Οι Βιολογικοί Παράγοντες στην Αντιμετώπιση της Παλαμοπελματιαίας Ψωρίασης:μετα-ανάλυση δικτύου

Efficacy of on-label use of biologic agents for palmoplantar psoriasis: a network meta-analysis

Department of Rheumatology and Clinical Immunology, Faculty of Medicine, University of Thessaly 2023

Efficacy of on-label psoriasis-approved biologic agents for palmoplantar psoriasis and palmoplantar pustulosis: a systematic review and network meta-analysis

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Introduction

- ✓ Psoriasis: chronic inflammatory disease of the skin
- ✓ Localized forms have been described, including **palmoplantar psoriasis** (PP)
- ✓ Palmoplantar lesions: *exclusively or concurrently*
- ✓ High impact on **quality of life**, frequently prescribed **systemic treatments**
- ✓ Management regularly supported by **biological agents**
- ✓ Determination of **efficacy of biologics for PP**: an unsatisfied need
- ✓ Limited evidence on the optimal treatment of localized palmoplantar lesions

Στόχος

Η συστηματική ανασκόπηση και σύνθεση των διαθέσιμων δεδομένων σχετικά με την αποτελεσματικότητα των εγκεκριμένων βιολογικών παραγόντων στη διαχείριση της εντοπισμένης παλαμοπελματιαίας ψωρίασης

Population:	Patients with **PP** (concomitant or not with psoriasis vulgaris).
Intervention:	**On-label use of biologic therapies** currently approved for the treatment of psoriasis (etanercept, infliximab, adalimumab, certolizumab, ustekinumab, secukinumab, ixekizumab, brodalumab, bimekizumab, guselkumab, tildrakizumab, risankizumab).
Comparison:	On-label biologic therapies, small molecules, conventional systemic treatment use (licensed for plaque psoriasis), placebo, or no treatment.
Outcomes:	
- *Main:*	1. Proportion of participants **cleared or almost cleared** of psoriatic lesions, measured as an objective score of disease severity (ppIGA or hfPGA of 0/1, PPASI100, PPASI90). 2. Proportion of participants achieving **PPASI50** and proportion of participants achieving **PPASI75**. 3. Proportion of participants with severe adverse events.
- *Secondary:*	Proportion of participants with at least 50% improvement in patient's QoL as measured by specific scales (e.g., DLQI).

Eligibility criteria and search strategy

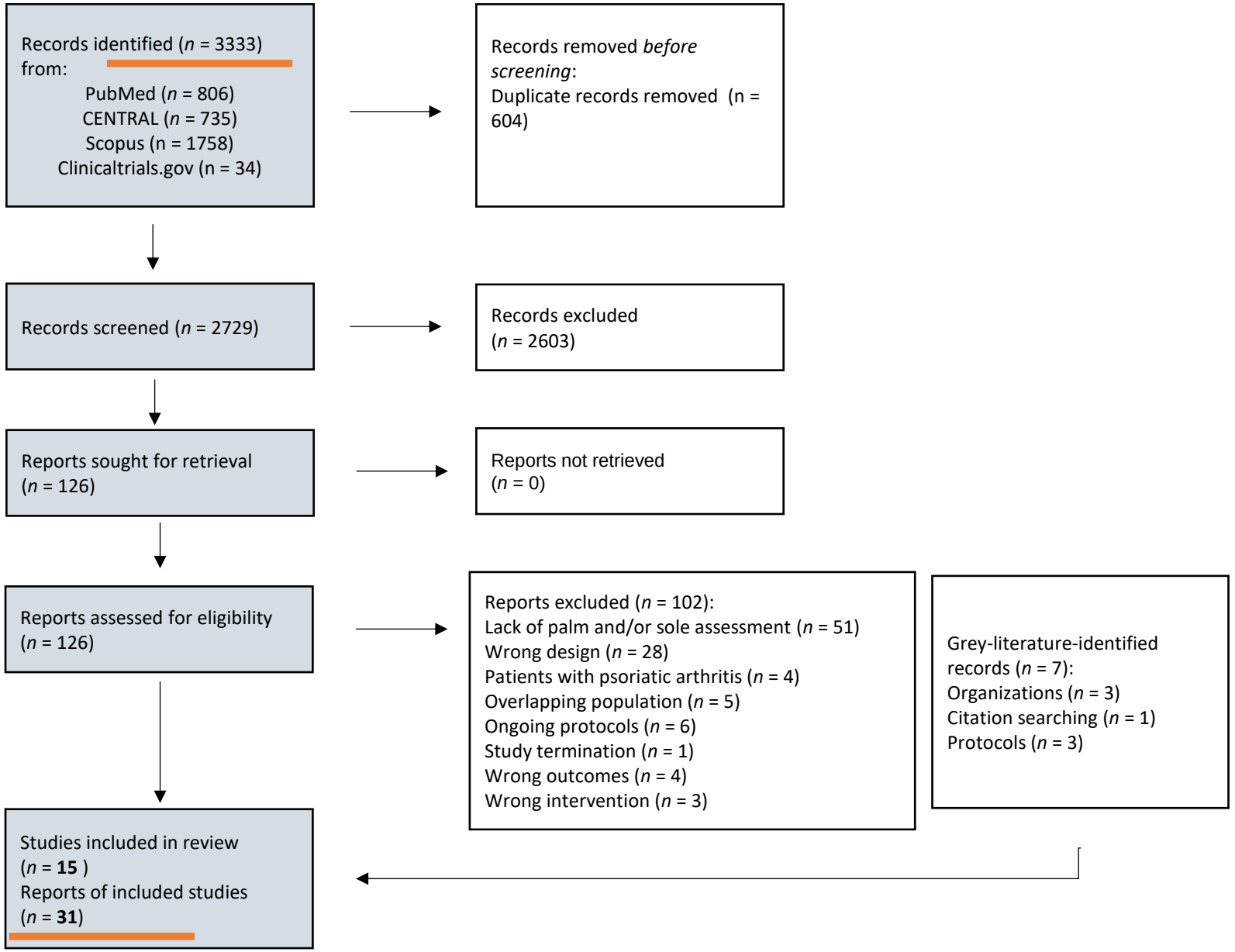
- Randomized controlled trials (RCTs)
- Terms: "palmoplantar", "psoriasis", "feet", "hands", "soles"
- Databases: MedLine (PubMed), Scopus, CENTRAL, clinicaltrials.gov

Data synthesis

- Frequentist, fixed and random-effects NMAs (**graph theory** approach)
- R (version 4.0.6), "**netmeta**"' package
- Risk ratios (RRs) and 95% confidence intervals (CI)
- Treatments ranked using **P-scores** (higher P-score, best ranking)
- Global inconsistency: design-by-treatment model
- Local inconsistency: **node-splitting** method
- 2 sensitivity analyses for the main outcome

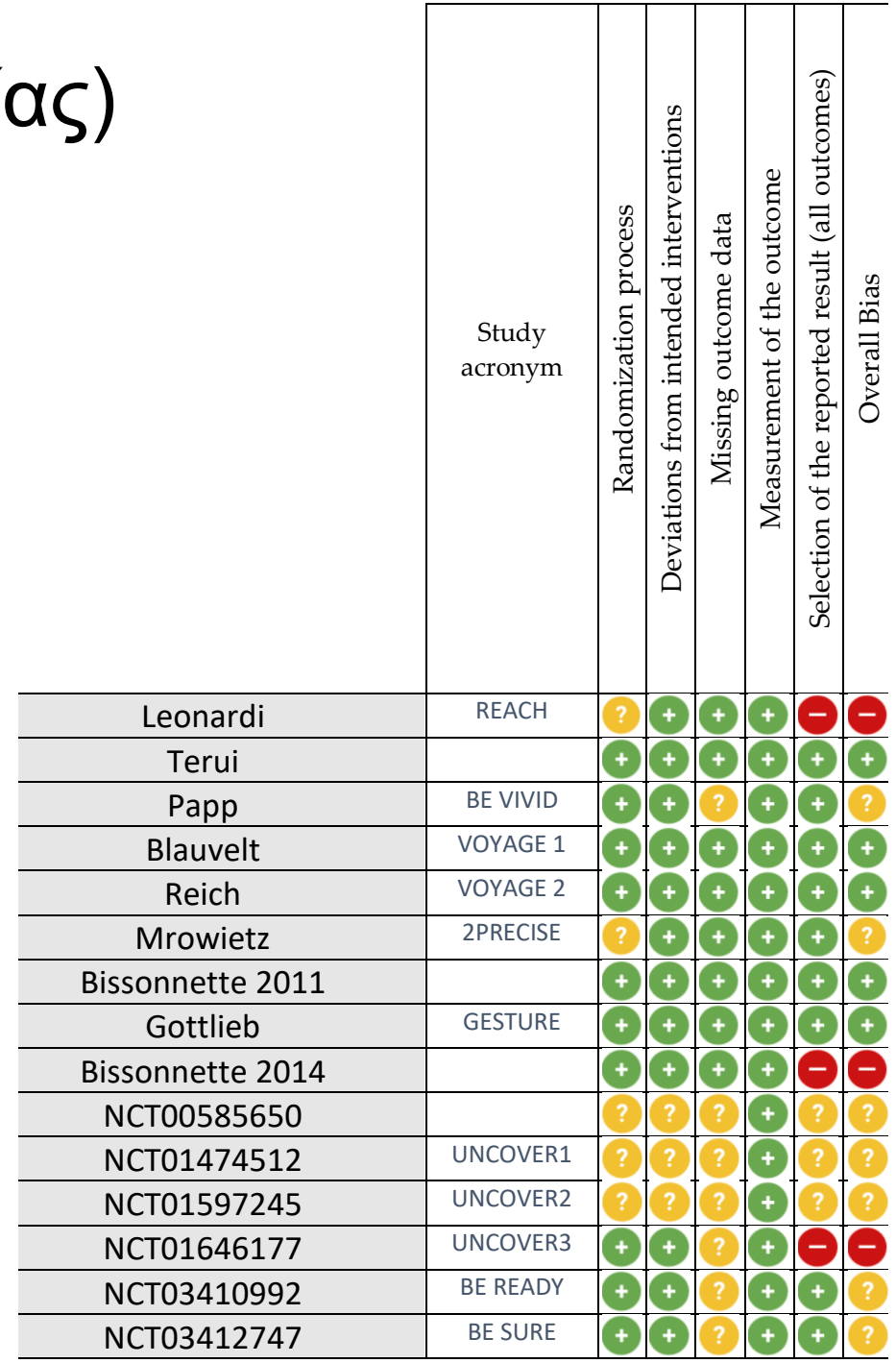
(1st, excluded studies of high risk of bias; 2nd,excluded a dose of an intervention)

Included studies (Διάγραμμα Ροής)



Risk of bias (Κίνδυνος Μεροληψίας)

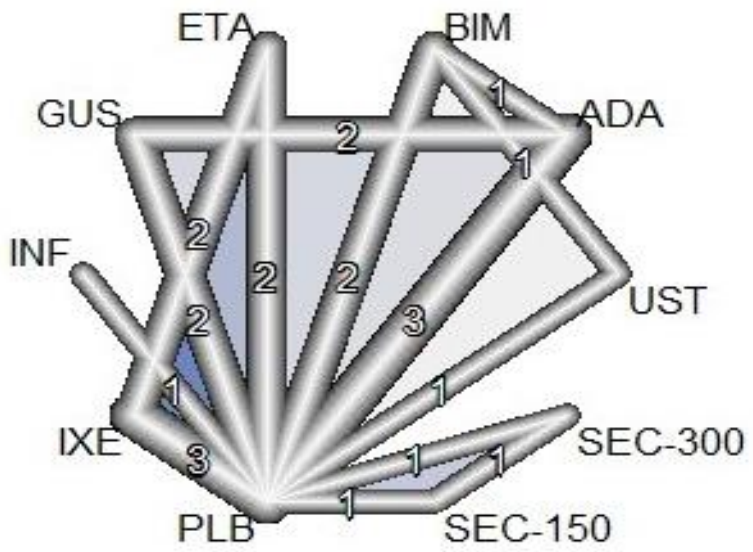
- rev. Cochrane Risk of Bias assessment tool 2.0
- Studies classified as being of "low", "high" risk, or exhibiting "some concerns“

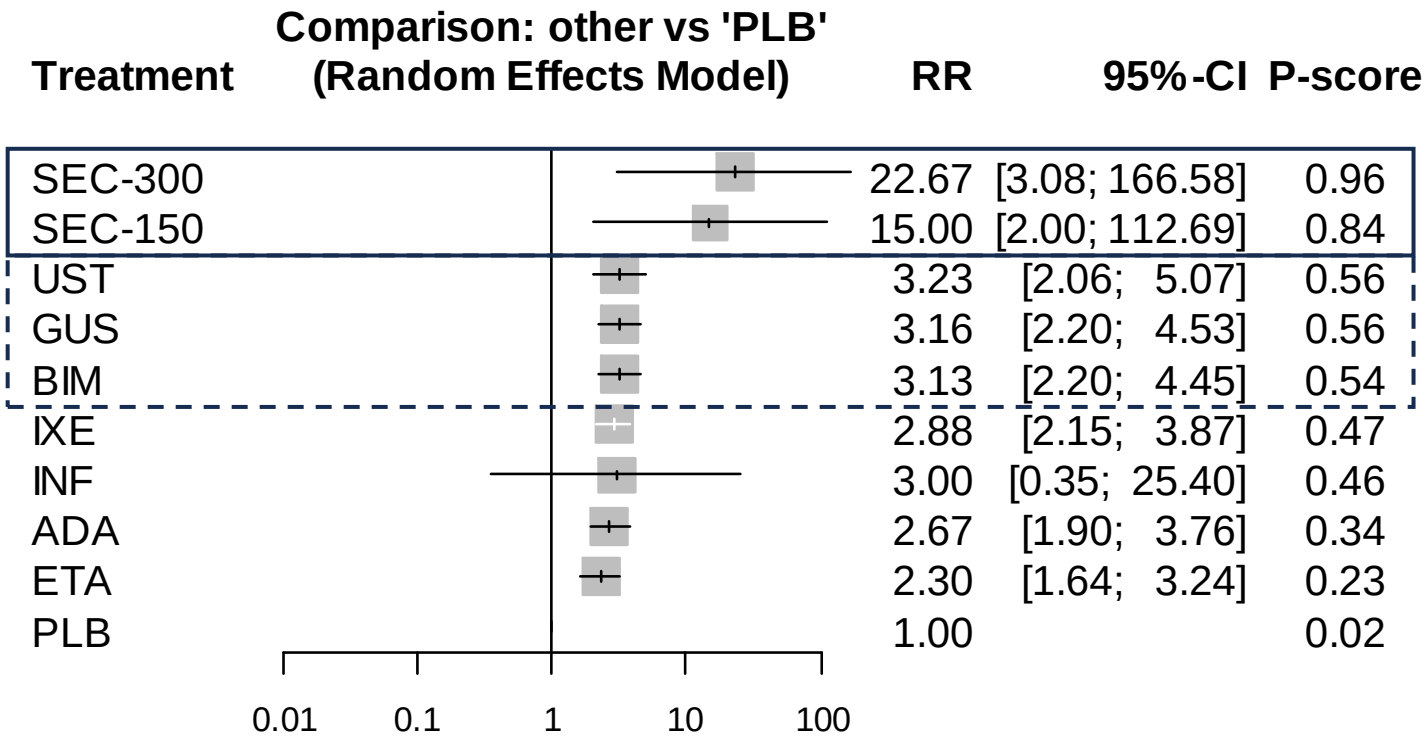


	Study acronym	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result (all outcomes)	Overall Bias
Leonardi	REACH	?	+	+	+	−	−
Terui		+	+	+	+	+	+
Papp	BE VIVID	+	+	?	+	+	?
Blauvelt	VOYAGE 1	+	+	+	+	+	+
Reich	VOYAGE 2	+	+	+	+	+	+
Mrowietz	2PRECISE	?	+	+	+	+	?
Bissonnette 2011		+	+	+	+	+	+
Gottlieb	GESTURE	+	+	+	+	+	+
Bissonnette 2014		+	+	+	+	−	−
NCT00585650		?	?	?	+	?	?
NCT01474512	UNCOVER1	?	?	?	+	?	?
NCT01597245	UNCOVER2	?	?	?	+	?	?
NCT01646177	UNCOVER3	+	+	?	+	−	−
NCT03410992	BE READY	+	+	?	+	+	?
NCT03412747	BE SURE	+	+	?	+	+	?

Primary outcome: Cleared or almost cleared skin

(δίκτυο των παρεμβάσεων για τη κύρια έκβαση)

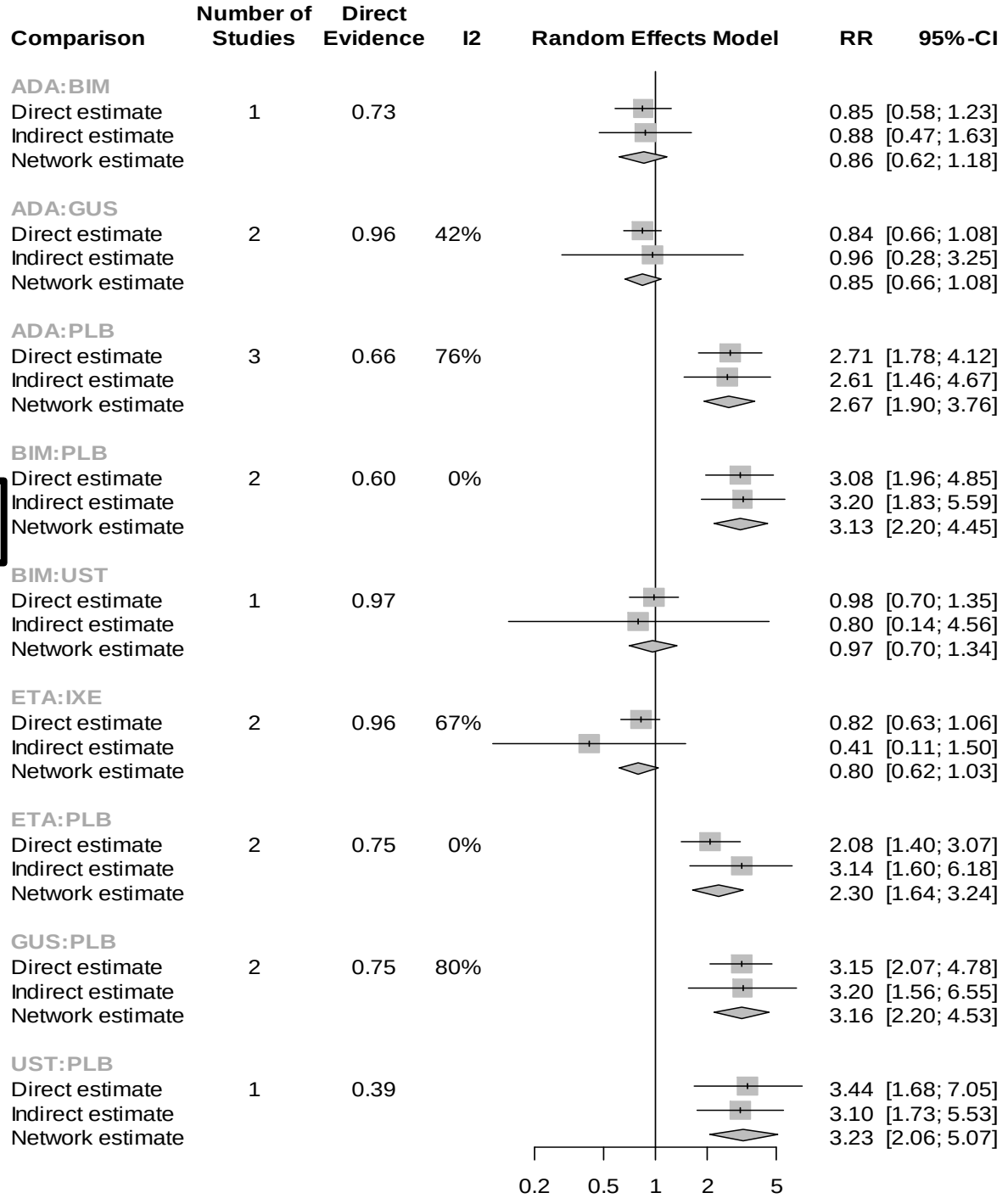




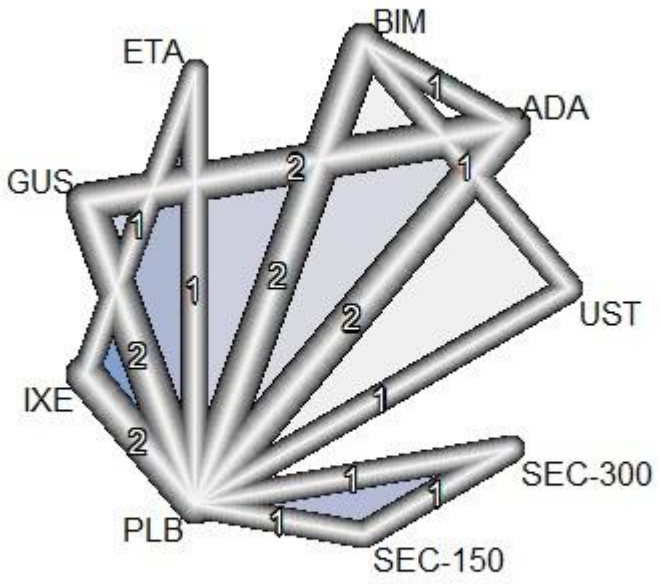
*ixekizumab, infliximab, guselkumab, etanercept, bimekizumab, adalimumab, ustekinumab και secukinumab.

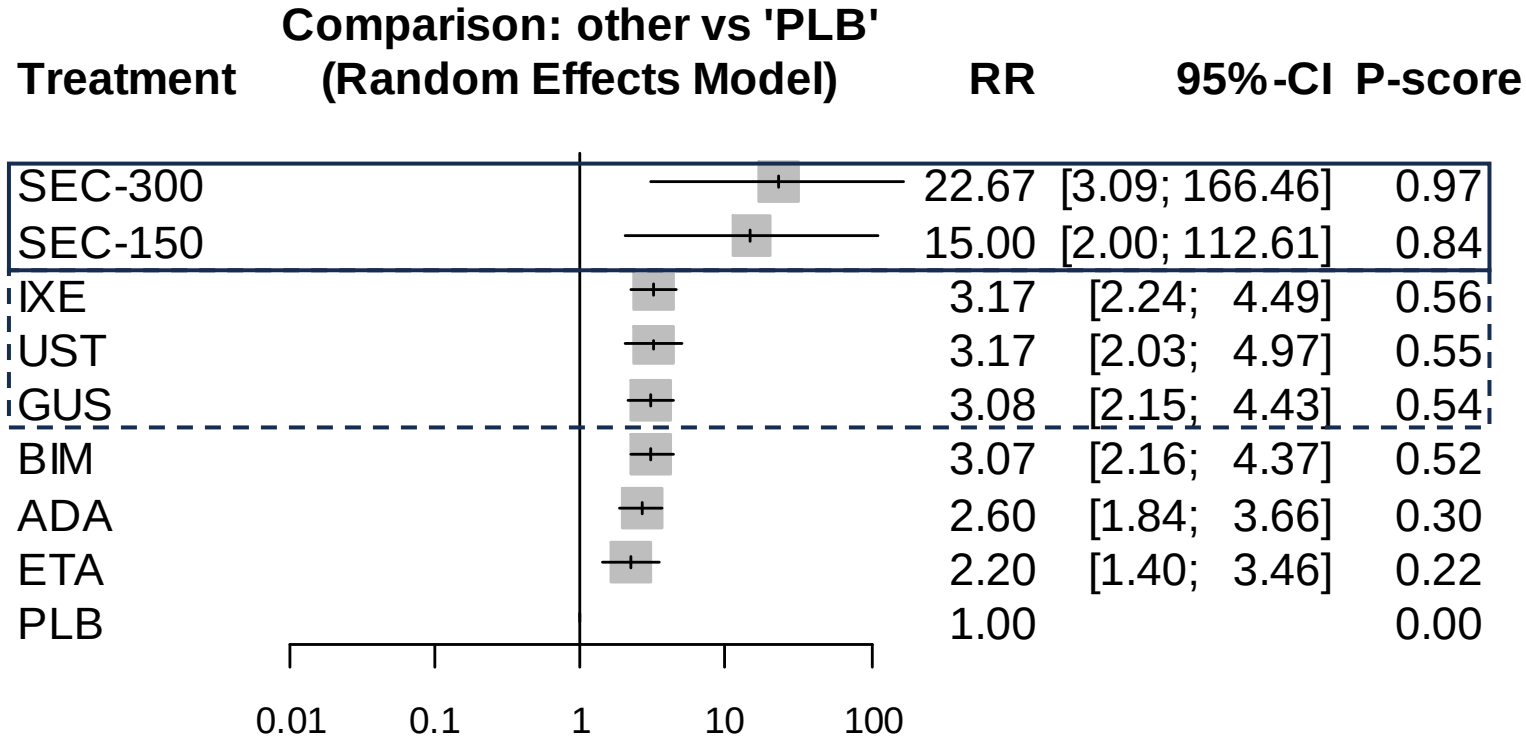
Direct vs. indirect evidence

✓ No significant differences observed

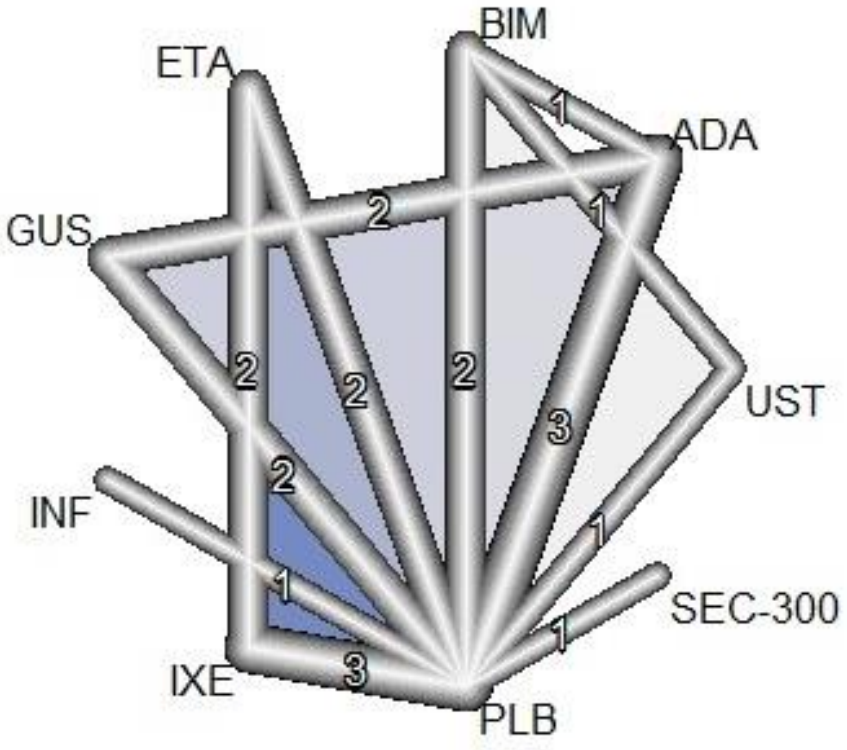


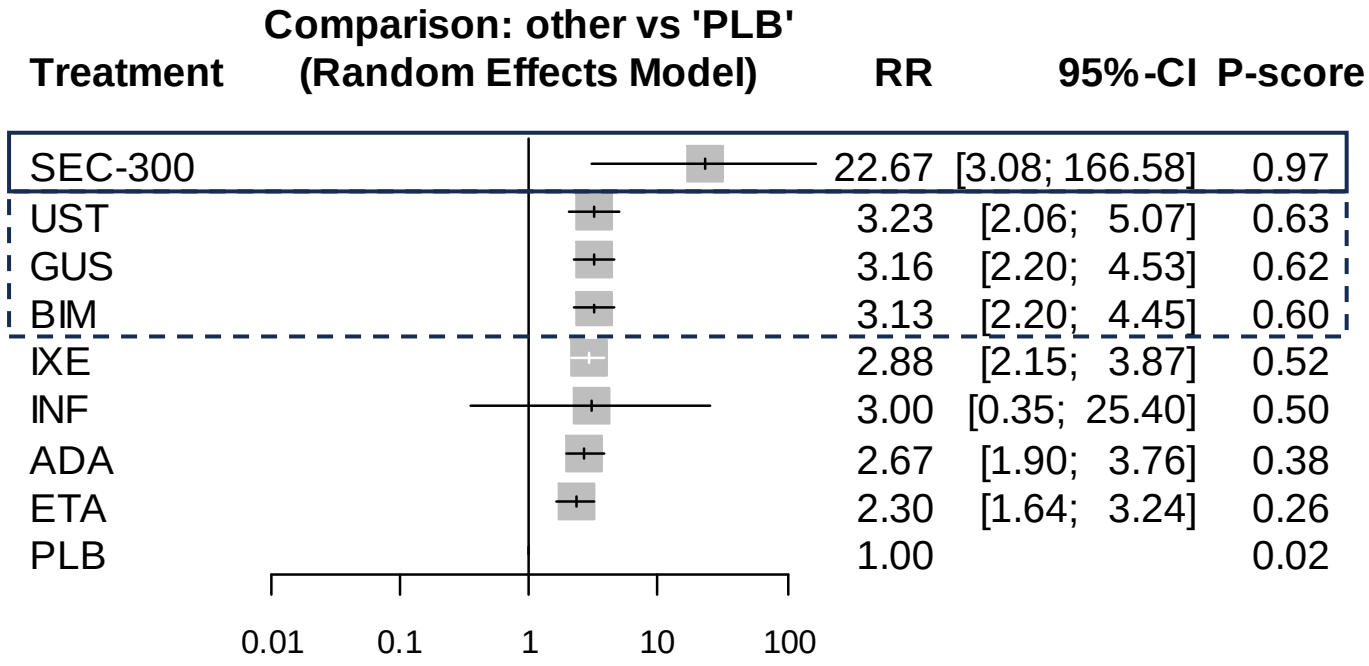
Sensitivity analysis: excluding “high” risk of bias RCTs



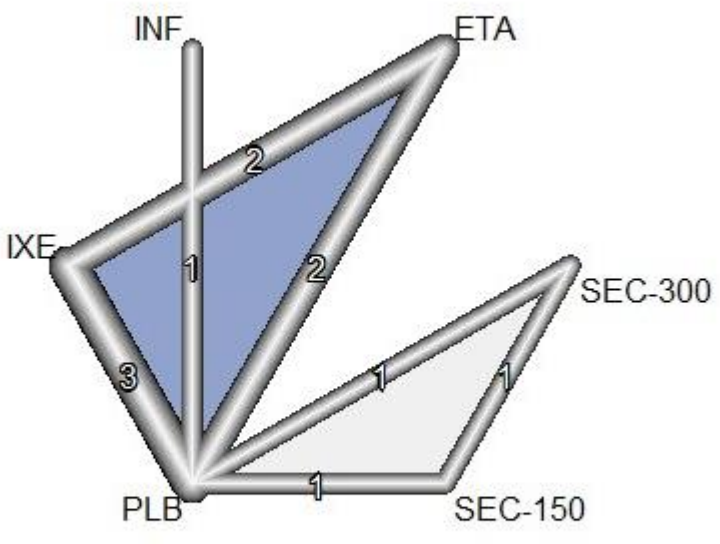


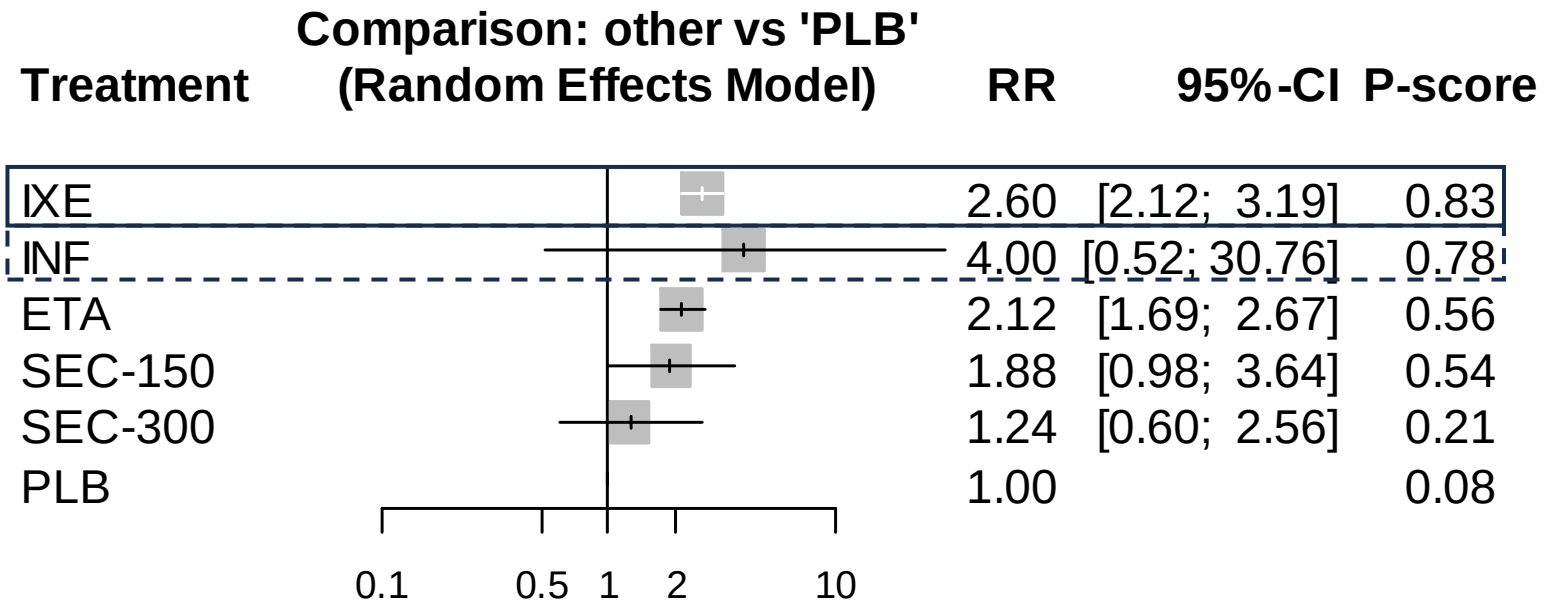
Sensitivity analysis: excluding SEC-150





PPASI75


INF
ETA
IXE
SEC-300
PLB
SEC-150
2
1
2
3
1
1
1


Comparison: other vs 'PLB'
Treatment
(Random Effects Model)
RR
95%-CI
P-score
IXE
2.60
[2.12; 3.19]
0.83
INF
4.00
[0.52; 30.76]
0.78
ETA
2.12
[1.69; 2.67]
0.56
SEC-150
1.88
[0.98; 3.64]
0.54
SEC-300
1.24
[0.60; 2.56]
0.21
PLB
1.00
0.08
0.1
0.5
1
2
10

Conclusions

- ✓ Greater comparative efficacy of on-label doses of secukinumab on clearing or almost clearing the palmoplantar skin
- ✓ ADA, BIM, GUS, IXE, and UST were more effective than PLB in clearing the skin
- ✓ PPASI50 and PPASI75 responses: IXE and INF are ranked best
- ✓ Secukinumab: most effective biologic in clearing the skin but not first for attenuation disease severity
- ✓ In NMAs investigating outcomes PPASI50 and PPASI75 the RCT that contributed data for secukinumab enrolled patients with pustular PP
- ✓ Varying efficacy of the agent between hyperkeratotic and pustular PP could justify these findings

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