Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

SHORT COMMUNICATION

OPEN ACCESS

Achieving remission with peach sublingual immunotherapy in adults and children with Lipid transfer protein syndrome without associated cofactor

Victoria Villalobos Violán[a*], Maria Frühbeck Muñoz[b], Maria Jesús Trujillo Trujillo[a], Ester Mohedano Vicente[a], Mar Gandolfo-Cano[a-c], Eloína González-Mancebo[a]

[a]*Department of Allergy. University Hospital of Fuenlabrada, Madrid, Spain*
[b]*University Hospital of Fuenlabrada. Rey Juan Carlos University, Madrid, Spain*
[c]*Department of Allergy. University Hospital of La Paz. IdiPAZ. Madrid, Spain*

Received 5 May 2025; Accepted 18 August 2025
Available online 1 January 2026

KEYWORDS
Pru p3 sublingual immunotherapy;
food allergy;
cofactors;
efficacy;
remission

Abstract
Introduction: Lipid transfer protein (LTP) allergy is the leading cause of food allergy and food anaphylaxis in adults in the Mediterranean region. Treatment options include avoidance of the implicated foods and specific sublingual peach immunotherapy (Pru p3 SLIT). This study aims to determine the effectiveness of Prup3 SLIT in patients with cofactor-induced and noncofactor-induced LTP syndrome, assessing the change in food tolerance before and after treatment.
Methods: We conducted a retrospective observational study of 23 patients diagnosed with LTP allergy who were treated with Pru p3 SLIT. To assess food tolerance before and after treatment, all patients underwent an oral challenge with unpeeled peach, as well as other foods to which they were allergic or sensitized.
Results: Fifty-five percent of patients were female, with a mean age of 25.8 years, 39% of whom were under 14 years of age. Thirteen percent were allergic only to pink fruits, 4.3% to nuts, 43.4% to two families, and 39.1% to more than two families of vegetables. Eighty-six percent of the reactions were systemic, including 47% anaphylaxis. After a mean of 2.7 years of treatment, 95.6% of the patients tolerated oral provocation with unpeeled peach and all foods to which they were allergic. However, none of the seven patients with cofactor-induced or cofactor-enhanced allergic reactions to food showed improved tolerance following Pru p3 SLIT.
Conclusion: Pru p3 SLIT can induce clinical remission of LTP food allergy in both adult and pediatric populations. However, it doesn´t resolve cofactor-triggered LTP reactions; therefore, patients with this profile should continue to avoid such triggers.

***Corresponding author:** Victoria Villalobos Violán, Department of Allergy. University Hospital of Fuenlabrada, Madrid, Spain.
Email address: vivillalobosviolan@gmail.com

https://doi.org/10.15586/aei.v54i1.1408

Introduction

Lipid transfer proteins (LTPs) are a family of panallergens widely distributed in the plant kingdom and are located in the outer layer of foods because of their protective function. Their clinical relevance is largely limited to the Mediterranean area, where they are the most frequent cause of food allergy and food-induced anaphylaxis in adults.[1]

LTPs can be found in foods such as *Rosaceae* fruits, nuts, vegetables, legumes, cereals, and several pollens.[2] Pru p3 (peach LTP) is the most relevant allergen in allergy to *Rosaceae* fruits among Spaniards and is usually the primary sensitizer that subsequently directs the immune response towards the recognition of other LTPs in most allergic patients. It is also a marker of severe systemic reactions to plant foods.[3]

LTP syndrome occurs in patients sensitized to LTPs from different plant foods because of cross-reactivity between their proteins. Clinical manifestations range from oral pruritus or contact urticaria to anaphylaxis.[4] A significant number of reactions also involve cofactors, most commonly physical exercise and the intake of nonsteroidal anti-inflammatory drugs (NSAIDs).

Classic treatment includes avoiding implicated foods and treating acute manifestations in case of a reaction. However, this approach leads to a loss of quality of life and does not ensure the absence of accidental-ingestion-related reactions.[5] Since sublingual immunotherapy with commercial allergenic extracts of Pru p3 (Pru p3 SLIT) was marketed in 2011, several studies have demonstrated its efficacy, even in those who had systemic reactions,[6] not only in clinical trials[7]but also in real-life conditions.[8] However, doubts remain about the management and indication of Pru p3 SLIT in patients with cofactor-associated LTP allergy.

Our study aimed to determine the effectiveness of Pru p3 SLIT in real-life conditions in patients with cofactor-induced and noncofactor-induced LTP syndrome, by evaluating the change in food tolerance before and after the treatment. As a secondary objective, we assessed the safety of Pru p3 SLIT through the occurrence of adverse effects and checked for the development of new food sensitizations during or after treatment.

Material and Methods

A retrospective observational study was carried out in routine clinical practice, with a pre-post design in which each patient acted as their own control, before and after treatment. We analyzed data from 80 patients diagnosed with LTP syndrome who were prescribed Pru p3 SLIT in the Allergology Unit of the Fuenlabrada University Hospital from its commercialization in 2011 to November 2023.

In 2022, we implemented a protocol for the management of these patients, starting with oral provocations with unpeeled peach and other reaction-implicated foods after they had been on treatment for 1 year (Figure 1). Prior to the protocol, each physician decided independently when to assess food tolerance.

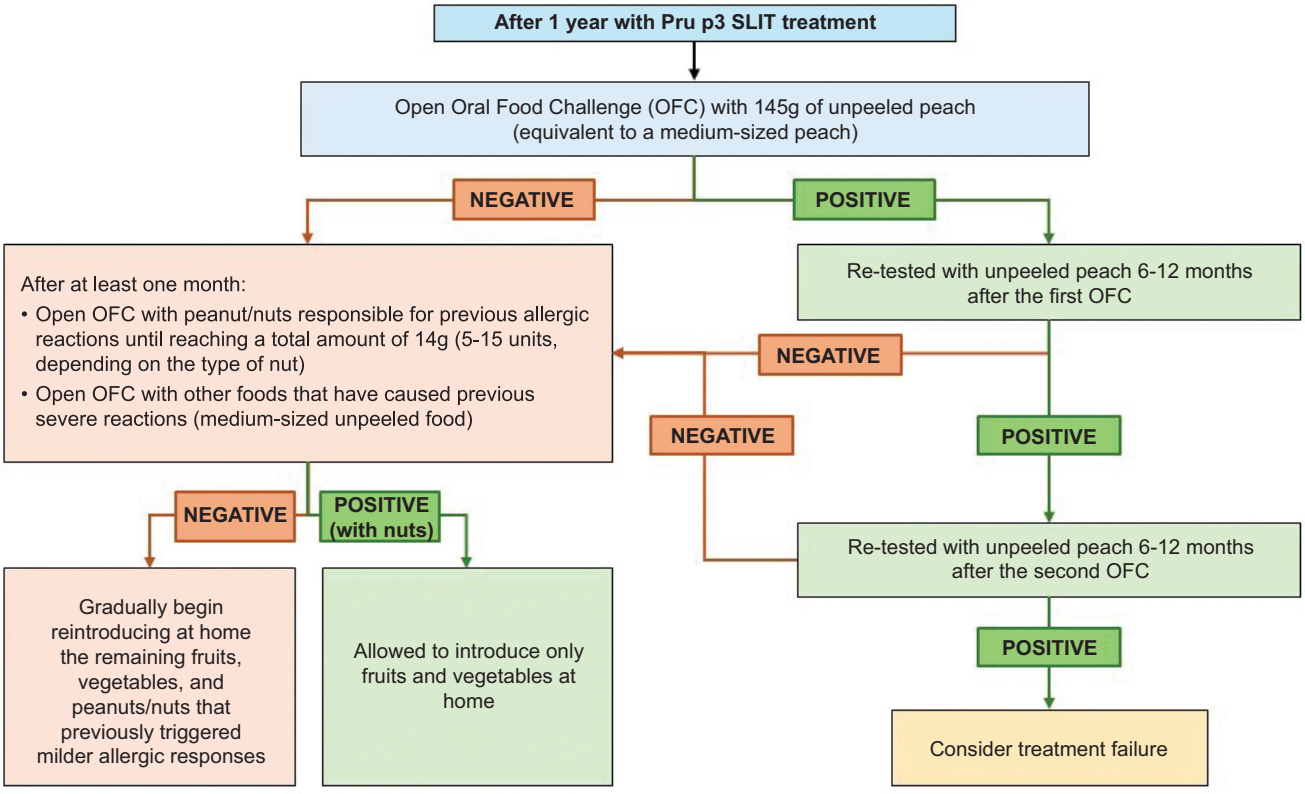

Figure 1 Oral challenge protocol of the allergology unit of the Fuenlabrada university hospital.

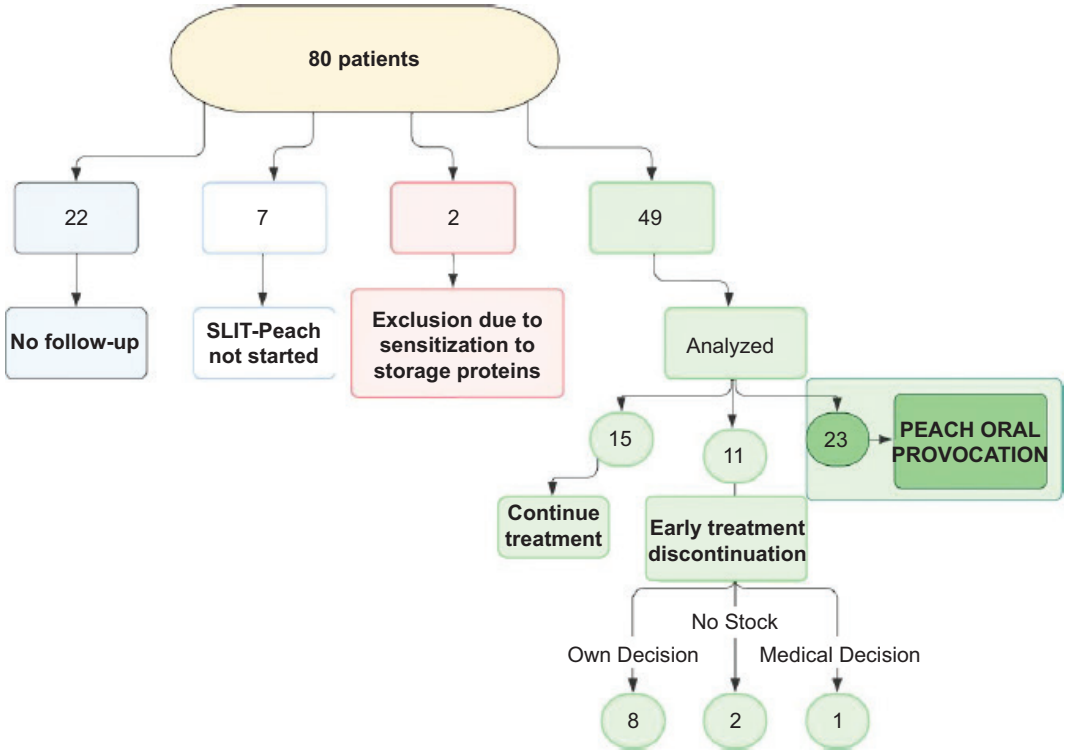

Figure 2 Patients finally included in the study.

As shown in the flow chart in Figure 2, only patients who could be orally challenged with unpeeled peach, as well as with other foods, were eligible for inclusion in the study, allowing us to evaluate the effectiveness of the treatment in a total of 23 patients.

Results

Fifty-five of the patients were female, with a mean age of 25.8 years (range: 7–55), including 9 patients (39%) younger than 14 years. Thirteen percent were allergic only *to Rosaceae* fruits, 4.3% to nuts, 43.3% to two families, and 39.1% to more than two, including reactions to other LTP foods such as citrus fruits and bananas, vegetables (lettuce and tomatoes), and grains (wheat and corn). Eighty-six percent of the reactions were systemic, including 39.1% of anaphylaxis. The presence of cofactors in the reaction was observed in 7 patients, with exercise being the main factor (6/7) and, to a lesser extent, NSAIDs' concomitant intake (1 of the previous 6) and menstruation (1/7). Of these patients, three reported a reaction only when ingesting the food in combination with the cofactor, and four reported mild allergic symptoms with food ingestion that worsened when the cofactor was present. All cofactor-related data were obtained from patients after a thorough medical history was taken.

The mean treatment duration with Pru p3 SLIT was 3.4 years. A total of 91.3% had no adverse reactions; only one local and one mild grade 2 systemic reaction (itchy lips and a few facial wheals) were observed. According to our protocol, after an average of 2.7 years of treatment, 95.7% of the patients tolerated oral challenge with unpeeled peach and all foods to which they were allergic. However, none of the seven patients with cofactor-induced or cofactor-enhanced allergic reactions to food showed improved tolerance to these plant foods in the presence of the cofactor. This information was specifically obtained in follow-ups, after instructing patients to cautiously re-expose themselves to the intake of food in the presence of the same cofactors. Finally, after a follow-up of 4–10 years, no new sensitization or allergic reactions to new foods were observed.

Discussion

In a recent 10-year follow-up study conducted to assess the natural history of 113 patients allergic to LTPs not treated with immunotherapy, Betancor et al. showed that all patients remained sensitized to the initial allergens and one-third developed sensitization to new plant foods.[9]

In contrast, a previous publication showed that after 1 year of treatment with Pru p3 SLIT in patients with LTP syndrome, 90.6% of patients tolerated a whole unpeeled peach.[6] Similar data were observed in another study, in which after 24 months of treatment, 95% also tolerated it.[8]

Although previous studies have demonstrated a relationship between the severity of the reactions and the presence of cofactors,[10] the mechanism remains unknown and, to date, avoidance remains the main recommendation, as there are no scientific publications addressing the indication of Pru p3 SLIT in the presence of these cofactors.

Our study suggests better outcomes, showing that both adult and pediatric patients can achieve remission of LTP food allergy, with tolerance to peach and other implicated foods reaching 95.6% after an average of 2.7 years

of treatment, and no new sensitizations or symptoms in a long-term follow-up of 4–10 years. Consequently, this study supports the indication of Pru p3 SLIT as the treatment of choice in patients with LTP syndrome.

However, it is noteworthy that among the seven patients with cofactor-induced or cofactor-enhanced reactions, all tolerated the food to which they were allergic or sensitized after Pru p3 SLIT, but none tolerated it if the cofactor was present.

Conclusions

Our study provides the first evidence that Pru p3 SLIT is a highly effective treatment, capable of inducing clinical remission of LTP food allergy in both adult and pediatric populations. However, it doesn´t resolve cofactor-triggered LTP reactions; therefore, we can suggest that patients with this profile should continue to avoid such triggers.

Author's Contribution

All authors contributed equally to this article.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to research, authorship, and/or publication of this article

Funding

None.

References

1. Cuesta-Herranz J, Lazaro M, Figueredo E, Igea JM, Umpierrez A, De-Las-Heras M. Allergy to plant-derived fresh foods in a birchand ragweed-free area. Clin. Exp. Allergy. 2000;30(10):1411–6. https://doi.org/10.1046/j.1365-2222.2000.00868.x
2. Rial MJ, Sastre J. Food allergies caused by allergenic lipid transfer proteins: what is behind the geographic restriction? Curr. Allergy Asthma Rep. 2018;18(11):56. https://doi.org/10.1007/s11882-018-0810-x
3. Mothes-Luksch N, Raith M, Stingl G, Focke-Tejkl M, Razzazi-Fazeli E, Zieglmayer R, et al. Pru p 3, a marker allergen for lipid transfer protein sensitization also in Central Europe. Allergy: Eur. J. Allergy Clin. Immunol. 2017 Sep 1;72(9):1415–8. https://doi.org/10.1111/all.13151
4. Basagaña Torrentó M, Elduque C, Teniente-Serra A, Casas I, Roger A. Clinical profile of lipid transfer protein syndrome in a Mediterranean area. J. Investig. Allergol. Clin. Immunol. 2018; 28:58–60. https://doi.org/10.18176/jiaci.0209
5. Rossi CM, Lenti MV, Merli S, Licari A, Marseglia GL, Di Sabatino A. Immunotherapy with Pru p 3 for food allergy to peach and non-specific lipid transfer protein: a systematic review. Clin Mol Allergy. 2023 May 31;21(1):3. https://doi.org/10.1186/s12948-023-00184-5
6. Gomez F, Bogas G, Gonzalez M, Campo P, Salas M, Diaz-Perales A, et al. The clinical and immunological effects of Pru p 3 sublingual immunotherapy on peach and peanut allergy in patients with systemic reactions. Clin. Exp. Allergy. 1 de marzo de 2017;47(3):339–50. https://doi.org/10.1111/cea.12901
7. Fernandez-Rivas M, Garrido Fernandez S, Nadal JA, Diaz de Durana MD, Garcia BE, Gonzalez-Mancebo E, et al. Randomized double-blind, placebo-controlled trial of sublingual immunotherapy with a Pru p 3 quantified peach extract. Allergy. 2009;64(6):876–83. https://doi.org/10.1111/j.1398-9995.2008.01921.x
8. Beitia JM, Vega Castro A, Cardenas R, Pena-Arellano MI. Pru p 3 sublingual immunotherapy in patients with lipid transfer protein syndrome: is it worth? Int. Arch. Allergy. Immunol. 1 de mayo de 2021;182(5):447–54. https://doi.org/10.1159/000512613
9. Betancor D, Gomez-Lopez A, Villalobos-Vilda C, Nuñez-Borque E, Fernández-Bravo S, De las Heras Gozalo M, et al. Ltp allergy follow-up study: development of allergy to new plant foods 10 years later. Nutrients. 2021 Jul 1;13(7):2165. https://doi.org/10.3390/nu13072165
10. Miralles-Lopez JC, Carbonell-Martínez A, Zamarro-Parra S, Navarro-Garrido C, Escudero-Pastor AI, Boulaich M, et al. Clinical and serological characteristics of patients allergic to LTP. Allergol. Immunopathol. 2024 Jul 1;52(4):9–14. https://doi.org/10.15586/aei.v52i4.1074