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Background: Upadacitinib (UPA), a Janus kinase inhibitor, has demonstrated efficacy and an acceptable safety profile in patients (pts) with ankylosing spondylitis (AS) in the phase 3 SELECT-AXIS 1 and 2 program, including pts with an inadequate response or intolerance to biologic disease-modifying antirheumatic drugs (bDMARD-IR).[1,2]
Objectives: To assess the 1-year efficacy and safety of UPA 15 mg once daily (QD) in bDMARD-IR pts with active AS in SELECT-AXIS 2.
Methods: The design of the SELECT-AXIS 2 AS bDMARD-IR study has been described previously.[1] Pts who completed the 14-wk placebo (PBO)-controlled period were eligible to enter an ongoing long-term extension and receive open-label UPA 15 mg QD for up to 90 wks. This analysis evaluated efficacy over 52 wks in pts who received continuous UPA, and those who switched from PBO to UPA at wk 14. Efficacy endpoints included proportion of pts achieving Assessment of SpondyloArthritis international Society 40 response (ASAS40), ASAS partial remission (PR), ASDAS (AS Disease Activity Score with C-reactive protein [CRP]) low disease activity (LDA; <2.1), ASDAS inactive disease (ID; <1.3), and changes from baseline in ASDAS and high-sensitivity CRP (hsCRP). As-observed (AO) and non-responder imputation with multiple imputation (NRI-MI) analyses are presented for binary endpoints and mixed model for repeated measures (MMRM) analyses for continuous endpoints. Safety was assessed through the cut-off date of May 19, 2022 in all pts who received ≥1 dose of UPA. Treatment-emergent adverse events (TEAEs) and TEAEs of special interest are presented as exposure-adjusted event rates (events/100 pt-years [E/100 PY]).
Results: A total of 420 pts were randomized and received study drug (PBO to UPA: n=209; continuous UPA: n=211). Response rates were maintained from wk 14 to wk 52 in the continuous UPA group, and responses were similar in the PBO to UPA group at wk 52. NRI-MI response rates at wk 52 for the PBO to UPA and continuous UPA groups, respectively, were: ASAS40 (64.6% and 65.9%), ASAS PR (29.2% and 30.3%), ASDAS LDA (55.3% and 56.9%), and ASDAS ID (25.2% and 26.0%) (**Figure 1**). Changes from baseline in ASDAS and hsCRP were also similar between groups (-1.9 and -2.0, and -10.6 and -10.0 for the PBO to UPA and continuous UPA groups, respectively). Safety was assessed in 414 pts (534.4 PY of exposure) who received ≥1 dose of UPA (**Table 1**). Rates of serious TEAEs and TEAEs leading to study drug discontinuation were 9.9 and 3.0 E/100 PY, respectively. Rates of malignancy, major adverse cardiovascular events, and venous thromboembolic events were low (0.2, 0.2, and 0.4 E/100 PY, respectively).
Conclusion: UPA 15 mg demonstrated sustained efficacy up to wk 52 in bDMARD-IR pts with active AS. Similar efficacy was observed at wk 52 in pts with continuous UPA exposure and those who switched from PBO to UPA. UPA 15 mg was generally well tolerated in this bDMARD-IR population, with no new safety signals identified.

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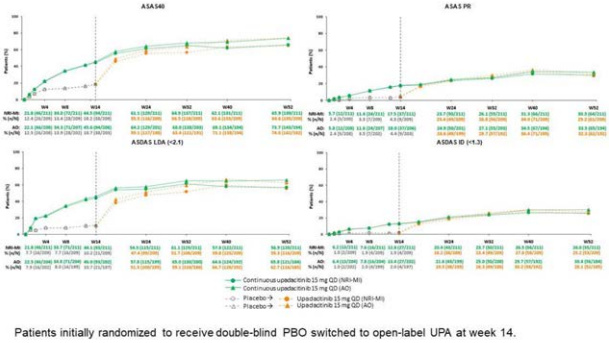
[1] van der Heijde D, et al. Lancet 2019;394:2108–2117.
[2] van der Heijde D, et al. Ann Rheum Dis 2022;81:1515–1523.

Figure. Efficacy over 52 weeks (NRI-MI and AO)



Patients initially randomized to receive double-blind PBO switched to open-label UPA at week 14.

AO, as observed; ASAS40, Assessment of SpondyloArthritis international Society 40 response; ASDAS, AS Disease Activity Score with C-reactive protein; ID, inactive disease; LDA, low disease activity; NRI-MI, non-responder imputation with multiple imputation; PBO, placebo; PR, partial remission; QD, once daily; UPA, upadacitinib; W, week.

Table 1. Treatment-emergent adverse events

Exposure-adjusted event rates, (E/100 PY)	Any upadacitinib 15 mg QD (n=414; PY=534.4)
Any AE	877 (164.1)
Serious AE	53 (9.9)
AE leading to discontinuation of study drug	16 (3.0)
Any death[a]	1 (0.2)
Infection	301 (56.3)
Serious infection	24 (4.5)
Herpes zoster	19 (3.6)
Malignancy other than NMSC	1 (0.2)
NMSC	2 (0.4)
Adjudicated MACE	1 (0.2)
Adjudicated VTE	2 (0.4)
Adjudicated gastrointestinal perforation	0
Renal dysfunction	1 (0.2)
Anemia	11 (2.1)
Lymphopenia	3 (0.6)
Neutropenia	19 (3.6)
Hepatic disorder	47 (8.8)
Uveitis	7 (1.3)
Inflammatory bowel disease	1 (0.2)
Psoriasis	2 (0.4)

[a]One patient died due to polytrauma.AE, adverse event; E, event; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PY, patient-years; QD, once daily; VTE, venous thromboembolic event.

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IMPACT OF THE TIME OF INITIATION AND LINE OF BIOLOGIC THERAPY ON THE RETENTION RATE OF SECUKINUMAB (SECU) IN AXIAL SPONDYLOARTHRITIS (AXSPA). DATA FROM THE FRENCH MULTICENTER RETROSPECTIVE FORSYA STUDY

Keywords: Prognostic factors, Spondyloarthritis, Real-world evidence

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Background: The characteristics of patients receiving a new therapy might differ overtime since its launch (date of its availability in a specific region/country); the differences in these characteristics might impact the efficiency of this treatment.
Objectives: To compare the one year retention rate of SECU in axSpA and its predisposing factors with regard to its time of initiation (e.g. right after its launch or later).
Methods: *Study design*: Retrospective multicenter French study of axSpA patients a) having initiated and received at least one dose of SECU b) with at least a one year follow-up. *Study periods*: Two cohorts were evaluated with regard to the time of initiation of SECU: *Cohort (C1)*: between August 11th, 2016 (time of the launch of SECU in France) and Aug 3st 2018; *Cohort 2 (C2)*: between sept 1st 2018 and Nov 13, 2020 (remotely from the launch). *Statistical analysis*: The one year retention rate of SECU was estimated using the Kaplan Meier technic and Cox models and was used to compare the retention rate performed in C1 and C2. Preselected factors of SECU retention at 1 year (≥1 Objective Sign of Inflammation [CRP> N, MRI-inflammation at the sacroiliac or spine level], age, sex, BMI, smoking, HLA B27, non-radiographic vs radiographic axSpA, past or present uveitis/ Inflammatory Bowel Disease (IBD)/ psoriasis/ arthritis or synovitis, diagnostic delay, disease duration, SEC line of biologic therapy, SECU maintenance dose, concomitant csDMARD/ oral corticosteroids/ proton pomp inhibitor at SECU initiation, history of depression/ fibromyalgia) were analyzed by univariate and multivariate cox model regression. Only variables with <20% missing data were included in the model after multiple imputation and stepwise selection (significance level for entering variables = 20%; for removing variables = 10%).
Results: In total, 906 pts in C1 and 758 pts in C2 from 50 centers were included in the analysis. Pts characteristics (male: 42.8%, mean age: 46.5 ± 11.9 years, mean disease duration: 9.2± 9.4 years) were similar between the 2 cohorts. The 1 year retention rate was better in C2 vs C1 (64% [61-68%] vs 59% [55-62%], Hazard Ratio (HR)=0.84 [0.72-0.98], p = 0.03). Between C1 and C2, the proportion of patients receiving SECU as the 1st or 2nd line of biologic therapy increased from 23% to 40%. In the multivariate analysis, line of biologic therapy was the single predictive factor of the 1 year retention rate of SECU in both cohorts with a better retention rate for the 1st line of biologic therapy (Table 1).
Conclusion: These data showing a better retention rate at 1 year remotely from the launch of SECU, probably explained by its use at an earlier stage of the disease, suggest a change in the behavior of prescribing physicians probably reflecting a better confidence in this treatment. These data also underline the interest of iterative evaluations of treatments used in daily practice.
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Table 1. Impact of SECU line on SECU retention rate at 1 year with regard of its time of initiation

SECU line (* reference)	Survival probability estimate at 1 year (95% CI)#	$HR_{adjusted}$ [95% CI]$	p vs ref	p type III
Cohort 1†				
1st L (n=68; 8%)*	70% [59%-81%]			0.084
2nd L (n=132, 15%)	62% [54%-70%]	1.53 [0.91; 2.57]	0.107	
≥ 3rd L (n=676, 77%)	57% [53%-61%]	1.67 [1.06; 2.62]	0.028	
Cohort 2†				
1st L (n=93, 13%)*	78% [69%-86%]			0.007
2nd L (n=192, 27%)	63% [56%-70%]	1.92 [1.18; 3.13]	0.009	
≥ 3rd L (n=437, 60%)	62% [57%-66%]	2.11 [1.32; 3.35]	0.002	

† See Methods for explanation# without imputation for missing data$ Adjustment on: C1 (OSI, IBD, History of depression or anti-depressive concomitant treatment); C2 (OSI, History of depression or anti-depressive concomitant treatment, disease duration, corticosteroids)Interpretation HR > 1: the hazard of discontinuation at 1 year is X times higher vs referenceL = Line of biologic therapy