ADALIMUMAB vs. IXEKIZUMAB EFFECTIVENESS IN PATIENTS WITH PSORIATIC ARTHRITIS: *A REAL-WORLD MULTICENTER STUDY WITH MATCH-ADJUSTED COMPARISONS*

GRAPPA Group for Research and Assessment of Psoriasis and Psoriatic Arthritis — Bogotà (CO), July 2025

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BACKGROUND

Real-world evidence (RWE) from routine clinical practice ***complements randomised controlled trials (RCTs),*** providing insights into more heterogeneous patient cohorts at lower operational cost. However, the lack of randomisation precludes direct drug comparisons. ***Developing reliable statistical methods for comparison would greatly enhance RWE's value.***

Direct RWE comparisons between Adalimumab (ADA) and Ixekizumab (IXE) in PsA are lacking.

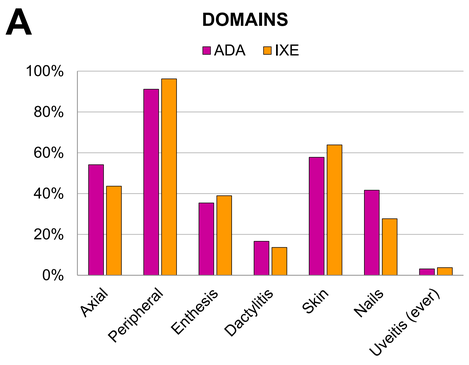
METHODS

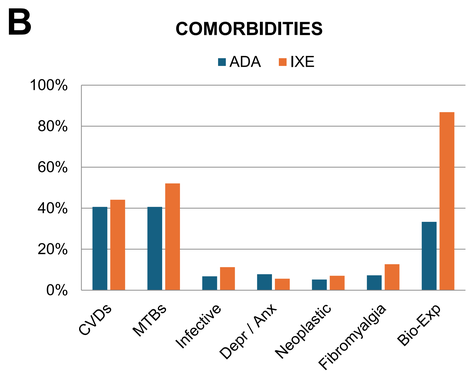
This multicentre real-world study ***aimed to compare*** the likelihood of patients achieving ***remission after treatment with ADA or IXE***, accounting for baseline characteristics and drug effectiveness.

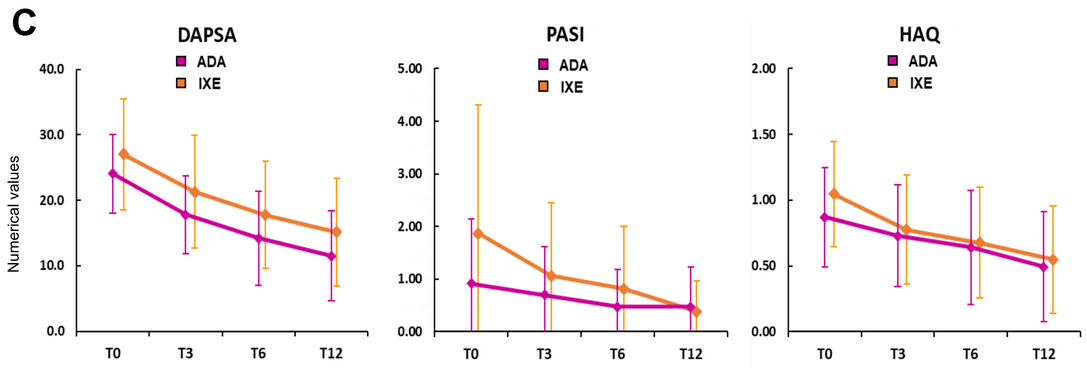
Clinical data, comorbidities, disease activity scores, and adverse events were retrospectively collected at ***baseline, 3, 6, and 12 months***. Primary outcomes included ***DAPSA, PASI, and HAQ scores***.

Logistic regression analysis assessed treatment allocation and ***factors associated with DAPSA remission at 1 year.***

The ***primary outcomes were then assessed using the average treatment effect (ATE)*** on the whole cohort ***after matching*** the study groups through a propensity score based on baseline covariates.







Figures: A. Distribution of PsA domains and **B.** comorbidities (from left to right) of interest in the ADA and IXE groups. **C.** Trend of DAPSA, PASI and HAQ scores (from left to right) from baseline to 12 months for ADA and IXE in visual comparison (not adjusted and not statistically relevant).

Abbreviations. ADA: Adalimumab; IXE: Ixekizumab; CVD: Cardiovascular Diseases; MTB: Metabolic Diseases; DAPSA: Disease Activity in Psoriatic Arthritis; DAPSA REM: DAPSA remission, expressed as DAPSA score ≤ 4; PASI: Psoriasis Area Severity Index; HAQ: Health Assessment Questionnaire; OR: Odds Ratio; SE: Standard Error; CI: Confidence Interval. Statistical analysis conducted by "R" software. P-values are considered significant and highlighted in bold when <0.05.

Table 1a. presents the ORs for the likelihood of being treated with IXE compared to ADA based on clinical factors. **Table 1b**. presents the ORs for the likelihood of achieving remission in terms of clinical characteristics. **Table 1c**. presents the average treatment effect (ATE) after full cohort matching using propensity score. For the binary outcome (DAPSA REM), results are reported as OR. For continuous outcomes (DAPSA, PASI, and HAQ at 1 year), results are given as mean differences (IXE vs. ADA).

RESULTS

A total of ***405 patients (47.4% ADA, 52.6% IXE)*** were enrolled.

Relevant differences at baseline between ADA and IXE groups (Fig. A-B):
- *Prevalence of bDMARD experienced patients higher in the IXE group* compared to ADA (66.7% vs 13.1%, respectively);
- *Metabolic comorbidieties more represented in the IXE group* (52.3% vs 41.1%, respectively);
- *Higher disease activity scores* (assessed by DAPSA, PASI and HAQ) in *the IXE group*.

PRE-MATCHING

Both ADA and IXE effectively *improved articular, cutaneous, and functional status* **at 1 year** (ΔDAPSA: -12.5 and -11.7, respectively, p < 0.0001; ΔPASI: -0.44 and -1.47, respectively, p < 0.01; ΔHAQ: -0.38 and -0.50, respectively, p < 0.0001) (Fig. C)

However, *numerically* higher proportion of DAPSA remission observed in the ADA group compared to IXE (21% vs 13%, respectively), **not statistically comparable pre-matching**.

Similar retention rates were observed for both drugs.

Logistic regression analysis (Tables 1 a-b) revealed that:
- Patients with *skin psoriasis and higher HAQ* score were *more likely to receive **IXE***;
- Patients with *axial or nail involvement*, as well as *smokers*, were *more likely to receive **ADA***;
- *Male gender* and the *absence of nail involvement* were associated with h*igher probability of **DAPSA remission**;*
- The ***probability of achieving DAPSA remission*** at 1 year was ***52% lower in the IXE group*** compared to the ADA group.

POST-MATCHING

*"Average Treatment Effect" (ATE) following propensity-score-matched analysis showed **no significant differences** in DAPSA remission rates* between ADA and IXE at **1 year** (Table 1c).

Furthermore, ***IXE*** *was significantly more effective than ADA in reducing* ***PASI*** (ΔPASI IXE vs ADA at 1 year: -0.28; p = 0.011; 95% CI: -0.503 to -0.065) and ***HAQ scores*** (ΔHAQ IXE vs ADA at 1 year: -0.10; p = 0.037; 95% CI: -0.189 to -0.006) (Table 1c).

Table 1a – Probability of being treated with IXE versus ADA based on patients' clinical characteristics.

	OR [IC95%]	p-value
Intercept	0.36 [0.11-1.09]	0.076
Smoker vs Non-smoker	0.40 [0.21-0.75]	**0.005**
Axial involvement, yes vs no	0.56 [0.35-0.87]	0.011
Skin psoriasis, yes vs no	2.29 [1.39-3.80]	**0.001**
Nail psoriasis, yes vs no	0.37 [0.22-0.61]	**<0.001**
Metabolic diseases, yes vs no	1.48 [0.94-2.39]	0.093
Baseline C-reactive protein	1.04 [0.91-1.22]	0.592
Baseline HAQ	1.83 [1.11-3.06]	**0.019**
Baseline DAPSA score	1.01 [0.99-1.04]	0.395

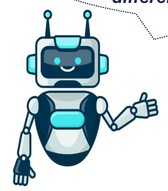
Table 1b – Factors associated with the probability of achieving remission.

	OR [CI 95%]	p-value
Intercept	1.19 [0.23-5.82]	0.828
IXE vs ADA	0.48 [0.24-0.94]	**0.035**
Male vs Female	2.45 [1.27-4.78]	**0.008**
Axial involvement, yes vs no	0.85 [0.42-1.69]	0.638
Peripheral involvement, yes vs no	1.09 [0.36-3.83]	0.886
Enthesitis, yes vs no	0.66 [0.31-1.37]	0.278
Nail psoriasis, yes vs no	0.38 [0.17-0.79]	**0.013**
Cardiovascular diseases, yes vs no	0.62 [0.29-1.28]	0.201
Metabolic diseases, yes vs no	0.69 [0.32-1.43]	0.320
Baseline HAQ	0.64 [0.3-1.34]	0.248
Baseline DAPSA score	0.97 [0.93-1.01]	0.196

Table 1c – Average Treatment Effect following propensity-score-matched analysis

	OR [CI 95%]	p-value
DAPSA REM (IXE vs ADA), yes vs no	0.62 [0.34-1.14]	0.120
	Mean Diff. ± SE	**p-value**
DAPSA at 1 year (IXE vs ADA)	0.78 ± 0.94	0.410
PASI at 1 year (IXE vs ADA)	-0.28 ± 0.11	**0.011**
HAQ at 1 year (IXE vs ADA)	-0.097 ± 0.047	**0.036**

«ATE represents the mean difference in outcomes between patients treated with a specific therapy (exposed) and those not treated (or receiving a different treatment) (unexposed)»



Propensity Bot 3000

DAPSA REM T12
OR: 0.62
CI: 0.34-1.14
p= 0.120

DAPSA SCORE T12
MD: 0.78
Err. Stand.: ± 0.94
p= 0.410

PASI SCORE T12
MD: -0.28
Err. Stand.: ± 0.11
p= 0.011

HAQ T12
MD: -0.097
Err. Stand.: ± 0.047
p= 0.036

CONCLUSION

In a «real-world» setting, ***both ADA and IXE*** demonstrated *similar improvements in disease activity and functional status* of PsA patients, although *ADA* appeared *more effective* in achieving *DAPSA remission*. *However*, ***no differences*** in achieving *DAPSA remission* were observed *after match-adjusting for baseline differences*; and ***IXE*** *showed* ***more effective*** *than ADA in* ***skin outcomes***, aligning with H2H RCT findings. Match-adjusted comparison is a promising strategy for evaluating drug effectiveness in real-world settings, but these findings require confirmation through additional studies.