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Efficacy and Safety of Secukinumab in Enthesitis-related Arthritis and Juvenile Psoriatic Arthritis: Primary Results from a Randomised, Double-blind, Placebo-controlled, Treatment Withdrawal, Phase 3 Study (JUNIPERA)

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Background:

Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) are two ILAR categories of juvenile idiopathic arthritis (JIA) and represent paediatric correlates of axial spondyloarthritis (axSpA) and adult psoriatic arthritis (PsA), respectively.[1,2] Secukinumab (SEC) has demonstrated efficacy and safety in adult patients (pts) with PsA, ankylosing spondylitis and non-radiographic axSpA.[3-5]

Objectives:

Evaluate efficacy and safety of SEC using a flare prevention design in pts with active ERA and JPsA.

Methods:

This 2-yr study consisted of an open-label (OL) s.c. SEC (75/150 mg in pts <50/ ≥50 kg) at baseline (BL), and at Weeks (Wk) 1, 2, 3, 4, 8 and 12 in treatment-period (TP) 1. Responder pts who achieved at least JIA ACR 30 response at Wk 12 were randomised into the double-blinded TP2 to continue SEC or placebo (PBO) q4w until a disease flare, or up to Wk 100. Pts (aged 2 to <18 yrs) classified as ERA or JPsA according to ILAR criteria of ≥6 months

duration with active disease were included. Primary endpoint was time to flare in TP2 and key secondary endpoints were JIA ACR 30/50/70/90/100, inactive disease, JADAS, enthesitis count and safety. Analysis of time to flare in TP2 included proportion of disease flare, Kaplan-Meier (KM) estimate of median time to flare in days, hazard ratio (95% CI) from Cox model, and *P*-value for the Stratified log-rank test. KM estimates of the probability to disease flare by treatment groups in TP2 were plotted against days. Observed data were used in all analyses. Post-hoc analyses using non-responder imputation (NRI) were performed for JIA ACR 30/50/70/90/100 responses.

Results:

86/97 (89%) pts were enrolled in the OL period TP1 (mean age, 13.1 yrs; female, 33.7%; ERA, n=52; JPsA, n=34). At BL, mean JADAS-27 score was 15.1 and enthesitis count was 2.6. At the end of TP1, 90.4% (75/83) of pts achieved JIA ACR 30 and 69.9% (58/83) achieved JIA ACR 70. There were 21 and 10 flares in TP2, respectively in PBO and SEC treated pts with a significantly longer time to flare and 72% risk of flare reduction in SEC treatment vs PBO (HR: 0.28; 95% CI: 0.13–0.63; *P*<0.001) (Figure). JIA ACR responses, disease activity and enthesitis count are reported in Table. NRI analyses showed that 87.2%, 83.7%, 67.4%, 38.4% and 24.4% of pts achieved JIA ACR 30/50/70/90/100, respectively. Rates of adverse events (AEs; 91.7% vs 92.1%) and serious AEs (14.6% vs 10.5%) in SEC and PBO groups were comparable in the entire TP. No new safety signals were observed.

Conclusion:

In children and adolescents with ERA and JPsA, efficacy of SEC was demonstrated with a significantly longer time to flare vs PBO with sustained improvement of signs and symptoms up to Wk 104 and a favourable safety profile.

References:

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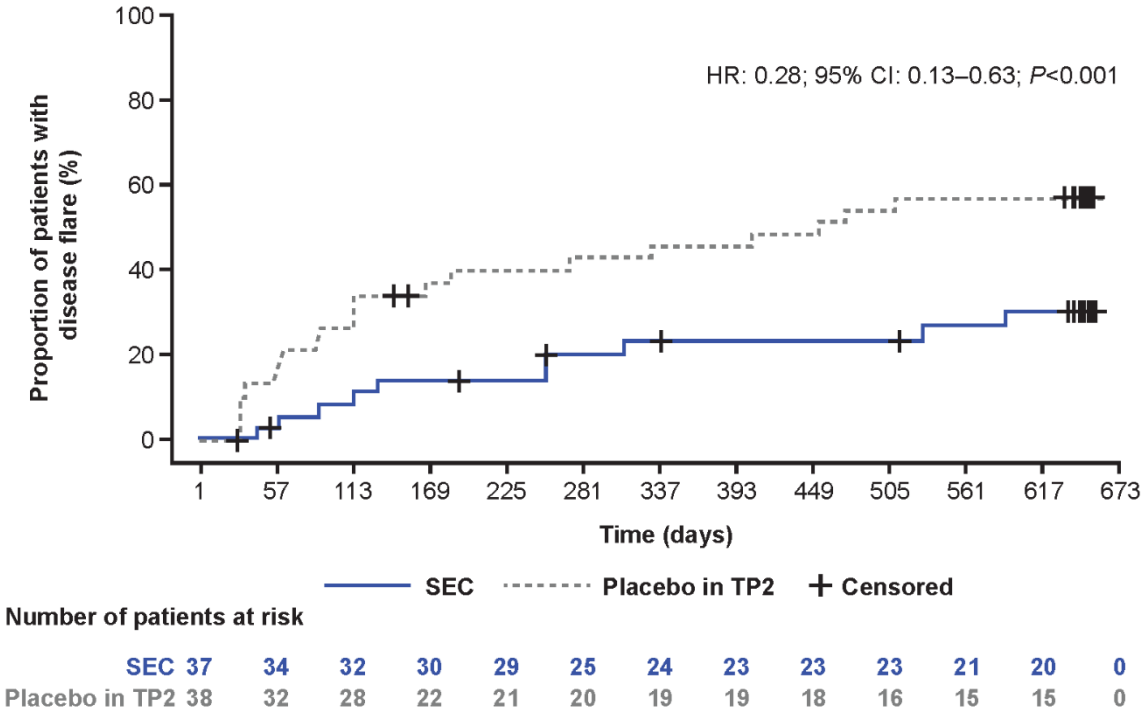
Figure. Time to flare in Treatment Period 2 (Primary Endpoint)



SEC: all subjects who did not take any placebo. Placebo in TP2: all subjects who took placebo in TP2 and SEC in other period/s. Day 1 = date of randomisation. Disease flare was derived relative to the end of TP1 (Week 12 visit). Patients who did not experience a disease flare in TP2 were censored at the date of their last non-missing flare evaluation in TP2. Patients at risk = patients in TP2 who did not have flare and were not censored before or at the start of the specified day.
NC, data not calculable

Table. Efficacy of secukinumab in Treatment Periods 1 and 2 (Key secondary endpoints)

Efficacy Outcomes, %	**TP1**	**TP2¥**		
	SEC (N=83)^	**SEC (N=37)**	**PBO (N=37)**	***P*-value**
JIA ACR 30	90.4	89.2	64.9	**0.014**
JIA ACR 50	86.7	78.4	62.2	0.152
JIA ACR 70	69.9	67.6	43.2	**0.042**
JIA ACR 90	39.8	51.4	40.5	0.431
JIA ACR 100	25.3	43.2	37.8	0.745
Inactive disease#	36.1	47.2	37.8	0.500
JADAS-27, mean (SD)	15.1 (7.2)	14.6 (8.1)	13.3 (5.8)	NA
Enthesitis count, mean change from BL (SD)	−1.8 (2.3)	−2.1 (2.0)	−1.9 (1.2)	NA

P-values: Cochran-Mantel-Haenszel test, adjusted for analysis factors: JIA category (ERA/ JPsA) and MTX use at BL
¥The N numbers are values at the end of TP2
^Efficacy outcomes (%) in TP1 calculated in patients with evaluable data at Wk 12 (N=83)
#Inactive disease: Definition adapted from JIA ACR criteria of Wallace et al., 2011. N=36 for SEC at the end of TP2
JADAS, Juvenile Arthritis Disease Activity Score; N, total number of patients in the treatment group; NA, data not available

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