Real-World Comparative Effectiveness of Upadacitinib in Psoriatic Arthritis: Evaluation of Switching to Upadacitinib Versus Tumor Necrosis Factor Inhibitors or Interleukin-17 Inhibitors After First-Line Tumor Necrosis Factor Inhibitors

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OBJECTIVE

To compare the effectiveness of switching from a first-line or initial TNF inhibitor to upadacitinib versus cycling to another TNF inhibitor or switching from a TNF inhibitor to an IL-17 inhibitor on tender and swollen joint involvement in patients with PsA

CONCLUSIONS

In patients with PsA, switching from a first-line TNF inhibitor to upadacitinib resulted in significantly more patients with both TJC ≤ 1 and SJC ≤ 1 than cycling to a second TNF inhibitor

Similarly, switching to upadacitinib after a first-line TNF inhibitor resulted in significantly more patients with both TJC ≤ 1 and SJC ≤ 1 than switching to an IL-17 inhibitor

These real-world data demonstrate that switching to upadacitinib after an initial TNF inhibitor may benefit patients with PsA

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INTRODUCTION

- For patients with PsA with an intolerance of or inadequate response to at least one biological DMARD (bDMARD), EULAR treatment guidelines recommend switching to a JAK inhibitor (JAKi) or to another bDMARD, including cycling within the TNF inhibitor (TNFi) class or switching to a bDMARD with another mechanism of action, such as an IL-17 inhibitor (IL-17i)[1]
- While there is mixed evidence that cycling to another TNFi after failure of a first-line TNFi is associated with lower response rates on joint symptoms,[2] there are limited studies comparing the effectiveness of cycling to another TNFi versus switching to a different mechanism of action
- This analysis compared the effectiveness of switching from an initial TNFi to upadacitinib (UPA), an oral JAKi with demonstrated safety and efficacy for the treatment of PsA in two phase 3 clinical trials,[3,4] versus cycling to another TNFi or switching from a TNFi to an IL-17i on tender and swollen joint involvement in patients with PsA

METHODS

Data Source and Inclusion Criteria

- Data were drawn from the Adelphi Real World Spondyloarthritis (SpA) V and VI Disease Specific Programmes™, cross-sectional surveys administered to physicians and their consulting patients in routine clinical practice in Germany, France, Italy, Spain, the United Kingdom, and the United States (SpA VI only)
  - Data were collected for SpA V from March 2021 to November 2021 and from June 2023 to June 2024 for SpA VI
- Adult patients with PsA who switched treatment from a TNFi in the first line of advanced therapy were stratified into three groups by the second-line therapy of interest:
  - TNFi to UPA
  - TNFi to TNFi
  - TNFi to IL-17i

Outcomes and Statistical Analysis

- The outcome of physician-reported assessment of both tender joint count (TJC) ≤ 1 and swollen joint count (SJC) ≤ 1 was evaluated ≥ 3 months after treatment switch
- Patient demographics and clinical characteristics were balanced using inverse-probability-weighted regression adjustment (IPWRA)
- The covariates balanced within the IPWRA were age, sex, Charlson Comorbidity Index, and disease severity at initiation of second-line therapy as reported by their physician for the weighting and regression adjustment stage; additionally, second-line treatment duration was used for the regression adjustment stage
- The regression analyses were conducted separately for comparisons between TNFi to UPA and TNFi to TNFi and between TNFi to UPA and TNFi to IL-17i
- Statistical analyses were run in Stata v18[6] and descriptive analysis was performed using UNICOM Intelligence Reporter version 7.5.1 (UNICOM Systems 2021)

RESULTS

Patients

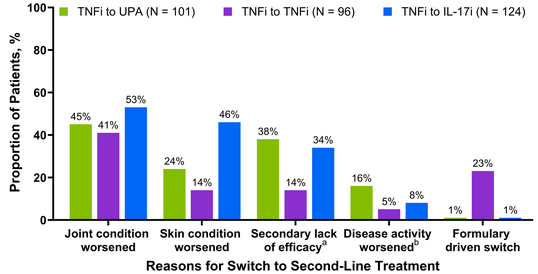
- Of the 320 eligible patients who used a TNFi in the first-line of advanced therapy, 101 patients switched to UPA, 96 switched to another TNFi, and 123 switched to an IL-17i as a second-line treatment (**Table 1**)
- Across the three groups, adalimumab was most commonly used as the first-line TNFi
- At the time of switch, physician-reported assessment of disease severity in most patients was moderate/severe (TNFi to UPA: 92%; TNFi to TNFi: 89%; TNFi to IL-17i: 93%)

Table 1. Patient Demographics and Characteristics

Parameter	TNFi to UPA N = 101	TNFi to TNFi N = 96	TNFi to IL-17i N = 123
Age, years, mean (SD)	45.9 (10.1)	51.1 (13.7)	48.4 (10.4)
Sex, n (%)			
Female	53 (52)	49 (51)	63 (51)
Male	48 (48)	47 (49)	60 (49)
Charlson Comorbidity Index, mean (SD)	0.1 (0.5)	0.1 (0.5)	0.2 (0.7)
Time since PsA diagnosis, years, mean (SD)	5.8 (3.7) n = 100	8.3 (7.1) n = 90	7.0 (5.4) n = 110
TNFi received as first-line treatment, n (%)			
Adalimumab	85 (84)	61 (64)	95 (77)
Etanercept	8 (8)	22 (23)	18 (15)
Infliximab	2 (2)	8 (8)	3 (2)
Certolizumab-pegol	3 (3)	2 (2)	5 (4)
Golimumab	3 (3)	3 (3)	2 (2)
Concurrent csDMARD use, n (%)	12 (12)	23 (24)	30 (24)
Prior csDMARD use, (n%)	77 (76)	69 (72)	95 (77)
Duration of first-line TNFi, years, mean (SD)	2.8 (2.7)	1.9 (2.0)	2.7 (2.6)
Duration of second-line advanced therapy, years, mean (SD)	0.9 (0.5)	2.6 (3.1)	2.1 (1.5)
Disease severity[a] at second-line treatment initiation, n (%)			
Mild	8 (8)	11 (11)	9 (7)
Moderate	57 (56)	56 (58)	83 (67)
Severe	36 (36)	29 (30)	31 (25)
TJC at second-line treatment initiation, mean (SD)	7.7 (7.8) n = 101	8.4 (8.8) n = 29	7.9 (9.3) n = 70
SJC at second-line treatment initiation, mean (SD)	5.0 (7.0) n = 101	5.6 (6.3) n = 29	4.6 (7.8) n = 70

csDMARD, conventional synthetic DMARD; IL-17i, IL-17 inhibitor; SJC, swollen joint count; TJC, tender joint count; TNFi, TNF inhibitor; UPA, upadacitinib.
[a]Disease severity was categorized as mild, moderate, or severe based on physician's assessment when completing the survey.

Figure 1. Reasons for Switch to Second-Line Treatment



IL-17i, IL-17 inhibitor; TNFi, TNF inhibitor; UPA, upadacitinib.
[a]Loss of response after initial response to first-line treatment.
[b]As assessed by physician, which may involve multiple factors.

Reasons for Switching From First-Line TNFi to Second-Line Treatment

- Across the three groups, the most frequent physician-reported reason for switching from a first-line TNFi was a worsening of the condition of the joints (**Figure 1**)
- Other reasons for switching were a secondary lack of efficacy (TNFi to UPA), a formulary driven switch (TNFi to TNFi), and a worsening in skin condition (TNFi to IL-17i)

Advanced Therapy Utilized in Second-Line Treatment

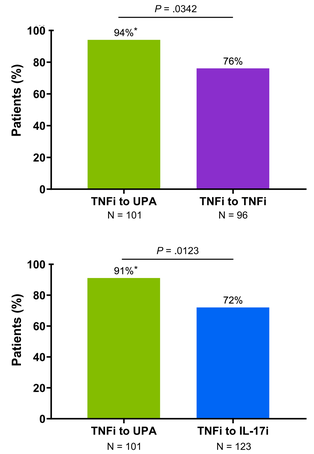
- In patients who cycled within the TNFi class, the most commonly utilized second-line TNFi was adalimumab (**Table 2**)
- For patients who switched from a TNFi to an IL-17i, the most commonly used IL-17i was secukinumab

Table 2. Advanced Therapy Used as Second-Line Treatment

Advanced therapy, n (%)	TNFi to UPA N = 101	TNFi to TNFi N = 96	TNFi to IL-17i N = 123
Adalimumab		58 (60)	
Etanercept		9 (9)	
Infliximab		9 (9)	
Certolizumab-pegol		9 (9)	
Golimumab		11 (11)	
Secukinumab			76 (62)
Ixekizumab			45 (37)
Bimekizumab			2 (2)
Upadacitinib	101 (100)		

IL-17i, IL-17 inhibitor; TNFi, TNF inhibitor; UPA, upadacitinib.

Figure 2. Adjusted Physician-Reported Assessment of Both TJC and SJC ≤ 1 at the Time of Data Collection



IL-17i, IL-17 inhibitor; SJC, swollen joint count; TJC, tender joint count; TNFi, TNF inhibitor; UPA, upadacitinib.
*$P < .05$.

Comparison of Tender and Swollen Joint Counts Between Treatment Groups

- After adjustment via IPWRA, the proportion of patients with a physician-reported assessment of both TJC ≤ 1 and SJC ≤ 1 was compared separately between the TNFi to UPA and TNFi to TNFi groups and TNFi to UPA and TNFi to IL-17i groups
- There were significantly more patients with both TJC ≤ 1 and SJC ≤ 1 in the TNFi to UPA group compared with the TNFi to TNFi group (94% vs 76%, $P = .0342$) (**Figure 2**)
- Similarly, there were significantly more patients with TJC ≤ 1 and SJC ≤ 1 in the TNFi to UPA group compared with the TNFi to IL-17i group (91% vs 72%, $P = .0123$)
- Achievement of SJC ≤ 1 alone was 91% vs 89%, $P = .8310$ for TNFi to UPA vs TNFi to TNFi and 91% vs 92%, $P = .7676$ for TNFi to UPA vs TNFi to IL17i
- Achievement of TJC ≤ 1 alone was 94% vs 82%, $P = .1493$ for TNFi to UPA vs TNFi to TNFi and 91% vs 73%, $P = .0145$ for TNFi to UPA vs TNFi to IL17i

Limitations

- Like many real-world data sets comprised of survey results, data reported here relies on physician participation in the Adelphi Real World SpA V and VI Disease Specific Programmes™, which may limit the representativeness of the patient population
- The quality and completeness of the data are dependent on accurate reporting by the participants, and thus may be influenced by recall bias
- Although this study did not report any measures of safety, long-term integrated safety studies of UPA have been reported across several immunological diseases[5]