Markers of IL-17 Signalling in the Blood of Patients with Psoriatic Arthritis with Inadequate Response to Tumour Necrosis Factor Inhibitors

Iain B. McInnes,[1,*] Ioana Cutcutache,[2,*] Leon Eyrich Jessen,[3] Magnus Petersen,[4] Melanie Randahl Nielsen,[3] Marie Skougaard,[4,5] Victoria Svinti MacLeod,[2] Andrew Skelton,[2] Adam R. Prickett,[2] Stevan Shaw[2]

[1]College of Medical Veterinary and Life Sciences, University of Glasgow, Glasgow, UK; [2]UCB, Slough, UK; [3]Department of Health Technology, Section for Bioinformatics, Technical University of Denmark, DTU, 2800 Kgs Lyngby, Denmark; [4]The Parker Institute, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Denmark; [5]Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark

*Iain B. McInnes and Ioana Cutcutache jointly contributed to this study

To access the presentation, scan the QR code

Link expiration: 12 September 2025

EULAR 2025 | Barcelona, Spain | 11–14 June 2025

Presentation number: OP0091

Disclosures & Acknowledgements

Disclosures

IBM: Consulting fees and honoraria from AbbVie, AstraZeneca, BMS, Boehringer Ingelheim, Cabaletta, Causeway Therapeutics, Celgene, Eli Lilly and Company, Evelo, Janssen, MoonLake Immunotherapeutics, Novartis and UCB; research support from BMS, Boehringer Ingelheim, Celgene, Janssen, Novartis and UCB. **IC, ARP, AS, SS:** Employees and shareholders of UCB. **LEJ:** Shareholder of Bavarian Nordic and Novo Nordisk; acted as speaker, paid instructor and consultant via role as co-founder and co-owner of a small consultancy (nordicdatalab); previously employed at Steno Diabetes Center (Novo Nordisk Foundation). **MP:** student internship at LEO Pharma; research support from LEO Pharma. **MRN:** None. **MS:** Research funding from Eli Lilly, Pfizer and UCB; speaker fees from Janssen-Cilag. **VSM:** Employee of UCB.

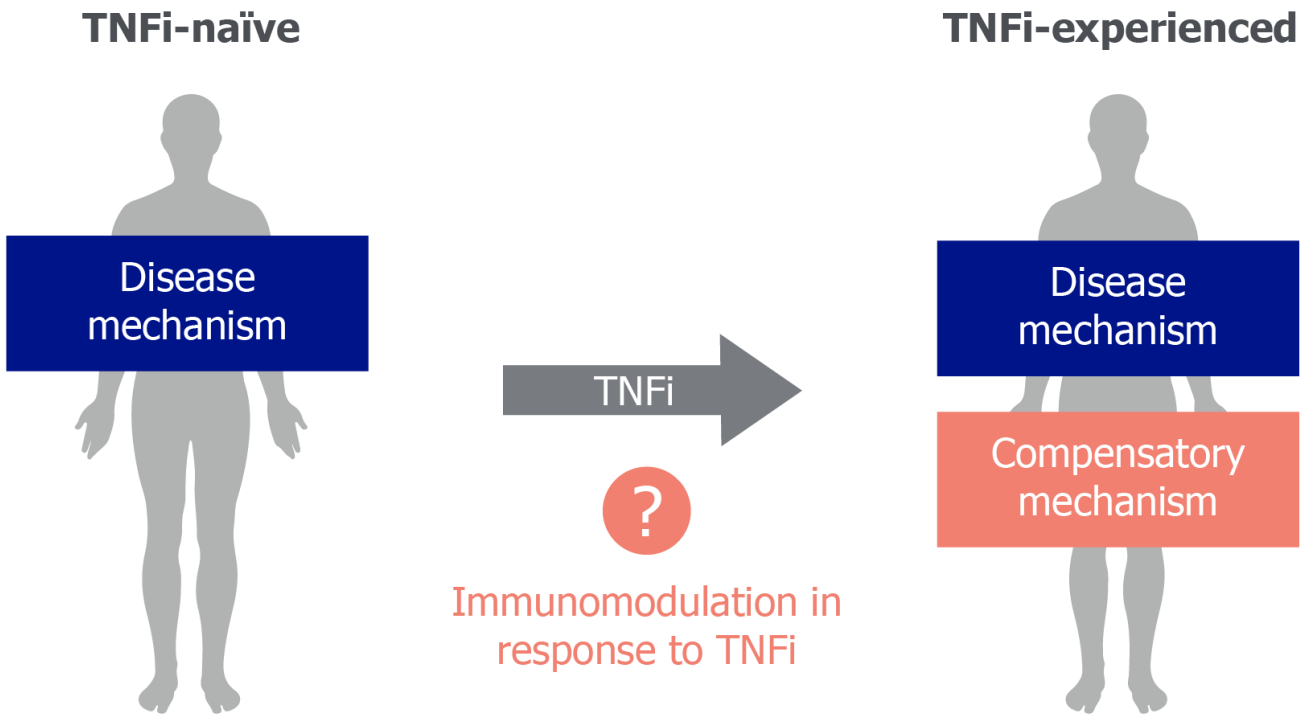
Acknowledgements

We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to this study. The authors acknowledge Heather Edens, PhD, UCB, Smyrna, Georgia, USA for publication coordination, Orla Woodward, PhD, Costello Medical, London, UK, for medical writing and editorial assistance, and the Costello Medical Creative team for design support. This study was funded by UCB. All costs associated with development of this presentation were funded by UCB.

Picture taking is **ALLOWED** during my presentation (including presented slides)

The pathogenetic mechanisms underlying lower treatment responses achieved in TNFi-experienced vs TNFi-naïve patients with PsA are poorly understood

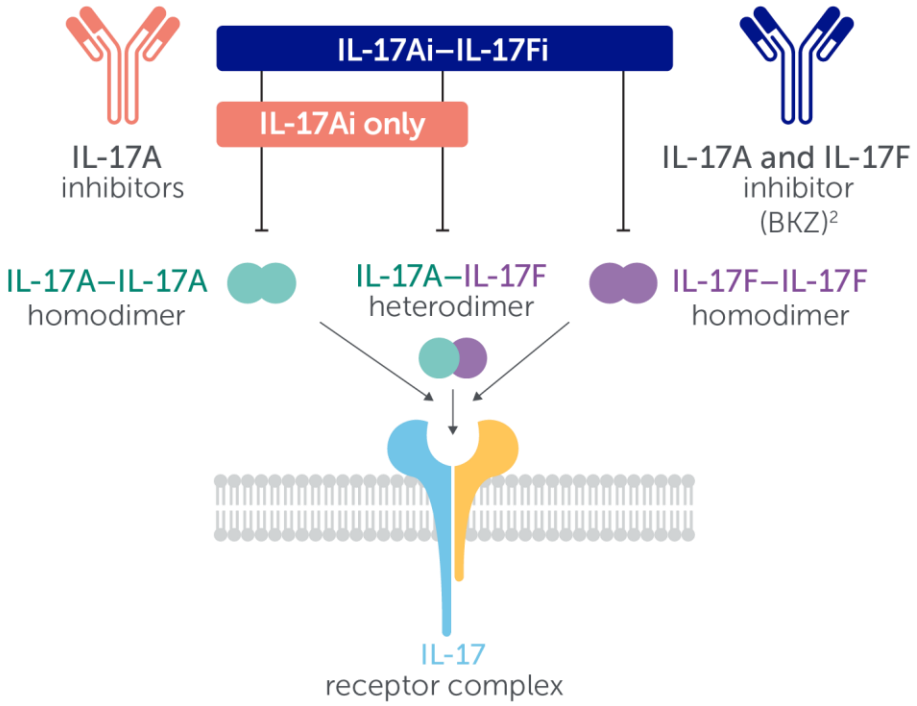
- Tumour necrosis factor inhibitor (TNFi)-experienced patients with psoriatic arthritis (PsA) are less likely to achieve treatment response targets following treatment with disease modifying antirheumatic drugs (bDMARDs) than TNFi-naïve patients[1,2]



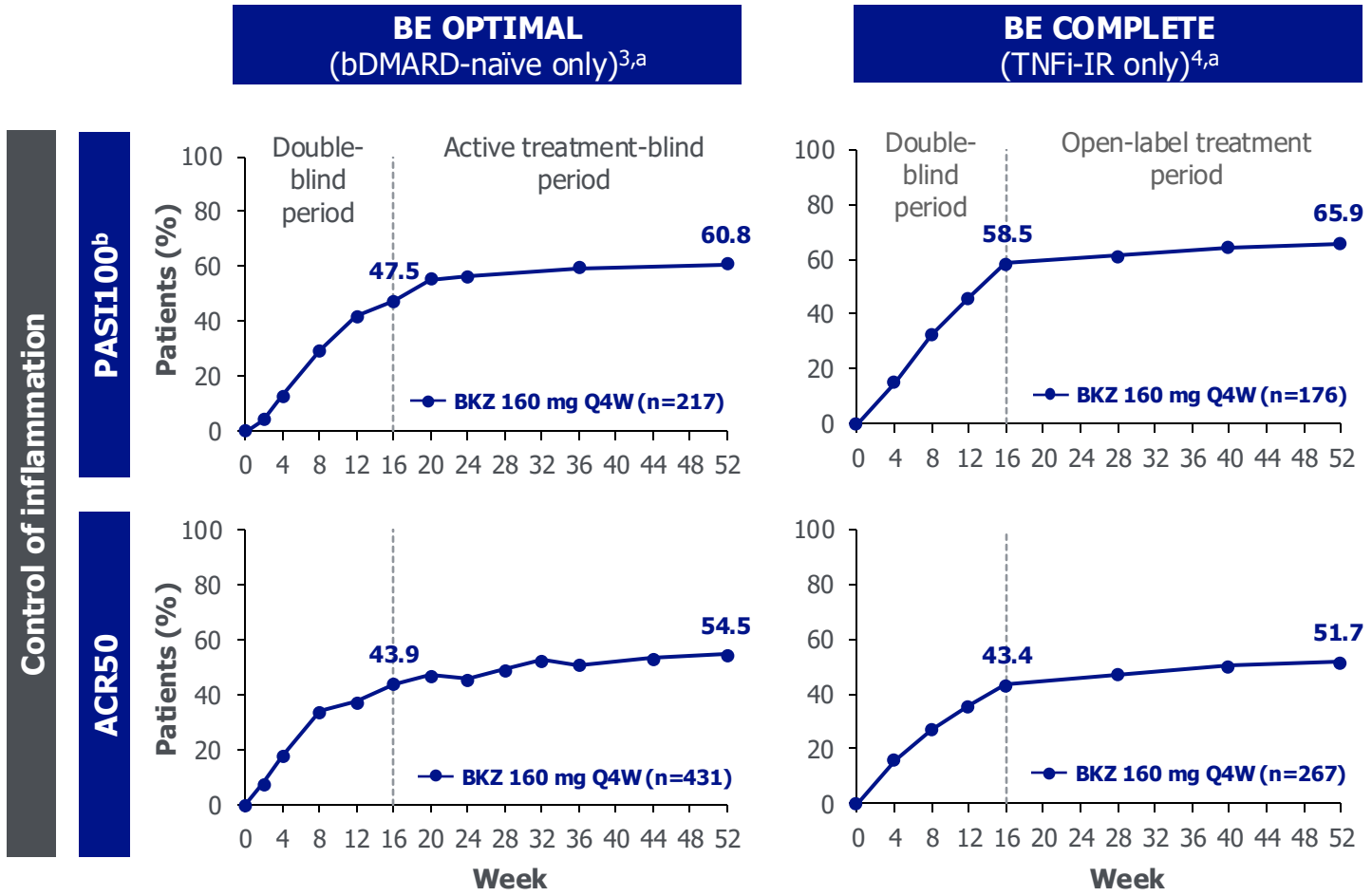
1. Xie Y. Clin Exp Dermatol 2022;47:1627–35; **2.** Merola JF. Semin Arthritis Rheum 2017;47:29–37. bDMARD: biologic disease-modifying antirheumatic drug; PsA: psoriatic arthritis; TNFi: tumour necrosis factor inhibitor.

Bimekizumab shows a consistent level of response in patients with PsA, regardless of prior TNFi exposure

Bimekizumab is a humanised monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A[1,2]



Bimekizumab has shown consistent efficacy in patients with PsA who were bDMARD-naïve or had inadequate response to TNFi (TNFi-IR)



[a] Randomised set; non-responder imputation data reported; **[b]** In patients with psoriasis affecting ≥3% of BSA at baseline. **1.** Glatt S. Ann Rheum Dis 2018;77:523–32; **2.** Adams R. Front Immunol. 2020;11:1894; **3.** Ritchlin CT. Ann Rheum Dis 2023;82:1404–14; **4.** Coates LC. RMD Open 2024;10:e003855. ACR50: ≥50% response in American College of Rheumatology response criteria; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BSA: body surface area; IL: interleukin; IL-17Xi: IL-17X inhibitor; PASI100: 100% improvement from baseline in Psoriasis Area and Severity Index; PsA: psoriatic arthritis; Q4W: every 4 weeks; TNFi: tumour necrosis factor inhibitor; TNFi-IR: prior inadequate response or intolerance to TNFi.

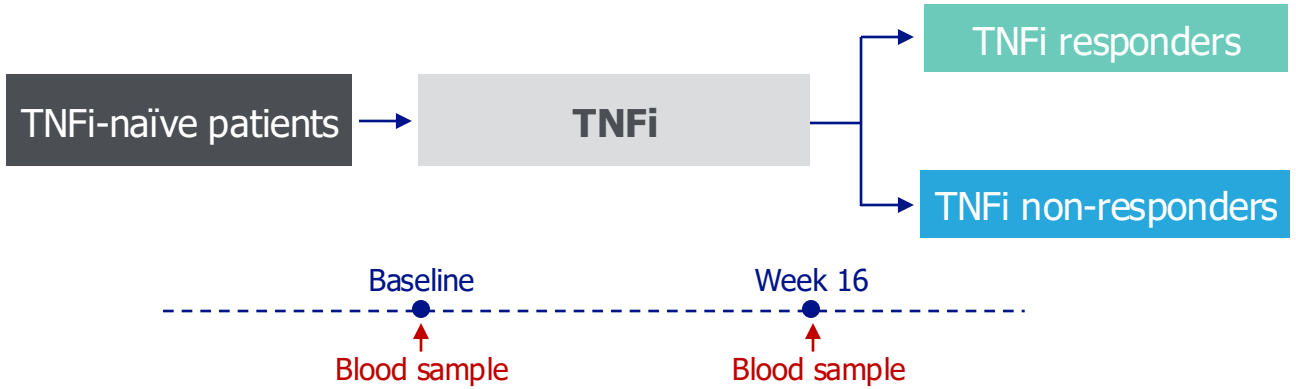
Using biomarkers in randomised controlled trials to explore clinically relevant immune pathways in PsA

OBJECTIVE: To test the hypothesis that immune signalling pathways, specifically IL-17F signalling, may be differentially regulated in patients with PsA following treatment with TNFi

IL: interleukin; PsA: psoriatic arthritis; TNFi: tumour necrosis factor inhibitor.

Immune signalling was assessed in two separate studies of TNFi-naïve patients with PsA initiating their first TNFi treatment (1/2)

EXAMINe-PsA
Immune Cell Composition Analysis Study Design



- EXploring Autoimmune disease Mechanisms IN Psoriatic Arthritis (EXAMINe-PsA) assessed a cohort of TNFi-naïve patients initiating TNFi treatment in a real-world clinical setting[1]
- Flow cytometry was performed on whole blood samples taken at baseline and at Week 16
- CD4+ Th1 and Th17 cell numbers were evaluated in TNFi responders vs non-responders[a]

[a] CD4+ Th1 and Th17 cells defined by measurement of cell surface markers (Th1 cell markers: CD3+CD4+CXCR3+CCR6-; Th17 cell markers: CD3+CD4+CXCR3-CCR6+).[2] **1.** Højgaard P. BMJ Open 2016;6:e010650; **2.** Maecker HT. Nat Rev Immunol 2012;12:191–200. EXAMINe-PsA: EXploring Autoimmune disease Mechanisms IN Psoriatic Arthritis; PsA: psoriatic arthritis; Th1: T helper cell type 1; Th17: T helper cell type 17; TNFi: tumour necrosis factor inhibitor.

Immune signalling was assessed in two separate studies of TNFi-naïve patients with PsA initiating their first TNFi treatment (2/2)

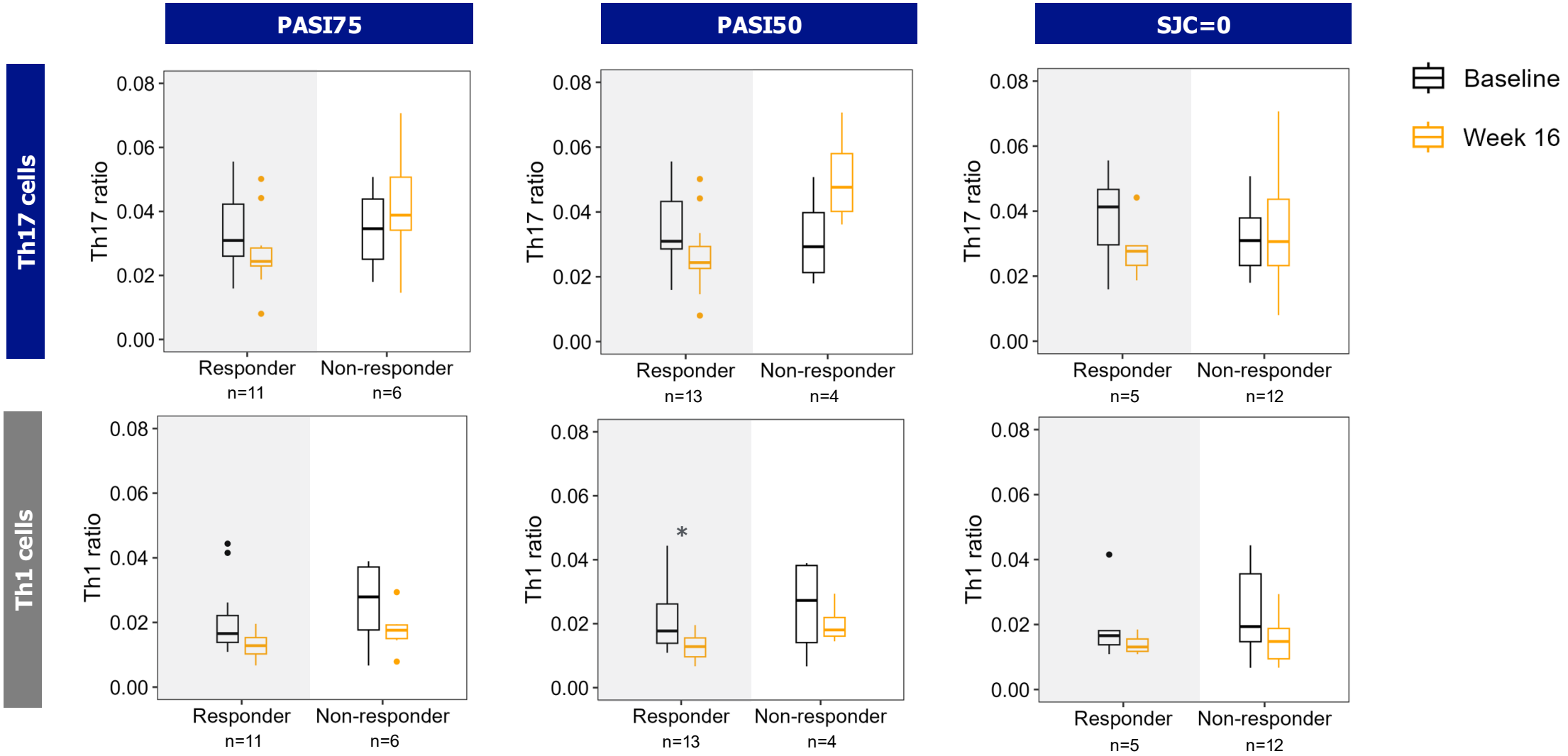
In both studies, **TNFi non-responders** at Week 16 were defined based on **lack of achievement** of either:

- **PASI75**: Psoriasis Area and Severity Index (PASI) ≥75% improvement from baseline[a]
- **PASI50**: PASI ≥50% improvement from baseline[a]
- **SJC=0**: resolution of swollen joint count

- Post hoc biomarker analysis of samples collected during BE OPTIMAL[1]
- Bulk RNA-seq was performed on whole blood samples taken at baseline and Week 16
- Geneset analyses for Th17 cell and *IL17F*-related gene signatures in TNFi non-responders was performed using Gene Set Variation Analysis (GSVA) and limma statistical methods[2,3]

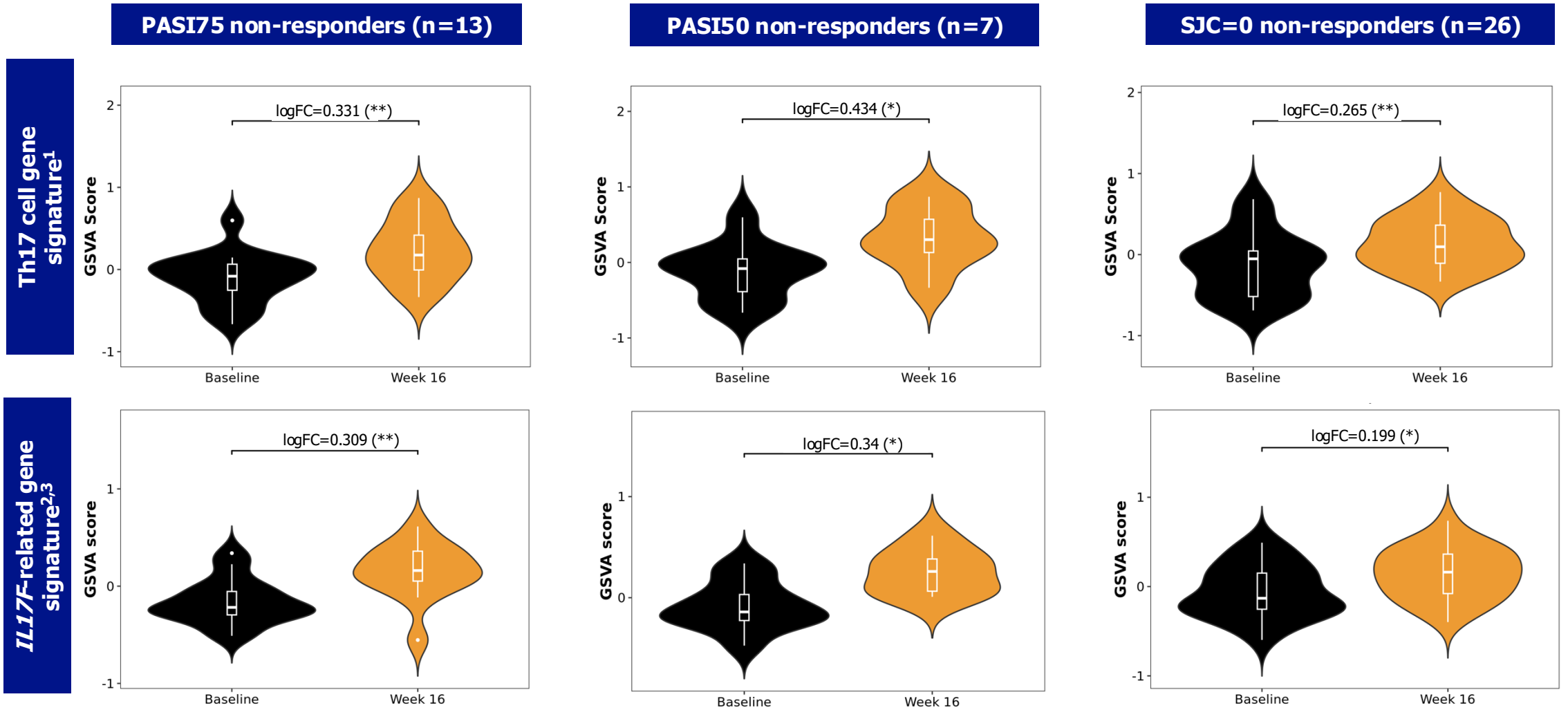
[a] In patients with psoriasis affecting ≥3% of BSA at baseline. **1.** McInnes IB. Lancet 2023;401:25–37 (NCT03895203); **2.** Hänzelmann S. BMC Bioinformatics 2013;14:7; **3.** Ritchie ME. Nucleic Acids Res 2015;43:e47. BSA: body surface area; GSVA: Gene Set Variation Analysis; IL: interleukin; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis; RNA-seq: RNA sequencing; SJC: swollen joint count; TNFi: tumour necrosis factor inhibitor.

In EXAMINe-PsA, immune cell composition trended towards increased levels of circulating Th17 cells in the blood from TNFi non-responders for PASI



Blood samples taken at baseline and Week 16. These box plots present the median and interquartile range. *p<0.05 for baseline vs Week 16 within each group. EXAMINe-PsA: EXploring Autoimmune disease Mechanisms IN Psoriatic Arthritis; IL: interleukin; PASI: Psoriasis Area and Severity Index; PASI50/75: ≥50/75% improvement from baseline in PASI; PsA: psoriatic arthritis; SJC: swollen joint count; Th1: T helper cell type 1; Th17: T helper cell type 17; TNFi: tumour necrosis factor inhibitor.

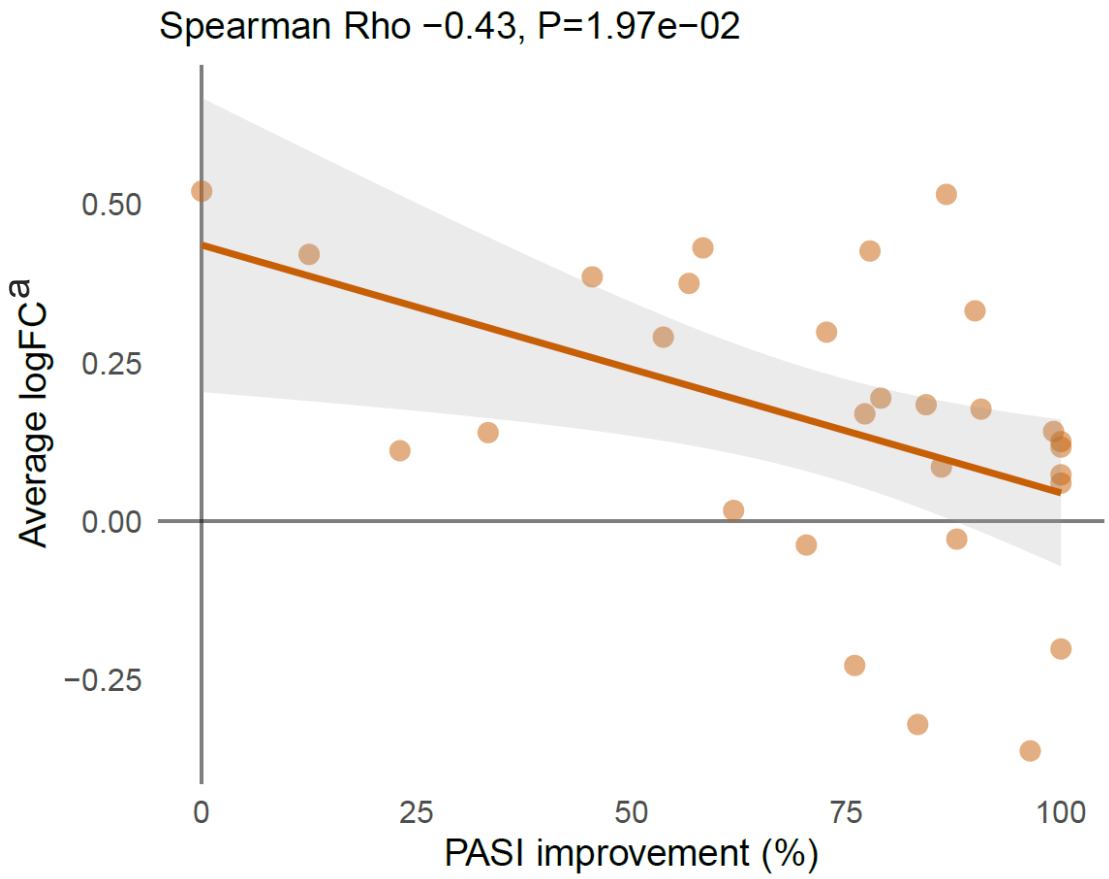
In BE OPTIMAL, expression of Th17 and *IL17F*-related gene signatures increased at Week 16 of TNFi exposure in blood from TNFi non-responders



Blood samples taken at baseline and Week 16. Data reported for patients who were non-responders at Week 16. These violin plots represent the distribution of the data and the box plots present the median and interquartile range. Th17 cell-related Dolcino gene signature: *CCL20, CCR6, LY9, IL12RB1, IL6ST*;[1] *IL17F*-related gene signature contains IL-17F regulatory genes and genes that are specific to IL-17F-producing T cells based on single cell data: *IL2, IL7, IL15, IL1A, IL1B, IL12A, IL12B, IL18, IL7R, TRBV7-6*.[2,3] **p<0.01, *p<0.05. **1.** Dolcino M. PLoS ONE 2015;10:e0128262; **2.** Cole S. J Allergy Clin Immunol 2023;152:783–98; **3.** Cutcutache I. ISDS 2023 (Poster 187). FC: fold change; GSVA: gene set variation analysis; IL: interleukin; PASI50/75: ≥50/75% improvement from baseline in Psoriasis Area and Severity Index; SJC: swollen joint count; Th17: T helper cell type 17; TNFi: tumour necrosis factor inhibitor.

In BE OPTIMAL, there was a negative correlation between PASI improvements and changes in *IL17F*-related gene signature expression at Week 16 of TNFi exposure

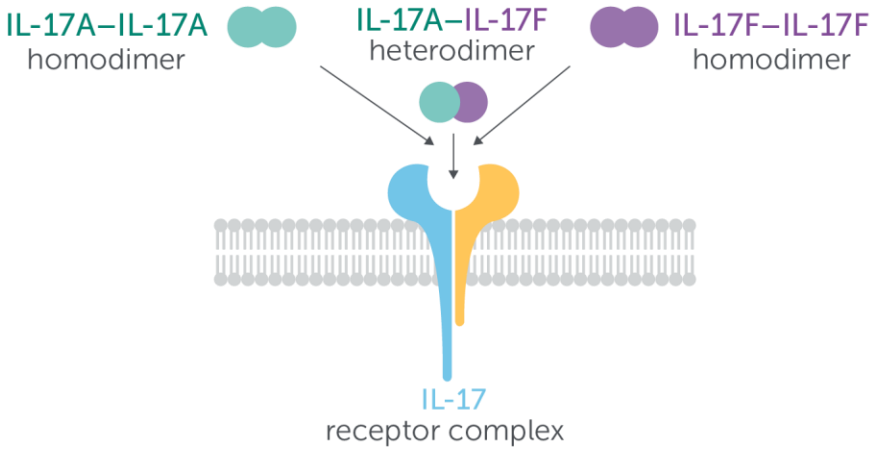
IL17F-related gene signature[1,2]



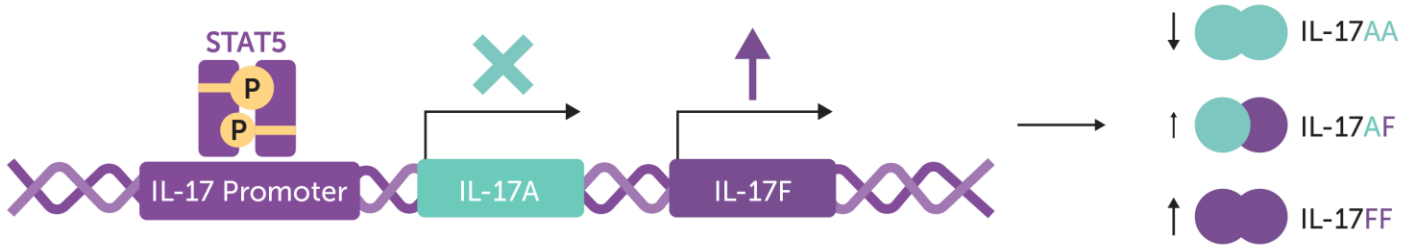
Each point represents a patient from BE OPTIMAL. Two points corresponding to patients with PASI improvement less than 0% are outside the plotting area; these patients are excluded from the statistical analysis shown here. *IL17F*-related gene signature contains IL-17F regulatory genes and genes that are specific to IL-17F-producing T cells based on single cell data: *IL2, IL7, IL15, IL1A, IL1B, IL12A, IL12B, IL18, IL7R, TRBV7-6*.[1,2] **[a]** Average logFC is the average logFC of gene expression between baseline and Week 16 across all genes in the signature. **1.** Cole S. J Allergy Clin Immunol 2023;152:783–98; **2.** Cutcutache I. ISDS 2023 (Poster 187). FC: fold change; IL: interleukin; PASI: Psoriasis Area and Severity Index; TNFi: tumour necrosis factor inhibitor.

IL-17A and IL-17F are dynamically regulated which may have functional significance in PsA pathogenesis

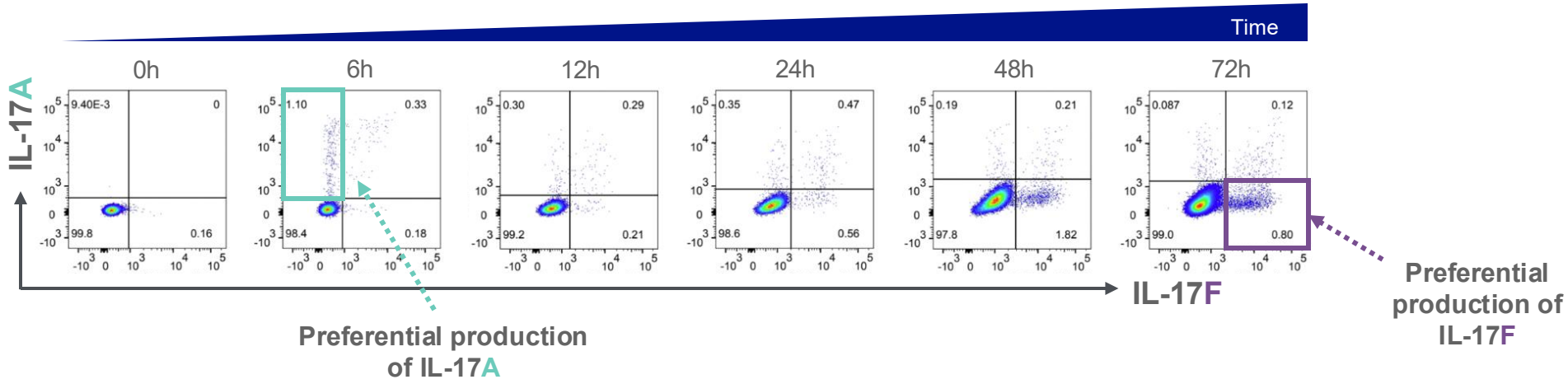
IL-17A and IL-17F share overlapping biology[1–3]



IL17A and *IL17F* expression can be dynamically regulated[4,a]

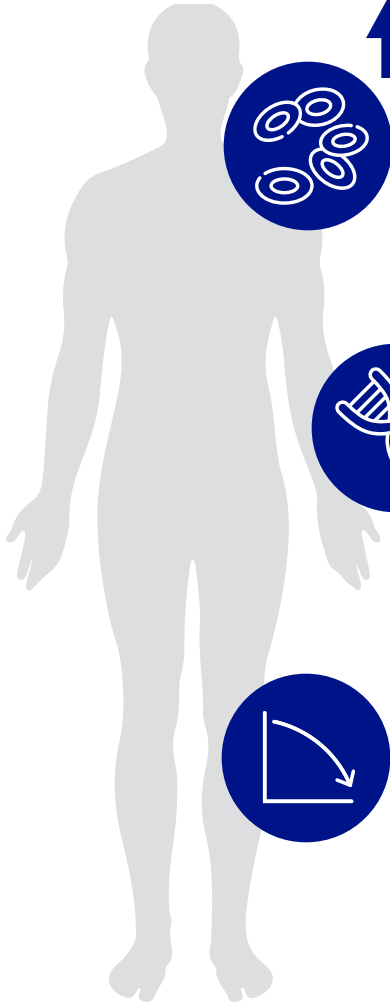


Over time, IL-17F becomes the dominant cytokine expressed by Th17 cells[4,a,b]



[a] Figure adapted from Cole S. 2023;[4] **[b]** CD4+ T cells stimulated with anti-CD3 and anti-CD28 between 0–72 hours in addition to brefeldin A for last 4 hours. **1.** Chang SH. Cell Res 2007;17:435–40; **2.** Wright JF. J Biol Chem 2007;282:13447–55; **3.** Kuestner RE. J Immunol 2007;179:5462–73; **4.** Cole S. J Allergy Clin Immunol. 2023;152:783–98. IL: interleukin; P: phosphate; PsA: psoriatic arthritis; STAT: signal transducer and activator of transcription; Th17: T helper cell type 17.

Conclusions



TNFi non-responders had numerically higher numbers of circulating **Th17 cells** vs TNFi responders at Week 16

TNFi non-responders had increased expression of **Th17- and *IL17F*-related gene signatures** at Week 16 vs baseline

Changes in *IL17F*-related gene signature expression were **negatively correlated** with PASI improvement at Week 16 of TNFi exposure

Together, these data suggest **IL-17F biology may be upregulated in response to TNFi exposure in TNFi non-responders**

This may provide an **explanatory mechanism** for the consistent clinical response to bimekizumab observed in TNFi-experienced and bDMARD-naïve patients with PsA

Further analyses of IL-17F production and activity at sites of inflammation in TNFi-experienced patients with PsA are required

To access the presentation, scan the QR code

Link expiration: 12 September 2025

bDMARD: biologic disease-modifying antirheumatic drug; IL: interleukin; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis; Th17: T helper cell type 17; TNFi: tumour necrosis factor inhibitor.