# Efficacy and safety of the SQ tree sublingual immunotherapy tablet in children and adolescents (5 through 17 years of age) with moderate to severe allergic rhinitis and/or conjunctivitis induced by pollen from birch and trees belonging to the birch homologous group

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To compare the efficacy of the SQ tree SLIT-tablet to placebo in the treatment of moderate to severe allergic rhinitis and/or conjunctivitis induced by pollen from birch and trees belonging to the birch homologous group in children and adolescents (...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Allergic conditions |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON51039

**Source**
ToetsingOnline

**Brief title**
TT-06

### Condition

- Allergic conditions

**Synonym**
allergic rhinitis, tree allergy

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** ALK-Abelló A/S
**Source(s) of monetary or material Support:** farmaceutische industrie

## Intervention

**Keyword:** birch pollen, phase 3, tree allergy

## Outcome measures

### Primary outcome

To compare the efficacy of the SQ tree SLIT-tablet to placebo in the treatment of moderate to severe allergic rhinitis and/or conjunctivitis induced by pollen from birch and trees belonging to the birch homologous group in children and adolescents (5 through 17 years of age) based on the average allergic rhinoconjunctivitis daily total combined score# (average TCS) during the birch pollen season (BPS)

### Secondary outcome

To compare the efficacy of the SQ tree SLIT-tablet to placebo based on:

• The average TCS during the tree pollen season (TPS)

• The average allergic rhinoconjunctivitis daily symptom score (average DSS) during the BPS and TPS

• The average allergic rhinoconjunctivitis daily medication score (average DMS) during the BPS and TPS

• To compare the safety and tolerability of the SQ tree SLIT-tablet to placebo

• To compare the efficacy of the SQ tree SLIT-tablet to placebo using additional endpoints based on daily allergic rhinoconjunctivitis symptoms and

rescue medication use

• To compare the efficacy of the SQ tree SLIT-tablet to placebo based on

assessments of quality of life

• To compare the efficacy of the SQ tree SLIT-tablet to placebo based on

patient treatment satisfaction

• To compare the effect of the SQ tree SLIT-tablet to placebo on immunological

parameters to birch, alder, hazel and oak pollen

# Study description

**Background summary**

Despite differences among countries, the incidence and prevalence of allergic rhinitis and asthma are increasing worldwide. AR/C affects between 10 to 30% of all adults and up to 40% of children (Pawankar et al. 2011). Sensitisation rates to 1 or more common allergens among school children are estimated to be 40%-50% (Pawankar et al. 2011). Tree pollen allergy is common across central and northern Europe and North America and is commonly caused by pollen from the birch and related trees, also commonly referred to as the birch homologous group (hereafter referred to as *birch group*). This group currently includes birch, alder, hornbeam, hazel, beech and oak (Lorenz et al. 2009), although more species may be included when additional data on cross-reactivity and allergen homology becomes available (Heath et al. 2015). AIT guidelines recommend treating allergic patients with AIT using a representative allergen within a homologous allergen group (Cox et al. 2011; EMEA 2008).
The trees in the birch group are characterised by having Bet v 1 homologous allergens with a high level of structural sequence identity, leading to extensive cross-reactivity at the immune response level. Thus, people who are sensitised to pollen from one of the trees often also experience symptoms in response to pollen from other members of the birch group. Sensitisation to Bet v 1 has been estimated up to 24% in adults (Burbach et al. 2009; Chan-Yeung et al. 2010), and between 14-16% in children (Schmitz et al. 2013; Stemeseder et al. 2017). The broad cross-reactivity and sequential pollen seasons of birch related allergens prolong the period of allergic symptoms for people with allergy to birch. In previous clinical trials conducted by ALK in Europe and North America with the SQ tree SLIT-tablet, more than 90% of participants with AR/C induced by birch pollen were also sensitised to alder and hazel (Biedermann et al. 2019a). Furthermore, Jantunen et al. showed that 95% of

patients diagnosed with birch pollen allergy presented with allergic symptoms during the alder season (Jantunen et al. 2012). Cross-reactivity of birch pollen allergens also extends to plant food allergens, resulting in the pollen food syndrome (Biedermann et al. 2019b).
Treatment options for AR/C include allergen avoidance, symptomatic medications such as antihistamines and corticosteroids, and AIT (Bousquet et al. 2008). Avoidance of pollen is difficult to achieve in a normal daily life, and symptom-relieving medication is widely used, however it does not offer causal treatment of the allergic disease and up to 44% of patients on optimal symptom-relieving medication report poor or only partial symptom control (Valovirta et al. 2008). AIT is the only available treatment modality that can modify the natural course of the allergic disease by induction of tolerance (Bousquet et al. 2008). The use of pollen extract for AIT is well-known, both in SCIT formulations (Blumberga et al. 2011; Bousquet et al. 1998a; Lang & Hawranek 2006; Winther et al. 2000a; Winther et al. 2000b) and as SLIT-tablets or drops (Demoly et al. 2016; Durham et al. 2012).

**Study objective**

To compare the efficacy of the SQ tree SLIT-tablet to placebo in the treatment of moderate to severe allergic rhinitis and/or conjunctivitis induced by pollen from birch and trees belonging to the birch homologous group in children and adolescents (5 through 17 years of age) based on the average allergic rhinoconjunctivitis daily total combined score# (average TCS) during the birch pollen season (BPS)

Key secondary objectives:
To compare the efficacy of the SQ tree SLIT-tablet to placebo based on:
• The average TCS during the tree pollen season (TPS)
• The average allergic rhinoconjunctivitis daily symptom score (average DSS) during the BPS and TPS
• The average allergic rhinoconjunctivitis daily medication score (average DMS) during the BPS and TPS
Secondary objectives:
• To compare the safety and tolerability of the SQ tree SLIT-tablet to placebo
• To compare the efficacy of the SQ tree SLIT-tablet to placebo using additional endpoints based on daily allergic rhinoconjunctivitis symptoms and rescue medication use
• To compare the efficacy of the SQ tree SLIT-tablet to placebo based on assessments of quality of life
• To compare the efficacy of the SQ tree SLIT-tablet to placebo based on patient treatment satisfaction
• To compare the effect of the SQ tree SLIT-tablet to placebo on immunological parameters to birch, alder, hazel and oak pollen

**Study design**

A phase III, randomised, parallel-group, double-blind, placebo-controlled, multi-regional trial in children and adolescents with AR/C (with or without asthma) induced by pollen from birch. The trial consists of 3 periods: a screening period, a treatment period, which includes pre-seasonal and co seasonal treatment, and a follow-up period. There may be multiple cohorts recruited over consecutive seasons to complete the enrolment goal.
The screening visit can take place up to approximately 6 months prior to randomisation. Eligible subjects will be randomised (1:1) to the SQ tree SLIT tablet or placebo. The randomisation will be stratified by geographical location and by age group.
Once randomised, subjects should receive at least 12 weeks pre-seasonal treatment prior to the TPS. Treatment will continue until 1 week after the end of the TPS for all subjects, corresponding to up to approximately 12 months of treatment.
For subjects recruited in the first season (cohort 1) also allergic to grass pollen, treatment will be extended until 1 week after the end of the grass pollen season (GPS), corresponding to up to approximately 13 months of treatment.
Open-label rescue medication for allergic rhinoconjunctivitis will be provided during the TPS and GPS. Open-label asthma medication will be provided to subjects with asthma during the TPS and GPS.
A follow-up phone visit will be conducted 1 week after the End-of-treatment visit.
At least 6 in-clinic visits and 4 telephone contacts are planned for each subject. The TPS includes hazel, alder, birch and oak pollen seasons.
A data monitoring committee will be established for the trial.

**Intervention**

SQ tree SLIT tablet (dose: 12 SQ-Bet) or placebo. Each randomised subject will receive IMP daily for a maximum of approximately 13 months.

**Study burden and risks**

The following side effects are very common (this means that it might happen in about 1 out of 10 people):
• Itching or irritating feeling in the throat
• Swelling of the mouth
• Prickling feeling or numbness in the mouth or tongue
• Itching in the mouth and ears
The following side effects are common (this means that it might happen in about 1 out of 100 people):
• Runny nose
• Pain in mouth and throat
• Prickling feeling in or loss of feeling in the throat
• Pain when swallowing or difficulty in swallowing

• Feeling of something stuck in the throat
• Pain or burning feeling of the tongue
• Loss of feeling in the mouth
• Swelling of the lips, tongue or throat
• Itchy lips
• Cough, dry throat or changes in the way you speak
• Mouth discomfort
• Changes to taste
• Itching and/or swelling in the mouth and throat after eating certain raw vegetables, fruits, or nuts (oral allergy syndrome)
• Blisters in the mouth or an area of the mouth that is swollen, red and painful (inflammation)
• Pain in the stomach
• Diarrhea
• Heartburn (a burning feeling in the throat)
• Swollen red bumps on the skin which can itch, burn or sting (hives) and itching of the skin
• Chest discomfort
• Nausea (feeling sick and like you might vomit)
• Shortness of breath (difficulty breathing)
• Eye symptoms (e.g. itching, swelling, redness, watery eyes)
Uncommon side effects (this means that it might happen in about 1 out of 1000 people)
• Tightness or swelling of the throat
• Blisters on the lip
• An area of the tongue that is swollen, red and painful (inflammation)
• Mouth ulcers
• Irritation of the oesophagus (the tube connecting your mouth to your stomach)
• Sudden swelling of face, mouth or throat
Other side effects (no information available for how often this occurs)
• Serious allergic reaction
• Allergic inflammation of the oesophagus (eosinophilic oesophagitis)

# Contacts

**Public**
ALK-Abelló A/S

Bøge Allé 6-8
Hørsholm DK-2970
DK
**Scientific**
ALK-Abelló A/S

Bøge Allé 6-8
Hørsholm DK-2970
DK

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

## Inclusion criteria

Subjects are eligible to be included in the trial only if all the following criteria apply:
• Male or female of any race/ethnicity aged >=4 to <18 years on the day informed consent is obtained from the parent/caregiver; the subject must be >=5 to <18 years old at the randomisation visit
• A documented , physician diagnosed, clinically relevant history of moderate to severe AR/C induced by birch pollen (with or without asthma) despite having received treatment with symptom-relieving medication during at least 1 previous tree pollen season for ages 4 through 6 years at screening or at least 2 previous tree pollen seasons for ages 7 through 17 years at screening
• Positive skin prick test (SPT) to Betula verrucosa at screening
• Positive specific IgE to Bet v at screening
• Presence of 1 or more of the following Allergic Rhinitis Impact on Asthma (ARIA) quality of life items due to AR/C during the previous BPS:
a. Sleep disturbance
b. Impairment of daily activities, leisure and/or sport
c. Impairment of school or work
d. Troublesome symptoms

## Exclusion criteria

Subjects are excluded from the trial if any of the following criteria apply:

• A clinically relevant history of symptomatic seasonal AR/C caused by an allergen source, other than tree pollen from the birch homologous group, with a season overlapping the TPS
• A clinically relevant history of symptomatic perennial AR/C caused by an allergen source such as animal hair and dander to which the subject is exposed during the TPS
• Any clinical deterioration of asthma (i.e. asthma exacerbation) that resulted in emergency treatment, hospitalisation or treatment with systemic corticosteroids within 3 months prior to randomisation
• Reduced lung function at randomisation defined as forced expiratory volume in 1 second (FEV1) <70% of predicted value. For subjects with asthma, this is assessed on subject*s usual asthma medication following at least a 6-hour wash-out of SABA. This criterion does not need to be fulfilled if the subject is <7 years old, cannot perform reproducible FEV1 manoeuvres despite coaching and is not considered as having a diagnosis of asthma
• Ongoing treatment with any allergy immunotherapy product
• Severe chronic oral inflammation
• A diagnosis of eosinophilic oesophagitis
• A relevant history of systemic allergic reaction e.g. anaphylaxis with cardiorespiratory symptoms, generalised urticaria or severe facial angioedema that in the opinion of the investigator may constitute an increased safety concern
• Immunosuppressive treatment (ATC code L04 or L01) within 3 months prior to the screening visit

# Study design

## Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

NL
Recruitment status: Recruitment stopped

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|---|---|
| Start date (anticipated): | 22-09-2022 |
| Enrollment: | 68 |
| Type: | Actual |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | SQ boom SLIT tablet |
| Generic name: | SLIT-tablet |
| Registration: | Yes - NL outside intended use |

## Ethics review

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| Approved WMO Date: | 07-07-2021 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 03-11-2021 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 22-12-2021 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 24-01-2022 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

## Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2020-004372-17-NL |
| CCMO | NL76040.078.21 |