National Institute for Health Research

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AR101– peanut allergy immunotherapy for adult and paediatric patients

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LAY SUMMARY

Food allergy occurs when the body's immune system reacts unusually to specific foods. Peanuts are one of the most common causes of food allergy. Symptoms of peanut allergy include: having an itchy mouth, developing a rash, bodily swelling, difficulty swallowing, wheezing or shortness of breath, feeling dizzy or light headed, feeling sick, abdominal pain and hay fever-like symptoms.

The prevalence of food allergy in Europe and North America has been reported to range from 6% to 8% in children up to the age of 3 years. Prevalence in adults has been estimated at 1 to 2%.

AR101 is a form of treatment for peanut allergy. This treatment is administered orally with the aim of re-educating the body's immune system, in order to increase the level at which the body reacts to peanuts, or to reduce the allergic response. The drug is targeted at adults and children with severe peanut allergy.

Phase III clinical trials are currently being conducted in adults and children.

A peanut desensitisation service is not currently provided by the NHS.

TARGET GROUP

Adults and children with severe peanut allergy.

TECHNOLOGY

DESCRIPTION

AR101 is a form of oral immunotherapy for the treatment of peanut hypersensitivity (peanut allergy). This treatment contains the protein profile found in peanuts.[1] A very small amount of an allergen (insufficient to cause a reaction) is administered in a gradual, controlled, up-dosing manner (with ongoing daily maintenance) until de-sensitisation to a certain amount of the allergen has been achieved. This process can re-educate the body's immune system, increasing the threshold of reactivity to an allergen or diminishing the allergic response.[2]

An on-going phase III clinical trial aims to evaluate the safety and efficacy of AR101 for desensitising peanut-allergic patients to a level sufficient to reliably protect them from allergic reactions upon accidental exposures to peanuts. In this trial, AR101 is administered orally in capsules and sachets using a dose escalation method for a period of approximately 22 weeks, to reach the maintenance dose of 300 mg per day. Subsequently, participants continue with daily maintenance at 300 mg per day for approximately six months. At the end of the maintenance period, patients will undergo an exit double-blind, placebo-controlled food challenge.[3]

A peanut desensitisation service is not currently provided by the NHS. However, current NICE guidelines state that some people may need allergen–specific immunotherapy, which should be supervised by allergy specialists and should only be provided by physicians and nurses with specialist knowledge.[4]

INNOVATION and/or ADVANTAGES

If licensed for this indication, AR101 could provide a novel way of treating adults and children with peanut allergy.

Reaching a tolerated dose of peanut protein of 300 mg could be a key milestone in the immunotherapy treatment of highly peanut-sensitive individuals at very high risk of allergic reactions, as this could mean ability to tolerate most trace levels of undeclared peanut protein in food products.[5]

DEVELOPER

Aimmune Therapeutics.

AVAILABILITY, LAUNCH or MARKETING

PATIENT GROUP

BACKGROUND

Food allergies occur when the body's immune system mistakenly treats proteins found in food as a threat.[1] Immunoglobulin E mediated food allergies are most common and involve a greater risk of rapid reactions and anaphylaxis, which is an acute, potentially fatal, allergic reaction that is characterised by rapidly developing airway, breathing and circulation problems.[6]

Peanut allergy is a major cause of food-induced deaths and having the allergy is associated with a reduced quality of life.[7]

CLINICAL NEED and BURDEN OF DISEASE

Reported prevalence of peanut allergy in children in the UK varies depending on the source; figures ranging from 2 in 1,000 to 19 per 1,000 have been reported.[8] About 20% of children outgrow their peanut allergy.[9]

In England in 2015/16, there were 4,673 hospital admissions due to adverse food reactions (T78.0 and T78.1), resulting in 1,882 bed days and 4,877 finished consultant episodes.[10] Over half of these episodes were in paediatric patients aged between 0 and 14. Annually, about 10 deaths are caused by food allergies in England and Wales.[6]

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE guidelines. Food allergy in under 19s: assessment and diagnosis (CG116). February 2011.
- NICE quality standard. Food allergy (QS118). March 2016.
- NICE quality standard. Anaphylaxis (QS119). March 2016.
- NICE diagnostics guidance. ImmunoCAP ISAC 112 and Microtest for multiplex allergen testing (DG24). May 2016.

NHS ENGLAND and POLICY GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Paediatric Medicine: Specialised Allergy services. E03/S/j.

OTHER GUIDANCE

- Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR, Beck LA et al. Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. *Journal of Allergy and Clinical Immunology* 2017;10(1):1.
- Muraro A, Roberts G, Worm M, Bilo MB, Brockow K, Fernández RM et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy* 2014;69(8): 1026-1045.
- European Academy of Allergy and Clinical Immunology. Food Allergy and Anaphylaxis Guidelines. 2014. Available from: http://www.eaaci.org/foodallergyandanaphylaxisguidelines/Food%20Allergy%20-%20web%20version.pdf [Accessed 02.05.2017]

CURRENT TREATMENT OPTIONS

There is currently no approved treatment for peanut allergy. Avoidance of the food through a peanut-free diet is the best way of preventing allergic reactions, and auto-injector pens (epinephrine) are used in emergency situations when a severe allergic reaction occurs. [6,7] However, avoidance of exposure to trace amounts of peanut protein capable of eliciting an allergic reaction is very difficult due to the nearly ubiquitous presence of peanuts in the food industry, the potential for cross-contamination, and incorrect ingredient information in restaurants and on product labels.

Other forms of immunotherapy have also been explored in an effort to find treatments for peanut allergy. Subcutaneous, sublingual and oral immunotherapy have all been trialled and have induced clinical benefits but with varying levels of adverse reactions. [7,11]

EFFICACY and SAFETY

Trial	**PALISADE; NCT02635776; AR101 vs placebo; phase III trial**
Sponsor	Aimmune Therapeutics Inc.
Status	Ongoing
Source of Information	Company website, [1,3] trial registry, [12] Adis Insight [2]
Location	Canada, Denmark, Ireland, Netherlands, Spain, Sweden, USA, United Kingdom
Design	Randomised, double-blind, placebo-controlled
Participants	Approximately 500 patients aged 4-55, with a clinical history of allergy to peanuts or peanut-containing foods.

Schedule	Patients undergo a dose escalation period of approximately 22 weeks to reach the maintenance dose of 300 mg per day, then continue with daily maintenance at 300 mg per day for approximately six months. At the end of the maintenance period, patients undergo an exit double-blind, placebo-controlled food challenge.
Follow-up	-
Primary Outcomes	Peanut allergy de-sensitisation [Time Frame: 12 months] The proportion of subjects who tolerate at least 1043 mg cumulative of peanut protein with no more than mild symptoms at the exit double blind placebo controlled food challenge.
Secondary Outcomes	Not reported
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Estimated Primary Completion Date: November 2017 (Final data collection date for primary outcome measure).

ESTIMATED COST and IMPACT

COST

The cost of AR101 is not yet known.

INFORMATION FROM

IMPACT – SPECULATIVE

IMPACT ON PATIENTS and CARERS

☐ Reduced mortality/increased length of survival

☒ Reduced symptoms or disability

☐ Other

☐ No impact identified

IMPACT ON HEALTH and SOCIAL CARE SERVICES

☐ Increased use of existing services

☒ Decreased use of existing services

☐ Re-organisation of existing services

☐ Need for new services

☒ Other: *potential requirement for new staff training*

☐ None identified

IMPACT ON COSTS and OTHER RESOURCE USE

☒ Increased drug treatment costs

☐ Reduced drug treatment costs

☒ Other increase in costs: *provision of a new mode of immunotherapy if provided within the NHS*

☒ Other reduction in costs: *potential reduction in peanut allergy related hospital attendance if desensitisation is achieved and anaphylaxis avoided*

☐ Other

☐ None identified

OTHER ISSUES

☐ Clinical uncertainty or other research question identified:

☒ None identified

REFERENCES

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