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| **Table 2. Specific characteristics of studies with Oral Immunotherapy\_** **The pre-specified outcomes of the review (desensitization: the change in the threshold of the tree nut in question required to elicit an allergic reaction while on treatment, and sustained unresponsiveness: the ability to consume foods containing the tree nut in question after discontinuing treatment) are marked in bold.** | | | | | | | | | | | | | | | |
| **Study ID** | **TreeNut and No of subjects** | **Inclusion Criteria** | **Exclusion Criteria** | **Comparator** | **Randomization** | **OFC at baseline** | **Initial Escalation** | **Build-up phase** | **Maintenance (mg of protein)** | **Time on Intervention** | **Discontinued** | **Results Primary outcome** | **Results Secondary outcomes** | **Doses administered** | **Adverse Reactions** |
| **Single tree nut OIT** | | | | | | | | | | | | | | | |
| Elizur et al.2019 | WN: 73 Active:  55 Control:18 | WNSPT>3mm, WNsIgE ≥0.35 kUA/L,  Positive OFC or history of reaction in the past year. | Uncontrolled asthma, Contraindication to receiving adrenaline. | SOC | 4:1 | 54 | 4-d. OFC to establish the highest tolerated dose (from 0.1 to 300mg of WN protein. | Monthly up to 4-fold escalations in clinic, until 4000mg WN protein. | 1200mg | (1) OIT:  5.9m.  (3.8–8.9), (2) Control: 7.1m.  (3.8–9.2) | 3 | (1) **49/55 (89%) participants in OIT were desensitized to 4000mg of WN protein** vs 0/18 (0%) participants in control, (OR: 9.2, 95% CI: 4.3–19.5; p<0·0001). | (1) OIT: **3 increased ≥10 times their single highest tolerated dose or were desensitized to ≥1000 mg but <4000 mg).** (2) 45/45 followed up for 6m. on 1200mg maintenance, passed OFC to 4000mg WN protein. (3)(a) co-PC desensitized: 46/46(100%), (b)co-HZ desensitized: 8/15 (53%), responded to treatment: 6/15 (40%), (c)co-CS desensitized or responded to treatment: 5/19 (26%). (4) (a) OIT ↓WSPT, WBAT, WsIgE, WsIgE/sIgG4, ↑WIgG4. (b) Control: non-significant change. (6) Quality of life (52 patients) : (a) 34 desensitized to all tested nuts: improve emotional impact (from 4.0 to 2.1; p=0,001), food anxiety (from 4.0 to 2.0; p=0·001), social and dietary limitation (from 3.0 to 1.0; p<0·0001) and total score (from 3.3 to 2.0; p<0·0001) (b) 18 allergic to at least one nut: statistically (not clinically) significant improvement only for the social and dietary limitation(from 3.0 to 2.6; p=0,034). | Hospital 2432,  Home 10605. | (1) Per patient:  (a) In hospital:  47/55(85%),  grade 1: 35(64%), grade 2:27 (49%), epinephrine use: 11(20%),  (b) At home: 40/55(73%), epinephrine use: 8(15%)  (2) Per dose:  (a) In hospital: 109/2432 (4%),  grade 1:63 (3%), grade 2: 46(2%), epinephrine use: 12 (<1%),  (b) At home: 244/10605 (2%), epinephrine use: 9 (<1%)  (3) EoE-like symptoms: 3/55.  (4) 6m. follow-up: 11/45 patients (24%), epinephrine use:1 (2%) |
| Sasamoto et al. 2021 | WN:3 | Children>5y.o, Positive OFC to 75 mg walnut protein | NR | BSL | NA | 3 | 3-d. OFC in hospital to establish the highest tolerated dose. | ~50% every month, until 75mg. | 75mg | At least 12m. | 0 | (1) Children 1, 2, and 3 received a home starting dose at 30, 18, and 18mg. (**2) 75mg was achieved after 3, 4, and 3 m. (3) 2-weeks SU to 450 mg achieved at 24, 14 and 12 m.** | (1) WN and Jug r 1 sIgEs increased after 1 m. and decreased gradually until 12 m. (2) WNsIgG4 tended to increase after starting OIT in all cases. | Child 1:  Hospital:3 Home:584  Child 2:  Hospital:3 Home:645  Child 3:  Hospital:3 Home:209 | Child 1: Hospital: 1 mild, Home: 14, 9 mild, 5 moderate (2 anaphylactic),  Child 2: Hospital: 1 mild, 1 moderate, Home: 4 mild,  Child 3:Hospital:1 mild, Home: 18 mild,Adverse reaction rate per intake at home: 3.1%. Epinephrine:0. |
| Moraly et al. 2019 | HZ: 100 | <18 y.o., Convincing history of HZ- IgE allergy, HZSPT>3 mm,  HZsIgE>0.35 kUA/L,  Positive HZ DBPCFC,  At least 6m. in HZ -OIT,  Open OFC after 6 m. of HZ OIT. | >18 y.o., Discontinued OIT during the first 6 m., No OFC at 6m.,  No consent. | BSL | NA | 100 | None | 25-50% every month until 50% of initial ED | 416mg 3 times a week | 6 m. | NA | **34 (95% CI, 25-44) participants were desensitized (Tolerated up to 695mg (1635mg CM) of hazelnut protein).** | **(1) median ED increased by 417 mg (IQR, 139-1386).** (2) 66 patients who were not considered desensitized had at least doubled their baseline ED at 6 m. (median ED, 259 mg IQR, 106-523). (2) median SPT decreased by 5 mm (IQR, 2-7). (3) 44%, 51%, and 59% of participants were desensitized at months 12, 18 and 24 respectively. | NR | 76 retrospective reports: (1) 30% at least one nonsevere (urticaria, 6.6%; oral angioedema, 1.3%; gastrointestinal symptoms including abdominal pain and nausea, 23.7%). (2) No EoE or symptoms suggestive of EoE. (3) No serious side effects. |
| Sabouraud et al. 2022 | HZ: 70 | < 18 y.o., Confirmed IgE-mediated allergy by: (a) history and (b)SPT>3 mm or sIgE>0.35 kU/L OR Strong presumption by: (a) allergy to another nut and (b)Positive sIgE to Cor a 9 or Cor a 14or (c)HZ PT>15 mm,  Started H-OIT lasting more than 1y.between 2015 and 2019. | NR | BSL | NA | 70 | None | 10% of the individualized intermediate target dose. Progressively increased to reach full dose at 6 months. | Individualized | NR | 15 | 16 (22.9%) entered the maintenance phase at 1-y. consultation. | (1) Proportion of patients in the maintenance phase during the study period: 42 patients (60%); median (IQR) daily dose: 154.4 mg [128.6-255] range: 46.4-1462.5 mg**). (2) Change of the cumulative dose of OFC: (a) 6m.: increased to 68.3 mg (31.2-175.1) from 21.4 mg (12.8-36.8); P < .001. (b) 1y.: increased to 220.9 mg (86.1-492.0) from 21.4 mg (12.8-3 6.8); P < .001). (3) 36/70 (51.4%) reached >120 mg of HZ proteins at the 1-y. consultation**. (4) Immunological changes at 1-y. vs BSL: (a) sIgE: (9.7 kU/L [2.4-25.3] vs 11.9 kU/L [3.7-36.5]; P = 0.73, (b) SPT: 4mm [0-7]) vs 6mm [3-10]; P = .02, (c)sIgG4: 1.2 mg/L [0.6-3.2]) vs 0.4 mg/L [0.2-0.9]; P = .003,(d)IgG4/IgE: 44,7 [12-177.9] vs 16.6 [7.4-53.8]; P < .001. (5) Satisfaction questionnaire score (63 children aged > 8y.o: (a)satisfaction: 5[4-6.8], (b)effectiveness: 6[5-7], (c) treatment recommendation: 7[5.3-7] (d) Enjoy eating hazelnut every day: 3[1-4]), (e) HZ-OIT as a strain: 5[3-6]), (f) HZ-OIT as a medication: 4[2-6]. | NR | Retrospective reports at consultations-grading by Ring and Messmer:  (1) Home:  40(57.1%) patients had at least 1 adverse effect:  36(51.4%) mild, 17(24.3%) aversion,  14(20%) recurrent abdominal pain; 2(2.9%) severe systemic allergic reactions,  1 used epinephrine.  (2) Hospital:  7/212 (3.3%) severe systemic reactions during OFCs; epinephrine use: 4 during OFCs.  (3) EoE: 1 |
| Elizur et al.2022 | CS: 65 Active: 50 Control: 15 | Positive OFC or a recent reaction to cashew,  CSSPT > 3mm, CSsIgE ≥0.35 kUA/L. | Uncontrolled asthma, Diagnosis of eosinophilic gastrointestinal disease,  Autoimmune diseases. | SOC | NA | 50 | 4-d. OFC to the highest tolerated dose (0.1-360mg CS protein). | Monthly 4-fold increases in clinic until 4000mg CS  protein. | 1200mg | OIT:12m. (range, 3- 57), Control: 17m. (range, 5-44.1) | OIT: 3 | **ITT: 44/50 (88%) OIT- treated and 0% controls tolerated 4000mg of CS protein** (Odds ratio 8.3, 95% CI 3.9- 17.7, p < 0.001). | (**1) 3 OIT and 0 control were partially desensitized to cashew (1200mg CS protein).**  (2) OIT: CS SPT (median 10 vs. 4 mm, p<0.001), BAT (median 23.2% vs. 1.25%, p<0.001), and sIgE (median 3.95 vs. 2.2 kU/L, p = 0.001) Ana o3sIgE(median 3.7-1.6 kU/L, p<0.001) decreased significantly, and sIgG4 to CS (median 0.32 vs. 23.4 mgA/L, p<0.001) and to Ana o3 (median 0.15-22.9 mgA/L, p<0.001) increased significantly. Controls: no significant changes were noted (CSSPT: median 12.5 vs. 12.5 mm, sIgE: median 8.2 vs. 6 kU/L, BAT: median 37.7% vs. 36%, sIgG4: 0.26 vs. 0.54 mgA/L, and Ana o3sIgE: median 8.3-5.9 kU/L, and Ana o3sIgG4: median 0.19-0.17 mgA/L, (3) OIT group: 35/44 patients who were fully desensitized to CS were fully desensitized to PS. 10/11 children with WN co-allergy, were fully desensitized to CS: 2/10 refused WN OFC, 4/8 reacted (3 at lower doses). (4) PSSPT (median 10 vs. 4 mm, p<0.001), BAT (median 28.6% vs. 0.6%, p<0.001), and sIgE (median 4.8 vs. 1.9 kU/L, p<0.001) decreased, and PSIgG4 (median 0.44 vs. 14.7 mgA/L, p<0.001) increased. (5) 44/44 children passed OFC to CS after 6 m. on 1200mg maintenance. | Hospital: 1913, Home: 17816 | WAO Subcutaneous Immunotherapy Systemic Reaction Grading System:(A) In hospital: (1) per patient: 44 (88%) reactions, 28 (56%) grade 1, 34 (68%) grade 2, 9 (18%) epinephrine use; (2) per dose: 80 (4.2%) reactions, 37 (1.9%) grade 1, 44 (2.3%) grade 2, 12 (0.63%) epinephrine use; (B) Home: (1) per patient: Any reaction: 26 (52%), A single reaction: 5 (10%),  2-4 reactions:12 (24%), ≥5 reactions: 9 (18%), Epinephrine: 3 (6%). (2) per dose: Any reaction:108 (0.61%), Epinephrine: 3 (0.017%). 1 patient OITIGER, 1 patient EOE. |
| **Multi OIT** | | | | | | | | | | | | | | | |
| Begin et al. 2014a | CS: 13, WN: 14, PE: 7, HZ: 3, AL: 5. | 4-55 y.o., PNSPT> 7mm, PNIgE>2ku/L, Positive DBPCFC up to 182mg of PN protein, DBPCFC to nuts, sesame seed, dairy or egg. | EoE, Autoimmune disease, Severe cardiac diseases, Chronic treatment with (a) b- antagonists, (b)steroids, History of anaphylaxis requiring ICU admission, Frequent allergic or non-allergic urticaria, Poorly controlled asthma. | PN-OIT | NA | 40 | 0.1-6mg of total food protein, or the highest tolerated dose. | 25-108% every 2 weeks. | 4000mg of food protein (20g max total food protein) | Individualized | mOIT: 3 PNOIT:3 | (1) Initial escalation: (a)mOIT: 15 reactions in 15/25 (60%) participants, adrenaline: 0, (b)PNOIT: 6 reactions in 6/15 (40%) participants, adrenaline: 0, (2) Hospital: (a) mOIT: reaction rate 3.4% (0-23.1), adrenaline: 0,  (b) PNOIT: reaction rate: 3.7% (0-16.6), adrenaline: 0,  (3) Home:  (a) mOIT: reaction rate 3.1% (0.6-29.2), adrenaline: 2, (b)PNOIT: reaction rate: 2.9% (0.1-59), adrenaline: 2. | (1) Participants in PNOIT reached a 10-fold increase in threshold dose of food allergen protein, as well as a dose of 300mg, 1000mg and 4000mg food allergen protein significantly faster than those on mOIT. (2) The dose progression in mOIT was unrelated to the number or combinations of foods in the OIT mix. (3) 12m. of OIT: increase PNIgG4 (both groups) and WNIgG4 (mOIT group) (p<0.05), **(4) All participants in mOIT tolerated 4000mg of treenut protein.** | (a) mOIT:  hospital:  603, home: 12030, rush:25, total: 12658  (b) PNOIT: hospital: 277, home: 7830, rush: 15, total:8122 | See Primary outcome |
| Andorf et al. 2017a | CS: 13, WN:15,  PE: 8, HZ: 3, AL: 5. | 0,5-60 y.o., PNSPT>7mm, PNsIgE>2ku/L, Positive DBPCFC up to 182mg of PN protein, DBPCFC to nuts, sesame seed, dairy or egg. | Moderate- severe allergic reaction in the last 6 months,  No decrease in skin tests and sIgE | 300mg daily/  2g daily/  300mg every other day | Individualized | 25 | 0.1-6mg of total food protein, or the highest tolerated dose. | 108-25% every 2 weeks. | 2000mg per allergen daily | Up to 72m., median: 48m. (27-72). | 1 | (1) Low dose: 10/25 (40%) High dose: 10(40%) were on a high long-term maintenance dose for all foods. (2) 1 stopped eating PN after 25m. on a high dose but ate traces. (3) 6 on low dose, returned to high dose after varying times. **(4) Per allergen on low dose at the end of the study: WN 67%, PE 63%,**  **PN 46%,**  **HZ 100%,**  **AL 60%,**  **CS 46%,**  **(5) All tolerated 2 g protein or more during OFC, independent of high vs. low long-term maintenance dose.** | (1) SPTs were significantly decreased during the active phase, and remained low over LTFU, except for PC, AL and sesame. (2) A significant trend of increasing sIgG4/sIgE ratios was observed at the end of active phase for all the food allergens and persisted over LTFU. (3) Neither SPT wheal diameter nor IgG4/IgE ratio was significantly associated with a low vs. a high dose. | 25598 | 1) 1207 reactions (2.29% of maintenance doses):1073(88.9%) mild, 129 (10.69%) moderate, 5 (0.41%) severe. No fatal or serious adverse events. No epinephrine use. (2) The frequency of allergic adverse events decreased over time. (3) Safety results did not differ based on low vs. high maintenance dose. (4) median reactions/participant: 25 (0-35) |
| **Multi OIT with Omalizumab** | | | | | | | | | | | | | | | |
| Begin et al. 2014b | Active: CS: 14 WN: 9 PE: 7 HZ:3 AL: 6 | 4-55 y.o.,  Sensitivity to at least two foods, documented by SPT>3 mm and sIgE>0.35 ku/L, and positive DBPCFC. | EoE, Autoimmune disease, Severe cardiac disease, Chronic treatment with b-antagonists or steroids, History of severe anaphylaxis requiring admission to an intensive care unit, Frequent allergic or non-allergic urticaria, Poorly controlled asthma. | BSL | NA | 25 | 1-250 mg of protein of each food, or the highest tolerated dose. | 80-14% every 2 weeks. | 4000mg of protein of each food | Individualized | 3 | (1) Initial escalation: (a) 13 mild reactions in 13/25 participants (52%) (b) 0 epinephrine use. (2) Hospital escalations: (a) 13 mild reactions/ 227 doses (5.7%), (b) median reaction rate 0% (0-25), (c) 0 epinephrine use. (3) Home dosing: (a) 401 reactions/7530 doses (5.3%), (b) mild: 385(5.1%), moderate: 15(0.2%), severe: 1 (0.01%), (c) median reaction rate 3.2% (0.1-18.5). (d) 1 epinephrine use (0.01%) | (**1) Time to reach and maintain (a) 300 mg: 2months, (b) 1000 mg: 3months, (c) 4000 mg: 9 months per food allergen protein, median 18 (7-36) weeks. (2) Time to reach a 10 fold increase from the baseline reactivity threshold: 2 months.**  **(3)** **All participants reached maintenance dose (4000 mg per allergen) by 9 months. All participants reached a dose equivalent to a 10-fold increase of all their allergens by 2 months of therapy.** | 7782 | In total 427 reactions |
| Andorf et al. 2017b | CS: 18 WN: 10 PE: 8 HZ: 7 AL: 6 | 0,5-60 y.o.  PNSPT>7mmPNsIgE>2ku/L positive DBPCFC up to 182mg PN protein. Further DBPCFC were also performed to nuts, sesame seed, dairy or egg. | Moderate to severe allergic reaction in the last 6 months, no decrease in skin tests and sIgE. | 300mg/ 2gr maintenance. | NA | 34 | 1-250mg of protein of each food, or the highest tolerated dose. | 80-14% every 2 weeks. | 2g -4g per allergen daily | Up to 62 m. after reaching the 2 g maintenance dose for the first food (median 53 m., range 32–62) | 0 | (1) Per allergen on low dose at the end of the study: WN: 80%, PE: 100%, PN: 92.3%, HZ: 85.7%, AL: 100%, CS: 94.4%,  **(2) Each participant on long-term maintenance dosing tolerated 2 g protein or more in an OFC, independent of high vs. low long-term maintenance dose.** | (1) The log10 IgG4/IgE ratio levels were not significantly different between a low and a high maintenance dose. (2) SPT decreased during the dose escalation phase and varied across a large range for the participants per allergen, however, it was not significantly dependent on a low or high maintenance dose. (3) Of the 8 participants with pecan in their OIT and 10 with walnut, 7 were desensitized to both foods. | NR | (1) 1126 reactions (3.5% of doses):  Mild:1076(95.6%), Moderate: 40(3.6%), Severe:5(0.4%), (4 skin reactions, 1 nasal congestion/ 2 gr group).  (2) No serious adverse events.  (3) No anaphylactic reactions.  (4) Epinephrine was used (no details provided). |
| Andorf et al. 2018 | Oma: CS: 25 WN: 20 HZ: 17 AL: 6 Control: CS: 11 WN: 5 HZ: 7 AL: 1 | 5-15 y.o., SPT≥6mm,  sIgE>4 kU/L, positive DBPCFC at ≤500mg of food protein. | EoE,  Severe asthma. | Multi-OIT | 1:3 | 48 | 5-1250mg food protein (divided equally among the number of foods included). | Every 2 weeks. | 2gr of protein of each food, max 10gr total food protein. | 36w. | Oma: 6,  Control:8 | **(1)Tolerated 2gr of ≥2** allergens: oma:30/36 vs control:4/12,  **(2) Per allergen:**  **(a)AL: oma:4/6 vs.control:0/1 (b)CS: oma:20/25vs.control: 4/11, (c)HZ: oma:16/17 vs.control:3/7(d)WN: oma:17/20**  **vs.control: 0/5** | (1)Tolerated 4g of ≥2 allergens: oma:30/36 vs.control:4/12.  (2)Tolerated 2g of (a)≥3allergens: oma:21/26 vs.control:2/7,(b)≥4 allergens: oma:13/17 vs.control:0/5, (c)5 allergens: oma:4/7 vs.control:0/1.  (3)Participants with only mild symptoms during build-up: oma:6(17%) vs control:0(0%). (4)Participants with only mild symptoms during build-up and maintenance: oma: 3(8%) vs.control 0(0%).(5)sIgG4/sIgE significantly increased between baseline and 36w. and SPTs were significant decrease. (6) 20/24 patients with PS co-allergy were desensitized to PS(18/20 oma, 2/4 control). 17/17 (100%) patients with PE co-allergy were desensitized to PE(all in oma). | NR | (1) Per patient: (a)8-16w.: oma:36/36, control:12/12,(b) 17-24w.:oma:33/36, control:4/12, (c)25-36w.:oma:33/36, control:4/12,(2)Median per-participant % of doses: (a)8-16w.: any:oma:24, control:68, grade1:oma:24,control:56, grade2:oma: 2,control:7,(b)17-24w.:any: oma:26,control:39,grade1:oma:22,control:19, grade 2: oma: 0, control:0, (c)25-36w: any: oma: 29, control: 29, grade1: oma:16,control:28, grade2: oma: 0,control:1 (3)Epinephrine use: (a)8-16w:oma:3 events/2 patients, pl: 2events/2patients,(b) 17-24w:oma:0 events/0patients,control:1event/1patient, (c)25-36w: oma:2events/2patients,control: 3events/2patients. |
| Andorf et al. 2019 | (1) 1g: CS:10 PS:3 WN: 11 PE: 4 HZ: 7 AL: 2 (2) 300mg: CS: 13 PS: 3 WN: 9 PE: 4 HZ: 4 AL:2  (3) 0mg: CS: 11 PS: 2 WN: 11 PE: 4 HZ: 6 AL: 1 | 5-55 y.o., sIgE>4kU/L, SPT≥6mml, positive DBPCFC at ≤125mg of food protein, tIgE< 2000kU/L, Reaching the maintenance dose (<1gr per food protein) by 28-29 w. | History of severe anaphylaxis (intubation or admission to an ICU), Frequent allergic or non-allergic urticaria,  Poorly controlled persistent asthma, Eosinophilic esophagitis, colitis, or gastritis. | 1gr/300mg/0mg maintenance | 1:1:1 | 70 | 1 d. (5-62mg total allergens) | 15-900% increase every 2 w. | Patients reached maintenance at 30 w. received OFC to 4gr per allergen. Tolerant randomized to 1g, 300mg and 0mg maintenance for 6w. | 36w. | 1gr: 2  300mg:1, 0mg:4 | **(1)Tolerated 2gr of ≥2 allergens**: (a)ITT: active (1gr+300mg) vs 0gr: 34/40 vs 11/20, (b)PP: active vs 0mg: 34/37vs 11/16, (c) 1gr vs 300mg : 17/19 vs 17/21  **(****d) CS: 1gr: 9/10, 300mg: 12/13, 0gr: 2/11, WN: 1gr:11/11, 300mg: 9/9, 0 gr:8/11,PE: 1gr: 4/4, 300mg: 5/5, 0gr: 1/4, HZ: 1gr: 6/7, 300mg: 3/4, 0gr: 3/6, AL: 1gr 2/2 ,300 mg: 1/1, 0 gr: 1/1.** | (1) Active vs 0gr: (a)Tolerated 4g of ≥2 allergens: 28/40 vs 9/20, OR: 2.8, 95% CI: 0.8–10.0, P = 0.09), (b)Tolerated 2g each of (i)≥3 allergens: 25/26 vs 8/16, p<0.05 (ii) ≥4 allergens: 15/18 vs 3/9, p<0.05 (iii) 5 allergens: 10/12 vs 0/3 p<0.05 (2) 1g vs 0g: (a)Tolerated 2g of ≥2 allergens: 17/19 vs 11/20, (b) Tolerated 4g of ≥2 allergens: 14/19 vs 9/20, (c)Tolerated 2g each of (i)≥3 allergens: 13/14 vs 8/16, (ii) ≥4 allergens: 7/8 vs 3/9, (iii) 5 allergens: 5/ vs 0/3, (3)300mg vs 0gr: (a)Tolerated 2g of ≥2 allergens: 17/21vs 11/20, (b) Tolerated 4g of ≥2 allergens: 14/21 vs 9/20, (c)Tolerated 2g each of (i)≥3 allergens: 12/12 vs 8/16, (ii) ≥4 allergens: 8/10 vs 3/9, (iii) 5 allergens: 5/6 vs 0/3. (**4a) 4/4 PE (WN in OIT) allergic patients (1-1gr, 1-300mg, 2-0mg) passed the PE challenge at 36w.(4b) 7/8 PS (CS in OIT) patients (3-1gr, 3-300mg, 1/2-0mg) passed the PS challenge at 36w**. (5)↑peanut sIgG4/IgE (↑ IgG4), SPT ↔ | NR | (A) Median per-participant % of doses with AE: (1) 1gr: a)8-16w.: total 78, Treated: 0, Grade1: 29, Grade2: 0, Grade3: 0, b)17-29w.: Total:53, Treated: 13, Grade1: 22, Grade2: 12, Grade3: 0 c)30-36w.: Total: 0,Treated: 0,Grade1: 0, Grade2: 0, Grade3: 0, (2)300mg: a)8-16w: total:78, Treated: 0, Grade1: 29, Grade2:0, Grade3: 0 b)17-29w: Total:53, Treated: 13, Grade1: 22, Grade2: 12, Grade3: 0, c)30-36w.: Total: 0, Treated: 0,Grade1: 0, Grade2: 0, Grade3: 0 (3)0gr: a)8-16w.: total 61, Treated: 0, Grade1: 44, Grade2: 0 , Grade3: 0, b)17-29w.: Total:68, Treated: 6, Grade1: 32, Grade2: 11, Grade3: 0, c)30-36w: Total:6,Treated:0, Grade1: 0, Grade2: 0, Grade3:0, (4)non- randomized: a)8-16w: total: 63, Treated: 23, Grade1: 38, Grade2: 15, Grade3: 0 b)17-29w: Total:59, Treated: 12, Grade1: 41, Grade2: 12, Grade3: 0 c) 30-36w: Total: 22,Treated: 0, Grade1:22, Grade2: 0, Grade3: 0. (B) Epinephrine use: 8 uses/6 patients (3: 1 gr, 2: non-randomized, 1: 0gr (before randomization)/6 during home maintenance/ 2 during build-up at home). |

*AL: almond, BSL: Baseline, CM: Cumulative Dose, CS: cashew, ED: Eliciting Dose, EOE: Eosinophilic Esophagitis, HZ: hazelnut, ITT: intention to treat, m: months, NA: non applicable, NR: not reported/not assessed, (m)OIT: (multi) Oral Immunotherapy , OITGER: oral immunotherapy-induced gastrointestinal and eosinophilic responses, PE: pecan, PN: peanut, PP: per protocol, PS: pistachio, QoL: Quality of Life, SOC: Standard of care, SU: Sustained Unresponsiveness, (t)TN: (test) tree nut, w: weeks, WN: walnut, y: years.*