registry

Aim
- To investigate the drug survival of the IL-17 inhibitors secukinumab and ixekizumab

Methodology
- Patients enrolled between April 1, 2015 and August 1, 2018, and treated with ixekizumab or secukinumab for at least 52 weeks were included in the study
- 368 patients were included for secukinumab, (40.7% bio-naïve), and 62 patients were included for ixekizumab (12.9% bio-naïve)
- Mean number of previous biologics was 1.3 for secukinumab and 3.6 for ixekizumab (p<.0001)
- Kaplan-Meier plots were used to present descriptive (unadjusted) survival curves stratified into bio-naïve patients (i.e. first ever treatment series) and non-naïve patients
- *Limitations*: Low number of patients especially for ixekizumab and a short follow-up

Conclusions
- Drug survival was higher for ixekizumab even though ixekizumab-treated patients had received significantly more previous treatments

Kaplan-Meier plot of drug survival for ixekizumab and secukinumab over 52 weeks



aNone of the biologic-naïve patients discontinued IXE during the follow-up period. exp=Experienced; IL=Interleukin; IXE=Ixekizumab; SEC=Secukinumab.

Egeberg A, et al. *J Am Acad Dermatol.* 2019; doi: 10.1016/j.jaad.2019.03.048 [

Συγκριτικά δεδομένα παραμονής στη θεραπεία
Ixe vs Sec, 2 χρόνια παρακολούθησης

Comparison of two-year treatment adherence, persistence, discontinuation, reinitiation, and switching between psoriasis patients treated with ixekizumab or secukinumab in real-world settings

Andrew Blauvelt, MD, MBA,[a] Nianwen Shi, PhD,[b] Najwa Somani, MD,[c] Russel Burge, PhD,[c,d] Baojin Zhu, PhD,[c] Terri L. Ridenour, MBA, BSN,[c] Carolyn R. Lew, PhD,[b] Nicole M. Zimmerman, MS,[b] Bilal Atiya, PharmD,[c] and Mwangi J. Murage, PhD, MPH[c]

Portland, Oregon; Cambridge, Massachusetts; Indianapolis, Indiana; and Cincinnati, Ohio

Συγκριτικά δεδομένα μακροχρόνιας παραμονής στη θεραπεία **Ixe vs Sec** , 2 έτη παρακολούθησης

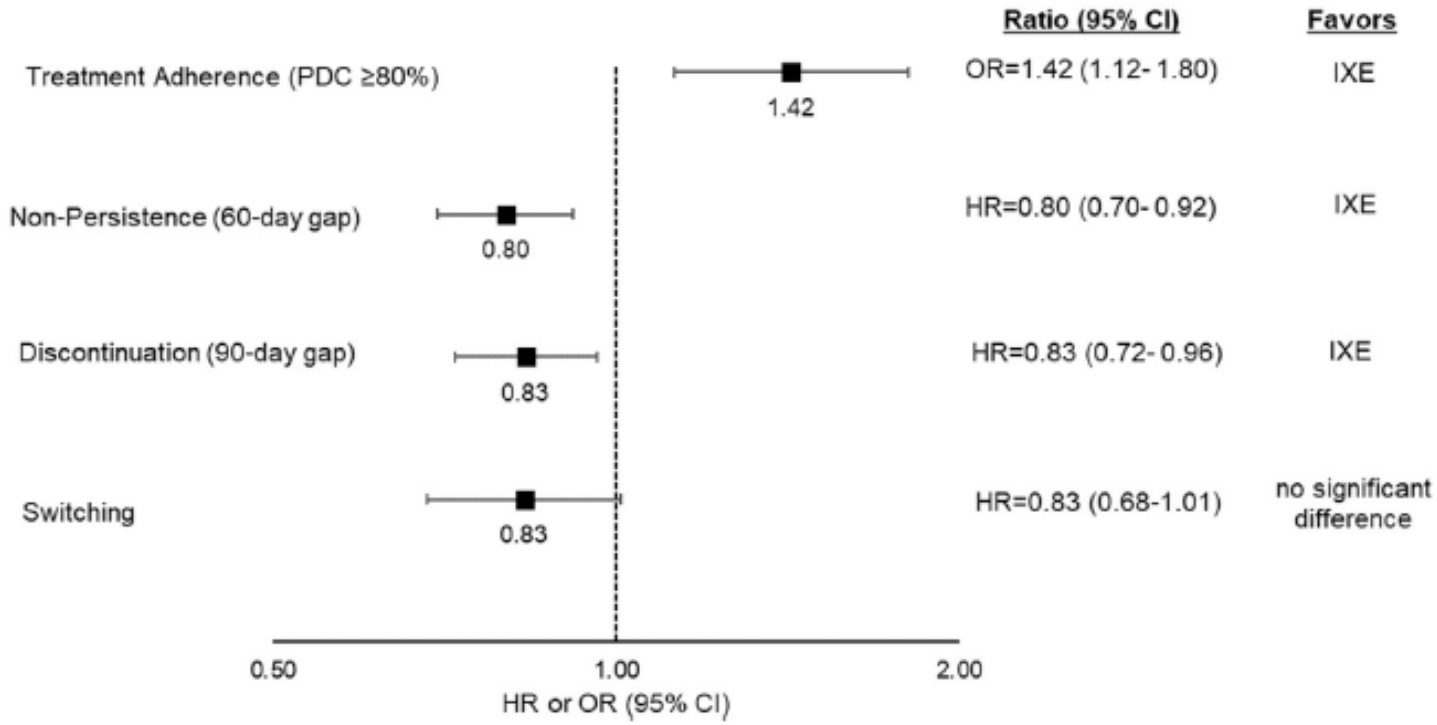


Fig 3. Multivariable analyses, treatment pattern outcomes over 24 months of follow-up (weighted), documenting psoriasis patients treated with ixekizumab vs. secukinumab. *HR*, Hazard ratio; *IXE*, ixekizumab; *OR*, odds ratio; *PDC*, Proportion of days covered.

1.Comparison of two-year treatment adherence, persistence, discontinuation, reinitiation, and switching between psoriasis patients treated with ixekizumab or secukinumab in real-world settings Andrew Blauvelt et al, JAAD2022 Mar;86(3):581-589.

- **Τα RWD μπορούν να δώσουν απαντήσεις και σε δύσκολα κλινικά σενάρια!**

Εξαντλείται το μονοπάτι της IL-17;

Πρόσφατα δεδομένα intra-class switch από την Ελλάδα!

J Eur Acad Dermatol Venereol. 2022 Jun 30. doi: 10.1111/jdv.18381. Online ahead of print.

Real-life intraclass switch among IL-17 inhibitors in psoriasis: results from a single-centre, 24-week, retrospective study

E Sotiriou [1], K Bakirtzi [1], I Papadimitriou [1], A Tsentemeidou [1], N Kougkas [2], A Panagopoulou [1], D Ioannides [1], E Vakirlis [1]

Table 2 Clinical outcomes after the anti-IL17 intraclass switch

	PASI 75 % (*n*)	PASI 90 (*n*) % (*n*)	PASI 100 (*n*) % (*n*)
12 weeks			
Brodalumab to Ixekizumab	83.3 (5/6)	66.7 (4/6)	33.3 (2/6)
Brodadumab to Secukinumab	94.1 (16/17)	88.2 (15/17)	82.4 (14/17)
Secukinumab to Ixekizumab	75.0 (12/16)	56.3 (9/16)	43.8 (7/16)
Secukinumab to Brodalumab	71.4 (5/7)	42.9 (3/7)	14.3 (1/7)
24 weeks			
Brodalumab to Ixekizumab	100 (6/6)	66.7 (4/6)	50.0 (3/6)
Brodalumab to Secukinumab	100 (17/17)	94.1 (16/17)	94.1 (16/17)
Secukinumab to Ixekizumab	81.3 (13/16)	68.8 (11/16)	50.0 (8/16)
Secukinumab to Brodalumab	85.7 (6/7)	71.4 (5/7)	14.3 (1/7)

- 1.Real-life intraclass switch among IL-17 inhibitors in psoriasis: results from a single-centre, 24-week, retrospective study, E Sotiriou et al, J Eur Acad Dermatol Venereol 2022 Jun 30. doi: 10.1111/jdv.18381. Online ahead of print.

American Journal of Clinical Dermatology
https://doi.org/10.1007/s40257-022-00722-y

Published online: 17 August 2022

ORIGINAL RESEARCH ARTICLE

Drug Survival of Interleukin (IL)-17 and IL-23 Inhibitors for the Treatment of Psoriasis: A Retrospective Multi-country, Multicentric Cohort Study

Tiago Torres[1,2] · Luis Puig[3] · Ron Vender[4] · Jensen Yeung[5] · José-Manuel Carrascosa[6] · Stefano Piaserico[7] · Paolo Gisondi[8] · Charles Lynde[9] · Paulo Ferreira[10] · Pedro Mendes Bastos[10] · Esteban Dauden[11] · Luiz Leite[12] · Joana Valerio[12] · Elena del Alcázar-Viladomiu[6] · Eva Vilarrasa Rull[3] · Mar Llamas-Velasco[11] · Federico Pirro[13,14] · Francesco Messina[7] · Manfredo Bruni[8] · Gaetano Licata[15] · Federica Ricceri[16] · Alessia Nidegger[17] · Jan Hugo[18] · Asfandyar Mufti[5] · Athina-Ioanna Daponte[19] · Laetitia Teixeira[20] · Anna Balato[21] · Marco Romanelli[22] · Francesca Prignano[16] · Spyridon Gkalpakiotis[18] · Curdin Conrad[17] · Elizabeth Lazaridou[19] · Natalia Rompoti[23] · Marina Papoutsaki[23] · Miguel Nogueira[1] · Andrea Chiricozzi[13,14]

Abstract

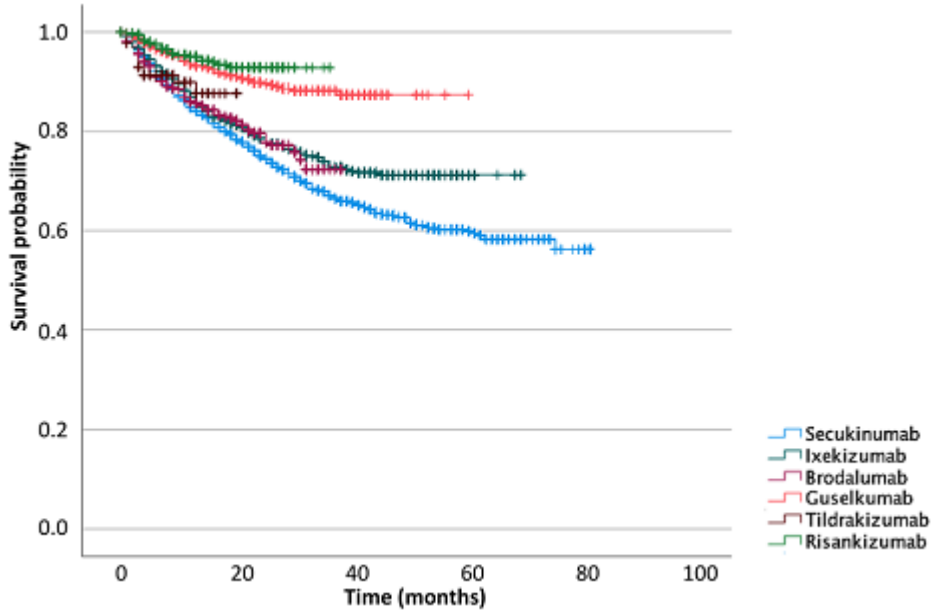
Background Drug survival, defined as the length of time from initiation to discontinuation of a given therapy, allows comparisons between drugs, helps to predict patient's likelihood of remaining on a specific treatment, and achieving the best decision for each patient in daily clinical practice.

Objective The aim of this study was to provide data on drug survival of secukinumab, ixekizumab, brodalumab, guselkumab, tildrakizumab, and risankizumab in a large international cohort, and to identify clinical predictors that might have an impact on the drug survival of these drugs.

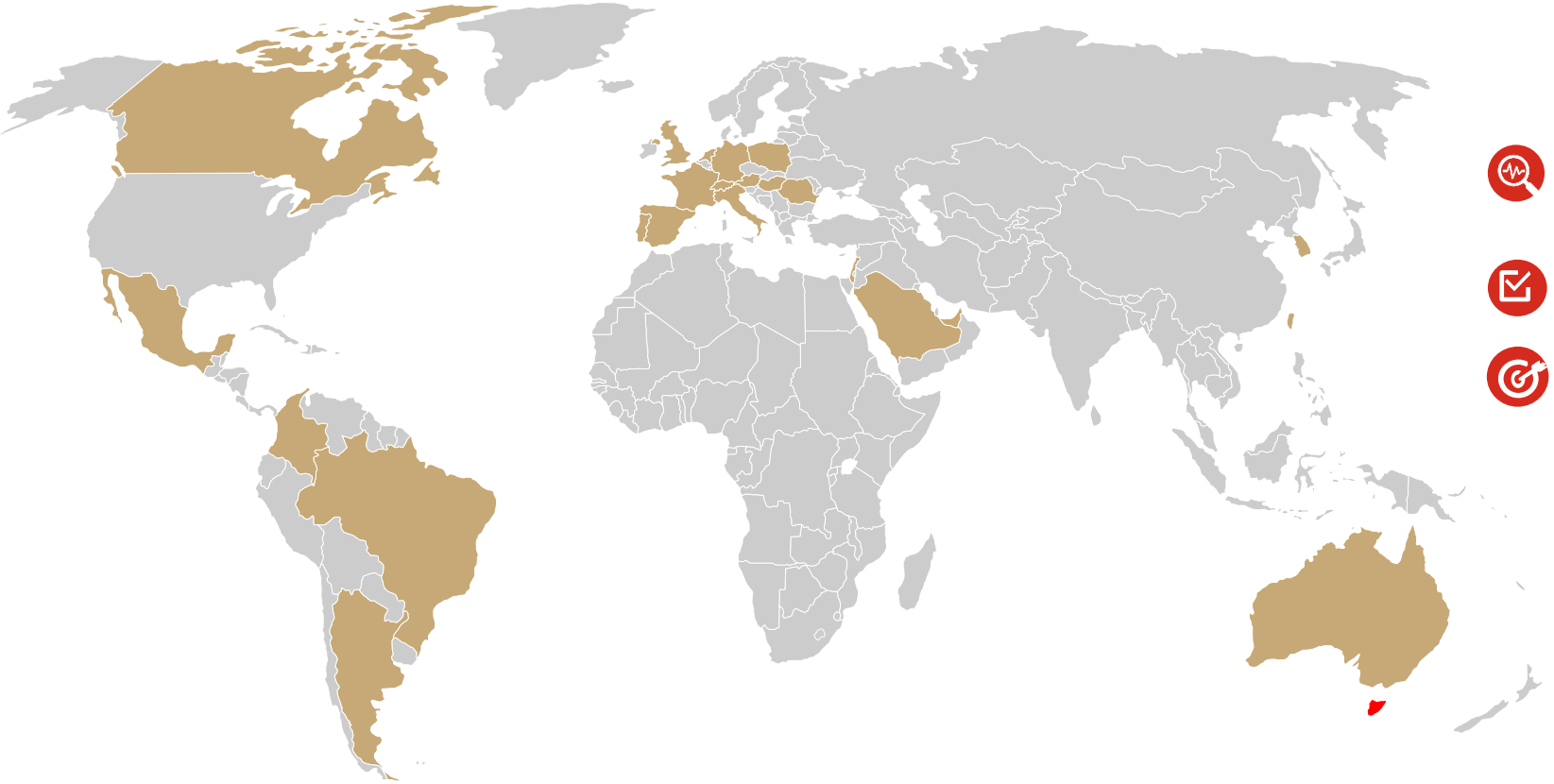
Methods This was a retrospective, multicentric, multi-country study that provides data of adult patients with moderate to severe psoriasis who started treatment with an interleukin (IL)-17 or IL-23 inhibitor between 1 February 2015 and 31 October 2021. Data were collected from 19 distinct hospital and non-hospital-based dermatology centers from Canada, Czech Republic, Italy, Greece, Portugal, Spain, and Switzerland. Kaplan–Meier estimator and proportional hazard Cox regression models were used for drug survival analysis.

Results A total of 4866 treatment courses (4178 patients)—overall time of exposure of 9500 patient-years—were included in this study, with 3164 corresponding to an IL-17 inhibitor (secukinumab, ixekizumab, brodalumab) and 1702 corresponding to an IL-23 inhibitor (guselkumab, risankizumab, tildrakizumab). IL-23 inhibitors had the highest drug survival rates during the entire study period. After 24 months of treatment, the cumulative probabilities of drug survival were 0.92 (95% confidence interval [CI] 0.89–0.95) for risankizumab, 0.90 (95% CI 0.88–0.92) for guselkumab, 0.80 (95% CI 0.76–0.84) for brodalumab, 0.79 (95% CI 0.76–0.82) for ixekizumab, and 0.75 (95% CI 0.73–0.77) for secukinumab. At 36 months, only guselkumab [0.88 (95% CI 0.85–0.91)], ixekizumab [0.73 (95% CI 0.70–0.76)], and secukinumab [0.67 (95% CI 0.65–0.70)] had more than 40 patients at risk of drug discontinuation. Only two drugs had more than 40 patients at risk of drug discontinuation at 48 months, with ixekizumab demonstrating to have a higher cumulative probability of drug survival [0.71 (95% CI 0.68–0.75)] when compared with secukinumab [0.63 (95% CI 0.60–0.66)]. Secondary failure was the main cause for drug discontinuation. According to the final multivariable model, patients receiving risankizumab, guselkumab, and ixekizumab were significantly less likely to discontinue treatment than those receiving secukinumab. Previous exposure to biologic agents, absent family history of psoriasis, higher baseline body mass index (BMI), and higher baseline Psoriasis Area and Severity Index (PASI) were identified as predictors of drug discontinuation.

Conclusion The cumulative probability of drug survival of both IL-17 and IL-23 inhibitors was higher than 75% at 24 months, with risankizumab and guselkumab demonstrating to have overall cumulative probabilities ≥ 90%. Biological agent chosen, prior exposure to biologic agents, higher baseline BMI and PASI values, and absence of family history of psoriasis were identified as predictors for drug discontinuation. Risankizumab, guselkumab, and ixekizumab were less likely to be discontinued than secukinumab.



Psoriasis Study of Health Outcomes (PSoHO)



- Προοπτική, πολυκεντρική, διεθνής, μη-παρεμβατική μελέτη διάρκειας 36 μηνών
- Συμμετοχή 23 χωρών
- Ποικιλία δεδομένων σχετικά με το ixekizumab,τη σύγκριση των IL-17i με τις άλλες θεραπευτικές κατηγορίες, τις δύσκολες ειδικές εντοπίσεις,την ποιότητα ζωής των ασθενών σε real-world settings.

Πρώτη δημοσίευση:Δεδομένα 12 Εβδομάδων,Ιούνιος 2022, JEADV

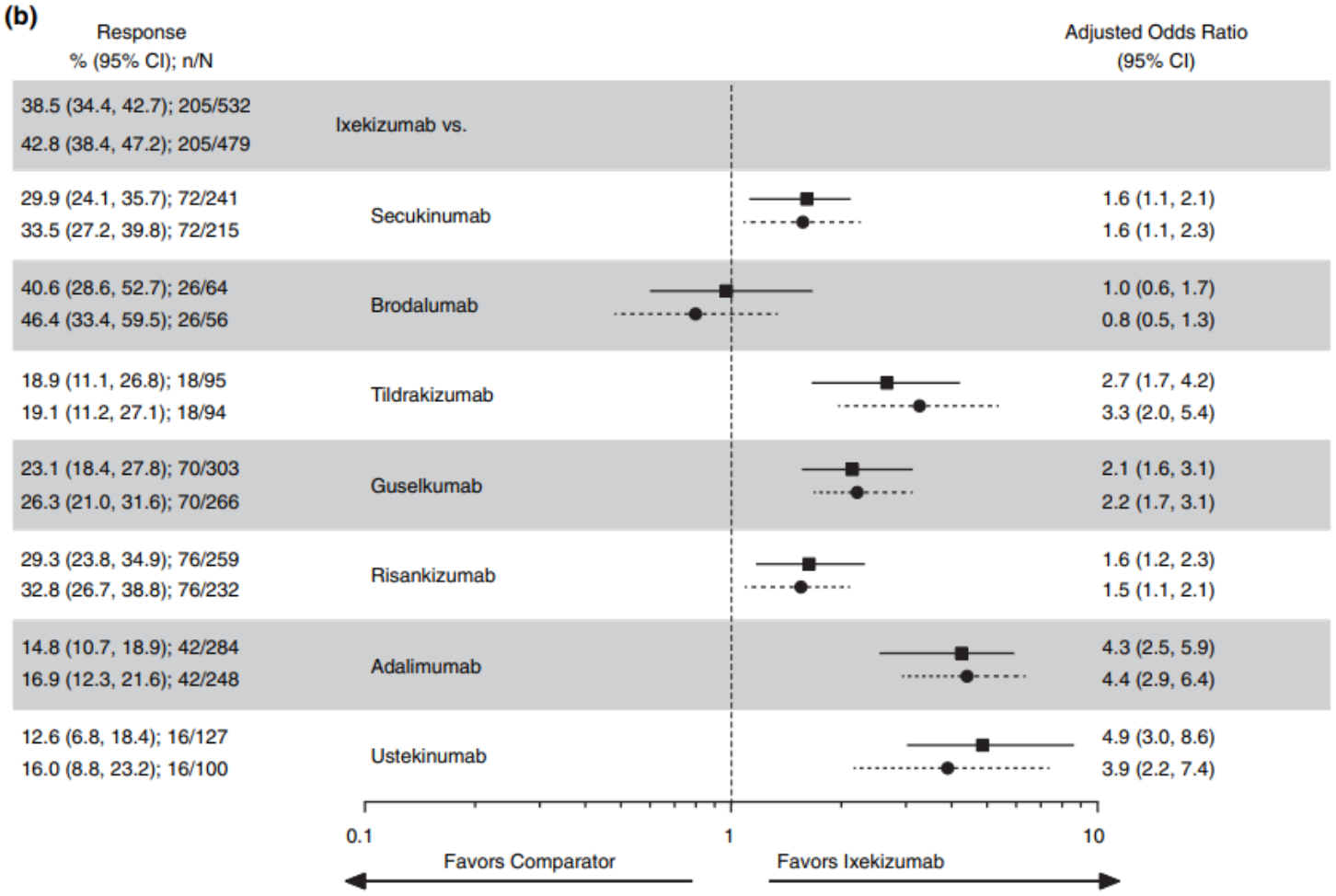
DOI: 10.1111/jdv.18376 JEADV

ORIGINAL ARTICLE

Comparative effectiveness of biologics in clinical practice: week 12 primary outcomes from an international observational *psoriasis study of health outcomes* (PSoHO)

Andreas Pinter,[1,*] Luis Puig,[2] Knut Schäkel,[3] Adam Reich,[4] Shirin Zaheri,[5] Antonio Costanzo,[6 7] Tsen Fang Tsai,[8] Saxon D. Smith,[9] Charles Lynde,[10] Alan Brnabic,[11] Catherine Reed,[11] Julie Hill,[11] Christopher Schuster,[11 12] Elisabeth Riedl,[11 12] Carle Paul[13]

Τα αποτελέσματα επίτευξης του PASI100 στις 12 Εβδομάδες επιβεβαιώνουν τα δεδομένα των μεταναλύσεων.



EADV 2022

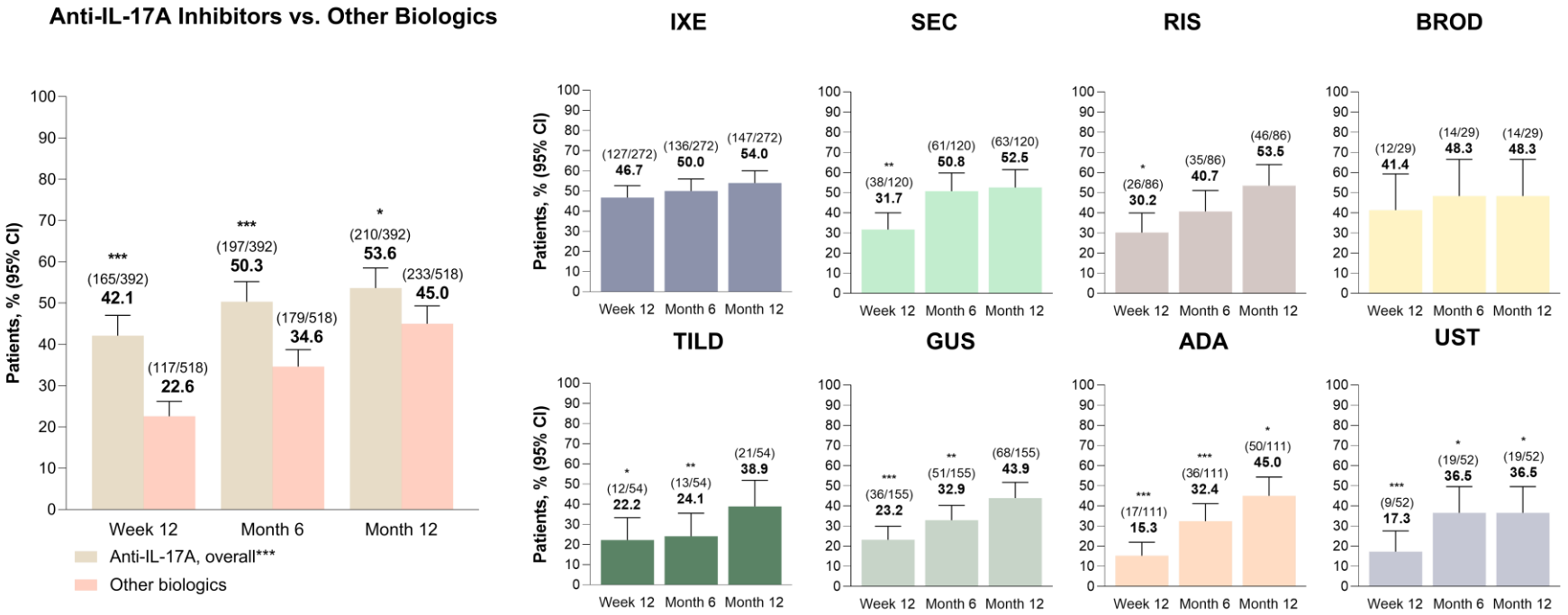
Initial Report on the Month 12 Results From the Psoriasis Study of Health Outcomes (PSoHO) for Patients With Moderate-to-Severe Psoriasis Treated With Biologics in the Real-World Setting

Antonio Costanzo,[1] Carle F. Paul,[2] Jose-Manuel Carrascosa,[3] Yayoi Tada,[4]
Alan Brnabic,[5] Christopher Schuster,[5,6] Catherine Reed,[5]
Michael Abrahamy,[5] Elisabeth Riedl,[5*,6] Andreas Pinter[7]

[1]Division of Dermatology, Humanitas Research Hospital, Pieve Emanuele, Milan, Italy,
and Dermatology IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy;
[2]Université Paul Sabatier Toulouse III, Toulouse, France;
[3]Department of Dermatology Hospital Universitari Germans Trias, Badalona, Spain;
[4]Department of Dermatology, Teikyo University School of Medicine, Tokyo, Japan;
[5]Eli Lilly and Company, Indianapolis, USA (*Former employee);
[6]Clinic for Dermatology, Venereology and Allergology, Department of Dermatology, Medical University of Vienna, Vienna, Austria;
[7]University Hospital Frankfurt, Frankfurt am Main, Germany

Study was sponsored by Eli Lilly and Company

Ποσοστό ασθενών (NRI) που πέτυχαν PASI 100 στις 12 Εβδομάδες και στους 6+12 Μήνες



* p<.05; *** p<.001 vs. other biologics (NRI) (GLMM)

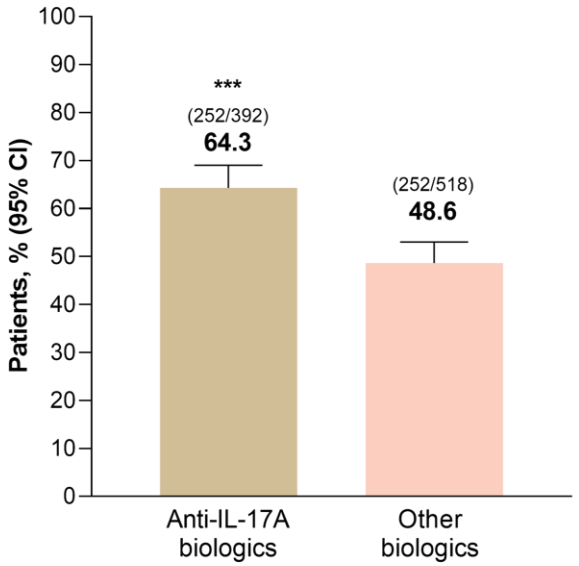
* p<.05; ** p<.01; *** p<.001 vs. IXE (NRI) (GLMM)

CIs are calculated from the normal approximation. Data were analyzed for a subset of patients with a result for the primary objective variable at Month 12

ADA=adalimumab; BROD=brodalumab; CI=confidence interval; GLMM=generalized linear mixed model; GUS=guselkumab; IL-17A=interleukin-17A; IXE=ixekizumab; NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index; RIS=risankizumab; SEC=secukinumab; TILD=tildrakizumab; UST=ustekinumab

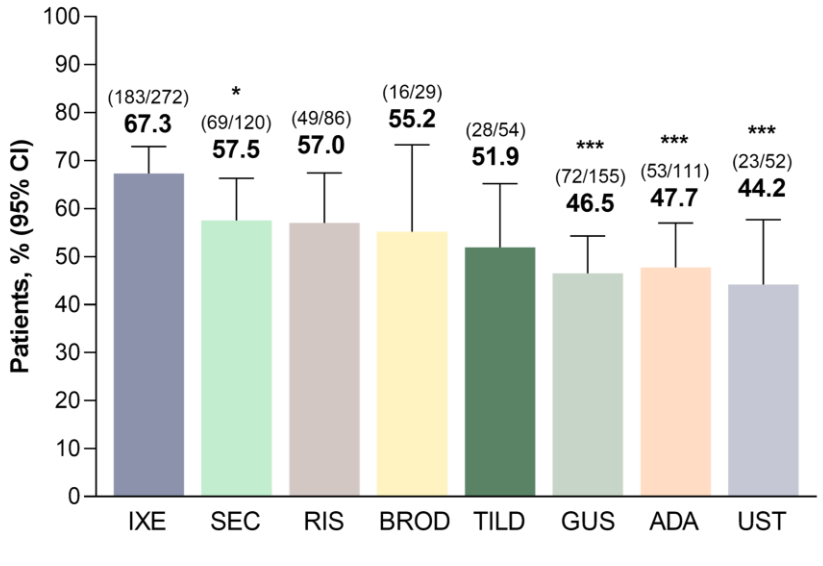
Ποσοστό ασθενών (NRI) που πέτυχαν **Διατήρηση της θεραπείας** στους 12 Μήνες

Anti-IL-17A Inhibitors vs. Other Biologics



*** p<.001 vs. other biologics (NRI) (logistic regression)

Individual Biologic Treatment Groups



* p<.05; *** p<.001 vs. IXE (NRI) (logistic regression)

CIs are calculated from the normal approximation. Data were analyzed for a subset of patients with a result for the primary objective variable at Month 12

[a] Durability of treatment effectiveness was defined as the percentage of patients achieving PASI 90 and/or sPGA (0,1) at Week 12 and PASI 75 and/or ≥2-point improvement in sPGA at Months 6 and 12

ADA=adalimumab; BROD=brodalumab; CI=confidence interval; GUS=guselkumab; IL-17A=interleukin-17A; IXE=ixekizumab; NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index; RIS=risankizumab; SEC=secukinumab; sPGA=static Physician's Global Assessment; TILD=tildrakizumab; UST=ustekinumab

Συμπερασματικά

IXE

RTCs

NMA

RWE

♦ H2H=Head-to-Head; IL=Interleukin; IXE=Ixekizumab; PASI 100=100% Improvement in Psoriasis Area and Severity Index; PsA=Psoriatic Arthritis. References listed in slide notes.

Σας ευχαριστώ πολύ για την προσοχή σας!

Ixekizumab SPC

Βοηθήστε να γίνουν τα φάρμακα πιο ασφαλή και
Αναφέρετε
ΟΛΕΣ τις ανεπιθύμητες ενέργειες για
ΟΛΑ τα φάρμακα
Συμπληρώνοντας την «ΚΙΤΡΙΝΗ ΚΑΡΤΑ»

Αξιολόγηση Δορυφορικής Διάλεξης

Η άποψή σας είναι πολύτιμη!

Σας ευχαριστούμε για το ενδιαφέρον σας να παρακολουθήσετε την εκδήλωσή μας