multivariable models, biologic-experienced patients were more likely to discontinue treatment (HR 1.21 [95% CI 1.04–1.43]; p=0.017) vs. biologic-naive patients, while PsA had no significant effect on TTD alone vs. no PsA (HR 1.12 [95% CI 0.9–1.4]; p=0.31). However, comorbid PsA increased the likelihood of treatment discontinuation for biologic-experienced patients (HR 1.45 [95% CI 1.06–1.97]; p=0.018). Obesity was a further predictor of discontinuation (HR 1.15 [95% CI 1.02–1.31]; p=0.027) and this was independent of comorbid PsA and prior biologic exposure (Table 1).

Conclusion: Comorbid PsA was associated with reduced time-to-discontinuation of UST in biologic-experienced patients, but not biologic-naive patients. Obesity also impacted TTD but independently of PsA status.

REFERENCES:

Table 1. Multivariate analysis of UST discontinuation in PsO patients (N=3,174).

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Status (n)</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbid PsA</td>
<td>No PsA</td>
<td>ref</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>PsA</td>
<td>1.12</td>
<td>0.90–1.40</td>
</tr>
<tr>
<td>(n=2609)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biologic experience</td>
<td>No prior biologic (n=2371)</td>
<td>ref</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Prior biologic (n=803)</td>
<td>1.21</td>
<td>1.04–1.43</td>
</tr>
<tr>
<td>(n=665)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PsA/Prior biologic experience</td>
<td>No PsA, prior biologic</td>
<td>ref</td>
<td>-</td>
</tr>
<tr>
<td>(n=539)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity (BMI, kg/m²)</td>
<td>&lt;30</td>
<td>ref</td>
<td>-</td>
</tr>
<tr>
<td>(n=1554)</td>
<td>≥30</td>
<td>1.15</td>
<td>1.02–1.31</td>
</tr>
<tr>
<td>(n=1620)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

BMI, body mass index; CI, confidence interval; HR, hazard ratio; PsA, psoriatic arthritis; PsO, psoriasis; ref, reference; UST, ustekinumab.


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POS1054 UPADACITINIB PHARMACOKINETICS AND EXPOSURE-RESPONSE RELATIONSHIPS FOR EFFICACY AND SAFETY IN PSORIATIC ARTHRITIS – ANALYSES OF THE PHASE 3 SELECT-PA STUDIES

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Background: Upadacitinib (UPA) is an oral, reversible, JAK inhibitor approved for the treatment of rheumatoid arthritis (RA). The efficacy and safety profile of UPA in psoriatic arthritis (PsA) has been established in the SELECT-PA program which includes two global Phase 3 studies.

Objectives: These analyses characterize UPA pharmacokinetics and exposure-response relationships for efficacy and safety endpoints using data from the SELECT-PA studies.

Methods: The SELECT-PA program enrolled patients with prior inadequate response (IR) or intolerance to ≥1 non-bDMARD (N=1705) and prior IR or intolerance to ≥1 bDMARD (N=642). Data from both trials were integrated for patients receiving placebo (PBO), UPA 15mg once daily (QD) and UPA 30mg QD; adalimumab data was excluded from this analysis. UPA pharmacokinetics were characterized in PsA patients using Bayesian population pharmacokinetics analyses and utilizing prior information from analyses in healthy subjects and RA patients. Exposure-response analyses were conducted using logistic regression to characterize the relationships between upadacitinib average plasma concentration during a dosing interval (Cavg) and the percentage of patients achieving apremilast in patients with PsA. Patients will be followed up for a maximum of 12 months. This interim analysis compared the baseline characteristics and experience on apremilast for two subgroups of patients, those remaining on apremilast versus the ones that discontinued.

Methods: In this interim analysis we included patients with data available at cut-off date of 03 November 2020. Patient enrollment and follow up of current subjects is ongoing. Descriptive statistics (n’s and percents for categorical data, means for continuous data) were used to summarize the baseline data by subgroup. Kaplan Meier plots are presented to show patients’ experience on apremilast by subgroup.

Results: 85 patients were included in the analysis. 30 patients have completed the study, 39 patients have discontinued and 16 are ongoing. At baseline 22 (26%) patients were biologic experienced and 62 (74%) were biologic naïve. Both groups had a comparable disease activity measure with clinical disease activity in psoriatic arthritis (cDAPSA) scores. Biologic experienced patients had a longer disease duration compared to biologic naïve patients (mean 9.7 vs 6.2 years). Inefficacy of previous medication was the main reason for starting apremilast in both subgroups. Overall, 86% (n=69) of patients were still receiving apremilast at month 3, 60% (n=46) at month 6, and 41% (n=26) at month 12 (Figure 1). Drug survival (length of time until discontinuation of apremilast) for biologic naïve patients was 93% at month 3, 73% at month 6 and 58% at month 12. Drug survival of biologic experienced patients was 67%, 20%, and 0% at months 3, 6, and 12, respectively. At baseline mean values of body mass index (BMI), swollen joint count (SJC), tender joint count (TJC), psoriatic arthritis impact of disease (PsAID) were comparable between both groups (Table 1). Reasons for discontinuation were mainly lack of efficacy (49%) and adverse events (44%). In this analysis the nature and frequency of adverse events is in line with the known profile of apremilast.

Conclusion: In this interim analysis, patients who were biologic naïve had a better probability to remain on treatment than those who were biologic experienced. Baseline characteristics were similar between the two groups, apart from disease duration that was longer in the biologic experienced group. Best drug survival is achieved when apremilast is prescribed earlier in the PsA treatment course, before biologics and after csDMARDS, as per apremilast EU label.

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ACR20/50/70 at Weeks 12 and 24, static Investigator Global Assessment of psoriasis (sIGA) of 0 or 1 (clear or almost clear) and at least a 2-point improvement from baseline, and PASI75 at Weeks 16 and 24 or experiencing selected clinically relevant safety events through week 24.

**Results:** Analyses were conducted using data from 1964 subjects (for pharmacokinetics) and 1916 subjects (for exposure-response analyses). UPA model-estimated plasma exposures in subjects with PsA who received 15mg and 30mg QD doses were comparable to previously estimated exposures in subjects with RA. Body weight and methotrexate use had no clinically relevant effects on UPA exposures. There was a statistically significant relationship between UPA Cavg and the percentage of subjects who achieved Week 12 ACR20/50/70, Week 16 sIGA 0/1, and Week 24 sIGA 0/1 (Figure 1). No statistically significant exposure-response relationship was observed for Week 12 ACR20, Week 16 PASI75, or Week 24 ACR20/50/70 or PASI75, indicating that the 15mg QD exposures are approximately at the plateau of response for these endpoints. No statistically significant relationships were observed between upadacitinib Cavg and the percentage of subjects experiencing pneumonia, herpes zoster, hemoglobin < 9 g/dL, Grade ≥3 lymphopenia, Grade ≥3 neutropenia. There was a shallow but statistically significant exposure-response relationships with the occurrence of serious infections and decrease in hemoglobin from baseline (>2 g/dL and >2 g/dL in combination with hemoglobin < lower limit for normal).

**Conclusion:** Exposure-response analyses demonstrated that plasma exposures associated with UPA 15mg QD achieves robust efficacy in subjects with PsA with limited effects on the evaluated safety endpoints. UPA plasma exposures associated with UPA 15 and 30mg QD are predicted to provide similar ACR responses and limited effects on the evaluated safety endpoints. UPA plasma exposures associated with UPA 15 and 30mg QD are predicted to provide similar ACR responses and limited effects on the evaluated safety endpoints.

**Disclosure of Interests:** None declared.

**References:**


[2] Fleischmann R, et al. Safety and Effectiveness of Upadacitinib or Adalimumab in Patients with Rheumatoid Arthritis: Results at 48 weeks from the SELECT-COMPARE Study. 2019 EULAR; FRIO147


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**POS1056**

**Title:** COMPARATIVE EFFICACY OF TNF INHIBITORS VERSUS OTHER CYTOKINE INHIBITOR dMDARs ON PSORIATIC ARTHRITIS IMPACT OF DISEASE (PsAID) SCORE AND DOMAINS

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**Background:** Psoriatic arthritis (PsA) has many consequences, reflecting musculoskeletal and skin inflammation, with the potential to adversely affect overall quality of life. Patient reported outcome measures (PROM) assess a holistic range of aspects of quality of life, including physical and mental components, and provide broad detailed information of the impact of disease. Biologic DMARDs (bDMARDs) targeting TNF have been used to treat PsA for over 10 years whereas inhibitors of IL-17, IL-12/23 and Janus kinases (JAK) have only been available more recently. They all target differing cytokines, including JAK inhibitors which inhibit IL-12 and IL-23 signaling but not TNF signaling. Their relative impact on PROMs is unknown.

**Objectives:** To assess, in routine care, the relative impact in PsA of TNF inhibitors (TNFi) versus non-TNF bDMARDs, targeting IL-17, IL-12/23 and JAK, on PROMs. Methods: We performed a cross section analysis of PsA patients with established disease treated with bDMARDs and JAKi, under routine care at St George’s University Hospital, London, UK. Patients completed the 12-item psoriatic arthritis impact of disease (PsAID) tool. The total PsAID score was calculated using the on-line EULAR toolkit (see reference). The PsAID total and individual domain scores were compared between TNFi and non-TNF groups using the