#0102 - High correlation between validated Rhinoconjunctivitis Quality Of Life (RQLQ) and EAACI recommended Combined Symptom Medication Score (CSMS) as clinical outcome measure in allergen immunotherapy trial

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Introduction
EAACI recommends the combined symptom and medication score (CSMS) as standardized clinical outcome measure in allergen immunotherapy trials for allergic rhinoconjunctivitis (ARC) and calls for further validation of this score (Pfaar, Allergy 2014). The first Phase III study with a sublingual immunotherapy (SLIT) in ARC with CSMS as primary outcome was recently completed. The primary results showed a clinically relevant and statistical significant 31% improvement in CSMS following SLIT with a liquid birch pollen extract compared to placebo ($p<0.0001$) (Pfaar et al. Allergy (2016); 71 (suppl.102): 45 (abstract 87). The validated Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ-S) assessed during the birch pollen season was correlated to the CSMS of this birch SLIT study and the minimal clinical important difference (MCID) for CSMS was estimated using the RQLQ-S as anchor.
Objectives
The data from the pivotal Phase III study were used after pre- and co-seasonal birch SLIT administration in 406 patients suffering from moderate to severe birch pollen induced ARC. Previously, a MCID of 23% in CSMS compared to placebo was justified based on clinical and statistical criteria and accepted by regulators. Pearson's correlation coefficient was calculated between the secondary RQLQ-S and CSMS and the MCID for CSMS was estimated using linear regression based on the consideration that an improvement of 0.5 points in the validated RQLQ-S score is accepted to be clinically relevant.
Results
A strong positive correlation was observed between the CSMS and the RQLQ-S scores during the pollen season ($r=0.68$ and $p<0.0001$). Based on regression analysis using the study results, a clinically relevant 0.5 point improvement in RQLQ-S corresponds to an MICD for CSMS of 21% (95% CI: 19-23%).
Conclusions
This is the first validation of the CSMS as proposed by the EAACI as primary endpoint in a Phase III field trial. Using the validated RQLQ-S score as anchor, the post-hoc results show that a 21% improvement in CSMS may be considered clinically relevant. Moreover, these results emphasize the clinical relevance of the 31% CSMS improvement realized after SLIT with a liquid birch pollen extract, the first pivotal Phase III study in ARC which used CSMS score as primary endpoint. Moreover, these results provide important guidance and support for the external validation of CSMS as primary outcome measure in allergen immunotherapy trials for ARC.