



AppleCare - Birch Pollen Immunotherapy by Consumption of Apples

Bettina Nothegger¹, Claudia E. Covaciu², Martin Tollinger³, Thomas Letschka⁴, Valentina Cova⁴, Klaus Eisendle², Norbert Reider¹

¹Department of Dermatology, Venerology and Allergology, Medical University of Innsbruck, Innsbruck, Austria;

²Department of Dermatology and Venerology, Central Teaching Hospital of Bolzano, Bolzano, Italy;

³Institute of Organic Chemistry and Center for Molecular Biosciences Innsbruck, University of Innsbruck, Innsbruck, Austria;

⁴Department of Applied Genomics and Molecular Biology, Laimburg Research Centre, Ora, Italy

BACKGROUND

The majority of birch-pollen-allergic patients develop also an allergy to raw apples and other Rosaceae fruits, known as oral allergy syndrome (OAS). This can be attributed to a strong homology between the Bet v 1 and Mal d 1 allergens. This cross-reactivity provides an opportunity to use apples in a controlled and established dosage to cure birch pollen- and apple allergy. The AppleCare Pilot-Study aims at developing a healthy and time-saving alternative therapeutic option for birch-pollen-allergic patients with apple allergy.

METHODS

- 49 participants with birch-pollen related apple allergy, aged between 18-70
- ImmunoCAP measurements (specific IgE and IgG of Bet v 1, Mal d 1, Mal d 3)
- Prick-to-Prick Test (PPT) with 23 low, middle and high allergenic apple cultivars [fig.3 b, c]. Three apple parts were tested: Flesh, Peel, Stem;
- Oral Provocation Tests with three selected apple cultivars of each allergenicity class (Red Moon®, Pink Lady®, Golden Delicious) in 25 patients [fig.3 a, fig.2]
- Immunotherapy (SIT) over > 6 months (daily apple intake in increasing allergen concentration).
- Further analyses to assess the tolerability of apples and their impact on pollinosis: Conjunctival provocation tests, pollen-diaries, visual analogue scores, NMR structure analysis of Mal d 1 isoforms;

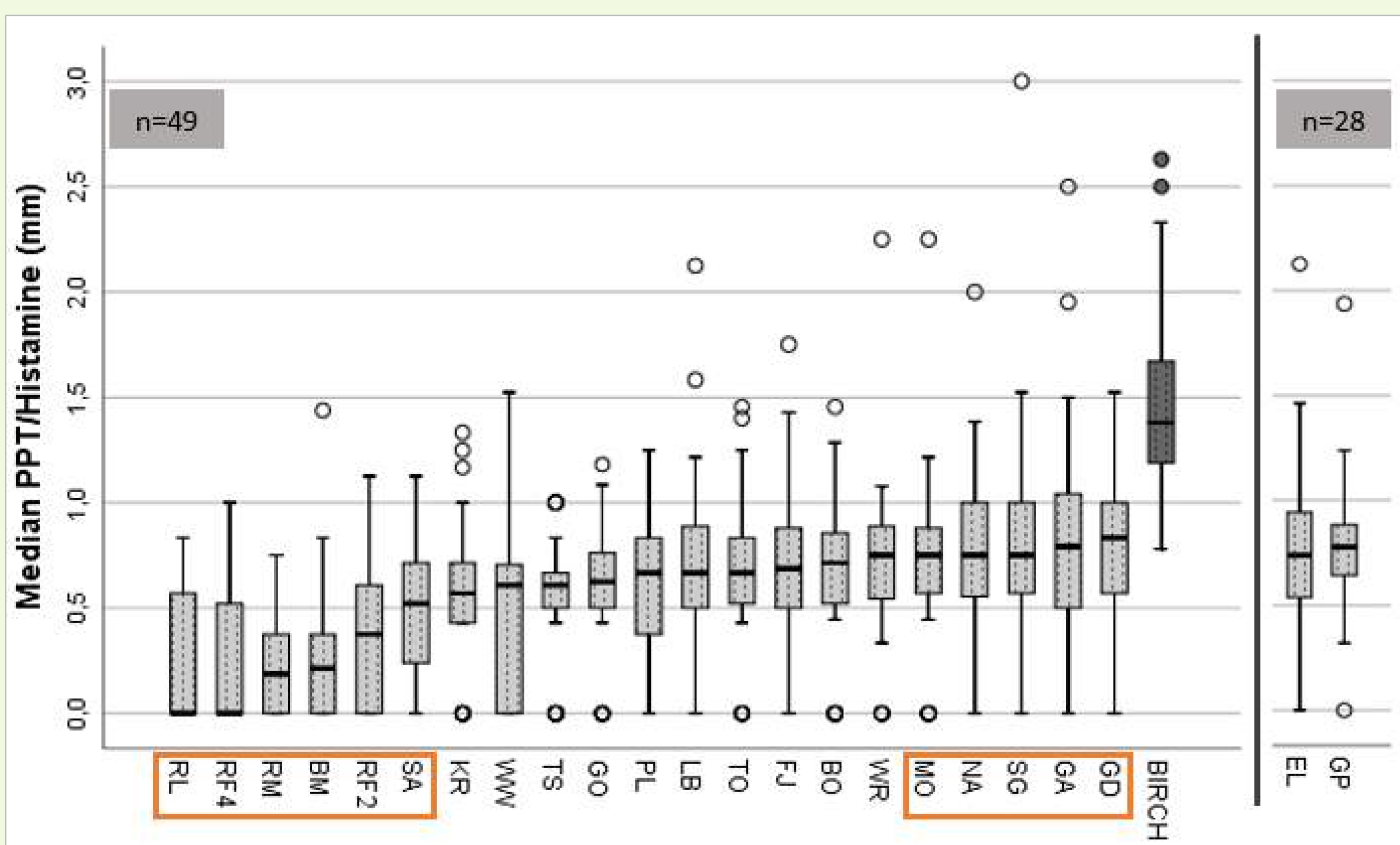


Figure 1. Apple Prick to Prick-Test (PPT) with 23 apple cultivars including Birch, Median PPT/Histamine (mm). The first 21 apple cultivars, RL to GD*, were tested in Austria and Italy, EL* and GP* only in Austria. Statistical outliers are shown in dots. The cultivars are divided into three groups: low allergenic (red fleshed cultivars RL to RF2 and SA), middle allergenic (KR to WR) and high allergenic (MO to GD). The low allergenic group is significantly different from the high allergenic group ($p < 0,001$, Friedman's two-way Anova and Post-hoc test with Bonferroni correction).

*RL=Redlove®, RF4=Red fleshed 4, RM=Red Moon®, BM=Baya Marisa®, RF2=Red Fleshed 2, SA=Santana, KR=Kanada Renette, WW=Weißer Winterkalvill, TS=Tiroler Spitzleederer, GO=Gloster, PL=Rosy Glow Pink Lady®, LB=LB 17906, TO=Topaz, FJ=Fuji®, BO=Bonita, WR=Weißer Rosmarin, MO=Modi®, NA=Natyra, SG=Sonnenglanz, GA=Gala, GD=Golden Delicious, EL=Elstar, GP=Goldparmäne;

RESULTS

Red-fleshed apples and the low allergen sort Santana are tolerated well and significantly different ($p < 0,001$) to the commercial apple sorts Modi®, Natyra®, Gala and Golden Delicious which are, in comparison classified as high allergenic. The commercials Pink Lady®, Topaz, Fuji®, Bonita, and Elstar are better tolerated. Of the tested old apple varieties, Kanada Renette, Weißer Winterkalvill, Tiroler Spitzleederer and Gloster are less reactive than Weißer Rosmarin and Goldparmäne. Different allergic reactions between Flesh, Peel or Stem could be found in over 16 tested apple sorts. The majority of PPT responses for peeled apple cubes was lower than for unpeeled apple cubes.

PPTs predicted the severity of OAS. The participants were able to eat higher amounts of Red Moon® than Pink Lady and Golden Delicious [fig.2]. Unpeeled apple pieces induced stronger allergic reactions. Six participants were able to eat more than one full Red Moon® apple. In some cases, also one full Pink Lady or Golden Delicious was tolerated. This shows that every participant is different and needs to be treated in his own way with a suitable therapy apple, respectively.

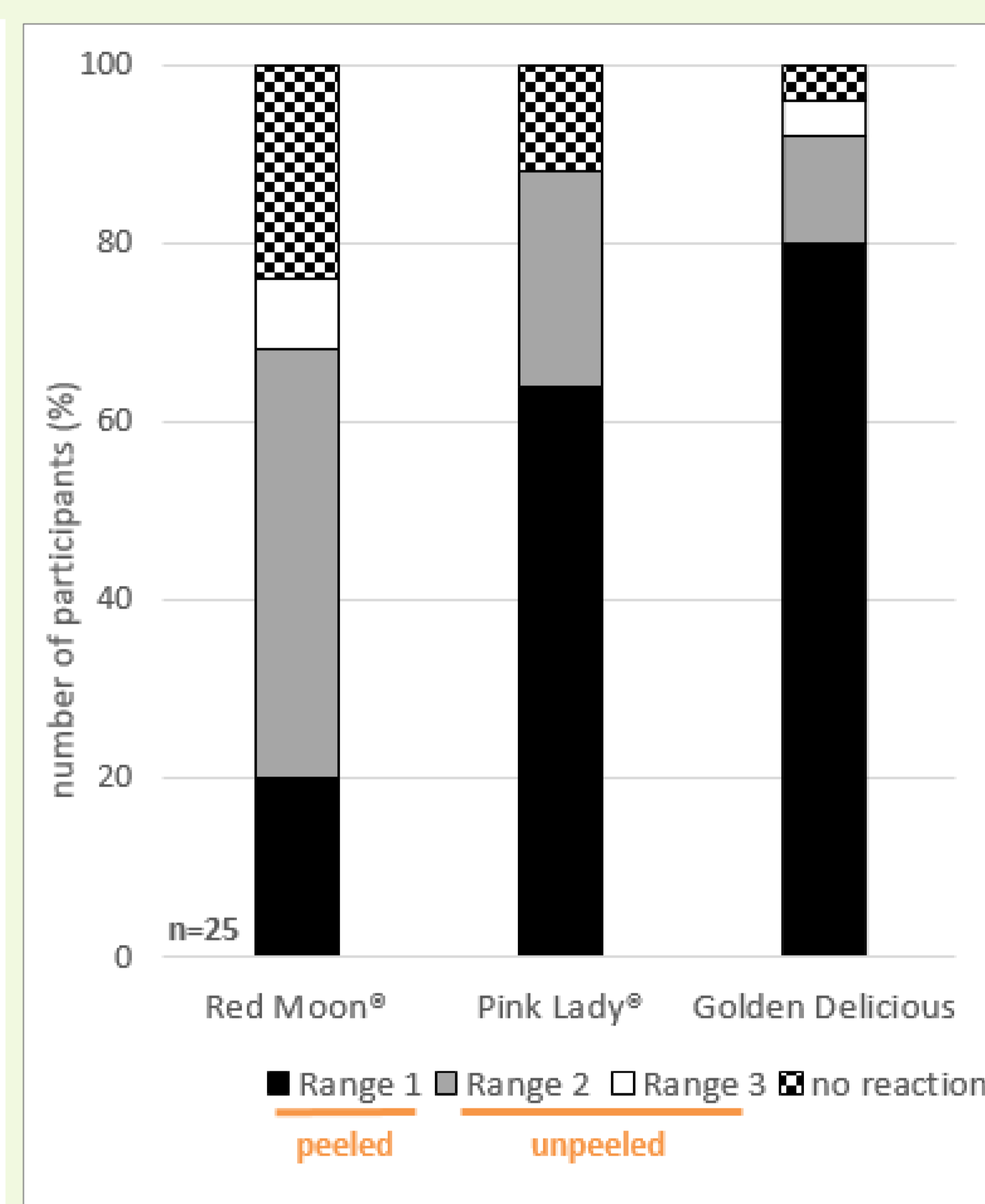


Figure 2. Number of participants (%) reacting on different amounts of apple. Low, middle and high allergenic apple sorts RM, PL and GD were tested by oral provocations. The respective apple amounts that induced first OAS symptoms (e.g. itching/scratching) are divided into three ranges: **Range 1 (0.1-8.6g) peeled**, **Range 2 (13.6-43.6g) unpeeled** and **Range 3 (83.6-163.6g) unpeeled**. In some cases, more than one full apple (163.6+100g) was tolerated without any symptoms (=no reaction).

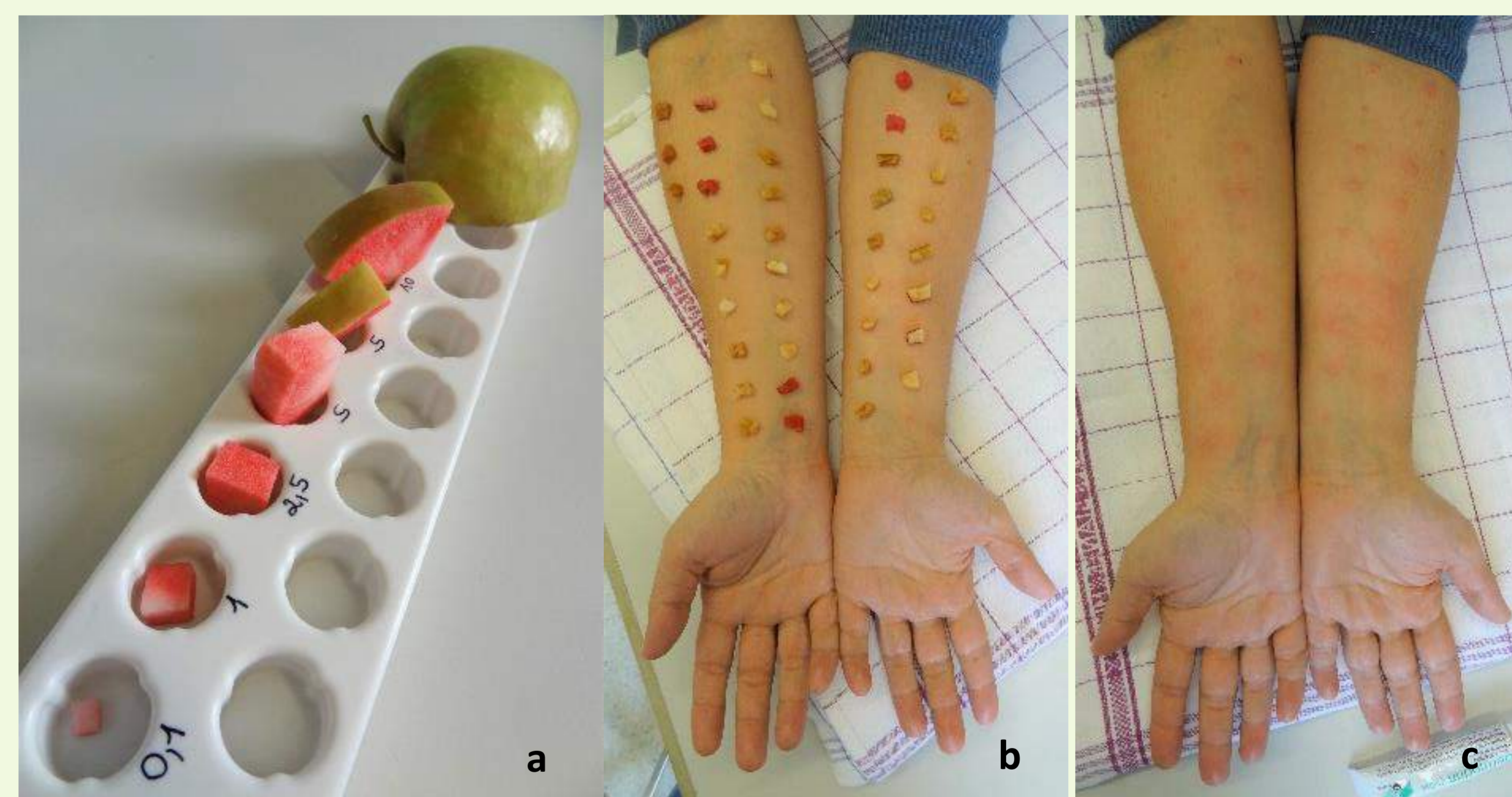


Figure 3. SCREENING. (a) Oral Provocation Test with Red Moon®; (b,c) Prick-to-Prick Test with apples;

CONCLUSION

So far, our results support the assumption that old apple cultivars are better tolerated and we were able to prove for the first time the low allergenicity of red-fleshed apples. In the next step, we focus on the SIT with specifically selected apple sorts in increasing allergen concentration. Initial results are expected in one year. This Pilot-Study was performed as part of the EU-funded Interreg V-A Italy-Austria 2014-2020 AppleCare-Project.