STG 320 for allergic rhinitis

LAY SUMMARY

Allergic rhinitis is caused by an allergic reaction. Symptoms include sneezing, and a runny, itchy or blocked nose. Common allergies include reactions to house dust mites, grass and tree pollens, and animals such as cats and dogs. Most people are able to control their symptoms with medicines bought from a chemist or prescribed by GPs, but some people with allergic rhinitis need to be referred to specialist allergy clinics for ‘desensitisation’, where small amounts of the allergy-causing substance are given over a long period of time as an injection under the skin or a tablet under the tongue. This may help reduce allergy symptoms.

STG 320 is a tablet which is designed to prevent allergic reactions to house dust mites. STG 320 is taken under the tongue, once daily for one year.

STG 320 is currently being studied to see how well it works and whether it is safe to use in people with allergic rhinitis due to house dust mites. If STG 320 is licensed for use in the UK, it will offer a new treatment option for people with house dust mite-sensitive allergic rhinitis. As it is taken as a tablet under the tongue, some patients may prefer this to some current treatments, which are given as injections.

NIHR HSRIC ID: 6990
TARGET GROUP

- Allergic rhinitis (AR); persistent – in adults and adolescents aged 12-17 years.

TECHNOLOGY

DESCRIPTION

STG 320 (house dust mite (HDM) allergy immunotherapy sublingual tablet; HDM SLIT; S524101) is an allergen immunotherapy preparation designed for sublingual administration to develop allergy desensitisation. In clinical trials, STG 320 was administered sublingually at 300 IR\(^a\), once daily for one year.

STG 320 is also in phase II trials for allergic asthma.

STG 320 does not currently have Marketing Authorisation in the EU for any indication.

INNOVATION and/or ADVANTAGES

If licensed, STG 320 will provide an additional treatment option for this patient group for whom current treatments are only partially effective.

DEVELOPER

Stallergenes.

AVAILABILITY, LAUNCH OR MARKETING

In phase III clinical trials.

PATIENT GROUP

BACKGROUND

Rhinitis is a common condition, often triggered by allergic sensitisation, when it is known as allergic rhinitis (AR)\(^b\). It commonly coexists with other nasal problems which contribute to symptoms in a varying degree\(^b\). AR is an inflammatory disorder of nasal mucosa, defined as an immunologic response modulated by immunoglobulin E (IgE)\(^2\) and characterised by pruritus, sneezing, rhinorrhoea, and nasal congestion\(^3\). It is caused by hypersensitivity responses to indoor and outdoor environmental allergens\(^3\). Typical allergens include house dust mites (HDM), grass and tree pollens, dander from animals, and occasionally, moulds\(^4\). AR used to be classified according to the type of exposure to aeroallergens as perennial, seasonal and occupational\(^5\). However, it is now classified as intermittent or persistent, depending on the frequency of symptoms\(^6\). Whilst certain allergens, such as HDM, are

\(^a\) Index of Reactivity (IR) defined as a measure of the allergenicity of an allergen extract. The allergen extract contains 100 IR/ml when, on a skin prick-test using a Stallergen point, it induces a wheal diameter of 7mm in 30 patients sensitised to this allergen (geometric mean). The cutaneous reactivity of these patients is simultaneously demonstrated by a positive skin prick-test to either 9% codeine phosphate or 10mg/ml histamine.

\(^b\) Expert personal opinion.
perennial, they may still show seasonal trends, and most people with AR are sensitive to several different allergens and are therefore exposed year-round. AR is associated with other inflammatory conditions, including allergic conjunctivitis, rhinosinusitis and asthma. Up to 40% of people with AR have or will have asthma, and atopic eczema often precedes AR. AR is a major cause of morbidity, affecting physical and psychological well-being and health-related quality of life, in direct correlation with allergen exposure.

NHS or GOVERNMENT PRIORITY AREA

This topic is relevant to:

CLINICAL NEED and BURDEN OF DISEASE

AR has the highest prevalence of all allergic respiratory disease, affecting over 20% of the UK population, and up to 40% of children. It affects people of all ages, with around 80% of people diagnosed before the age of 20, and for 80-90%, symptoms continue into adulthood. HDM is one of the most frequent inhalant allergens, affecting up to 49% of people with AR. In childhood, boys are more likely than girls to have AR, however by adulthood, men and women are affected equally. 80% of people affected by AR develop symptoms before age 20 years. Approximately 20% of people with AR are not adequately controlled on currently available pharmacotherapy, and are therefore eligible for immunotherapy.

AR represents a significant healthcare burden. In 2004, treatment costs for allergic diseases and asthma accounted for 10% of all primary care prescribing costs and direct NHS costs for managing allergic disease were estimated at more than £1 billion per year. For many people, rhinitis is minor and managed by patients without any intervention, and patients are very rarely admitted into hospital specifically for AR. In 2013-14, there were 795 hospital admissions for AR (ICD10: J30.3) in England, accounting for 795 finished consultant episodes and 34 bed days.

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE Guidance

None identified.

Other Guidance

- PRACTALL. Update on allergy immunotherapy: American Academy of Allergy, Asthma & Immunology/European Academy of Allergy and Clinical Immunology/PRACTALL consensus report. 2013.

c Expert personal opinion.
CURRENT TREATMENT OPTIONS

An accurate aetiological diagnosis is crucial in determining whether a patient’s symptoms are genuinely driven by allergic sensitisation. Allergen avoidance is recommended as first line treatment for AR, followed by pharmacotherapy aimed at symptom control. Many patients with mild symptoms do not seek medical therapy for their condition, and manage their condition with over-the-counter products. For patients with severe symptoms, who do not respond to first line therapy, immunotherapy is recommended. Immunotherapy is the only disease-modifying treatment available and can provide long term benefits. Current treatment options for AR include:

- Saline nasal douching.
- Oral and nasal H1-antihistamines – first line therapy for intermittent and persistent symptoms – non-sedating (e.g. bilastine, desloratadine, rupatadine) or sedating (e.g. ketotifen).
- Oral decongestants – adjuvant, intermittent use – ephedrine, phenylephrine, phenylpropanolamine and pseudoephedrine.
- Intranasal decongestants – adjuvant, intermittent use – e.g. oxymetazoline, xylometazoline and ipratropium.
- Specific immunotherapy – where AR symptoms are driven by exposure to the allergen used. Different preparations may be administered via subcutaneous injection or sublingual tablet. These routes of administration are believed to have equivalent efficacy.

EFFECTIVENESS and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT00674700, VO57.07; HDM allergy immunotherapy vs placebo; phase III.</th>
<th>NCT02443805, SL75.14; HDM allergy immunotherapy vs placebo; phase III.</th>
<th>NCT01199133, VO64.08, 2009-011999-30; HDM allergy immunotherapy vs placebo; phase III.</th>
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d Mechanisms of the Development of ALLergy collaborative project.

Global Allergy and Asthma European Network.

Allergic Rhinitis and its Impact on Asthma.

Expert personal opinion.
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<tbody>
<tr>
<td>Status</td>
<td>Published.</td>
<td>Ongoing.</td>
<td>Terminated.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Publication&lt;sup&gt;11&lt;/sup&gt;, trial registry&lt;sup&gt;28&lt;/sup&gt;.</td>
<td>Trial registry&lt;sup&gt;7&lt;/sup&gt;.</td>
<td>Trial registry&lt;sup&gt;29&lt;/sup&gt;.</td>
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<tr>
<td>Location</td>
<td>EU (not UK).</td>
<td>USA and France.</td>
<td>EU (not UK).</td>
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<tr>
<td>Participants</td>
<td>n=509; aged 18-50 years; HDM-associated allergic rhinitis for ≥1 year.</td>
<td>n=990 (planned); aged 12-65 years; HDM-associated allergic rhinitis for ≥1 year.</td>
<td>n=471 (planned); aged 5-17 years; HDM-associated allergic rhinitis for ≥1 year requiring regular intake of symptomatic treatments.</td>
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<tr>
<td>Schedule</td>
<td>Randomised to HDM allergy immunotherapy, 300 IR or 500 IR, sublingual, once daily; or placebo, sublingual, once daily.</td>
<td>Randomised to HDM allergy immunotherapy, 300 IR, sublingual, once daily; or placebo, sublingual, once daily.</td>
<td>Randomised to HDM allergy immunotherapy, 300 IR, sublingual, once daily; or placebo, sublingual, once daily.</td>
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<tr>
<td>Follow-up</td>
<td>Active treatment for 1 year; follow-up for 1 year.</td>
<td>Active treatment for 1 year; 2 weeks follow-up.</td>
<td>Active treatment for 1 year.</td>
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<tr>
<td>Primary outcome/s</td>
<td>Average rhinitis total symptom score (AAdSS)&lt;sup&gt;1&lt;/sup&gt;.</td>
<td>Total combined score&lt;sup&gt;1&lt;/sup&gt;.</td>
<td>Average adjusted symptom score.</td>
</tr>
<tr>
<td>Secondary outcome/s</td>
<td>Average rescue medication score; average combined score&lt;sup&gt;3&lt;/sup&gt;; five individual average symptom score; overall RQLQ&lt;sup&gt;1&lt;/sup&gt;; global evaluation of efficacy by patient; skin prick test; immunological markers; asthma status; Asthma Control Test Questionnaire.</td>
<td>Safety and tolerability.</td>
<td>Average rhinitis total symptom score; average rescue medications score; individual average rhinoconjunctivitis symptom score; rhinoconjunctivitis quality of life questionnaire score.</td>
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<tr>
<td>Key results</td>
<td>For 500 IR vs placebo and 300 IR vs placebo, respectively, AAdSS mean difference: -0.78 (95% CI -1.34,-0.22; p=0.0066), corresponding to -20.2%; -0.69 (95% CI -1.25,-0.14; p=0.0150), corresponding to -17.9%.</td>
<td>-</td>
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<td>Adverse effects (AEs)</td>
<td>AEs among patients sensitised prior to immunotherapy included oral pruritus, throat irritation, pharyngolaryngeal pain. Systemic AEs reported in</td>
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</table>

<sup>1</sup> Study population insufficiently symptomatic to enable differentiation between treatment and placebo. No safety concerns.

<sup>2</sup> AAdSS – measures severity of patient-reported rhinitis symptoms (sneezing, rhinorrhoea, nasal pruritus and nasal congestion).

<sup>3</sup> Sum of daily rhinitis total symptom score and daily rescue medication score.

<sup>4</sup> The average between the rhinoconjunctivitis total symptom score and the rescue medication score.

<sup>5</sup> Rhinoconjunctivitis Quality of Life Questionnaire – measures functional problems of seasonal or perennial rhinoconjunctivitis.
4 of these patients included asthma, urticarial and cough.

Expected reporting date - Last patient visit is expected in Q1 2017.

ESTIMATED COST and IMPACT

COST

The cost of STG 320 is not yet known. The 2010 costs of other selected immunotherapies (unlicensed in the UK) obtained from a BSACI survey of immunotherapy clinics in the UK are as follows:

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<th>Drug</th>
<th>Dose</th>
<th>Annual cost (2010)</th>
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<tr>
<td>Der p 1 via Oralvac Compact pump (Allergy Therapeutics).</td>
<td>2.9µg sublingually, daily (3 pumps per day) for 8 months (0.71mg per year).</td>
<td>£629</td>
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<tr>
<td>Der p 1 and Der f 1 via Staloral 300 pump (Stallergenes).</td>
<td>120IR (~84µg) sublingually, daily; or 240IR (~168µg) sublingually three times weekly (30.7mg and 61.3mg per year, respectively).</td>
<td>£985</td>
</tr>
<tr>
<td>Alutard SQ (ALK).</td>
<td>25 injections (90µg Der p 1 allergen per year).</td>
<td>£1,359</td>
</tr>
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</table>

IMPACT - SPECULATIVE

Impact on Patients and Carers

☐ Reduced mortality/increased length of survival
☒ Other: patients may prefer sublingual immunotherapy to subcutaneous immunotherapy as it is less invasive and requires fewer visits to specialist clinics for administration.
☐ Reduced symptoms or disability
☐ No impact identified

Impact on Health and Social Care Services

☐ Increased use of existing services
☒ Decreased use of existing services: sublingual immunotherapy requires fewer visits to specialist allergy clinics than subcutaneous immunotherapy, and much of the course may be delivered in community settings.
☐ Need for new services
☐ None identified

Impact on Costs and Other Resource Use

☐ Increased drug treatment costs
☐ Reduced drug treatment costs
☐ Other increase in costs:
☐ Other reduction in costs:
☒ Other: uncertain unit cost compared to existing treatments.
☐ None identified
Clinical uncertainty or other research question identified: sublingual immunotherapy may be less costly for the health service overall as it requires fewer visits to specialist clinics.

REFERENCES


2. Ozdoganoglu T and Songu M. The burden of allergic rhinitis and asthma. Therapeutic Advances in Respiratory Disease 2012;6(1):11-23.


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13. Scadding GK and Williams A. the burden of allergic rhinitis as reported by UK patients compared with their doctors. Rhinology 2008;46(2):99-106.


28 ClinicalTrials.gov. Safety and efficacy study of sublingual immunotherapy (SLIT) to treat house dust mite allergic rhinitis. clinicaltrials.gov/ct2/show/NCT00674700 Accessed 3 September 2015.
29 ClinicalTrials.gov. Safety and efficacy study of sublingual immunotherapy (SLIT) to treat house dust mite allergic rhinitis in adolescents and children. clinicaltrials.gov/ct2/show/NCT01199133 Accessed 4 September 2015.