**Supplementary information**

**Table 1: Summary of study results**

| **Biomarker** | | | **Allergen** | | | **Immunologic response** | | | | | **Clinical outcome** | | | | | | | **Correlation** | | | | | **Tolerance** | | | | **Number of treated patients** | | | | **Type of study** | | | | | **Level of evidence** | | | | **Material** | | **Reference** | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Domain i: IgE** | | |  | | |  | | | | |  | | | | | | |  | | | | |  | | | |  | | | |  | | | | |  | | | |  | |  | | | | | |
| Total IgE | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 472 | | | | RDBPC | | | | | A | | | | Serum | | (145) | | | | | |
|  | | | Grass | | | ↔ | | | | | Not reported | | | | | | | n.a. | | | | | Not included | | | | 17 | | | | RDBPC | | | | | A | | | | Serum | | (59) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 279 | | | | Retrospective | | | | | D | | | | Serum | | (33) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 11 | | | | PC | | | | | B | | | | Serum | | (42) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 22 | | | | PC | | | | | B | | | | Serum | | (68) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 27 | | | | PC | | | | | B | | | | Serum | | (146) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 702 | | | | RDBPC | | | | | A | | | | Serum | | (147) | | | | | |
|  | | | HDM | | | ↑Return to baseline after 3 months | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 34 | | | | CC | | | | | C | | | | Serum | | (41) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 10 | | | | RDBPC | | | | | A | | | | Serum | | (148) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 279 | | | | Retrospective | | | | | D | | | | Serum | | (33) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation: decision point, 965kU/l; sensitivity, 90.7%; specificity, 54.9% | | | | | Not included | | | | 185 | | | | Retrospective | | | | | D | | | | Serum | | (35) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 32 | | | | ROLPC | | | | | B | | | | Serum | | (36) | | | | | |
|  | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 43 | | | | CC | | | | | C | | | | Serum | | (149) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 12 | | | | RC | | | | | C | | | | Serum | | (94) | | | | | |
|  | | | Birch | | | ↑ Return to baseline | | | | | Improved | | | | | | | No correlation | | | | | + | | | | 30 | | | | PC | | | | | B | | | | Serum | | (150) | | | | | |
|  | | | Palm | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 18 | | | | RDBPC | | | | | A | | | | Serum | | (151) | | | | | |
| sIgE | | | Grass | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | + | | | | 156 | | | | DBPC | | | | | A | | | | Serum | | (6) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 279 | | | | Retrospective | | | | | D | | | | Serum | | (33) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 16 | | | | RDBPC | | | | | A | | | | Serum | | (81) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 30 | | | | RNBC | | | | | B | | | | Serum | | (82) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 18 | | | | PC | | | | | B | | | | Serum | | (69) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 40 | | | | RDBPC | | | | | A | | | | Serum | | (152) | | | | | |
|  | | | Grass | | | ↑ | | | | | Stable | | | | | | | n.r. | | | | | Not included | | | | 210 | | | | RDBPC | | | | | A | | | | Serum | | (153) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 29 | | | | RDBPC | | | | | A | | | | Serum | | (39) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 12 | | | | RDBPC | | | | | A | | | | Serum | | (154) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 13 | | | | RDBPC | | | | | A | | | | Serum | | (155) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 132 | | | | RDBPC | | | | | A | | | | Serum | | (156) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 207 | | | | RDBPC | | | | | A | | | | Serum | | (157) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 99 | | | | RDBPC | | | | | A | | | | Serum | | (158) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 48 | | | | RDBPC | | | | | A | | | | Serum | | (159) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 44 | | | | RDBPC | | | | | A | | | | Serum | | (160) | | | | | |
|  | | | Grass/ birch | | | ↔ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 186 | | | | RDBPC | | | | | A | | | | Serum | | (161) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 10 | | | | RDBPC | | | | | A | | | | Serum | | (148) | | | | | |
|  | | | HDM | | | ↑Return to baseline after 3 months | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 34 | | | | CC | | | | | C | | | | Serum | | (41) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 279 | | | | Retrospective | | | | | D | | | | Serum | | (33) | | | | | |
|  | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 31 | | | | CC | | | | | C | | | | Serum | | (58) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation: decision point, 90.3kU/l; sensitivity, 70.9%; specificity, 55.8% | | | | | Not included | | | | 185 | | | | Retrospective | | | | | D | | | | Serum | | (35) | | | | | |
|  | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 32 | | | | ROLPC | | | | | B | | | | Serum | | (36) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 42 | | | | RDBPC | | | | | A | | | | Serum | | (162) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 54 | | | | RDBPC | | | | | A | | | | Serum | | (163) | | | | | |
|  | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 20 | | | | RDBPC | | | | | A | | | | Serum | | (164) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 45 | | | | RDBPC | | | | | A | | | | Serum | | (165) | | | | | |
|  | | | HDM | | | ↔ | | | | | Stable | | | | | | | n.a. | | | | | Not included | | | | 16 | | | | RDBPC | | | | | A | | | | Serum | | (166) | | | | | |
|  | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 33 | | | | RPC | | | | | B | | | | Serum | | (167) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | RDBPC | | | | | A | | | | Serum | | (112) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 55 | | | | RDBPC | | | | | A | | | | Serum | | (168) | | | | | |
|  | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 12 | | | | RC | | | | | C | | | | Serum | | (94) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 64 | | | | RDBPC | | | | | A | | | | Serum | | (169) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 20 | | | | RDBPC | | | | | A | | | | Serum | | (170) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 60 | | | | RDBPC | | | | | A | | | | Serum | | (171) | | | | | |
|  | | | Birch | | | ↑ Return to baseline | | | | | Improved | | | | | | | No correlation | | | | | + | | | | 30 | | | | PC | | | | | B | | | | Serum | | (150) | | | | | |
|  | | | Birch | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 24 | | | | PC | | | | | B | | | | Serum | | (43) | | | | | |
|  | | | Birch | | | ↔ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 31 | | | | RDBPC | | | | | A | | | | Serum | | (172) | | | | | |
|  | | | Birch | | | ↔ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 28 | | | | RDBPC | | | | | A | | | | Serum | | (83) | | | | | |
|  | | | Combined tree | | | ↔ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 117 | | | | RDBPC | | | | | A | | | | Serum | | (173) | | | | | |
|  | | | Japanese Cedar | | | ↔ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 43 | | | | RSBPC | | | | | A | | | | Serum | | (174) | | | | | |
|  | | | Alternaria | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | RDBPC | | | | | A | | | | Serum | | (175) | | | | | |
|  | | | Palm | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 18 | | | | RDBPC | | | | | A | | | | Serum | | (151) | | | | | |
|  | | | Cockroach | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 50 | | | | RDBPC | | | | | A | | | | Serum | | (176) | | | | | |
| sIgE/tIgE | | | Grass | | | ↑ | | | | | Improved | | | | | | | Correlation: decision point, 16.2%; sensitivity, 97.2%; specificity, 88.1% | | | | | Not included | | | | 279 | | | | Retrospective | | | | | D | | | | Serum | | (33) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation: decision point, 16.2%; sensitivity, 97.2%; specificity, 88.1% | | | | | Not included | | | | 279 | | | | Retrospective | | | | | D | | | | Serum | | (33) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation: decision point, 6%; sensitivity, 82.9%; specificity, 50% | | | | | Not included | | | | 185 | | | | Retrospective | | | | | D | | | | Serum | | (35) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 32 | | | | ROLPC | | | | | B | | | | Serum | | (36) | | | | | |
| **Domain ii: IgG subtypes** | | |  | | |  | | | | |  | | | | | | |  | | | | |  | | | |  | | | |  | | | | |  | | | |  | |  | | | | | |
| sIgG4 | | | Grass | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | + | | | | 32 | | | | Cross sectional | | | | | D | | | | Serum | | (84) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 472 | | | | RDBPC | | | | | A | | | | Serum | | (145) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 189 | | | | RDBPC | | | | | A | | | | Serum | | (177) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 282 | | | | DBPC | | | | | A | | | | Serum | | (63) | | | | | |
|  | | | Grass | | | ↑ | | | | | Not reported | | | | | | | n.a. | | | | | Not included | | | | 17 | | | | RDBPC | | | | | A | | | | Serum | | (59) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 145 | | | | RDBPC | | | | | A | | | | Serum | | (178) | | | | | |
|  | | | Grass | | | ↑ | | | | | Not reported | | | | | | | n.a. | | | | | Not included | | | | 7 | | | | Cross sectional | | | | | C | | | | Nasal fluid | | (179) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 20 | | | | CC | | | | | C | | | | Serum | | (85) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 30 | | | | RNBC | | | | | B | | | | Serum | | (82) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | Weak correlation MS | | | | | Not included | | | | 16 | | | | RDBPC | | | | | A | | | | Serum | | (81) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | + | | | | 156 | | | | DBPC | | | | | A | | | | Serum | | (6) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 28 | | | | DBPC | | | | | A | | | | Serum | | (115) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 22 | | | | PC | | | | | B | | | | Serum | | (68) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | Correlated with ratio sIgG4/sIgG1 | | | | | Not included | | | | 11 | | | | PC | | | | | B | | | | Serum | | (42) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 175 | | | | RDBPC | | | | | A | | | | Serum | | (44) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 40 | | | | RDBPC | | | | | A | | | | Serum | | (152) | | | | | |
|  | | | Grass | | | ↑ | | | | | Stable | | | | | | | n.r. | | | | | Not included | | | | 210 | | | | RDBPC | | | | | A | | | | Serum | | (153) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 175 | | | | RDBPC | | | | | A | | | | Serum | | (180) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 47 | | | | RDBPC | | | | | A | | | | Serum | | (181) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 29 | | | | RDBPC | | | | | A | | | | Serum | | (39) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 13 | | | | RDBPC | | | | | A | | | | Serum | | (155) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 132 | | | | RDBPC | | | | | A | | | | Serum | | (156) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 207 | | | | RDBPC | | | | | A | | | | Serum | | (157) | | | | | |
|  | | | Grass | | | ↔  temporary increase | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 99 | | | | RDBPC | | | | | A | | | | Serum | | (158) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 36 | | | | RDBPC | | | | | A | | | | Serum | | (182) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 48 | | | | RDBPC | | | | | A | | | | Serum | | (159) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 27 | | | | PC | | | | | B | | | | Serum | | (146) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 44 | | | | RDBPC | | | | | A | | | | Serum | | (160) | | | | | |
|  | | |  | | |  | | | | |  | | | | | | |  | | | | |  | | | |  | | | |  | | | | |  | | | |  | |  | | | | | |
|  | | | Grass/ birch | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 186 | | | | RDBPC | | | | | A | | | | Serum | | (161) | | | | | |
|  | | | Combined tree | | | ↑ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 117 | | | | RDBPC | | | | | A | | | | Serum | | (173) | | | | | |
|  | | | Japanese Cedar | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 43 | | | | RSBPC | | | | | A | | | | Serum | | (174) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation responders/ non-responders | | | | | Not included | | | | 34 | | | | CC | | | | | C | | | | Serum | | (41) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 10 | | | | RDBPC | | | | | A | | | | Serum | | (148) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 31 | | | | CC | | | | | C | | | | Serum | | (58) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 42 | | | | RDBPC | | | | | A | | | | Serum | | (162) | | | | | |
|  | | | HDM | | | ↑ SCIT | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 10 | | | | RDBPC | | | | | A | | | | Serum | | (164) | | | | | |
|  | | | HDM | | | ↔ SLIT | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 10 | | | | RDBPC | | | | | A | | | | Serum | | (164) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 45 | | | | RDBPC | | | | | A | | | | Serum | | (165) | | | | | |
|  | | | HDM | | | ↑ | | | | | Stable | | | | | | | n.a. | | | | | Not included | | | | 16 | | | | RDBPC | | | | | A | | | | Serum | | (166) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 33 | | | | RC | | | | | C | | | | Serum | | (167) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | RDBPC | | | | | A | | | | Serum | | (112) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 55 | | | | RDBPC | | | | | A | | | | Serum | | (168) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 12 | | | | RC | | | | | C | | | | Serum | | (94) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 20 | | | | RDBPC | | | | | A | | | | Serum | | (170) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 60 | | | | RDBPC | | | | | A | | | | Serum | | (171) | | | | | |
|  | | |  | | |  | | | | |  | | | | | | |  | | | | |  | | | |  | | | |  | | | | |  | | | |  | |  | | | | | |
|  | | | Birch | | | ↑ | | | | | Improved | | | | | | | Correlation, also with baseline sIgG4 | | | | | + | | | | 30 | | | | PC | | | | | B | | | | Serum | | (150) | | | | | |
|  | | | Birch | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 31 | | | | RDBPC | | | | | A | | | | Serum | | (172) | | | | | |
|  | | | Birch | | | ↑ | | | | | Improved | | | | | | | n.r | | | | | Not included | | | 217 | | | | | RDBPC | | | | A | | | | - | | (131) | | | | |
|  | | |  | | |  | | | | |  | | | | | | |  | | | | |  | | | |  | | | |  | | | | |  | | | |  | |  | | | | | |
|  | | | Birch | | | ↑ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 98 | | | | RDBPC | | | | | A | | | | Serum | | (183) | | | | | |
|  | | | Birch | | | ↑ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 28 | | | | RDBPC | | | | | A | | | | Serum | | (83) | | | | | |
|  | | |  | | |  | | | | |  | | | | | | |  | | | | |  | | | |  | | | |  | | | | |  | | | |  | |  | | | | | |
|  | | | Alternaria | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | RDBPC | | | | | A | | | | Serum | | (175) | | | | | |
|  | | | Palm | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 18 | | | | RDBPC | | | | | A | | | | Serum | | (151) | | | | | |
|  | | | Cockroach | | | ↑ | | | | | Improved | | | | | | | Correlation sIgG4/sIgG1 | | | | | Not included | | | | 50 | | | | RDBPC | | | | | A | | | | Serum | | (176) | | | | | |
| IgG1 | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 31 | | | | CC | | | | | C | | | | Serum | | (58) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | RDBPC | | | | | A | | | | Serum | | (112) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 33 | | | | RC | | | | | C | | | | Serum | | (167) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | Correlated with ratio sIgG4/sIgG1 | | | | | Not included | | | | 11 | | | | PC | | | | | B | | | | Serum | | (42) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 29 | | | | RDBPC | | | | | A | | | | Serum | | (39) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 40 | | | | RDBPC | | | | | A | | | | Serum | | (152) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 47 | | | | RDBPC | | | | | A | | | | Serum | | (181) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 27 | | | | PC | | | | | B | | | | Serum | | (146) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 132 | | | | RDBPC | | | | | A | | | | Serum | | (156) | | | | | |
|  | | | Birch | | | ↑ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 98 | | | | RDBPC | | | | | A | | | | Serum | | (183) | | | | | |
|  | | | Birch | | | ↑(SCIT) | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 31 | | | | RDBPC | | | | | A | | | | Serum | | (172) | | | | | |
|  | | | Palm | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 18 | | | | RDBPC | | | | | A | | | | Serum | | (151) | | | | | |
|  | | | Cockroach | | | ↔ | | | | | Improved | | | | | | | Correlation sIgG4/sIgG1 | | | | | Not included | | | | 50 | | | | RDBPC | | | | | A | | | | Serum | | (176) | | | | | |
| **Domain iii:**  **Serum inhibitory activity for IgE** | | | | | | | | | | | | | | | | | | | | | | |  | | | |  | | | |  | | | | |  | | | |  | |  | | | | | |
| IgE-BF | | | Grass | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | + | | | | 156 | | | | DBPC | | | | | A | | | | Serum | | (6) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 189 | | | | RDBPC | | | | | A | | | | Serum | | (177) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 282 | | | | DPBC | | | | | A | | | | Serum | | (63) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 145 | | | | RDBPC | | | | | A | | | | Serum | | (178) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 30 | | | | RNBC | | | | | A | | | | Serum | | (82) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 175 | | | | RDBPC | | | | | A | | | | Serum | | (44) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 18 | | | | PC | | | | | B | | | | Serum | | (69) | | | | | |
|  | | | Grass | | | ↑ | | | | | Stable | | | | | | | n.r. | | | | | Not included | | | | 210 | | | | RDBPC | | | | | A | | | | Serum | | (153) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 175 | | | | RDBPC | | | | | A | | | | Serum | | (180) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 54 | | | | RDBPC | | | | | A | | | | Serum | | (163) | | | | | |
| IgE-FAB | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 32 | | | | Cross sectional | | | | | C | | | | Serum | | (84) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | + | | | | 156 | | | | DBPC | | | | | A | | | | Serum | | (6) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 22 | | | | PC | | | | | B | | | | Serum | | (68) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 28 | | | | DBPC | | | | | A | | | | Serum | | (115) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | + | | | | 282 | | | | DPBC | | | | | A | | | | Serum | | (63) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 30 | | | | RNBC | | | | | B | | | | Serum | | (82) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 18 | | | | PC | | | | | B | | | | Serum | | (69) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 10 | | | | RDBPC | | | | | A | | | | Serum | | (67) | | | | | |
|  | | | Grass | | | ↓ | | | | | Not reported | | | | | | | n.a. | | | | | Not included | | | | 7 | | | | Cross sectional | | | | | C | | | | Nasal fluid | | (179) | | | | | |
|  | | | Birch | | | ↓ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 12 | | | | RDBPC | | | | | A | | | | Serum | | (34) | | | | | |
| **Domain iv:**  **Basophil activation** | | | | | | | | | | |  | | | | | | |  | | | | |  | | | |  | | | |  | | | | |  | | | |  | |  | | | | | |
| CD203c | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | + | | | | 32 | | | | Cross sectional | | | | | D | | | | WB | | (84) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 16 | | | | RDBPC | | | | | A | | | | WB | | (81) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 45 | | | | RDBPC | | | | | A | | | | WB | | (37) | | | | | |
| ΔEC50 | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation. | | | | | Not included | | | | 18 | | | | PC | | | | | B | | | | WB | | (69) | | | | | |
| DOA | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | + | | | | 32 | | | | Cross sectional | | | | | D | | | | WB | | (84) | | | | | |
| CD63 | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | + | | | | 32 | | | | Cross sectional | | | | | D | | | | WB | | (84) | | | | | |
|  | | | Birch | | | ↓ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 5 | | | | RDBPC | | | | | A | | | | WB | | (83) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 34 | | | | CC | | | | | C | | | | WB | | (41) | | | | | |
| CD107a | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | + | | | | 32 | | | | Cross sectional | | | | | D | | | | Serum | | (84) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 30 | | | | RDBPC | | | | | A | | | | WB | | (149) | | | | | |
| **Domain v:**  **Cytokines and Chemokines** | | | | | | | | | | | | | | | | | |  | | | | |  | | | |  | | | |  | | | | |  | | | |  | |  | | | | | |
| IL-2R | | | Jap.Ced. | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 22 | | | | CC | | | | | C | | | | Serum | | (184) | | | | | |
| IL-2 | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | CC | | | | | C | | | | Serum | | (185) | | | | | |
| IL-4 | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | CC | | | | | C | | | | Serum | | (185) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 12 | | | | CC | | | | | C | | | | PBMC | | (94) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 32 | | | | PC | | | | | B | | | | PBMC | | (36) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 20 | | | | PC | | | | | B | | | | PBMC | | (186) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 45 | | | | RDBPC | | | | | A | | | | PBMC | | (187) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 14 | | | | PC | | | | | B | | | | Nasal fluid | | (105) | | | | | |
|  | | | Ragweed | | | ↓ | | | | | Challenge Chamber | | | | | | | No correlation | | | | | Not included | | | | 18 | | | | RDBPC | | | | | A | | | | PBMC | | (188) | | | | | |
|  | | | Ragweed | | | ↓ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 48 | | | | CC | | | | | C | | | | PBMC | | (126) | | | | | |
|  | | | Jap ced. | | | ↓ | | | | | no symptom scores | | | | | | | n.r. | | | | | Not included | | | | 22 | | | | CC | | | | | C | | | | PBMC | | (189) | | | | | |
|  | | | Olea | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 24 | | | | CC | | | | | C | | | | Nasal lavage; nasal biopsies; | | (111) | | | | | |
|  | | | Dog | | | ↓ | | | | | Stable | | | | | | | n.r. | | | | | Not included | | | | 21 | | | | RDBPC | | | | | A | | | | PBMC | | (190) | | | | | |
| IL-4/IFNg ratio | | | HDM | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 32 | | | | RPC | | | | | B | | | | PBMC | | (191) | | | | | |
| IL-5 | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 20 | | | | PC | | | | | B | | | | PBMC | | (186) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 45 | | | | RDBPC | | | | | A | | | | Serum | | (187) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 12 | | | | RDBPC | | | | | A | | | | PBMC | | (192) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 9 | | | | CC | | | | | C | | | | PBMC | | (193) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 28 | | | | RPC | | | | | B | | | | PBMC | | (194) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 32 | | | | PC | | | | | B | | | | PBMC | | (36) | | | | | |
|  | | | HDM | | | ↓; higher basal levels in SCIT-responders than in non-responders and AR | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 34 | | | | CC | | | | | C | | | | PBMC | | (41) | | | | | |
|  | | | Ragweed | | | ↓ | | | | | Challenge Chamber | | | | | | | No correlation | | | | | Not included | | | | 18 | | | | RDBPC | | | | | A | | | | PBMC | | (188) | | | | | |
|  | | | Jap ced. | | | ↓ | | | | | no symptom scores | | | | | | | n.r. | | | | | Not included | | | | 22 | | | | CC | | | | | C | | | | PBMC | | (189) | | | | | |
|  | | | Dog | | | ↓ | | | | | Stable | | | | | | | n.r. | | | | | Not included | | | | 21 | | | | RDBPC | | | | | A | | | | PBMC | | (190) | | | | | |
|  | | | birch, alder, and hazel mix | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 20 | | | | RDBPC | | | | | A | | | | PBMC | | (195) | | | | | |
| IL-5/IFNg ratio | | | HDM | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 32 | | | | RPC | | | | | B | | | | PBMC | | (191) | | | | | |
| IL-6 | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | CC | | | | | C | | | | Serum | | (185) | | | | | |
| IL-8 | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | CC | | | | | C | | | | Serum | | (185) | | | | | |
| IL-9 | | | Grass | | | ↓ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 14 | | | | PC | | | | | C | | | | Nasal fluid | | (105) | | | | | |
|  | | | HDM | | | ↓; higher basal levels in SCIT-responders than in non-responders and AR | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 34 | | | | CC | | | | | C | | | | PBMC | | (41) | | | | | |
|  | | | Parietaria judaica | | | ↓ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 29 | | | | RCC | | | | | C | | | | PBMC | | (196) | | | | | |
| IL-10 | | | HDM | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 21 | | | | RDBPC | | | | | A | | | | Serum | | (164) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 13 | | | | RDBPC | | | | | A | | | | Serum | | (197) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | CC | | | | | C | | | | Serum | | (185) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 9 | | | | CC | | | | | C | | | | Serum | | (198) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 9 | | | | CC | | | | | C | | | | PBMC | | (199) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 12 | | | | CC | | | | | C | | | | Serum | | (94) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 32 | | | | PC | | | | | B | | | | PBMC | | (36) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 28 | | | | RPC | | | | | B | | | | PBMC | | (194) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 45 | | | | RDBPC | | | | | A | | | | PBMC | | (187) | | | | | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 12 | | | | RDBPC | | | | | A | | | | PBMC | | (192) | | | | | |
|  | | | Grass | | | ↓  ↔ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 20 | | | | PC | | | | | B | | | | PBMC | | (186) | | | | | |
|  | | | birch,  grass,  birch and grass | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 30 | | | | CC | | | | | C | | | | PBMC | | (200) | | | | | |
|  | | | birch, alder and hazel mix | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 20 | | | | RDBPC | | | | | A | | | | PBMC | | (201) | | | | | |
|  | | | Ragweed | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 48 | | | | CC | | | | | C | | | | PBMC | | (126) | | | | | |
|  | | | Jap. cedar | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 19 | | | | CC | | | | | C | | | | PBMC | | (202) | | | | | |
|  | | | birch, alder, and hazel mix | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 20 | | | | RDBPC | | | | | A | | | | PBMC | | (195) | | | | | |
|  | | | Olea | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 24 | | | | CC | | | | | C | | | | Nasal lavage; nasal biopsies; | | (111) | | | | | |
|  | | | Dog | | | ↓ | | | | | Stable | | | | | | | n.r. | | | | | Not included | | | | 21 | | | | RDBPC | | | | | A | | | | PBMC | | (190) | | | | | |
| IL-13 | | | Grass | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 20 | | | | PC | | | | | B | | | | PBMC | | (186) | | | | | |
|  | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 14 | | | | PC | | | | | B | | | | Nasal fluid | | (105) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 28 | | | | RPC | | | | | B | | | | PBMC | | (194) | | | | | |
|  | | | HDM | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 34 | | | | CC | | | | | C | | | | PBMC | | (41) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 32 | | | | PC | | | | | B | | | | PBMC | | (36) | | | | | |
|  | | | Ragweed | | | ↓ | | | | | Challenge Chamber | | | | | | | No correlation | | | | | Not included | | | | 18 | | | | RDBPC | | | | | A | | | | PBMC | | (188) | | | | | |
| IL-13/IFNg ratio | | | HDM | | | ↓ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 32 | | | | RPC | | | | | B | | | | PBMC | | (191) | | | | | |
| IL-17 | | | birch, alder and hazel mix | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 20 | | | | RDBPC | | | | | A | | | | PBMC | | (201) | | | | | |
| IL-18 | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 13 | | | | RDBPC | | | | | A | | | | Serum | | (197) | | | | | |
|  | | | birch,  grass,  birch and grass | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 30 | | | | CC | | | | | C | | | | PBMC | | (200) | | | | | |
| IFN-y | | | Grass | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 20 | | | | PC | | | | | B | | | | PBMC | | (186) | | | | | |
|  | | | Grass | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 12 | | | | RDBPC | | | | | A | | | | PBMC | | (192) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 32 | | | | RPC | | | | | B | | | | PBMC | | (191) | | | | | |
|  | | | HDM | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 12 | | | | CC | | | | | C | | | | PBMC | | (94) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 32 | | | | PC | | | | | B | | | | PBMC | | (36) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 13 | | | | RDBPC | | | | | A | | | | Serum | | (197) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | CC | | | | | C | | | | Serum | | (185) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 21 | | | | RDBPC | | | | | A | | | | Serum/ nasal | | (164) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 28 | | | | RPC | | | | | B | | | | PBMC | | (194) | | | | | |
|  | | | Dog | | | ↔ | | | | | Stable | | | | | | | n.r. | | | | | Not included | | | | 21 | | | | RDBPC | | | | | A | | | | PBMC | | (190) | | | | | |
| TGF-B | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 32 | | | | PC | | | | | B | | | | PBMC | | (36) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 28 | | | | RPC | | | | | B | | | | PBMC | | (194) | | | | | |
|  | | | HDM | | | ↔ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 12 | | | | CC | | | | | C | | | | PBMC | | (94) | | | | | |
|  | | | birch,  grass,  birch and grass | | | ↔ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 30 | | | | CC | | | | | C | | | | PBMC | | (200) | | | | | |
|  | | | birch, alder and hazel mix | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 20 | | | | RDBPC | | | | | A | | | | PBMC | | (201) | | | | | |
|  | | | Dog | | | ↑ | | | | | Stable | | | | | | | No correlation | | | | | Not included | | | | 21 | | | | RDBPC | | | | | A | | | | PBMC | | (190) | | | | | |
| TNF-a | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | CC | | | | | C | | | | PBMC | | (185) | | | | | |
| CCR3 | | | Birch | | | ↔SCIT, ↑AR | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 16 | | | | RDBPC | | | | | A | | | | nasal biopsies | | (97) | | | | | |
| CCR3 | | | Birch | | | ↑SCIT, ↑AR | | | | | Improved | | | | | | | n.a. | | | | | Not included | | | | 16 | | | | RDBPC | | | | | A | | | | nasal biopsies | | (97) | | | | | |
| apolipoprotein A-I | | | Jap. cedar | | | ↑ | | | | | Improved | | | | | | | Correlation | | | | | Not included | | | | 15 | | | | RPC | | | | | B | | | | Serum | | (99) | | | | | |
| C4a | | | Jap. cedar | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 15 | | | | RPC | | | | | B | | | | Serum | | (99) | | | | | |
| Eosinophil cationic protein ECP | | | Jap. cedar | | | ↔ | | | | | n.r. | | | | | | | n.a. | | | | | Not included | | | | 47 | | | | CC | | | | | C | | | | Serum | | (104) | | | | | |
| Eotaxin | | | Grass | | | ↓ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 14 | | | | PC | | | | | B | | | | Nasal fluid | | (105) | | | | | |
| MCP-1 | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r. | | | | | Not included | | | | 15 | | | | CC | | | | | C | | | | Serum | | (185) | | | | | |
| Transthyretin | | | Jap. cedar | | | ↑ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 15 | | | | RPC | | | | | B | | | | Serum | | (99) | | | | | |
| Tryptase | | | Grass | | | ↔ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | | 14 | | | | PC | | | | | B | | | | Nasal fluid | | (105) | | | | | |
| thymus and activation-regulated chemokine (TARC) | | | | | | | | | birch | | | | | ↑ | | Improved | | | | |  | | |  | | | | | 16 | |  | | |  | | | | nasal biopsies IHC | | | | | | (97) | |
| **Domain vi:**  **Cellular markers** | | | | | | | |  | | | | |  | |  | | | | |  | | | |  | | | |  | |  | | |  | | | |  | | | | | |  | |
| Treg  (FOXP3) | | | | | | | | HDM | | | | | ↑ | | Improved | | | | | n.r. | | | | Not included | | | | 15 | | RDBPC | | | A | | | | Serum | | | | | | (112) | |
|  | | | | | | | | | Grass | | | | | ↑ | | Improved | | | | | n.r. | | | Not included | | | | | 9 | | CC | | | C | | | | Nasal mucosa | | | | | | (114) | |
|  | | | Grass | | | ↑ | | | | | Improved | | | | | | | n.r. | | | | Not included | | | | 28 | | | | DBPC | | | | | A | | | | Sublingual biopsy | | (115) | | | | | |
|  | | | Ragweed | | | ↔ | | | | | Improved | | | | | | | No correlation | | | | | Not included | | | 48 | | | | | CC | | | | C | | | | PBMC | | (126) | | | | |
| CQ10 | | | Grass | | | ↑ | | | | | Improved | | | | | | | Correlation with responders | | | | | Not included | | | 41 | | | | | RDBPC | | | | A | | | | Serum | | (123) | | | | |
| **Domain vii:**  **In vivo biomarker** | | | | | |  | | | | |  | | | | | | |  | | | | |  | | |  | | | | |  | | | |  | | | |  | |  | | | | |
| ***Provocation tests*** | | |  | | |  | | | | |  | | | | | | |  | | | | |  | | |  | | | | |  | | | |  | | | |  | |  | | | | |
| ICAM-1 | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r | | | | | Not included | | | 10 | | | | | RDBPC | | | | A | | | | Conjuntical epithelium | | (128) | | | | |
| Eosinophils | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r | | | | | Not included | | | 10 | | | | | RDBPC | | | | A | | | | Conjuntical epithelium | | (128) | | | | |
| Neutrophils | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r | | | | | Not included | | | 10 | | | | | RDBPC | | | | A | | | | Conjuntical epithelium | | (128) | | | | |
| ***ECC*** | | |  | | |  | | | | |  | | | | | | |  | | | | |  | | |  | | | | |  | | | |  | | | |  | |  | | | | |
| Symptom score | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r | | | | | Not included | | | 52 | | | | | RDBPC | | | | A | | | | - | | (141) | | | | |
| Symptom score | | | HDM | | | ↓ | | | | | Improved | | | | | | | n.r | | | | | Not included | | | 118 | | | | | RDBPC | | | | A | | | | - | | (142) | | | | |
| Symptom score | | | Cat | | | ↓ | | | | | Improved | | | | | | | n.r | | | | | Not included | | | 52 | | | | | RDBPC | | | | A | | | | - | | (129) | | | | |
| ***TNPT*** | | |  | | |  | | | | |  | | | | | | |  | | | | |  | | |  | | | | |  | | | |  | | | |  | |  | | | | |
| Symptom score | | | Grass | | | ↓ | | | | | Improved | | | | | | | n.r | | | | | Not included | | | 14 | | | | | RDBPC | | | | A | | | | - | | (105) | | | | |
| Symptom score | | | Birch | | | ↓ | | | | | Improved | | | | | | | n.r | | | | | Not included | | | 217 | | | | | RDBPC | | | | A | | | | - | | (131) | | | | |

n.r.: not reported; n.a.: not applicable

WB: Whole blood

**Table 2: Study overview**

| **Study** | | | | **Type** | | | | **Adult/ Child** | | | | **Subjects\*** | | | | **Allergen** | | | | **Biomarkers tested** | | | | **Clinical outcome** | | | | **Duration** | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |
| (82) Aasbjerg *et al 2014* | | | | RNBC | | | | Adults | | | | SCIT: 15  SLIT: 15  SAR: 10 | | | | SCIT: Phleum pratense; Alutard  SLIT: Phleum pretense, Grazax | | | | sIgG4  sIgE  IgE-FAB  BAT  IgE-BF | | | | Nasal challenge improved | | | | 15 months | | | |
| (182) Amar  *et al 2009* | | | | RDBPC | | | | Adults | | | | SLIT (mono): 19  SLIT (multi): 17  SARP: 17 | | | | Mono: Phl p 5  Multi: Phl p5 + 9 additional pollen | | | | sIgG4  IFN-y | | | | Symptom score improved  Medication score improved | | | | 1 year | | | |
| (155) Ariano *et al 1999* | | | | RDBPC | | | | Adults/ children | | | | SCIT: 13  SARP: 12 | | | | SIT (Purethal) | | | | sIgE  sIgG4 | | | | Symptom score improved  Medication score improved | | | | 3 years | | | |
| (58) Bahceciler *et al 2005* | | | | CC | | | | Children | | | | SLIT (6 months): 17  SLIT (12 months): 14  NAC: 8 | | | | D. Pteronys./ D. Farinae. Staloral | | | | sIgG4  sIgE  sIgG1  sIgA | | | | Symptom score improved only in 12 months group  Medication score improved in 12 months group | | | | 1 year | | | |
| (185) Barberi et al, 2011 | | | | CC | | | | Child | | | | SLIT+D: 15  (drugs on demand)  ARD: 15 | | | | SLIT: HDM  Staloral, Stallergenes | | | | IL-4  IL-10  IL-2, IL-6, IL-8  TNFa, MCP  IFNg | | | | VAS  SMS | | | | 2 years | | | |
| (180) Blaiss *et al 2011* | | | | RDPBC | | | | Adults/ children | | | | SLIT: 142  SARP: 140 | | | | Phleum prat (Schering-Plough) | | | | sIgG4  IgE-BF | | | | TCS (total combined score) improved  RQLQ: Improved | | | | 23 weeks | | | |
| (187) Bonvalet et al., 2012 | | | | RDBPC | | | | Adult | | | | SLIT: 45  ARP: 44 | | | | five-grass pollen  extract (Stallergenes SA) | | | | IL-4  IL-10 | | | | TSS  Challenge chamber | | | | 2-4 months | | | |
| (162) Bousquet *et al 1999* | | | | RDBPC | | | | Adults | | | | SLIT:42  AAP: 43 | | | | Der p1, der f1 | | | | sIgE  sIgG4 | | | | Asthma scores improved  Medcation scores improved  QoL improved | | | | 25 months | | | |
| (166) Bush *et al* | | | | RDBPC | | | | Adults | | | | SLIT (high dose): 9  SLIT (low dose): 7  ARP | | | | Der f | | | | sIgE  sIgG4 | | | | Symptom scores and medication score stable | | | | 18 months | | | |
| (188) Campbell et al, 2010 | | | | RDBPC | | | | Adult | | | | SCIT: 17  ARP: 15 | | | | Ragweed: Amb a 1-imm-unostimulatory  oligodeoxynucle otide conjugate | | | | IL-4  IL-5  IL-13  IFNg | | | | Challenge chamber | | | | 7 months | | | |
| (83) Ceuppens *et al 2009* | | | | RDBPC | | | | Adults | | | | SCIT: 28  SARP: 30 | | | | Birch pollen extract | | | | sIgE  sIgG4  sIgG  BAT-CD63 (n=5) | | | | CIS eye en nose improved | | | | 18 months | | | |
| (151) Chakraborty *et al 2006* | | | | RDBPC | | | | Adults | | | | SCIT: 18  SARP: 17 | | | | P Sylvestris | | | | IgE  sIgE  sIgG4  sIgG1 | | | | Symptom scores improved  Medicaiton scores improved | | | | 2 years | | | |
| (198) Ciprandi et al, 2006 | | | | CC | | | | adult | | | | SLIT HDM: 9  AR: 10 | | | | HDM: Staloral | | | | IL-10 | | | | FEV(25-75) | | | | 3 years | | | |
| (199) Ciprandi et al, 2007 | | | | CC | | | | adult | | | | SLIT HDM: 9  AR: 10  NAC: 9 | | | | SLIT HDM, Staloral | | | | IL-10 | | | | NSS  Rhinomanometry | | | | 3 years | | | |
| (196) Ciprandi et al, 2011 | | | | RDBPC | | | | adult | | | | SLIT: 29, ARD: 34 | | | | Parietaria judaica pollen allergen extract (Anallergo, Florence, Italy) | | | | TGF-b | | | | VAS  NSMS | | | | 3 months preseasonal | | | |
| (175) Cortellini *et al 2010* | | | | RDBPC | | | | Adults | | | | SLIT: 15  ARP | | | | Alternaria (Anallergo) | | | | sIgE  sIgG4 | | | | Symptom score improved  Medication scores improved | | | | 10 months | | | |
| (163) Corzo *et al 2014* | | | | RDBPC | | | | Adults/ children | | | | SLIT: 54  AAP | | | | Der p, der f | | | | sIgE  gE-BF | | | | Medicatio score improved | | | | 2 weeks | | | |
| (94) Cosmi *et al 2006* | | | | RC | | | | Adults | | | | SLIT: 12  AR: 13 | | | | DP and D far. LAIS | | | | IgE  sIgE  sIgG4  IL-10  IFN-y | | | | Symptom score improved  Medication score improved | | | | 18 months | | | |
| (157) Cox *et al 2012* | | | | RDBPC | | | | Adults | | | | SLIT: 207  SARP: 223 | | | | Dact gl, dact gl, l per, Phl prat, Poa prat | | | | sIgE  sIgG4 | | | | Combined symptom score improved  RQLQ improve | | | | 8 months | | | |
| (177) Dahl *et al. 2008* | | | | RDBPC | | | | Adults | | | | SLIT: 189  SAR: 162 | | | | Phleum pretense, Grazax | | | | sIgG4  IgE-BF | | | | Symptom scores improved  RQLQ improved | | | | 2 years | | | |
| (33) Di Lorenzo *et al 2009* | | | | Retrospective | | | | Adult | | | | SCIT: 76  SLIT: 203  Responders vs non-responders | | | | Grass (P. judaica, O Europea)  HDM (D. Pteronys./ D. Farinae) | | | | IgE  sIgE  IgE-ratio | | | | VAS improved  ROC curve | | | | n.a. | | | |
| (145) Didier *et al. 2007* | | | | RDBPC | | | | Adults | | | | SLIT (100 IR): 157  SLIT (300 IR): 155  SLIT (500 IR): 160  SAR: 156 | | | | 5 grass pollens | | | | sIgG4  IgE | | | | RTSS improved  Rescue medication lower  RQLQ improved | | | | 6 months | | | |
| (178) Durham *et al 2010* | | | | RDBPC | | | | Adults | | | | SLIT: 145  SARP: 145 | | | | Phleum pretense, Grazax | | | | sIgG4  IgE-BF | | | | DSS improved  MDS improved  RQLQ improved | | | | 3 years | | | |
| (147) Durham *et al.* | | | | RDBPC | | | | Adults | | | | SLIT:702  SARP: 153 | | | | Phl. P (Grazax) | | | | IgE  IgE | | | | Symptom score improved  Medication score stable | | | | 18 weeks | | | |
| (63) Durham *et al. 2012* | | | | DBPC | | | | Adults | | | | SLIT: 282 – 137\*\*\*  SARP: 286 - 104 | | | | Phleum pretense, Grazax | | | | sIgG4  IgE-FAB  IgE-BF | | | | DSS improved  MDS improved  RQLQ improved | | | | 5 years | | | |
| (36) Eifan *et al. 2010* | | | | ROLPC | | | | Children | | | | SCIT 16  SLIT 16  ARP: 16 | | | | SLIT and SCIT: D. Pteronys./ D. Farinae, ALK | | | | IgE  sIgE  IgE-ratio  IL10  TGF-beta | | | | TASS, TRSS, TSS, TMS, VAS score improved | | | | 1 year | | | |
| (193) Francis et al, 2007 | | | | CC | | | | Adult | | | | SCIT: 9 (high dose)  AR: 9  NAC: 9  All: 34 (blood and nasal biopsies) | | | | High dose grass pollen SCIT | | | | IL-4  IFNg | | | | SS | | | | 2 years | | | |
| (192) Francis et al, 2008 | | | | RDBPC | | | | Adult | | | | SCIT: 12  ARP: 6 | | | | SCIT Alutard grass | | | | IL-10  IgG4  IgA | | | | SS  Provocation | | | | 2 years | | | |
| (42) Gehlar *et al 1999* | | | | PC | | | | Children | | | | SCIT: 11  SAR: 9 | | | | Novo-Helisen depot, allergopharma | | | | sIgG4  sIgG1  sIgG2  IgE | | | | Symptom score (analogue and questionnaire) improved  VAS improved | | | | 1 year | | | |
| (41) Gomez *et al 2015* | | | | CC | | | | Adults | | | | SCIT: 34  SAR: 14 | | | | Acaroid, Allergopharma | | | | sIgG4  sIgE  IgE  BAT-CD63 | | | | 82.3% responders  17.7% non responders | | | | 1 year | | | |
| (172) Hoiby *et al 2010* | | | | RDBPC | | | | Adults/ children | | | | SCIT: 31  ARP: 30 | | | | Bet alba (depigoid) | | | | sIgE  sIgG4  sIgG1  IL-4,10,12,13. | | | | Symptom score improved  Medication score improved | | | | 2 year | | | |
| (141) Horak *et al. 2009* | | | | RDBPC | | | | Adults | | | | SLIT: 45  SARP: 44 | | | | 300-IR 5 grass | | | | ECC | | | | Symptom scores | | | | 4 months | | | |
| (174) Horichuchi *et al 2008* | | | | RSBPC | | | | Adult | | | | SLIT: 43  SARP: 24 | | | | Cedar pollen extract | | | | sIgG4  sIgE | | | | Nasal symptom scores improved | | | | 6 months | | | |
| (68) James *et al. 2011* | | | | PC | | | | Adults | | | | SCIT only: 9  SCIT + placebo: 6  SCIT + SCIT: 7 | | | | Phleum pratense; Alutard | | | | sIgG4  sIgE  IgE-FAB | | | | Combined symptom and medication scores improved | | | | 2+2 years \*\* | | | |
| (39) Jutel *et al 2005* | | | | RDBPC | | | | Adults | | | | SCIT: 29  SAR: 28 | | | | Phl prat | | | | sIgE  sIgG4  sIgG1 | | | | Sympton score improved  Medication score improved  RQLQ improved | | | | 6 months | | | |
| (165) Keles *et al 2011* | | | | RDBPC | | | | Children | | | | SCIT: 15  SLIT: 15  SLIT + SCIT: 15  ARP | | | | Der p, der f (ALK) | | | | sIgE  sIgG4  TGF-B  IFN-y | | | | VAS improved  Medicaiton scores improved | | | | 1 year | | | |
| (111) Kirmaz et al, 2011 | | | | CC | | | | adult | | | | SCIT Olea: 24  ARD: 15 | | | | Allergopharma Novo-Helisen Depot | | | | IL-4  IL-10  IFNg | | | | NSS | | | | 1 years | | | |
| (146) Keskin *et al 2006* | | | | PC | | | | Children | | | | SCIT: 27  SAR: 26 | | | | Grass pollen (Allergovit) | | | | IgE  sIgG4  sIgG1 | | | | Rhinitis symptom and medication score improved | | | | 27 months | | | |
| (152) Klimek *et al 2012* | | | | RDBPC | | | | Adults | | | | SCIT: 40  SARP: 10 | | | | rPhl p1, rPhl p2, rPhl p5a, rPhl p5b, rPhl p6 | | | | sIgE  sIgG4  sIgG1 | | | | CPT improved | | | | 1 month | | | |
| (190) Lent et al, 2006 | | | | RDBPC | | | | Adult | | | | SCIT 21  (3 dosage groups)  ARP: 7 | | | | AP dog (cluster): (Hollister-Stier Laboratories) | | | | IL-4  IL-5  IL-10  IFNg  TGF-b | | | | SSS (Bousquet) | | | | 5 weeks | | | |
| (35) Li *et al. 2014* | | | | Retrospective | | | | Children | | | | SCIT: 185 | | | | D. Pteronys, alutard | | | | IgE  sIgE  IgE-ratio | | | | Symptom scores improved  ROC curve | | | | n.a. | | | |
| (148) Lue *et al 2006* | | | | RDBPC | | | | Children | | | | SLIT: 10  ARP: 10 | | | | D. Pteronys./ D. Farinae. Staloral | | | | sIgG4  IgE  sIgE | | | | Symptom score improved  Medication score improved  Skin prick test showed no difference | | | | 6 months | | | |
| (99) Makino et al, 2010 | | | | RPC | | | | adult | | | | SLIT Jap cedar: 15  ARP: 9  (1 withdrawal) | | | | Jap. cedar pollen extract, manufacturer | | | | C4a | | | | SMS  QoL | | | | before and during pollen season | | | |
| (130) Meyer *et al. 2013* | | | | RDBPC | | | | Adults | | | | SCIT: 30  SARP: 7 | | | | rBET v 1-FV | | | | ECC | | | | Sympton scores | | | | 10 weeks | | | |
| (194) Moed et al, 2013 | | | | RPC | | | | Child | | | | SLIT: 28  ARP: 30 | | | | HDM, Artu Biologicals Europe B.V. | | | | IL-5  IL-13  IL-10  TGF-b | | | | SPT  NSS, ASS  Eye SS | | | | 2 years | | | |
| (159) Mosges *et al 2007* | | | | RDBPC | | | | Adults | | | | SLIT: 48  SARP: 53 | | | | Staloral | | | | sIgE  sIgG4 | | | | Medication score improved  Symptom core improved | | | | 9 months | | | |
| (150) Moverare *et al 2001* | | | | PC | | | | Children/ Adults | | | | SCIT: 30  SAR: 16 | | | | Birch and timothy pollen extract (ALK) | | | | sIgG4  IgE  sIgE  sIgG | | | | Symptom score improved  Medication score improved | | | | 3 year | | | |
| (43) Moverare *et al 2002* | | | | PC | | | | Children/ Adults | | | | SCIT: 24  SAR: 15 | | | | Birch pollen Aquagen | | | | sIgE | | | | Symptom scores improved | | | | 3 years | | | |
| (202) Murakami et al, 2014 | | | | CC | | | | Adult | | | | OIT: 19  ARD: 10 | | | | OIT Jap cedar: Cry j 1-galactomannan conjugate (Wako Filter Technology Ltd, Ibaraki, Japan | | | | IL-10  IgG4 | | | | NSMS  Eye SMS | | | | 5 months | | | |
| (44) Nelson *et al 2011* | | | | RDBPC | | | | Adults | | | | SCIT: 175  SARP: 192 | | | | Phleum pretense: Schering-Plough | | | | sIgG4  IgE-BF | | | | Symptom scores improved  Medication scores improved  RQLQ improved | | | | 6 months | | | |
| (142) Nolte *et al. 2015* | | | | RDBPC | | | | Adults | | | | SLIT: 118 (2 doses)  ARP: 42 | | | | MK-8237 | | | | ECC | | | | Symptom scores | | | | 24 weeks | | | |
| (189) Nomura et al, 2013 | | | | open-label controlled | | | | child and adult | | | | SCIT Jap cedar  SCIT: 22,  AR: 6 | | | | SCIT:  rush followed by maintenance schedule, Japanese cedar extract (Torii Pharmaceutical,  Tokyo, Japan). | | | | IL-4  IL-5 | | | | None | | | | n.r. | | | |
| (112) O’Hehir *et al 2009* | | | | RDBPC | | | | Adults | | | | SLIT: 15  SARP: 15 | | | | Staloral | | | | sIgE  sIgG4  sIgG1  sIgA  Treg (FOXP3) | | | | Symptom score improved  Medication score improved  VAS improved | | | | 2 years | | | |
| (104) Ohashi, Nakai et al, 1997 | | | | CC | | | | Adult | | | | SCIT: 47  ARD: 34 | | | | SCIT: Jap. cedar | | | | ECP | | | | None | | | | 2-3 years | | | |
| (184) Ohashi, Tanaka et al, 1997 | | | | CC | | | | Adult | | | | SCIT: 47  ARD: 34 | | | | SCIT: Jap.cedar | | | | IgE  IL2R | | | | None | | | | 1 season | | | |
| (158) Ott *et al. 2009* | | | | RDBPC | | | | Adults/ childs | | | | SLIT: 99  SARP: 46 | | | | Phl. Prat (Staloral) | | | | sIgE  sIgG4 | | | | Combined symptom score improved, also after cessation | | | | 1 year | | | |
| (37) Overtvelt *et al 2011* | | | | RDBPC | | | | Adults | | | | SLIT number of patients not reported | | | | Stallergenes | | | | CD203c | | | | ARTSS improved | | | | 4 months | | | |
| (149) Ozdemir  *et al 2007* | | | | CC | | | | Children | | | | SLIT: 43  AAP: 23 | | | | Der p, der f (Stallergenes) | | | | IgE | | | | Medication score improved | | | | 3 years | | | |
| (81) Ozdemir *et al 2014* | | | | RDBPC | | | | Adults | | | | SCIT: 16  SARP: 15 | | | | 6 grass pollen extract: Allergovit | | | | sIgG4  sIgE  BAT-CD203c | | | | ARTSS no difference  Rescue medication score improved  ACS improved  RQLQ improved | | | | 4 months | | | |
| (170) Pajno *et al 2000* | | | | RDBPC | | | | Children | | | | SLIT: 12  AAP: 12 | | | | Der p1, der p2 (ALK) | | | | sIgE  sIgG4  sIgG | | | | Symptom score improved  Medication use decreased | | | | 2 years | | | |
| (128) Passalacqua *et al. 2008* | | | | RDBPC | | | | Adult | | | | SLIT: 10  SARP: 9 | | | | Der P, D Far LAIS | | | | ICAM-1  Eosinophils  Neutrophils | | | | Symptom scores | | | | 2 years | | | |
| (129) Patel *et al. 2013* | | | | RDBPC | | | | Adults | | | | SCIT: 52  ARP: 21 | | | | Cat-PAD | | | | ECC | | | | Symptom scores | | | | 1 year | | | |
|  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |
| (183) Pauli *et al* | | | | RDBPC | | | | Adults | | | | SCIT: 98  SARP 36 | | | | nBETv1  rBETv1  Birch | | | | sIgG4, sIgG1, sIgG2 | | | | Combined symptom en medication score improved | | | | 2 years | | | |
| (173) Pfaar *et al 2010* | | | | RDBPC | | | | Adults | | | | SCIT: 117  SARP: 40 | | | | Co rave, aln glut, bet alba | | | | sIgE  sIgG4 | | | | Combined symptom en medication score improved | | | | 18 months | | | |
| (161) Pfaar *et al* 2013 | | | | RDBPC | | | | Adults | | | | SCIT: 186  SARP: 99 | | | | Bet. Ver. (50%)  Dact gl, fest gl, l per, Phl prat, Poa prat (50%) | | | | sIgE  sIgG4 | | | | Combined symtpm and medication score improved  QoL improved | | | | 2 years | | | |
| (131) Pfaar *et al. 2016* | | | | RDBPC | | | | Adults | | | | SLIT: 217 (3 doses)  SARP: 52 | | | | SB | | | | IgG4 | | | | PNIF  TNPT  Symptom scores | | | | 5 months | | | |
| (168) Pham-Thi *et al 2007* | | | | RDBPC | | | | Children | | | | SLIT: 55  AAP: 56 | | | | Der p, der f (Stallergenes) | | | | sIgE  sIgG4 | | | | Medication score stable  QoL improved | | | | 18 months | | | |
| (126) Piconi et al, 2010 | | | | CC | | | | adult | | | | SLIT1 preseasonal 18  SLIT seasonal: 17  SLIT prologued: 13  ARD: 12 | | | | ragweed: Staloral (Stallergen SA) | | | | IL-4  IL-10  IgG4  PCDL-1  Tregs (FOXP3) | | | | VAS  SMS | | | | 3 years | | | |
| (97) Plewako et al, 2008 ; Follow up of (203) Arvidsson MB et al, 2002 | | | | RDBPC | | | | adult | | | | SCIT (+D):  (3 years after treatment): 16  ARD: 12 | | | | Birch: Alutard SQ Betula verrucosa (ALK, Hoersholm, DK) | | | | CCR3 | | | | NSMS | | | | 3 years | | | |
| (191) Potter et al, 2015 | | | | RPC | | | | adult | | | | SLIT HDM 32/34 completed  AR: 16/21 completed | | | | SLIT HDM, Der.p; Staloral, Stallergenes | | | | IL-5/IFNg  IL-13/IFNg  IL-4/IFNg | | | | TSS5  QoL | | | | 2 years | | | |
| (181) Purohit  *et al 2008* | | | | RDBPC | | | | Adults | | | | SCIT: 47  SARP: 37 | | | | Bet v 1 clone | | | | sIgG4  sIgG1 | | | | Combined symptom medication score improved | | | | 5 months | | | |
| (114) Radulovic *et al 2009* | | | | CC | | | | Adults | | | | SCIT: 9  SAR: 13  NAC: 9 | | | | Alutard SQ | | | | Treg (FOXP3) in nasal mucosa | | | | Symptom score  Skin response | | | | 2 years | | | |
|  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |
| (153) Reich *et al 2011* | | | | RDBPC | | | | Adults | | | | SCIT: 210  SARP: 52 | | | | Phleum pratanse Grazax | | | | sIgE  sIgG4  IgE-BF | | | | Symtpom score stable (before pollen season) | | | | 10 weeks | | | |
| (59) Rolinck- Werninghaus *et al 2005* | | | | RDBPC | | | | Children | | | | SLIT: 17  SARP: 12 | | | | 5-grass mixture Dactylis glomerata, Festuca praten- sis, Lolium perenne, Phleum pratense and Poa pratensis; Pangramin | | | | sIgG4  IgE | | | | Not reported | | | | 2 years | | | |
| (179) Saleem *et al. 2013* | | | | Cross sectional | | | | Adults | | | | SLIT: 7  SAR: 7  NAC: 8 | | | | Not reported | | | | sIgG4  IgE-FAB | | | | Not reported | | | | n.a. | | | |
| (200)Savolainen et al, 2004 | | | | CC | | | | adult | | | | SCIT birch: 18  SCIT grass: 6  SCIT birch+grass: 6  AR: 10  NAC: 10 | | | | SCIT Alutard SQ birch, grass, or birch+grass, (ALK Abello, H**oe**rsholm, Denmark)  conventional or rush | | | | IL-10  IL-18 | | | | VAS  SMS | | | | 5-15 weeks and 1-2 years after | | | |
| (195) Savolainen et al, 2006 | | | | RDBPC | | | | child: A: | | | | SLIT (low dose): 10  SLIT (high dose): 10  ARP: 10 | | | | SQ-standardized tree pollen extract: birch, alder, hazel mix | | | | IL-5  IL-10  TGF-b | | | | SMS | | | | 2 years | | | |
| (115) Scadding  *et al. 2010* | | | | DBPC | | | | Adult | | | | SLIT: 28  SARP: 28  NAC: 8 | | | | Phleum pratense; Alutard | | | | sIgG4  IgE-Fab  IgA2  Treg (FOXP3) | | | | Symptom score improved  Decreases LPR | | | | 18 months | | | |
| (105) Scadding et al, 2015 | | | | PC | | | | adult | | | | SCIT grass: 14  AR: 14,  NAC: 14 | | | | SCIT Grass Phl.p; Aquagen SQ, or Grazax, ALK-Abello, Hørsholm, Denmark | | | | IL-4  IL-9  Eotaxin  PNPT | | | | SS  PNIF | | | | at least 6 months | | | |
| (69) Schmid *et al. 2014* | | | | PC | | | | Adults | | | | SCIT: 18  SAR: 6 | | | | Grass pollen | | | | sIgE  IgE-FAB  IgE-BF  BAT-CD63  ΔEC50 | | | | Somptom score improved  Skin prick test improved  Nasal challenge improved | | | | 1 year | | | |
| (186) Schulten et al, 2014 | | | | PC | | | | adult | | | | SCIT: 40  AR: 40 | | | | SCIT grass pollen extract (Phl p) | | | | IL-4  IL-5  IgE  IgG4 | | | | Questionair | | | | 1 year | | | |
| (6) Shamji *et al. 2012* | | | | DBPC | | | | Adults | | | | SCIT (l): 54  SCIT (h): 112  SARP: 55 | | | | Phleum pratense; Alutard  (l) 10.000 SQ-U  (h) 100.000 SQ-U | | | | sIgG4  sIgE  IgE-FAB  IgE-BF | | | | Combined symptom and medication scores improved | | | | 8 months | | | |
| (84) Shamji *et al. 2015* | | | | Cross sectional | | | | Adults | | | | SCIT: 14  SLIT: 12  SLIT-TOL: 6  SAR: 24  NAC: 12 | | | | SCIT: Phleum pratense; Alutard  SLIT: Grazax | | | | sIgG4  IgE-FAB  BAT-DOA  BAT-CD63  BAT-CD107A | | | | RTSS improved | | | | n.a. | | | |
| (160) Smith *et al 2004* | | | | RDBPC | | | | Adults | | | | SLIT: 44  SARP: 45 | | | | Timothy grass (stallergenes) | | | | sIgE  sIgG4 | | | | Symptom score improved | | | | 2 years | | | |
| (176) Srivastava *et al 2011* | | | | RDBPC | | | | Adults | | | | SCIT: 50  ARP: 50 | | | | P. Americana (cockroach) | | | | sIgE  sIgG4  sIgG1 | | | | Symptom scores improved  Medication score improved | | | | 2 years | | | |
| (154) Tepas *et al 2004* | | | | RDBPC | | | | Adults | | | | SLIT:12  SARP: 12 | | | | Timothy grass microbeads | | | | sIgE  sIgG | | | | Combined symptom and medication score improved | | | | 10 weeks | | | |
| (67) Wachholz *et al 2003* | | | | RDBPC | | | | Adults | | | | SCIT: 10  ARP: 8 | | | | Phleum pretense, ALK | | | | IgE-FAB | | | | Sympton scores improve  Medication scores improved | | | | 1 year | | | |
| (156) Wahn  *et al 2012* | | | | RDBPC | | | | Children | | | | SLIT: 132  SARP: 47 | | | | Dact gl, fest gl, l per, Phl prat, Poa prat | | | | sIgE  sIgG4  sIgG1 | | | | Symptom-medication score improved | | | | 1.5 years | | | |
| (169) Wang *et al 2006* | | | | RDBPC | | | | Adults | | | | SCIT: 64  AAP: 65 | | | | D. pter (ALK) | | | | sIgE | | | | Peak flow improved | | | | 1 year | | | |
| (171) Wang *et al 2013* | | | | RDBPC | | | | Adults/ children | | | | SLIT: 60  ARP: 60 | | | | D pter d far | | | | sIgE  sIgG4 | | | | Symptom score improved  VAS improved | | | | 24 weeks | | | |
| (34) Wurtzen *et al 2008* | | | | RDBPC | | | | Adults | | | | SCIT: 21  SARP: 21 | | | | Bet. Verrucosa, Alutard | | | | IgE-FAB | | | | Medication score improved  Symptom score trend | | | | 2 years | | | |
| (164) Yukselen *et al 2012* | | | | RDBPC | | | | Children | | | | SCIT: 10  SLIT: 10  ARP: 10 | | | | D. pt D f. (Novohelisen) | | | | sIgE  sIgG4  IL10 | | | | RSS ASS (symptom score) improved  RMS, AMS (medication scores) improved | | | | 1 year | | | |
| (197)Yukselen et al, 2013 | | | | RDBPC | | | | Child | | | | SCIT (+D): 6/9 completed  SLIT (+D): 7/8 completed  ARP (+D): 10 | | | | SCIT and SLIT: D.p.+D.f. 50/50, NovoHelisen Depot and Oral, Allergopharma | | | | IL-10  IgG4  IgE | | | | VAS  NSMS  ASMS  Nasal provocation | | | | 2 years | | | |
| (85) Zidarn *et al 2015* | | | | CC | | | | Adults | | | | SCIT: 20  SAR: 13 | | | | Purethal Mixed Grasses,  HAL Allergy | | | | sIgG4  BAT-CD63 | | | | Symptom score improved  RQLQ improved | | | | 7 years | | | |
| (167) Zielen  *et al 2010* | | | | RC | | | | Children | | | | SCIT: 33  AAP: 32 | | | | D. pter (allergopharma) | | | | sIgE  IgG4  IgG1 | | | | Medicaiton score improved | | | | 2 years | | | |
| (123) Zimmer *et al. 2012* | | | | RDBPC | | | | Adults | | | | SLIT: 41  SARP: 38 | | | | n.r. | | | | C1Q  STAB1 | | | | Symptom score | | | | 4 months | | | |
|  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |  | | | |

\* NAC: Nonatopic control subject, SCIT: SCIT treated patients, SLIT: SLIT treated patients, SLIT-TOL: participants who completed 3 years of SLIT treatment, SAR: untreated seasonal allergic rhinitis, SARP untreated seasonal allergic rhinitis receiving placebo, ARP untreated allergic rhinitis receiving placebo, AAP allergic asthma receiving placebo

\*\* 22 patients received SCIT for 2 years, after 2 years 13 patients continued, 6 received placebo and 7 SCIT

\*\*\* Number of patients entering the study – number of patients after 5 years

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