Title: Grass pollen subcutaneous immunotherapy results in faster and greater suppression of allergen-induced skin responses compared to sublingual immunotherapy: a randomised controlled trial. Guy Scadding¹, Moises Calderon¹, Mohamed H. Shamji¹, Martin Penagos¹, Aarif Eifan ¹, Deborah Phippard², Kristina M. Harris², Nadia Tchao³, Noha Lim³, Alkis Togias⁴, Henry T. Bahnson⁵, Michelle L. Sever⁵, Kaitie Lawson⁵, and Stephen R. Durham¹.

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Background: We undertook a randomised, double-blind, double-dummy, controlled trial of subcutaneous (SCIT) and sublingual (SLIT) grass pollen immunotherapy in participants with moderate-severe seasonal allergic rhinitis.

Methods: 106 participants were randomised to one of three arms: active-SCIT (Alutard SQ, ALK), active-SLIT (Grazax, ALK) or double-placebo. Early (EPR, 15 minute) and late (LPR, 8 hour) skin responses to intradermal injection with grass pollen extract (Aquagen SQ, Phleum pratense [10 SQ units containing 7ng Phl p 5], ALK, Denmark) were recorded at baseline, at year 1 and year 2 during treatment and at year 3 (one year after stopping treatment). Serum was assessed for ability to block IgE-facilitated grass pollen allergen binding to EBV-transformed B-cells (IgE-FAB) in vitro.

Results: At year 1, SCIT suppressed skin EPR compared to both placebo (26.1%) and SLIT (22.6%), p<0.05. SLIT had a suppressive effect at year 2 (18.2% vs placebo), but the effect of SCIT was greater (17.4% vs SLIT), both p<0.05. Both active treatments had significant persistent effects at year 3 (SCIT 18.6%, SLIT 8.4% vs placebo, both p<0.05). Both treatments reduced skin LPR at all 3 years, peaking at year 2 (SCIT 63.5%, SLIT 39.7% vs placebo), persisting at year 3 (SCIT 49.7%, SLIT 32.5% vs placebo); SCIT had a greater effect than SLIT throughout (all p<0.01). SCIT sera showed strong inhibition of IgE-FAB at year 1 (p<0.05 vs placebo and SLIT), whereas SLIT sera showed modest, but significant inhibition (p<0.05 vs placebo). By year 2, the effect of SLIT had increased, showing no difference from SCIT. A significant effect was maintained at year 3 by SCIT and SLIT sera.
**Conclusion:** SCIT compared to SLIT results in faster and greater suppression of skin EPR and LPR, and faster suppression of IgE-FAB. Two years with SCIT or SLIT result in persistent suppression (albeit of lower magnitude) of skin EPR, LPR and IgE-FAB one year after discontinuation.