The SQ tree SLIT-tablet reduces rhinoconjunctivitis symptoms and medication use during the tree pollen season (hazel, alder and birch pollen seasons) – Results from a large multi-center phase III trial

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Background

The SQ tree SLIT-tablet (ALK, Denmark) is being developed for treatment of moderate-to-severe allergic rhinitis and/or conjunctivitis induced by pollen from the birch homologous group. We report the results of a phase III trial.

Methods

TT-04 (EudraCT 2015-004821-15) was a randomized, parallel-group, double-blind, placebo-controlled trial. Institutional review board approval was obtained from 57 sites. In September and October 2016, 634 subjects were randomized 1:1 to the SQ tree SLIT-tablet (12 DU dose) or placebo. Subjects received ≥16 weeks of treatment before the start of the hazel, alder and birch pollen seasons; i.e., tree pollen season (TPS) in 2017 (**Figure 1**). Treatment duration was between 6.5 months and 9.5 months for subjects completing the trial. Daily symptom score (DSS, max=18), daily medication score (DMS, max=20) and the sum of these; i.e., total combined score (TCS, max=38) were assessed during the birch pollen season (BPS), TPS, and alder-hazel pollen season. The primary endpoint was average TCS during the BPS. Key secondary endpoints were DSS during BPS, TCS during TPS, and DSS during TPS.

For each pollen region the start date of the BPS was defined as the first day of 3 consecutive days with birch pollen count larger than or equal to 30 grains/m^3 and the stop date of the BPS was defined as the last day in the last occurrence of three consecutive days with birch pollen count larger than or equal to 30 grains/m^3. Alder and hazel pollen seasons were defined the same way but with a pollen count cutoff of 10 grains/m^3.

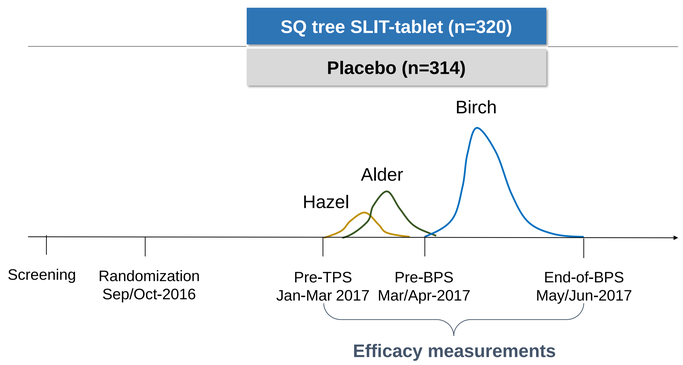

Figure 1. Trial design. Subjects were treated for at least 16 weeks before and during the 2018 tree pollen season (TPS). Efficacy was assessed throughout the TPS.

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Conflict of Interest: K Rance is an employee of ALK.

Results

Average TCS was improved with the SQ tree SLIT-tablet versus placebo throughout the TPS (**Figure 2**). Treatment effects on the average TCS, DSS, and DMS in the BPS, TPS, and alder-hazel pollen season were all statistically significantly greater for the SQ tree SLIT-tablet versus placebo (**Figures 3-5**). Average TCS during the BPS showed an estimated absolute difference of 3.02 corresponding to a reduction of 39.6% in favor of the SQ tree SLIT-tablet relative to placebo (p<.0001). For the average TCS during the TPS the estimated absolute difference was 2.27 (36.5% relative to placebo; p<.0001). For the average DSS, the estimated absolute differences were 1.32 for the BPS (36.8% relative to placebo; p <.0001), and 0.99 for the TPS (32.7% relative to placebo; p<.0001). DSS and DMS contributed almost equally to the observed treatment effect in both the BPS and TPS.

Figure 2. Average TCS throughout the tree pollen season.

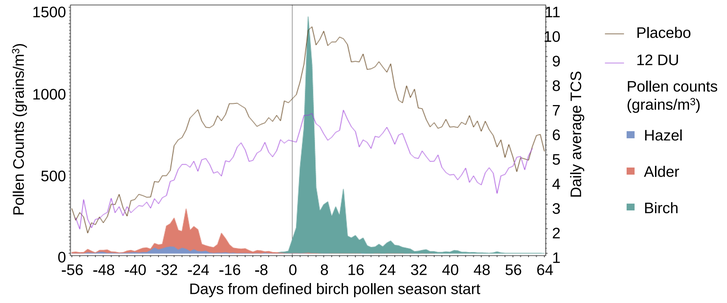


Figure 3. Efficacy during birch pollen season (BPS).

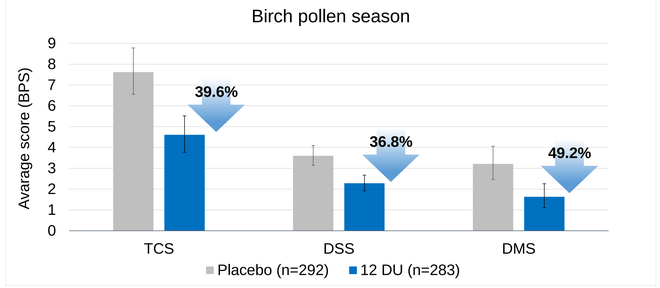


Figure 4. Efficacy during tree pollen season (TPS).

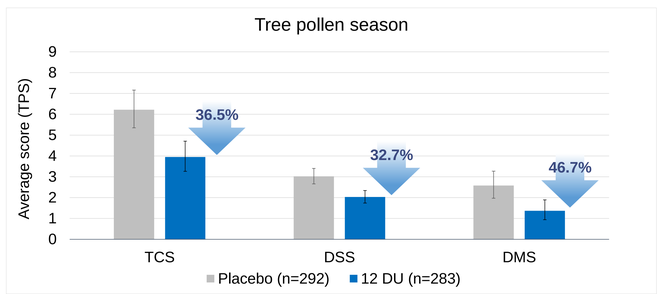
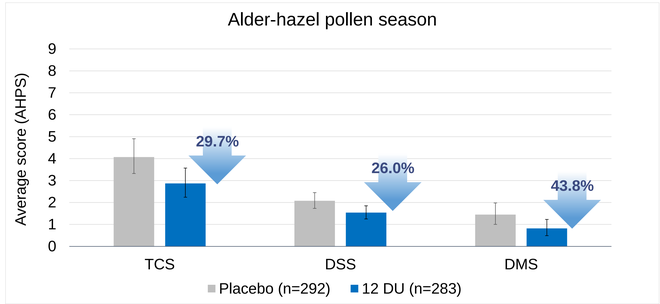


Figure 5. Efficacy during alder-hazel pollen season (AHPS).



Treatment was well-tolerated. Local reactions were the most common treatment-related events (**Figure 6**); the majority were mild or moderate in severity (**Table 1**). No deaths or anaphylactic reactions were reported with the SQ tree SLIT-tablet.

Figure 6. Proportion of subjects reporting treatment-related adverse events (safety analysis set)

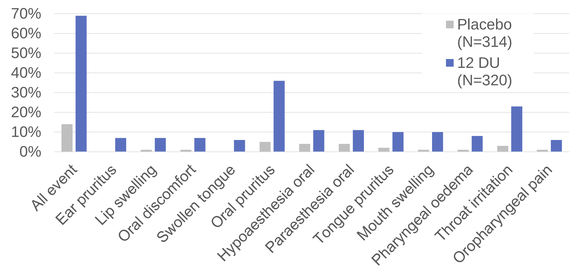


Table 1. Proportion of subjects reporting treatment-related adverse events (safety analysis set)

	Placebo N=314		12 DU N=320	
All treatment-related AEs, n (%n)	73	(23%)	239	(75%)
Mild	66	(21%)	192	(60%)
Moderate	11	(4%)	97	(30%)
Severe	2	(<1%)	16	(5%)
Serious	1	(<1%)	1	(<1%)
Leading to discontinuation	5	(2%)	24	(8%)

Conclusion

There was a statistically significant treatment effect of the tree SLIT-tablet compared with placebo for the primary and key secondary endpoints.

Clinical benefit was demonstrated for the birch pollen season, during the combined tree pollen season, and during the separately assessed alder-hazel season.

The tree SLIT-tablet was well tolerated in tree pollen allergic subjects, with a safety profile resembling that of other SLIT-tablets.