# Randomized Controlled Trial of Ragweed Sublingual Immunotherapy Tablet in Subpopulation of Canadian Children with Allergic Rhinoconjunctivitis

Rémi Gagnon[1], Anne K. Ellis[2], David I. Bernstein[3], Hendrik Nolte[4]

[1]Clinique Spécialisée en Allergie de la Capitale, Québec, QC, Canada;
[2]Department of Medicine, Queen's University, Kingston, ON, Canada;
[3]Department of Internal Medicine, University of Cincinnati College of Medicine and Bernstein Clinical Research Center, Cincinnati, OH, USA;
[4]ALK, Bedminster, NJ, USA

R. Gagnon has served as a speaker and/or advisor for ALK-Abello, AstraZeneca, Aralez, CSL Behring, GlaxoSmithKline, Merck, Novartis, Pediapharm, Pfizer, Sanofi, and Shire, and served as an investigator for AstraZeneca, Biocryst, DBV, GlaxoSmithKline, Green Cross Pharmaceuticals, Merck, Novartis, Regeneron, Shire, Stallergenes, and Sanofi Genzyme/Regeneron. A.K. Ellis has participated in advisory boards for Abbvie, ALK-Abelló, AstraZeneca, Aralez, Bausch Health, Circassia Ltd, GlaxoSmithKline, LEO Pharma, Johnson & Johnson, Merck, Mylan, Novartis, Pediapharm and Pfizer, has been a speaker for ALK, Aralez, AstraZeneca, Bausch Health, Boehringer-Ingelheim, CACME, Meda, Medexus, Mylan, Merck, Novartis, Pediapharm, Pfizer, The ACADEMY, and Takeda. Her institution has received research grants from AstraZeneca, Bayer, LLC, Circassia Ltd, Green Cross Pharmaceuticals, GlaxoSmithKline, Sun Pharma, Merck, Novartis, Pfizer, Regeneron and Sanofi. She has also served as an independent consultant to Allergy Therapeutics, Bayer, LLC, Ora Inc., and Regeneron in the past. D.I. Bernstein has received grant support from Aimmune, Allergy Therapeutics, ALK, Amgen, AstraZeneca, Avillion, Biocryst, Boehringer Ingelheim, Cipla, Genentech, GlaxoSmithKline, Gossamer, Leo, Lupin, Menlo, Merck, Mylan, Novartis, Novum, Pearl, Regeneron, Shire, and TEVA, served as an advisor for ALK America, Gerson-Lehman, GlaxoSmithKline, and Guidepoint Global, and been a speaker for ALK and GlaxoSmithKline. H. Nolte is an employee of ALK.

Hendrik.nolte@alk.net

Funding for this study was provided by ALK, Hørsholm, Denmark

# Introduction

- Ragweed pollen is a common cause of allergic rhinitis/conjunctivitis (AR/C)[1]
- AR/C in children can interfere with sleep and daily activities and negatively impact school attendance and performance[1]
- Post hoc analyses of randomized, double-blind, placebo-controlled trials[2,3] have demonstrated the efficacy and tolerability of the 12 Amb a 1-U ragweed sublingual immunotherapy (SLIT)-tablet in Canadian adults with ragweed pollen-induced AR/C [4]
- An international, double-blind, placebo-controlled trial of the ragweed SLIT-tablet was conducted in children with ragweed pollen-induced AR/C with or without asthma[5]
  - This post hoc analysis evaluated the efficacy and tolerability of the ragweed SLIT-tablet in the subpopulation of Canadian children

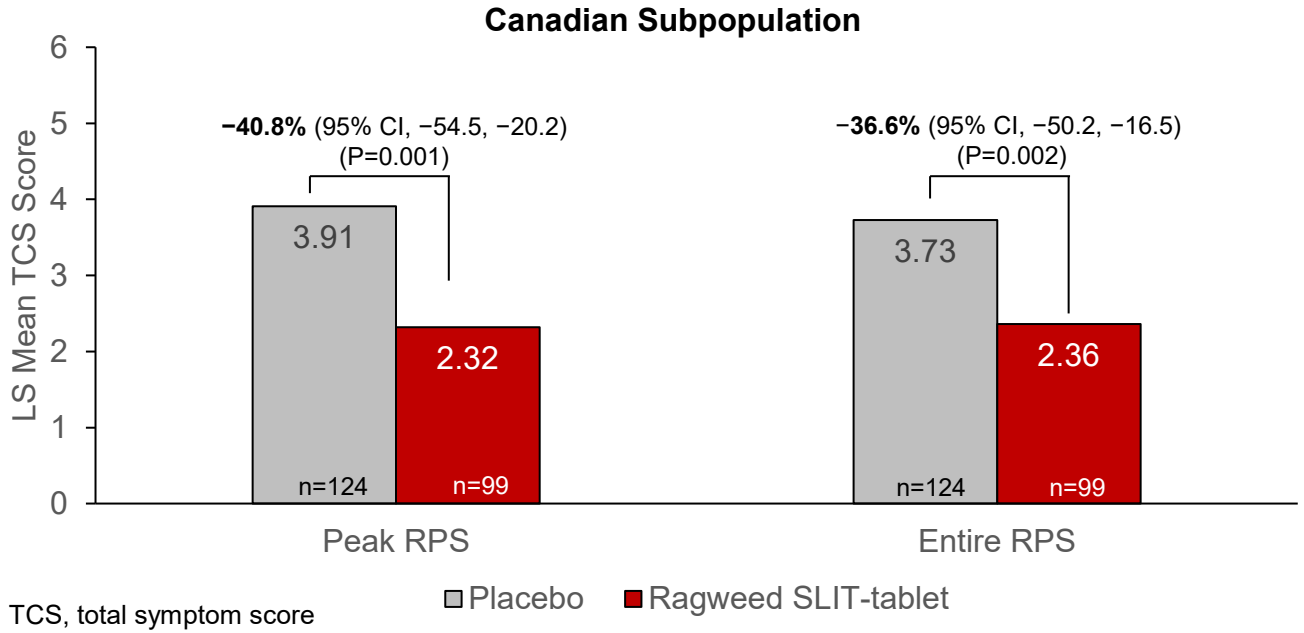

1. Meltzer, EO, et al. *J Allergy Clin Immunol Pract*. 2017;5:779-789.
2. Creticos PS, et al. *J Allergy Clin Immunol.* 2013;131:1342-9.
3. Nolte H, et al. *Ann Allergy Asthma Immunol.* 2013;110:450-456.
4. Kim H, et al. *Allergy Asthma Clin Immunol*. 2014;10:55.
5. Nolte H, et al. *J Allergy Clin Immunol Pract*. 2020;8:2322-2331.

# Methods

- Children aged 5-17 years with ragweed pollen-induced AR/C with or without asthma were randomized 1:1 to daily ragweed SLIT-tablet (12 Amb a 1-Unit dose) or placebo for up to 28 weeks (NCT02478398)
  - AR/C symptom-relieving medication was provided to both treatment groups
- Primary endpoint was the total combined daily symptom and medication score (TCS) during peak ragweed pollen season (RPS)
  - Six rhinoconjunctivitis symptoms were measured on a scale of 0 to 3
  - Symptom-relieving medication use was recorded in an e-diary once-daily
  - TCS is the sum of the rhinoconjunctivitis daily symptom score (DSS) and daily medication score (DMS)
- Post hoc analyses were conducted in the Canadian participants using per protocol statistical methods

# Rhinoconjunctivitis TCS during RPS in Canadian children

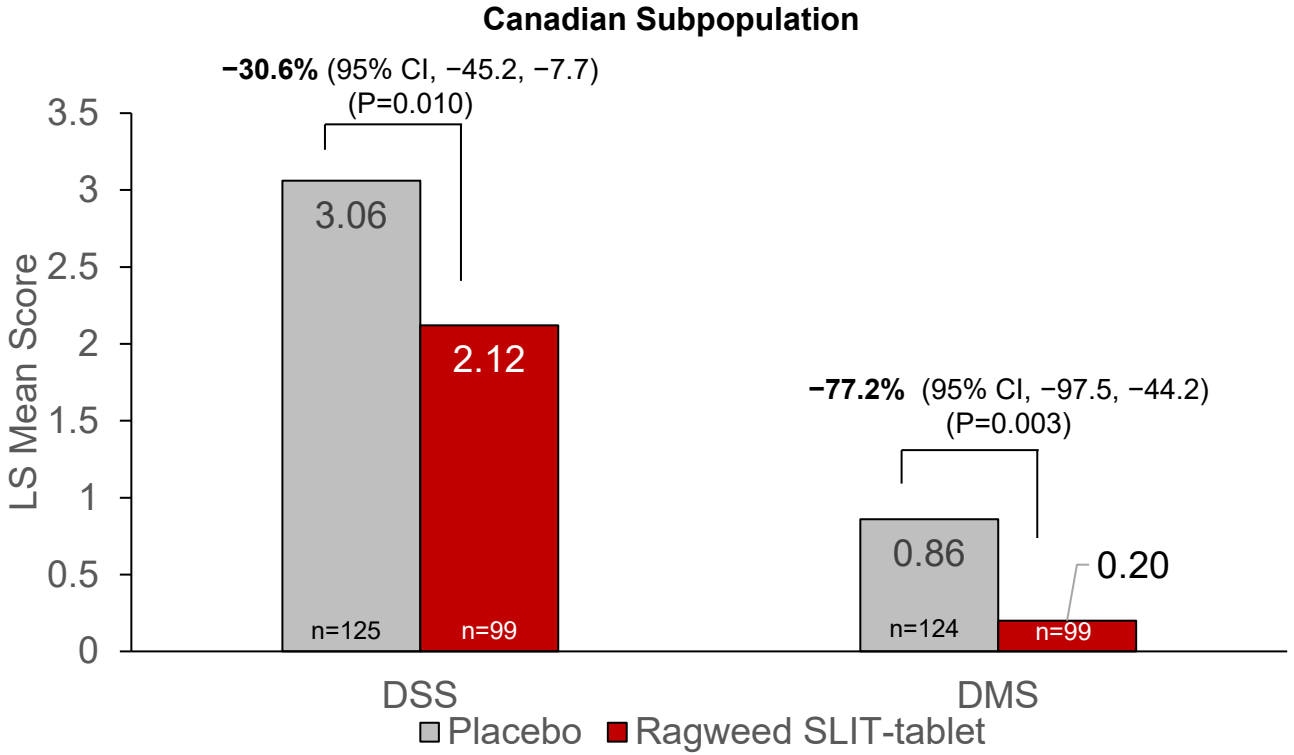
- Of the 1025 randomized participants, 246 (SLIT-tablet, n=116; placebo, n=130) were in the Canadian subpopulation
  - 90.7% of Canadian participants were polysensitized
  - 35.8% of Canadian participants had asthma
- In the total study population, relative TCS improvements with the ragweed SLIT-tablet vs placebo were 38.3% (P<0.001) during peak RPS and 32.4% (P<0.001) during the entire RPS
- In the Canadian subpopulation, relative TCS improvements with the ragweed SLIT-tablet vs placebo were 40.8% during peak RPS and 36.6% during the entire RPS




LS, least square; RPS, ragweed pollen season; TCS, total symptom score

# Rhinoconjunctivitis DSS and DMS during peak RPS in Canadian children

- In the total study population, DSS and DMS improved with SLIT-tablet versus placebo by 35.4% and 47.7%, respectively, during peak RPS (both P<0.001)
- In the Canadian subpopulation, DSS and DMS improved with SLIT-tablet versus placebo by 30.6% and 77.2%, respectively, during peak RPS




DMS, daily medication score; DSS, daily symptoms score; LS, least square; RPS, ragweed pollen season

# Safety of ragweed SLIT-tablet in Canadian children

- The ragweed SLIT-tablet was well tolerated in the overall population and Canadian subpopulation
- No events of anaphylaxis, airway compromise, eosinophilic esophagitis, intramuscular epinephrine, or severe treatment-related systemic allergic reactions were reported in the overall population or Canadian subpopulation

| AE, No. (%) | Ragweed SLIT-Tablet (n=117)* | Placebo (n=129)* |
|---|---|---|
| Treatment-emergent AE | 108 (92.3) | 96 (74.4) |
| Treatment-related AE | 89 (76.1) | 47 (36.4) |
| SAE | 0 | 0 |
| Treatment-related SAE | 0 | 0 |
| AE leading to treatment discontinuation | 6 (5.1) | 0 |
| Treatment-related AE leading to treatment discontinuation | 6 (5.1) | 0 |
| Discontinued treatment due to SAE | 0 | 0 |
| Discontinued treatment due to a treatment-related SAE | 0 | 0 |

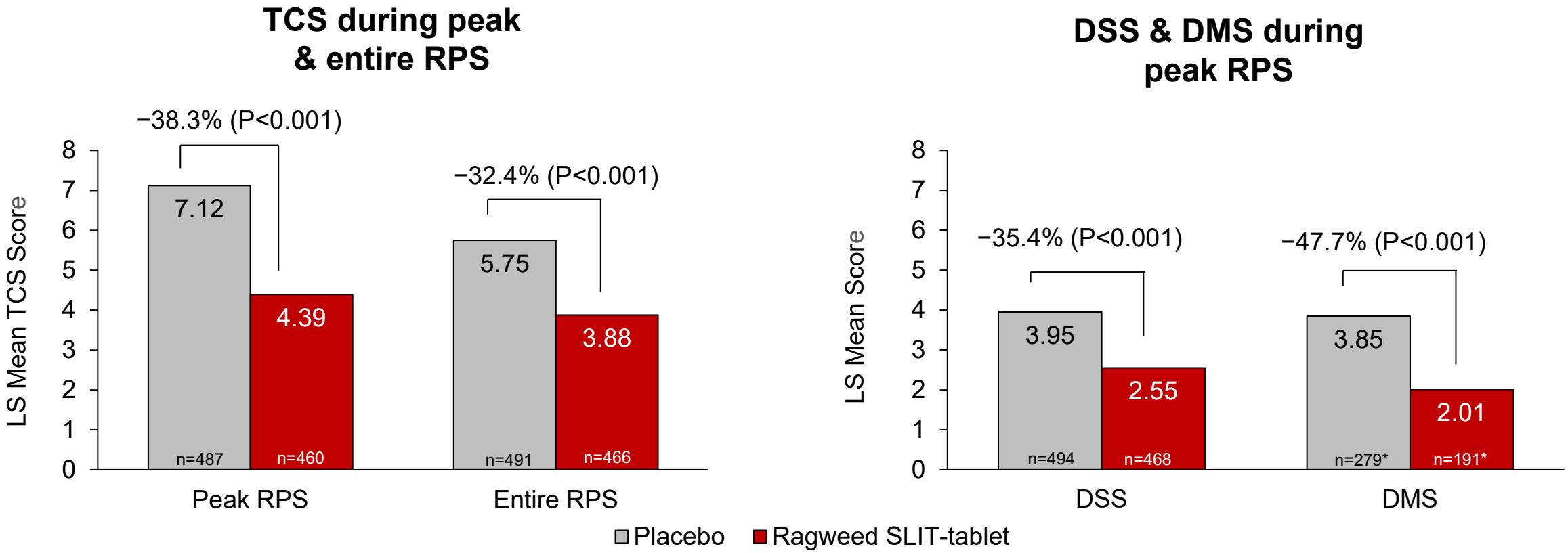
AE, adverse event; SAE, serious adverse event.
*One subject randomized to placebo received the ragweed SLIT-tablet by mistake.

# Conclusions

- The ragweed SLIT-tablet resulted in clinically meaningful improvement in symptoms and decreased symptom-relieving medication use in Canadian children with AR/C
- Treatment was well tolerated
- The efficacy and tolerability of the ragweed SLIT-tablet in the subpopulation of Canadian children was consistent with the full study population that included children from North America and Europe
- The magnitude of TCS improvement in the Canadian children was similar to that of Canadian adults (39.5%; $p<0.0001$ vs placebo)[1]
- The proportion of treatment-emergent and treatment-related AEs in the Canadian children was similar to that of Canadian adults[1]

1. Kim H, et al. *Allergy Asthma Clin Immunol*. 2014;10:55.

# Backup Slide:
# TCS, DSS, and DMS in overall study population




DMS, daily medication score; DSS, daily symptom score; LS, least square; RPS, ragweed pollen season; TCS, total symptom score

* 269 participants on ragweed SLIT-tablet and 208 participants on placebo had no rescue medication use. DMS analysis is based on the zero-inflated log-normal model.