5° ΠΑΝΕΛΛΗΝΙΟ ΘΕΡΙΝΟ ΣΥΜΠΟΣΙΟ
ΜΥΟΣΚΕΛΕΤΙΚΗΣ ΥΓΕΙΑΣ

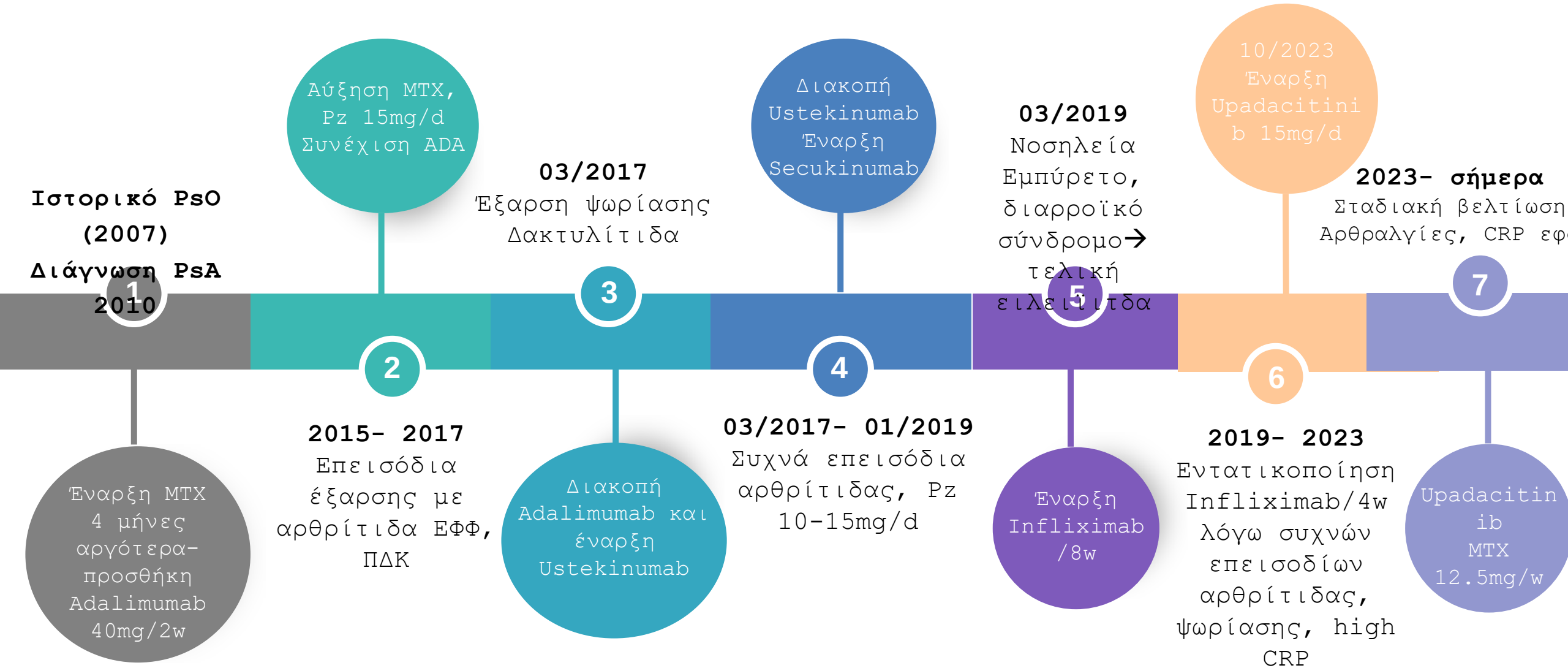
Νεότερες θεραπευτικές εξελίξεις στις ΣπΑ: νεότεροι JAK αναστολείς, διπλή αναστολή Il-17, νανοσωματίδια

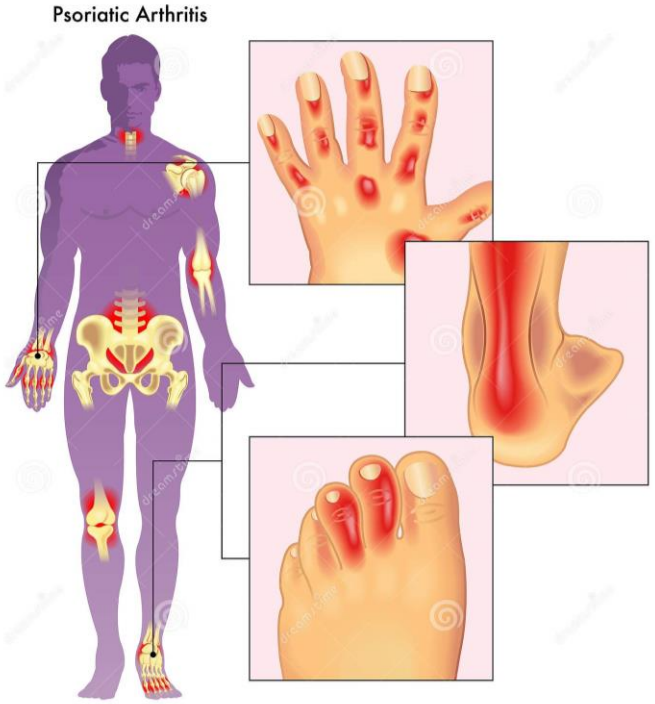
Μαρία Παππά

Επιμελήτρια Β' Ρευματολογίας
Μονάδα Ρευματολογίας- ΠΓΝ «ΑΤΤΙΚΟΝ»

11.05.2025

Περίπτωση ασθενούς #1





Ψωριασική Αρθρίτιδα

Εγκεκριμένες Θεραπείες της ΨΑ

Immunosuppressants	Methotrexate, Leflunomide, Sulfasalazine, Cyclosporine
PDE4 Inhibitors	Apremilast
JAK/ TYK2 inhibitors	Tofacitinib, Upadacitinib

Biologic Therapies

TNF-a inhibitor	Adalimumab, Certolizumab pegol, Etanercept, Infliximab, Golimumab
IL-12/23	Ustekinumab
IL-17 inhibitor	Secukinumab, Ixekizumab, Bimekizumab
IL-23 inhibitor	Guselkumab, Risankizumab

Table 1. JAK inhibitors currently approved by the European Medicines Agency for adult rheumatic diseases.

JAK Inhibitor	Selectivity	Diseases						First Approval in EMA
		RA	PsA	UC	nr-AxSpA	AS	CD	
Tofacitinib	JAK 1,2,3	✓	✓	✓		✔		2017
Baricitinib	JAK 1,2	✓				□		2017
Upadacitinib	JAK 1	✓	✓	✓	✓	✓	✓	2019
Filgotinib	JAK 1	✓		✓				2020

Efficacy Results (SELECT-PsA 1)

Biologic-naïve PsA patients

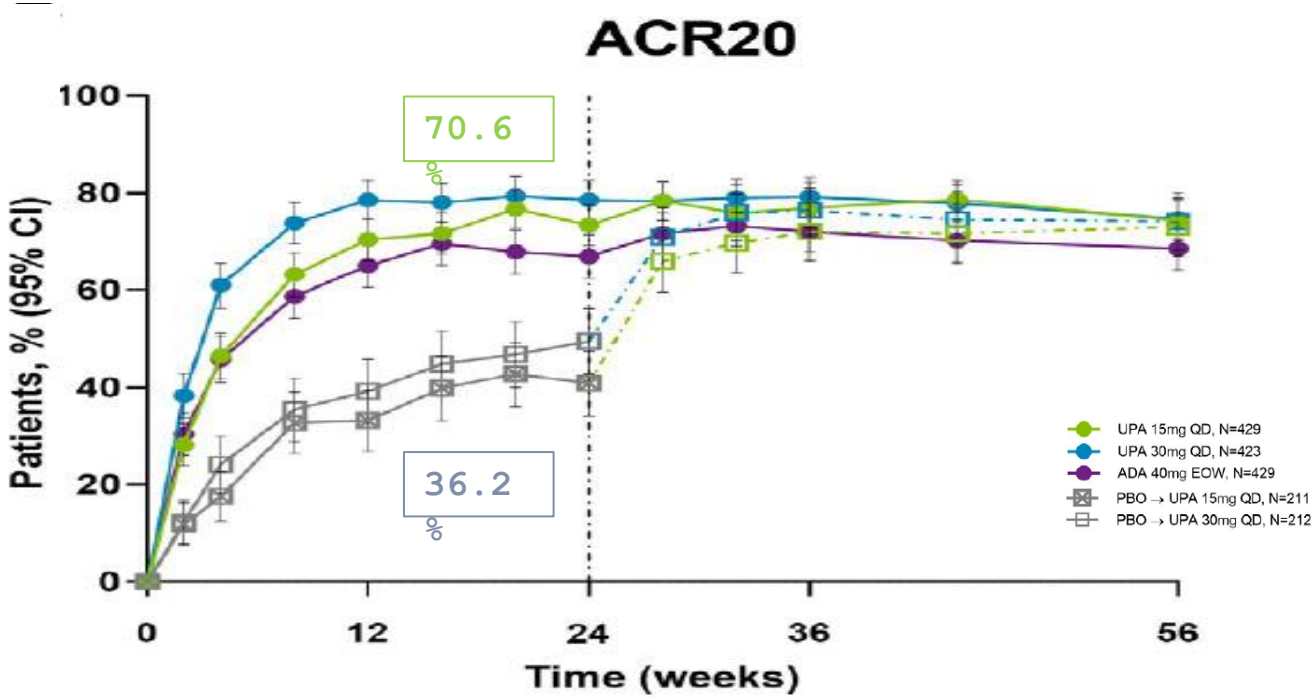
ACR20 Response at Week 12:

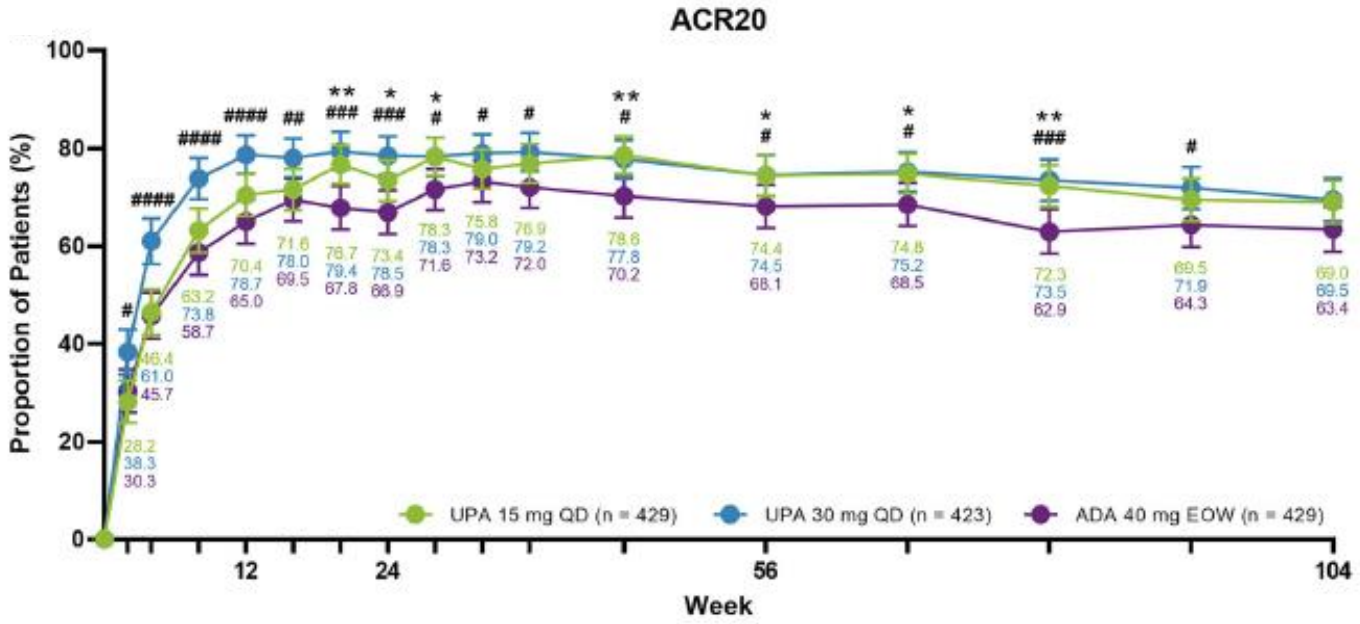
- Upadacitinib 15 mg: ~71%
- Adalimumab: ~65%
- Placebo: ~36%

Significant improvements in:

- Skin lesions (PASI scores)
- Physical function (HAQ-DI)
- Enthesitis and dactylitis

Response was maintained throughout w104





McInnes IB et al. RMD Open 2021;7:e001838

Efficacy Results (SELECT-PsA 2)

bDMARD-IR PsA patients

ACR 20 Response at Week 12:

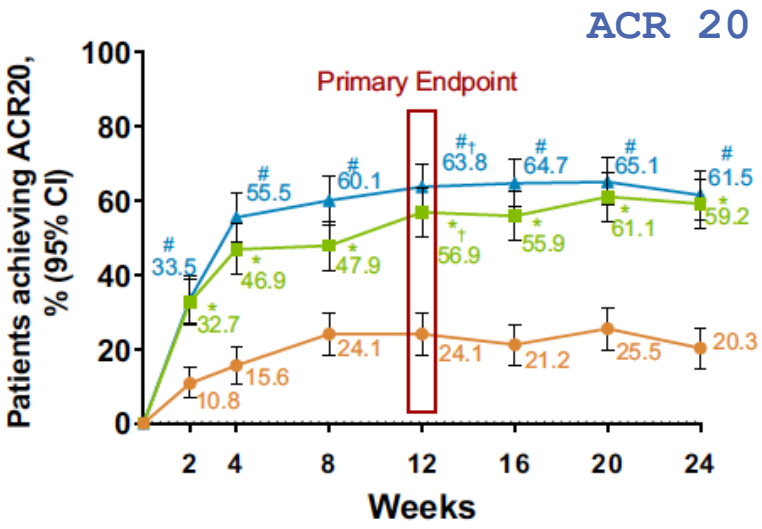
- Upadacitinib 15 mg: ~57%
- Upadacitinib 30 mg : ~64%
- Placebo: ~24%

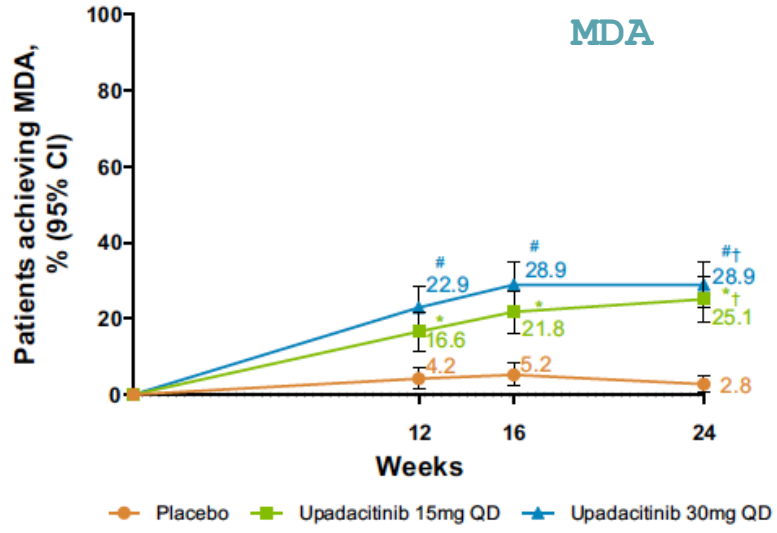
Open- Label extension study until week 152:

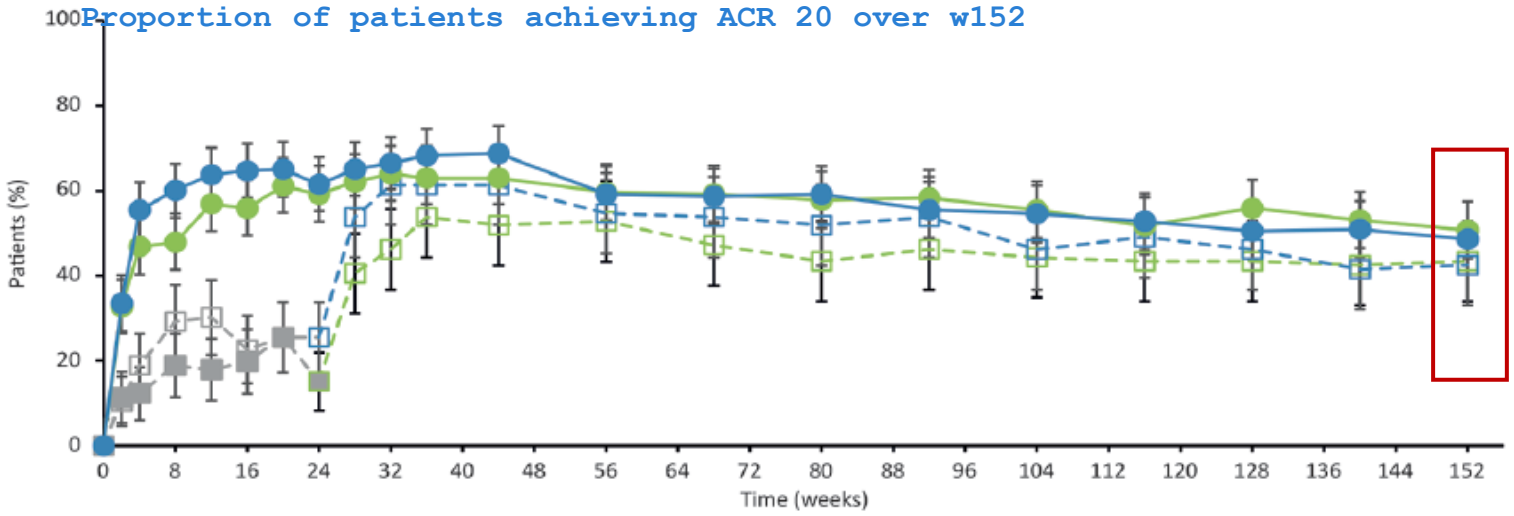
ACR 20 Responses sustained

- Upadacitinib 15 mg: ~50%
- Upadacitinib 30 mg : ~48%

MDA achieved by up to 44%







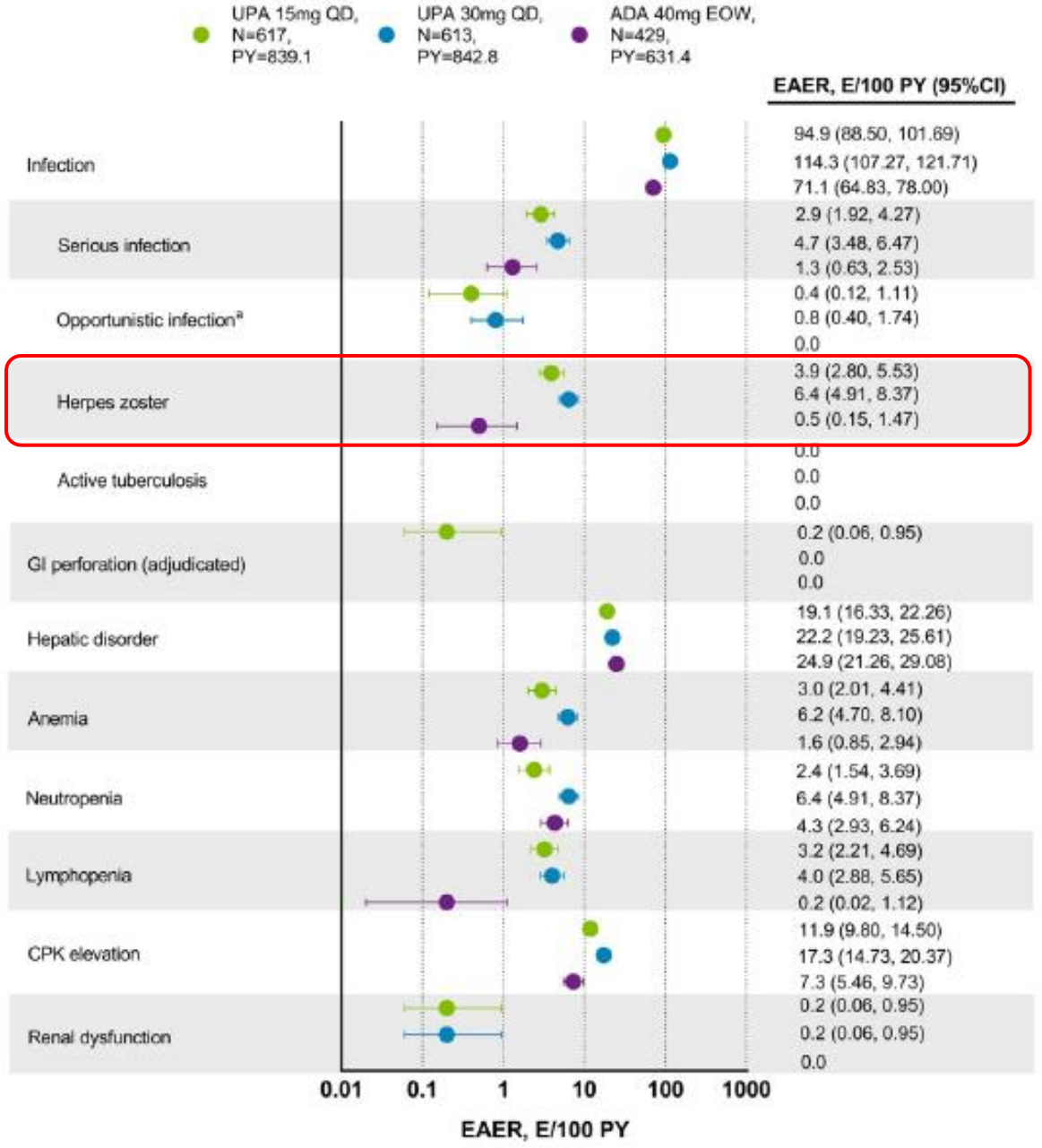
Mease PJ et al. ARD 2021;80:312-320

Προφίλ Ασφάλειας

- Common adverse events:
  - Upper respiratory infections
  - Nausea
  - Creatine phosphokinase elevation

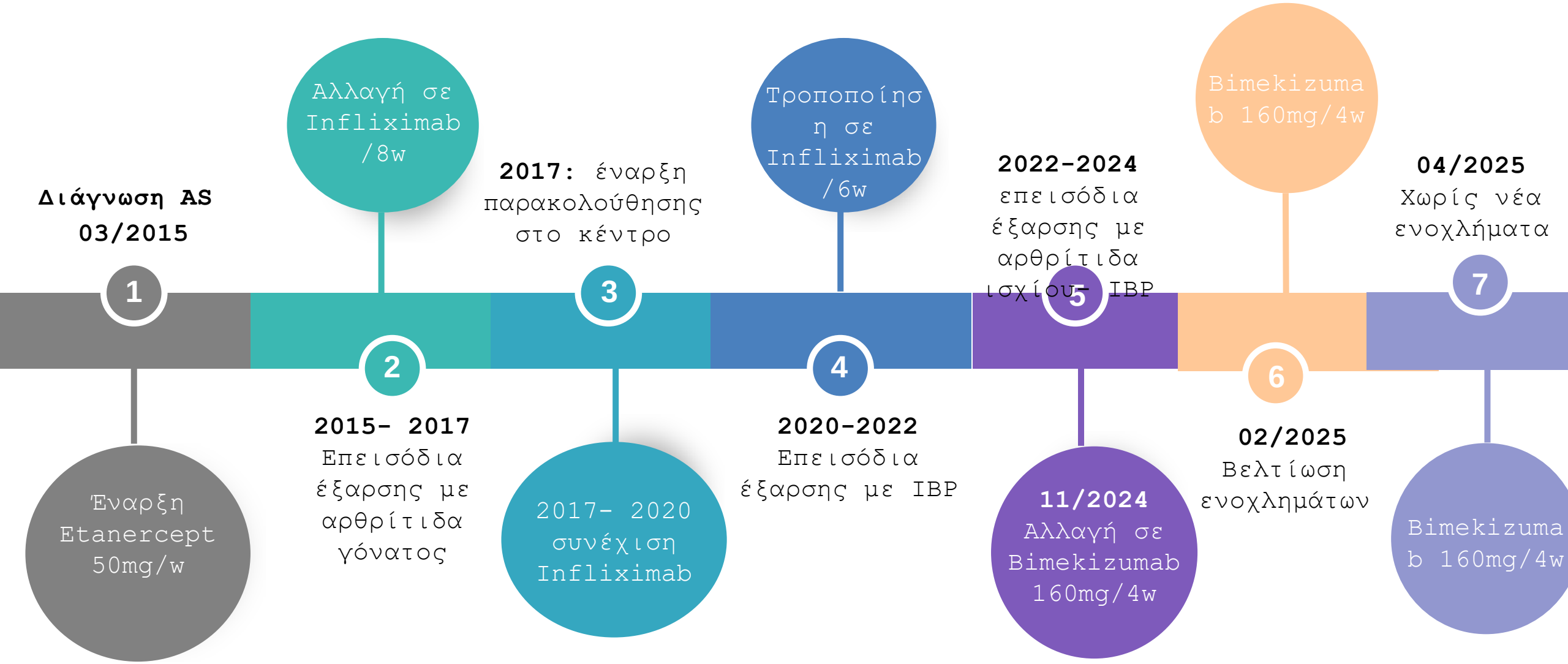
- Serious adverse events:
- - Infections (e.g., herpes zoster)

- Comparable safety profile to other JAK inhibitors

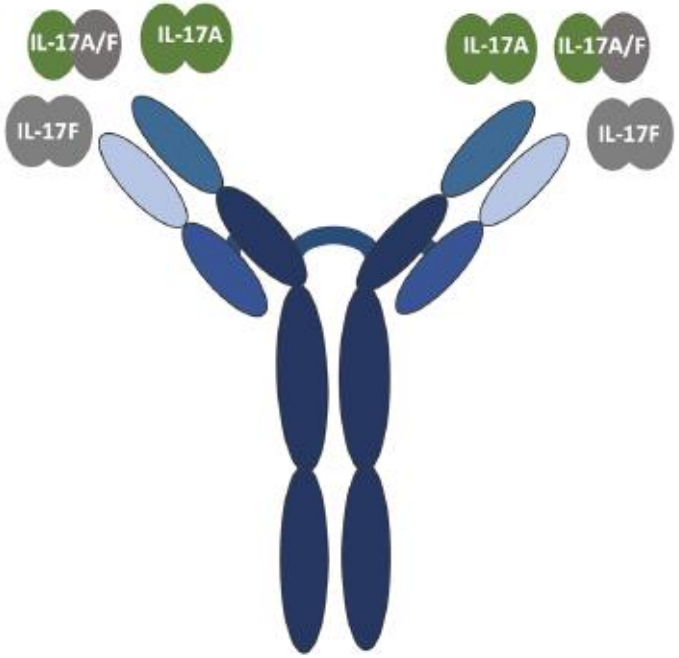


McInnes IB et al. RMD Open 2021;7:e001838

Περίπτωση ασθενούς #2



What is Bimekizumab



- Μονοκλωνικό αντίσωμα έναντι Il-17A και IL-17F

- Ενδείξεις:
  - plaque psoriasis
  - PsA
  - axial SpA
  - hidradenitis suppurativa

- *Μηχανισμός δράσης:* Διπλή εξουδετέρωση Il-17A και IL-17F

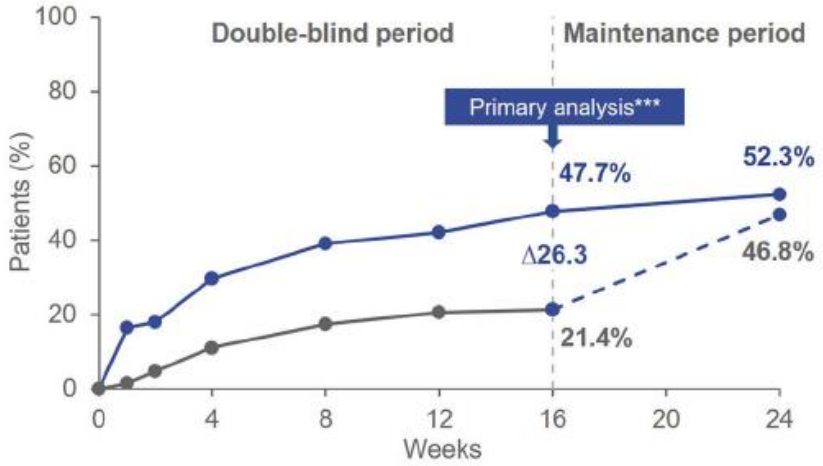
EXTENDED REPORT

Dual IL-17A and IL-17F neutralisation by bimekizumab in psoriatic arthritis: evidence from preclinical experiments and a randomised placebo-controlled clinical trial that IL-17F contributes to human chronic tissue inflammation

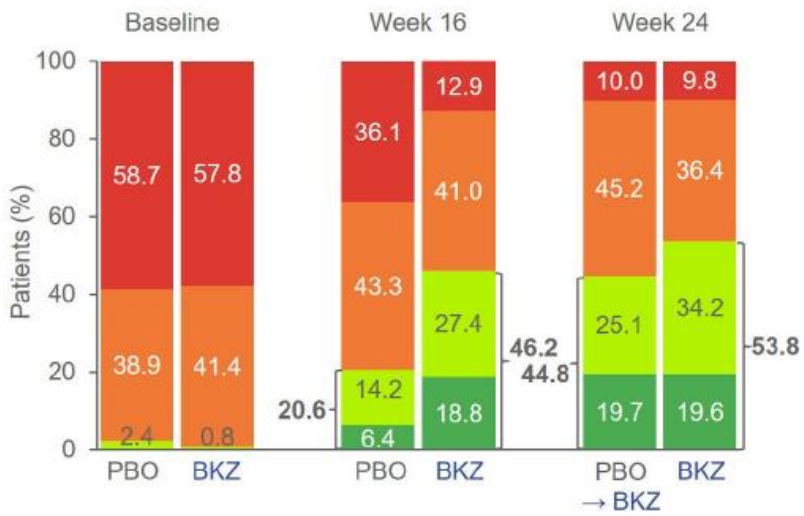
Sophie Glatt,[1] Dominique Baeten,[2,3] Terry Baker,[4] Meryn Griffiths,[5] Lucian Ionescu,[3] Alastair D G Lawson,[4] Ash Maroof,[5] Ruth Oliver,[1] Serghei Popa,[6] Foteini Strimenopoulou,[1] Pavan Vajjah,[1] Mark I L Watling,[1] Nataliya Yeremenko,[2] Pierre Miossec,[7] Stevan Shaw[5]

BE MOBILE 1 (nr-axSpA)- 254

ASAS 40

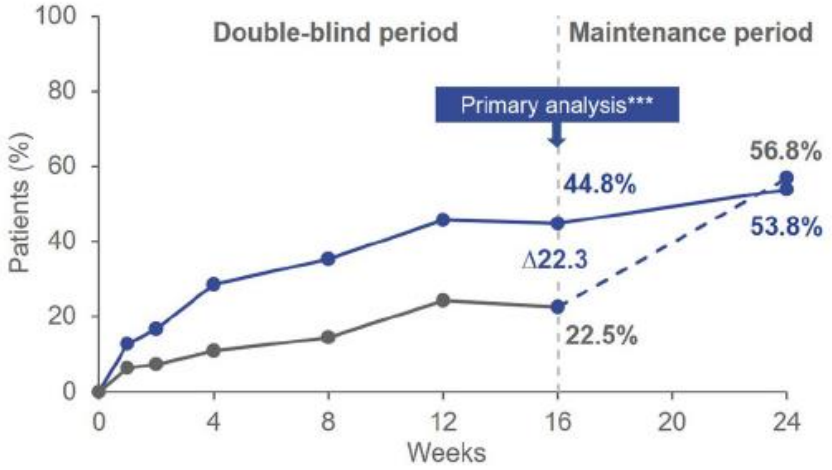


ASDAS

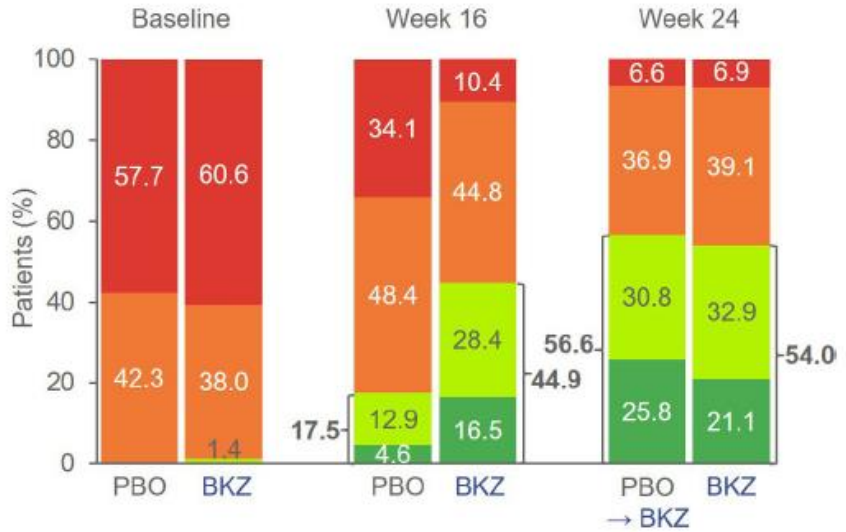


BE MOBILE 2 (r-axSpA)- 332

ASAS 40



ASDAS



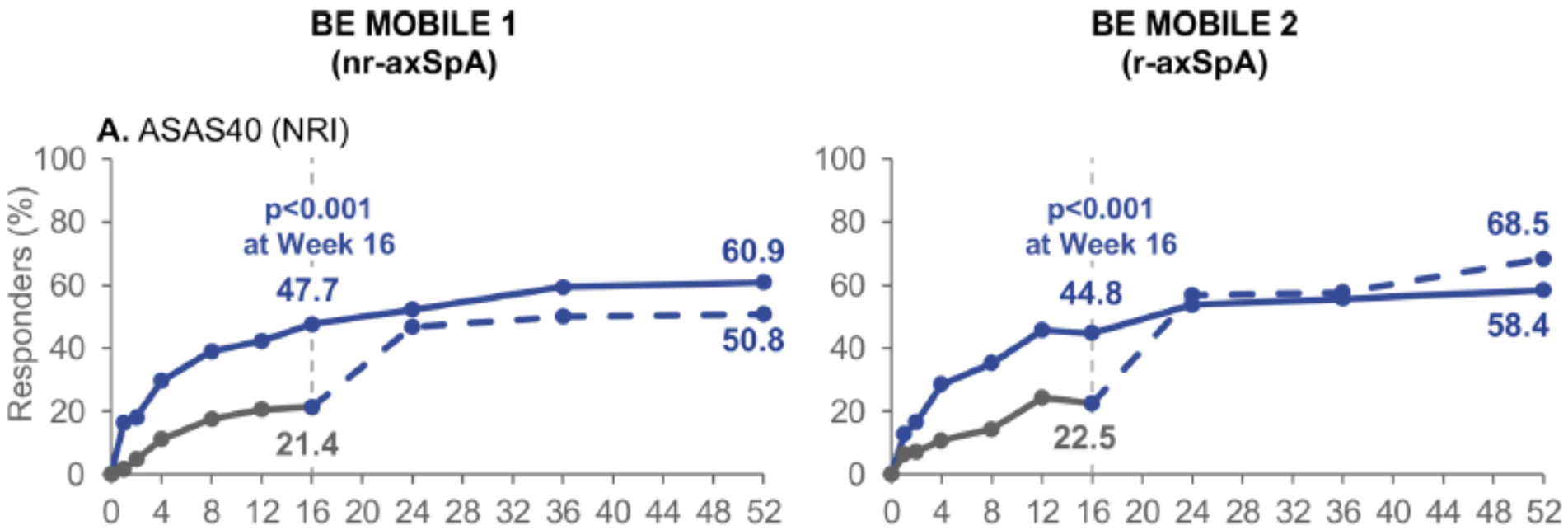
Van de Heijde et al. ARD 2023;82:515- 526

CLINICAL SCIENCE

Bimekizumab treatment in patients with active axial spondyloarthritis: 52-week efficacy and safety from the randomised parallel phase 3 BE MOBILE 1 and BE MOBILE 2 studies

Xenofon Baraliakos ,[1] Atul Deodhar ,[2] Désirée van der Heijde ,[3] Marina Magrey,[4] Walter P Maksymowych ,[5] Tetsuya Tomita,[6] Huji Xu ,[7] Ute Massow,[8] Carmen Fleurinck,[9] Alicia M Ellis,[10] Thomas Vaux,[11] Julie Shepherd-Smith,[11] Alexander Marten,[8] Lianne S Gensler [12]

BKZ demonstrated sustained efficacy over 52 weeks in axSpA

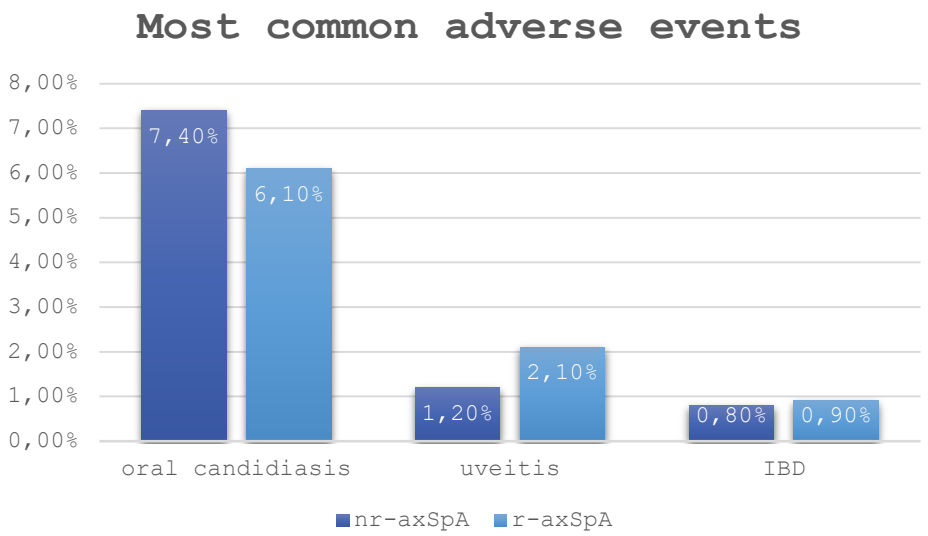


Προφίλ ασφάλειας

CLINICAL SCIENCE

Bimekizumab treatment in patients with active axial spondyloarthritis: 52-week efficacy and safety from the randomised parallel phase 3 BE MOBILE 1 and BE MOBILE 2 studies[1]

Xenofon Baraliakos ,[1] Atul Deodhar ,[2] Désirée van der Heijde ,[3] Marina Magrey,[4] Walter P Maksymowych ,[5] Tetsuya Tomita,[6] Huji Xu ,[7] Ute Massow,[8] Carmen Fleurinck,[9] Alicia M Ellis,[10] Thomas Vaux,[11] Julie Shepherd-Smith,[11] Alexander Marten,[8] Lianne S Gensler [12]



RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Long-term safety of bimekizumab in adult patients with axial spondyloarthritis or psoriatic arthritis: pooled results from integrated phase IIb/III clinical studies[2]

Philip J Mease ,[1,2] Lianne S Gensler,[3] Ana-Maria Orbai ,[4] Richard B Warren,[5,6] Rajan Bajracharya,[7] Barbara Ink,[7] Alexander Marten,[8] Ute Massow,[8] Vishvesh Shende,[7] Myriam Manente,[9] Luke Peterson,[10] Katy White,[7] Robert Landewé ,[11,12] Denis Poddubnyy [13,14]

Results

In patients receiving bimekizumab across all treatment periods:

Patients with ≥1 TEAE:

axSpA	PsA
752 (88.7%)	1,170 (83.2%)

Discontinued study due to TEAEs:

axSpA	PsA
54 (6.4%)	79 (5.6%)

The **3 most frequent** TEAEs with bimekizumab across axSpA and PsA were:

- SARS-CoV-2 (COVID-19) infection
- Nasopharyngitis (common cold)
- Upper respiratory tract infection

Incidence rates (EAIR/100 PY) of safety topics of interest **were low** and **decreased or remained stable with longer bimekizumab exposure:**

- Oral candidiasis: axSpA: **3.7** PsA: **4.2**
- Adjudicated probable/definite inflammatory bowel disease: axSpA: **0.8** PsA: **0.3**
- Uveitis: axSpA: **1.2** PsA: **0.0**

Most fungal infections (including *Candida* infections) were **mild/moderate; none were systemic**

EAIRs of **hepatic events, adjudicated MACE** and **adjudicated suicidal ideation/behaviour** remained **low**

[1] Baraliakos X et al. Ard-2023-224803

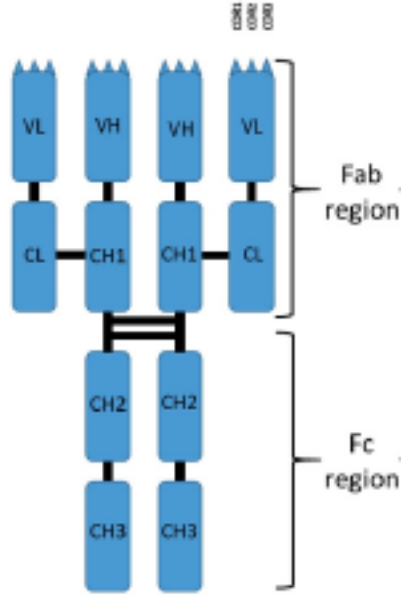
[2] Mease PJ et al. Rmdopen-2024-005026

Nanobodies

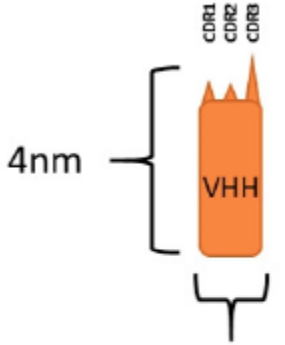
A Revolutionary Class of Therapeutic and Diagnostic Tools

What are Nanobodies

- Small (~15 kDa) antibody fragments from heavy-chain-only antibodies
- No light chains
- **Compact and stable**
- Unique CDR3 for enhanced antigen recognition
- **High solubility and protease resistance**



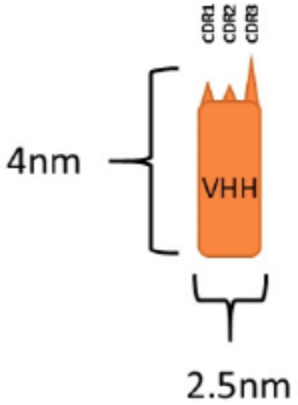
Conventional m(IgG)Ab
~150 kDa



VHH (Nb)
~15 kDa

Alexander Elena, et al. Journal of Nanobiotechnology (2024)22;661

Advantages and Applications



Advantages over conventional Abs

- ✓ Smaller size: 15 kDa
- ✓ Higher stability
- ✓ Excellent tissue penetration
- ✓ Low immunogenicity
- ✓ Blood- brain barrier penetration: Possible
- ✓ Easier production

Applications

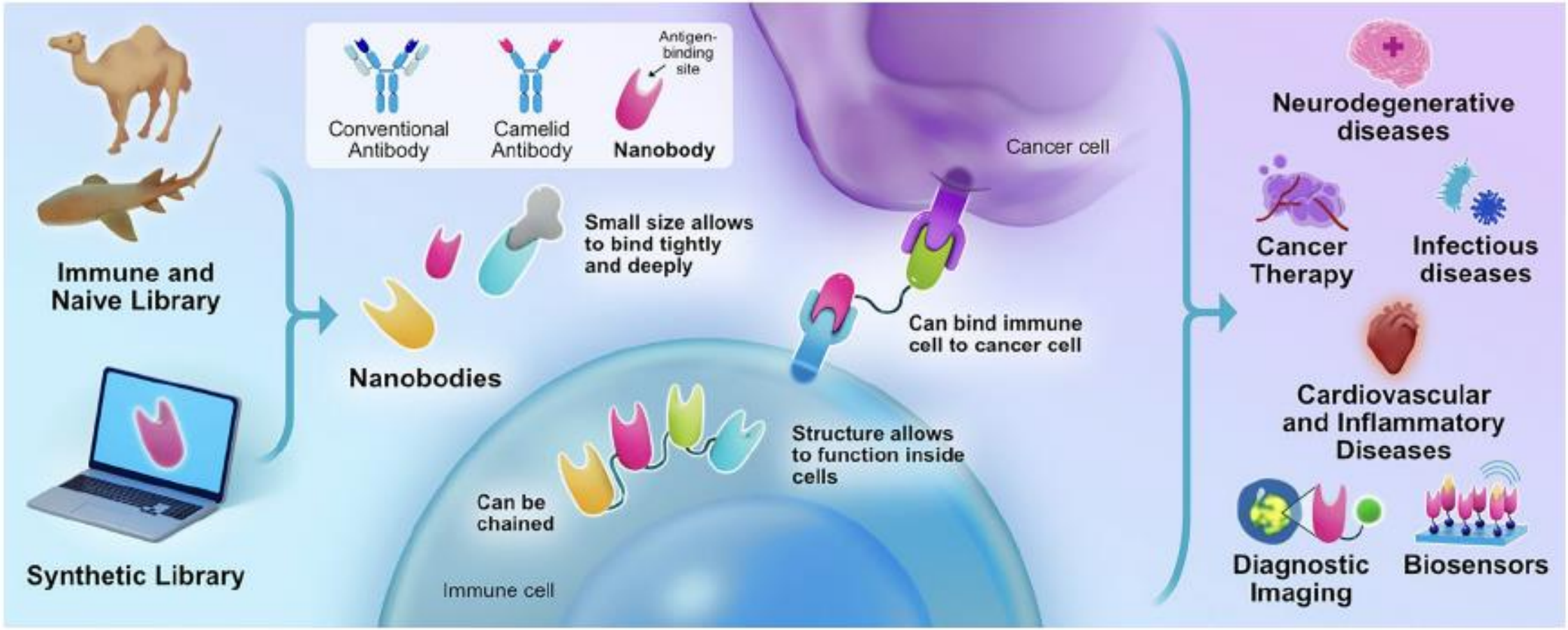
Therapeutic:

- ✓Hematology- oncology
- ✓Infectious Diseases
- ✓Neurology
- ✓Autoimmune diseases

Diagnostic

Alexander Elena, et al. Journal of Nanobiotechnology (2024)22;661

Production, structure and applications of nanobodies



Alexander Elena, et al. Journal of Nanobiotechnology (2024)22;661

Izokibep demonstrates efficacy benefits in patients with active PsA: results from a 16-week randomized, placebo-controlled phase 2 clinical trial

- Izokibep is an IL-17A inhibitor fusion protein, attached to albumin
- Multicenter, randomized, double-blind, placebo-controlled, study of placebo, izokibep 40mg Q2W or 80mg Q2W in active PsA pts csDMARD-IR and/or bDMARD-IR. ACR50 was the primary endpoint at W16
- ACR50 at W16: 13% in PBO vs 48% (p=0.0014) in 40mg vs 52% (p=0.0006) in 80mg. MDA at W16 was achieved in 42% (40mg) vs 39% (80mg) vs 5% (PBO)
- Izokibep showed **high levels of response rates** across multiple

Composite Endpoint	Placebo Q2W	Izokibep 40 mg Q2W	Izokibep 80 mg Q2W	Placebo Q2W	Izokibep 40 mg Q2W *p-value**	Izokibep 80 mg Q2W *p-value**
Number observations	*N=44*	*N=44*	*N=47*	*N=43*	*N=42*	*N=46*
	Week 4 (descriptive)			Week 16		
ACR20, % Response	16%	41%	45%	26%	60% *0.0028*	75% *<0.0001*
ACR50, % Response	1%	18%	21%	13%	48% *0.0014*	52% *0.0006*
ACR70, % Response	0%	9%	4%	5%	27% *0.0101*	18% *0.0678*
DAS28-CRP, Mean CFB**	0.19	0.88	0.96	0.64	1.54	1.66
DAPSA, Mean CFB**	4.6	15.4	17.7	13.0	24.8	28.6
MDA, % Response	3%	23%	20%	5%	42% *0.0020*	39% *0.0032*
	Subpopulation with Psoriasis-BSA > 3% at Baseline (74 of 135, 55%)					
Number observations	*N=23*	*N=28*	*N=23*	*N=23*	*N=23*	*N=28*
PASI75, % Response	0%	35%	25%	14%	83%	85%
PASI90, % Response	0%	22%	14%	14%	57%	48%
PASI100, % Response	0%	9%	7%	5%	39%	38%

Full Analysis Set (FAS)
Logistic regression model with fixed factors treatment, visit, treatment by visit interaction, previous TNFi exposure, concomitant csDMARD use, country (pooled), baseline covariate and baseline by visit interaction and random factor subject
* Two-sided p-value derived by using estimated difference between treatments and Placebo at Week 16
** Change from baseline

Behrens F, Taylor P, et al. Arthritis Rheumatology 2022; 74

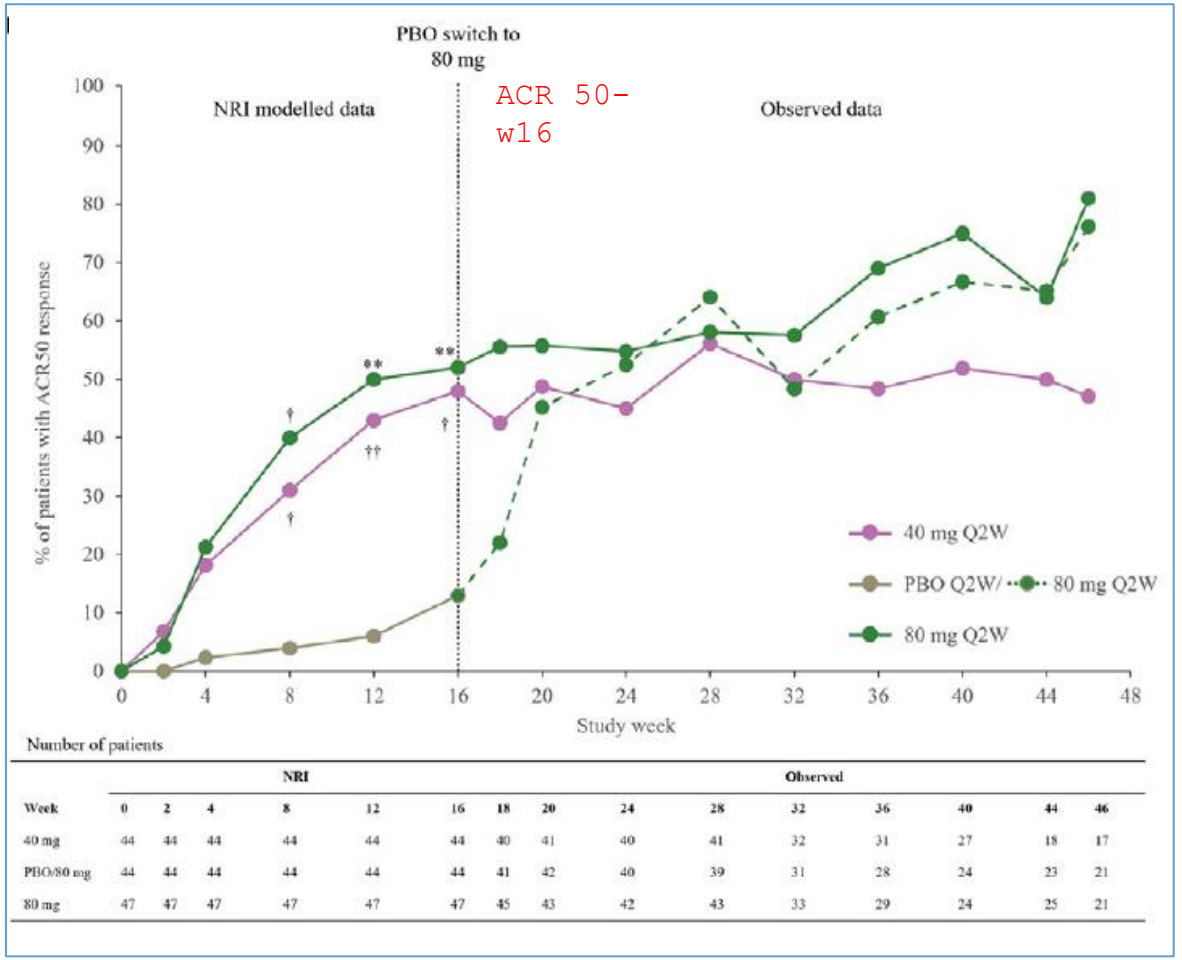
Psoriatic arthritis

Efficacy and safety of izokibep in patients with active psoriatic arthritis: a randomised, double-blind, placebo-controlled, phase 2 study

Peter C. Taylor[1,*], Philip J. Mease[2], Kurt de Vlam[3,4], Shephard Mpofu[5], Dieter Wetzel[6], Anne M. Stevens[5,7], Brian Wiens[5], Lisa Osterling Koskinen[8], Sven Ohlman[8], Joachim Feldwisch[8], Fredrik Y. Frejd[8], Nikolai C. Brun[8], Jan Brandt-Juergens[9], Edit Drescher[10], Eva Dokoupilova[11,12], Anna Rowińska-Osuch[13], Nadia Abdel-Kader Martin[14], Frank Behrens[15,16]

Phase 2, double-blind, placebo-controlled study: 135 patients:

- ✓ Primary end-point: **52%** in Izokibep 80mg vs **13%** in PBO (p=0.0006)
- ✓ Improvements in PASI 100, enthesitis, dactylitis
- ✓ PROs also showed improvements



Number of patients

	NRI										Observed					
Week	0	2	4	8	12	16	18	20	24	28	32	36	40	44	46	
40 mg	44	44	44	44	44	44	40	41	40	41	32	31	27	18	17	
PBO/80 mg	44	44	44	44	44	44	41	42	40	39	31	28	24	23	21	
80 mg	47	47	47	47	47	47	45	43	42	43	33	29	24	25	21	

Taylor P, et al. ARD 2025

Efficacy and safety of **Sonelokimab**, a novel IL-17A and IL-17F inhibiting nanobody in patients with active PsA: Results from the global, randomized, double- blind, placebo- controlled phase 2 ARGO trial

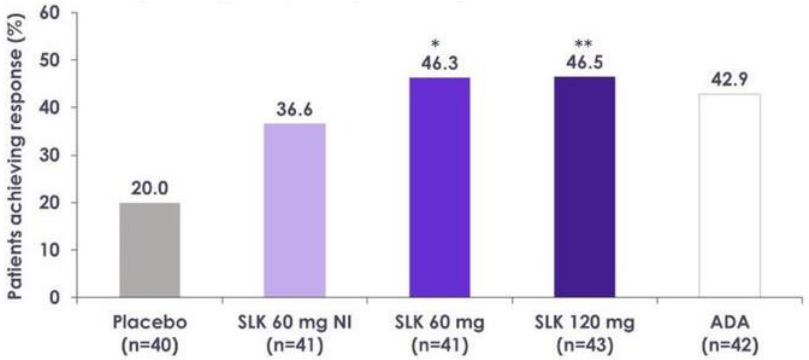
- Sonelokimab is a trivalent nanobody with 3 binding components to Il-17F, Il-17A/F and albumin

- ARGO trial: study of placebo, sonelokimab 60mg Q4W or sonelokimab 120mg Q4W or ADA Q2W in active PsA pts. ACR50 was the primary endpoint at W12.

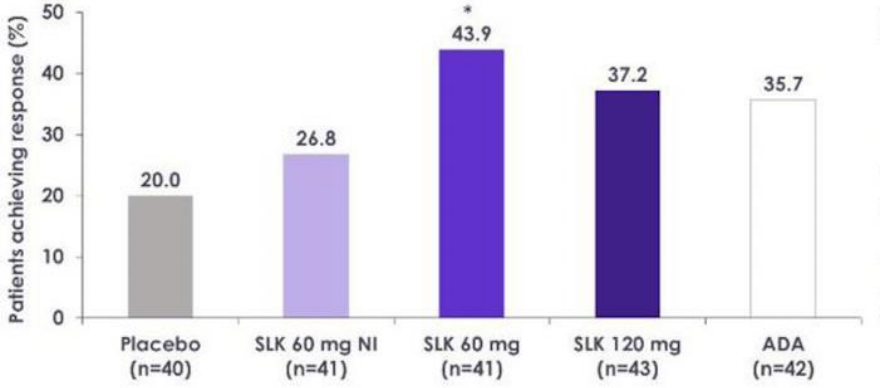
- ACR50 at W12: 20% in PBO vs 46.3% (p=0.012) in 60mg vs 46.5% (p=0.009) in 120mg. MDA at W12 was achieved in 44% (60mg) vs 37% (120mg) vs 20% (PBO)

- Sonelokimab showed **rapid onset** and **high levels of response rates** in

ACR50 at W12



MDA at W12



Mc Innes I. B, et al. ARD 2024