Health Technology Briefing
February 2023

WP1048 for treating grass pollen allergy

Company/Developer	Worg Pharma (Hangzhou) Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 6635	NICE ID: 10467	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase IIb clinical trials.

Summary

WP1048 is in clinical development for the treatment of adults with grass pollen allergy. Grass pollen allergy, also known as hay fever or allergic rhinitis, is caused by an immune reaction to proteins found in pollen from various types of grass. The allergy presents symptoms such as itchy eyes, blocked and inflamed nose and persistent sneezing. This can confer a significant health burden on patients, as it affects daily functions such as sleep and concentration, thus affecting quality of life. Allergic rhinitis is greatly under-recognised and poorly managed, as there is a high prevalence rate in the UK. Management of grass pollen allergy is important to help improve patient clinical outcomes and quality of life as many patients often have co-morbidities associated with this allergy such as asthma and eczema, whose symptoms can be exacerbated in episodes of allergic reaction to grass pollen. Currently, most treatments for grass pollen allergy are not curative and are mainly focused on symptom relief.

WP1048 is a treatment for allergic reactions (immunotherapy) administered by subcutaneous injection and is designed to expose the patient to the disease-inducing antigens (allergens) in order to induce gradual clinical and immunological tolerance (a state of unresponsiveness of the immune system to specific antigens) and obtain disease modification. If licensed, WP1048 would offer an additional treatment option to provide sustained relief from grass pollen allergy.

Proposed Indication

Treatment of grass pollen allergy in adults aged 18 – 60 years old.[1,2]

Technology

Description

WP1048 (BM32) is a hypoallergenic grass pollen allergy vaccine which consists of an aluminium hydroxide-adsorbed equimolar mix of four active ingredients, BM321, BM322, BM325 and BM326. The four active ingredients are purified recombinant proteins which have been designed to elicit IgG antibodies and contain non-allergenic peptides from the four major timothy grass pollen allergens, Phl p 1 (BM321), Phl p 2 (BM322), Phl p 5 (BM325) and Phl p 6 (BM326) which are fused to the PreS domain of hepatitis B virus, a protein used in childhood vaccines.[3,4] Selected epitopes from timothy grass allergens have been shown to be cross-reactive with other grass species.[3] WP1048 holds promise not to induce IgE mediated immediate type (for example, anaphylactic reactions) or T-cell mediated late phase side effects during immunotherapy.[4]

WP1048 is in clinical development for the treatment of grass pollen allergy in adults. In the phase IIb clinical trial (NCT02643641), patients were administered either three, four or five doses with 20 micrograms each of BM321, BM322, BM325 and BM326 by subcutaneous (SC) injection.[1,3,5]

Key Innovation

WP1048 has been designed to protect patients from the debilitating effects of grass pollen exposure and possibly provide long term cure. It is very convenient to use for patients and doctors, as only a very small number of subcutaneous applications are needed to achieve efficient desensitisation.[5] In comparison to allergen extract–based forms of allergen-specific immunotherapy (AIT) which require administration of multiple doses and thus makes treatment cumbersome, leading to poor compliance in patients. WP1048 can be injected into allergic patients without need for up-dosing. Sufficient levels of grass pollen allergen–specific IgG responses can be achieved with only few injections of WP1048, whereas traditional allergy vaccines require more than double the number of up-dosing injections. Treatment schedules based on WP1048 will be more convenient for patients and should increase their compliance.[6] If licensed, WP1048 will offer an additional treatment option for patients aged 18-60 years with grass pollen allergy who currently have limited treatment options.

Regulatory & Development Status

WP1048 does not currently have Marketing Authorisation in the UK/EU for any indication.

Patient Group

Disease Area and Clinical Need

Grass pollen allergy, also commonly known as hay fever or seasonal allergic rhinitis, is the most prevalent allergy in moderate climate areas in Europe and North America.[3,7] Grass pollen allergy is caused by an overreactive immune response to pollen, triggering an allergic reaction.[8] Symptoms include sneezing, coughing, runny or blocked nose, itchy and/or watery eyes and itchy mouth or throat.[9] Those who suffer from allergic rhinitis are also four times as likely to suffer from other conditions such as asthma, eczema and food allergy.[7] The symptoms can be exacerbated in individuals who also have asthma and can lead to shortness of breath, wheezing and tightness of the chest.[10] Most people with this allergy have mild

symptoms that can be easily and effectively treated. For some people, however, symptoms can be severe and persistent and have a significant impact on quality of life.[11] Sleep problems including micro-arousals, leading to daytime fatigue and somnolence, and decreased cognitive functioning are usually associated with most people with allergic rhinitis.[12]

Allergic rhinitis affects 20% of the population in the UK and symptoms of this allergy usually worsen between late March and September when the pollen count is at its highest.[10,13] In England, 2021-2022, there were 2,188 finished consultant episodes (FCE) and 2,167 admissions for allergic rhinitis due to pollen (ICD-10 code J30.1) which resulted in 118 FCE bed days and 1,864 day cases.[14]

Recommended Treatment Options

NICE currently recommends medications such as antihistamines and intranasal corticosteroids as first-line treatments for allergic rhinitis. For more severe or persistent symptoms that do not respond to medication, immunotherapy (sublingual or subcutaneous) is sometimes used.[11]

Clinical Trial Information

Trial	NCT01350635; Evaluation of BM32, a Recombinant Hypoallergenic Grass Pollen Vaccine, by Skin Testing **Phase I/II** - Completed **Location(s):** Austria **Study completion date:** September 2011
Trial Design	Open label, non-randomised, parallel assignment.
Population	N=60 (actual); aged 18 to 60 years old; Subjects a positive history of grass pollen allergy and positive skin prick test reaction to grass pollen extract
Intervention(s)	WP1048 applied in sterile phosphate buffer solution in concentrations of 11,33 and 100 micrograms/ml
Comparator(s)	No comparator
Outcome(s)	Primary outcome measure: • Wheal size of immediate type skin reactions to the mix of BM32 proteins [Time Frame: 20 minutes].
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information

Trial	NCT01445002; **EudraCT** 2011-003368-64; Safety and Dose Finding Study Based on the Effects of Three Subcutaneous Injections of BM32, a Recombinant Hypoallergenic Grass Pollen Vaccine, on Responses to Allergen Challenge by Skin Testing and in the Vienna Challenge Chamber (VCC) as Well as Immunological Response in Subjects Know to Suffer From Grass-pollen Induced Allergic Rhinitis **Phase II** - Completed **Location(s):** Austria **Study completion date:** October 2012

Trial Design	Quadruple masked, randomised, parallel assignment.
Population	N=79 (actual); aged 18 to 60 years old; Subjects with a history of seasonal allergic rhinitis from grass pollen.
Intervention(s)	• Three (SC) injections of 10 micrograms each of BM321, BM322, BM325 and BM326 in a time span of 8 weeks • Three (SC) injections of 20 micrograms each of BM321, BM322, BM325 and BM326 in a time span of 8 weeks • Three (SC) injections of 40 micrograms each of BM321, BM322, BM325 and BM326 in a time span of 8 weeks
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: • Minimum effective dose for reduction of total nasal symptom score (TNSS) after inhalation challenge with grass pollen [Time Frame: Baseline and 14 weeks]. See trial record for full list of other outcomes.
Results (efficacy)	Sixty-eight patients completed the trial. Total nasal symptom score (TNSS) significantly decreased with mean changes of -1.41 (BM32/20µg) (P=0.03) and -1.34 (BM32/40µg) (P=0.003) whereas mean changes in the BM32/10µg and placebo group were not significant. Total ocular symptom score (TOSS) and skin prick testing (SPT) reactions showed a dose-dependent decrease. BM32 induced highly significant allergen-specific IgG responses (P<0.0001) but no allergen-specific IgE. Allergen-induced basophil activation was reduced in BM32 treated patients and addition of therapy-induced IgG significantly suppressed T cell activation (P=0.0063).[15]
Results (safety)	No systemic immediate type side effects were observed. Only few grade 1 systemic late phase reactions occurred in BM32 treated patients. The number of local injection site reactions was similar in actively and placebo-treated patients.[15]
Clinical Trial Information	
Trial	NCT01538979; **EudraCT** 2012-000442-35; Phase IIb Study on the Safety and Efficacy of BM32, a Recombinant Hypoallergenic Vaccine for Immunotherapy of Grass Pollen Allergy **Phase IIb –** Completed **Location(s):** 6 EU countries **Study completion date:** March 2015
Trial Design	Quadruple masked, randomised, parallel assignment.
Population	N=181 (actual); aged 18 to 60 years old; Subjects with a positive history of grass pollen allergy.
Intervention(s)	• Seven (SC) injections of 20 micrograms of each of BM321, BM322, BM325 and BM326 before each pollen season and one boost injection after pollen season

	• Seven (SC) injections of 40 micrograms of each of BM321, BM322, BM325 and BM326 before each pollen season and one boost injection after pollen season
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: • Mean daily combined symptom medication score (SMS)during the peak of the pollen season. [Time Frame: Up to 3 months]. See trial record for full list of other outcomes.
Results (efficacy)	Rhinoconjunctivitis Symptom Score (SS) during the peak pollen season in the second treatment year was reduced by 25% compared to the placebo (p=0.042, statistically significant). The treatment also significantly improved patients' well-being measured by two independent methods (Visual Analogue Scale (VAS, p=0.014) and the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), p<0.005). A 22% difference of a Combined Symptom and Medication Score (SMS) to the placebo was also found (p=0.085).[16]
Results (safety)	The treatment was safe and very well tolerated. Most side-effects were mild to moderate and resolved within a short period after drug application.[16]

Clinical Trial Information

Trial	NCT02643641; Study to Evaluate the Effect of Different Pre-seasonal BM32 Dosing Schedules on the Rapid Induction of a Protective IgG Immune Response **Phase IIb –** Completed **Location(s):** Austria **Study completion date:** January 2017
Trial Design	Triple masked, randomised, parallel assignment.
Population	N=130 (actual); aged 18 to 60 years old; Subjects with grass pollen allergy.
Intervention(s)	• Two placebo injections followed by three injections (SC) with 20 micrograms each of BM321, BM322, BM325 and BM326 • One placebo injection followed by four injections (SC) with 20 micrograms each of BM321, BM322, BM325 and BM326 • Five injections (SC) with 20 micrograms each of BM321, BM322, BM325 and BM326
Comparator(s)	Five placebo injections (alhydrogel)
Outcome(s)	Primary outcome measure: • Titre of allergen specific IgG4 antibodies [Time Frame: approximately 6 months]. See trial record for full list of other outcomes.
Results (efficacy)	The study reached its primary endpoint: it was observed that a regimen of five monthly injections of 80 µg of BM32 was statistically significantly superior to all other

	dosing schemes in terms of induction of allergen specific IgG4 ($p<0.05$ vs. three and four injections; $p<0.0001$ vs placebo). This dose regimen also provided for a statistically significant and clinically meaningful improvement of combined rhinoconjunctivitis symptom and medication score (SMS) vs. placebo during the peak pollen season ($p<0.0001$) and the whole pollen season (>100 grains/m3/24hrs, $p<0.0001$) measured by area under the curve (AUC). Patients' well-being evaluated by visual analog scale (VAS) was significantly improved by 50% during the days of highest pollen exposure ($p<0.05$) in this dose group.[5]
Results (safety)	The treatment was safe and very well tolerated. Most side-effects were local injection site reactions, were mild to moderate and resolved within a short period after drug application.[5]

Estimated Cost

The cost of WP1048 is not yet known.

Relevant Guidance

NICE Guidance

- NICE interventional procedures guidance. Intranasal phototherapy for allergic rhinitis (IPG616). June 2018.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Specialised Allergy Services (All Ages). B09/S/b.

Other Guidance

- BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007.[17]

Additional Information

Worg Pharma (Hangzhou) Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR innovation observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

1 ClinicalTrials.gov. *Effect of Different Pre-seasonal BM32 Dosings on the Induction of a Protective Immune Response*. *Trial ID: NCT02643641*. 2015. Status: Completed. Available

from: https://clinicaltrials.gov/ct2/show/study/NCT02643641 [Accessed 22 December 2022].

2 ClinicalTrials.gov. *Phase II Study of Grass Pollen Allergy Vaccine BM32*. *Trial ID: NCT01538979*. 2012. Available from: https://clinicaltrials.gov/ct2/show/study/NCT01538979 [Accessed 22 December 2022].

3 Worg Pharmaceuticals. *WP1048*. 2022. Available from: http://www.worgpharma.com/index.php?c=category&id=81 [Accessed 22 December 2022].

4 ClinicalTrials.gov. *Skin Test Study of BM32*. *Trial ID: NCT01350635*. 2011. Status: Completed. Available from: https://clinicaltrials.gov/ct2/show/study/NCT01350635 [Accessed 22 December 2022].

5 Medical Xpress. *Successful phase IIB trial with third-generation grass pollen allergy vaccine BM32*. 2017. Available from: https://medicalxpress.com/news/2017-01-successful-phase-iib-trial-third-generation.html [Accessed 31 January 2023].

6 Weber M, Niespodziana K, Linhart B, Neubauer A, Huber H, Henning R, et al. Comparison of the immunogenicity of BM32, a recombinant hypoallergenic B cell epitope–based grass pollen allergy vaccine with allergen extract–based vaccines. *Journal of Allergy and Clinical Immunology*. 2017;140(5):1433-6.e6. Available from: https://doi.org/10.1016/j.jaci.2017.03.048.

7 Natasha Allergy Research Foundation. *Allergies - The Facts.* 2023. Available from: https://www.narf.org.uk/the-allergy-explosion [Accessed 27 January 2023].

8 NHS Inform. *Hay fever: causes of hay fever*. 2023. Available from: https://www.nhsinform.scot/illnesses-and-conditions/immune-system/hay-fever#causes-of-hay-fever [Accessed 19 January 2023].

9 NHS Inform. *Hay fever: symptoms of hay fever*. 2023. Available from: https://www.nhsinform.scot/illnesses-and-conditions/immune-system/hay-fever#symptoms-of-hay-fever [Accessed 31 January 2023].

10 National Health Service. *Hay fever*. 2021. Available from: https://www.nhs.uk/conditions/hay-fever/ [Accessed 6 January 2023].

11 National Institute for Health and Care Excellence (NICE). *Intranasal phototherapy for allergic rhinitis* (*IPG616)*. Available from: https://www.nice.org.uk/guidance/ipg616/chapter/2-The-condition-current-treatments-and-procedure [Accessed 10 January 2023].

12 Allergy UK. *Statistics and Figures | Allergy Prevalence: Useful facts and figures*. 2023. Available from: https://www.allergyuk.org/about-allergy/statistics-and-figures/ [Accessed 27 January 2023].

13 Siddiqui ZA, Walker A, Pirwani MM, Tahiri M, Syed I. Allergic rhinitis: diagnosis and management. *British Journal of Hospital Medicine*. 2022;83(2):1-9. Available from: https://doi.org/10.12968/hmed.2021.0570.

14 NHS Digital. *Hospital Admitted Patient Care Activity, 2021-22: Diagnosis*. 2023. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2021-22 [Accessed 27 January 2023].

15 Zieglmayer P, Focke-Tejkl M, Schmutz R, Lemell P, Zieglmayer R, Weber M, et al. Mechanisms, safety and efficacy of a B cell epitope-based vaccine for immunotherapy of grass pollen allergy. *EBioMedicine*. 2016;11:43-57. Available from: https://doi.org/10.1016/j.ebiom.2016.08.022.

16 PipelineReview.com. *Biomay AG Reports Positive Phase IIB Data With The Innovative 3rd Generation Grass Pollen Allergy Vaccine BM32*. 2015. Available from: https://pipelinereview.com/index.php/2015012956790/Vaccines/BIOMAY-AG-REPORTS-POSITIVE-PHASE-IIB-DATA-WITH-THE-INNOVATIVE-3RD-GENERATION-GRASS-POLLEN-ALLERGY-VACCINE-BM32.html [Accessed 31 January 2023].

17 Scadding GK, Kariyawasam HH, Scadding G, Mirakian R, Buckley RJ, Dixon T, et al. BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised

Edition 2017; First edition 2007). *Clinical & Experimental Allergy*. 2017;47(7):856-89. Available from: https://doi.org/10.1111/cea.12953.

NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.