Innovation Observatory

NHS National Institute for Health Research

HEALTH TECHNOLOGY BRIEFING FEBRUARY 2019

BIIB092 for progressive supranuclear palsy

NIHRIO ID	15108	**NICE ID**	9824
Developer/Company	Biogen Idec Ltd	**UKPS ID**	647011

Licensing and market availability plans	Currently in phase II clinical trials

SUMMARY

BIIB092 is a product that is being investigated for the treatment of progressive supranuclear palsy (PSP). PSP is a rare condition that is a result of destruction of nerve cells in certain parts of the brain causing problems with balance, movement, vision, speech and swallowing. In patients with PSP, an abnormal form of a protein called tau accumulates in specific areas of the brain by spreading from brain cell to brain cell leading to their damage. Over time, PSP gets progressively worse, with people becoming severely disabled within three to five years of onset. Currently, there is no cure for PSP and no treatment to slow down the disease.

BIIB092 is a monoclonal antibody that acts by recognising, binding to and neutralising a specific type of tau protein responsible for the nerve cells damage and gradual worsening of PSP. This action of BIIB092 is thought to prevent the spread of the disorder and potentially slow the progression of PSP. Tau-directed immunotherapy like BIIB092 offers a promising disease-modifying treatment strategy for PSP and similar conditions. BIIB092 is given by intravenous infusion and if licensed, will offer a more targeted treatment option for patients with PSP.

PROPOSED INDICATION

Treatment of progressive supranuclear palsy (PSP).[1]

TECHNOLOGY

DESCRIPTION

BIIB092 is a humanised monoclonal antibody that binds to extracellular, N-terminally fragmented forms of tau. Tau is believed to cause neuronal dysfunction directly and may be partially responsible for the spreading of tau pathology from nerve cell to nerve cell.[2 3]

BIIB092 is being developed for the treatment of PSP. In the phase II clinical trial (NCT03068468; PASSPORT), BIIB092 is given as 50 mg/ml by intravenous (IV) infusion once every 4 weeks for 48 weeks in double blind treatment period followed by BIIB092 50 mg/ml IV infusion once every 4 weeks starting at Week 52 up to Week 208.[1]

INNOVATION AND/OR ADVANTAGES

There is currently no cure for PSP and no treatment to slow it down.[4] Tau-directed immunotherapy is a promising disease-modifying treatment strategy for tauopathies such as PSP.[5] At the time of orphan designation, no satisfactory methods were authorised in the EU for the treatment of PSP. BIIB092 has been designed to recognise and attach to some of the tau protein and to neutralise it, thereby potentially slowing disease progression of PSP.[1,6]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

BIIB092 does not currently have Marketing Authorisation in the EU/UK for any indication.

BIIB092 is currently in phase II clinical development for early Alzheimer's Disease.[7]

BIIB092 has an orphan drug designation in the EU awarded in 2015 for the treatment of progressive supranuclear palsy.[6]

PATIENT GROUP

DISEASE BACKGROUND

Progressive supranuclear palsy (PSP) is a rare progressive neurodegenerative condition that can cause problems with balance, movement, vision, speech and swallowing. It is caused by increasing numbers of brain cells becoming damaged over time.[8] The disorder's long name indicates that the disease worsens (progressive) and causes weakness (palsy) by damaging certain parts of the brain above nerve cell clusters called nuclei (supranuclear).[2]

PSP occurs when brain cells in certain parts of the brain are damaged as a result of an abnormal deposits of a protein called tau. The condition has been linked to changes in certain genes, but these genetic faults are not inherited and the risk to other family members, including the children or siblings of someone with PSP, is very low.[8]

The amount of abnormal tau in the brain can vary among people with PSP, as can the location of these clumps. This means the condition can have a wide range of symptoms.[8] Symptoms of PSP

usually begin around the age of 65 years, but may occur earlier.[2,9] The symptoms of PSP usually get gradually worse over time. At first, they can be similar to some other conditions, which makes it difficult to diagnose early on. One of the classic signs of the disease is an inability to aim and move the eyes properly, which individuals may experience as blurring of vision. Some of the main symptoms of PSP include problems with balance and mobility, including frequent falls, changes in behaviour, such as irritability or apathy (lack of interest), muscle stiffness, an inability to control eye and eyelid movement, including focusing on specific objects or looking up or down at something slow, quiet or slurred speech, difficulty swallowing (dysphagia), slowness of thought and some memory problems. The rate at which the symptoms progress can vary widely from person to person.[2,8]

The disease gets progressively worse, with people becoming severely disabled within three to five years of onset. Affected individuals are predisposed to serious complications such as pneumonia, choking, head injury, and fractures. The most common cause of death is pneumonia.[2]

CLINICAL NEED AND BURDEN OF DISEASE

There are believed to be around 4,000 people living with PSP in the UK at any one time.[10] A large descriptive cross-sectional population-based prevalence study extended between 2003 to 2012 as well as a retrospective incidence study between 2009 to 2012 in Geneva, Switzerland indicated that the age-adjusted incidence rate was 1.3 per 100,000 (95%CI 0.9-1.8) and the age-adjusted prevalence rate was approximately 5.7 per 100,000 (95% CI 3.8-7.6) - standardised to the European standard population.[11] Applying this to the estimated population in England using the UK midyear estimate for 2017,[12] the number of patients diagnosed with PSP in England annually would be about 723.

In England in 2017 - 2018, there were 280 hospital admissions, 737 finished consultant episodes, and 26 day cases for progressive supranuclear ophthalmoplegia [Steele-Richardson-Olszewski]; (ICD10: G23.1).[13]

Although the clinical course is variable, the typical presentation is usually associated with mortality 5-9 years after the onset of symptoms.[14] The grand total registered mortalities in England and Wales due to ICD10: G23.1 between 2001 and 2017 is 509.[15]

A journal article that describes a clinical rating scale for PSP patients referred to a Movement Disorders Centre in USA from 1994 through 2005 reported that mean survival for the 98 patients who died during the observation period was 6.8 years (Standard Deviation 3.06, median 6.5, range 1.5–20.2). The actuarially corrected median survival from onset was 7.3 years. This calculation included all 162 patients: those deceased, those known to be alive as of the censoring date and those lost to follow-up.[16]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

Currently, there is no cure for PSP. PSP can affect many different areas of the patient's health. Some of the main treatments include medications for symptom management, physiotherapy, speech and language therapy, dietary advice and management of severe swallowing problems, occupational therapy, treatment of eye problems, and palliative care.[8]

A PSP patient will be cared for by a team of health and social care professionals working together. This is known as a multidisciplinary team (MDT) which may include a neurologist, a physiotherapist, a speech and language therapist, an occupational therapist, a social worker, an ophthalmologist or orthoptist, and a specialist neurology nurse.[8]

CURRENT TREATMENT OPTIONS

There are currently no medications that treat PSP specifically, but some people in the early stages of the condition may benefit from taking levodopa, amantadine or other medications used to treat Parkinson's disease. These medications can improve balance and stiffness for some people with PSP, although the effect is often limited and only lasts for up to a few years.[8]

PLACE OF TECHNOLOGY

If licensed, BIIB092 will offer disease modifying therapy option for patients with PSP.

CLINICAL TRIAL INFORMATION

Trial	PASSPORT, NCT03068468 , EudraCT 2016-002554-21; BIIB092 vs placebo; phase II
Sponsor	Biogen.
Status	Ongoing
Source of Information	Trial registry.[1]
Location	EU (incl UK), USA, Canada and other countries.
Design	Randomised, placebo-controlled, parallel assignment, double-blind.
Participants	n= 396 (planned); aged 41-86 years; probable or possible PSP; able to ambulate independently or with assistance; able to tolerate magnetic resonance imaging (MRI); score greater or equal to 20 on the Mini Mental State Exam (MMSE) at screening.
Schedule	Randomised to BIIB092 50 mg/ml given by intravenous (IV) infusion once every 4 weeks for 48 weeks in double blind treatment period followed by BIIB092 50 mg/ml IV infusion once every 4 weeks starting at week 52 up to week 208.; or placebo IV infusion once every 4 weeks for 48 weeks in double blind treatment period followed by BIIB092 50 mg/ml IV infusion once every 4 weeks starting at week 52 up to week 208.
Follow-up	Active treatment period up to 208 weeks and overall follow-up 52 weeks.
Primary Outcomes	- Change from baseline in progressive supranuclear palsy rating scale (PSPRS) at week 52 [time frame: baseline, week 52] Percentage of participants with death, serious adverse events (SAES), adverse events leading to discontinuation, and grade 3 and 4 laboratory abnormalities [time frame: up to 52 weeks]
Secondary Outcomes	Time frame: baseline, week 52 - Change from baseline in movement disorder society (MDS)-sponsored revision of the unified Parkinson's disease rating scale (MDS-UPDRS) Part II at week 52

	- Change from baseline in repeatable battery for the assessment of neuropsychological disease severity (RBANS) scale at week 52 - Change from baseline in progressive supranuclear palsy quality of life scale (PSP-QoL) score - Change from baseline in clinical global impression of severity (CGI-S) score at week 52 Time frame: week 52 - Clinical global impression of change (CGI-C) scale score Time frame: baseline, week 48 - Change From Baseline in Schwab and England Activities of Daily Living (SEADL) Scale Score at Week 48 - Change from baseline in phonemic fluency test score at week 48 - Change from baseline in letter-number sequencing test at week 48 - Change from baseline in color trails test at week 48 - Change from baseline in montreal cognitive assessment (MoCA) score at week 48 Time frame: up to week 52 - Number of participants with drug antibodies (anti-BIIB092) in serum - Percent change from baseline of brain volumes as determined by MRI
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study completion date expected in March 2020

ESTIMATED COST

The cost of BIIB092 is not yet known.

ADDITIONAL INFORMATION

RELEVANT GUIDANCE

NICE GUIDANCE

No relevant guidance identified.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

No relevant guidance identified.

OTHER GUIDANCE

PSPA. Pathway of care for PSP: a guide for health and social care professionals.[17]

REFERENCES

1 ClinicalTrials.gov. *Study of BIIB092 in participants with progressive supranuclear palsy (PASSPORT). Trial ID: NCT03068468*. 2017. Available from: https://clinicaltrials.gov/ct2/show/NCT03068468 [Accessed 11 January 2019].

2 National Institute of Neurological Disorders and Stroke. *Progressive supranuclear palsy fact sheet.* Available from: https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Progressive-Supranuclear-Palsy-Fact-Sheet [Accessed 11 January 2019].

3 Dam T, Boxer A, Golbe LI, et al. Efficacy and Safety of BIIB092 in Patients with Progressive Supranuclear Palsy: PASSPORT Phase 2 Study Design (P6.073). *Neurology*. 2018;90(15 Supplement):P6.073. Available from: http://n.neurology.org/content/90/15_Supplement/P6.073.

4 NHS. *Progressive supranuclear palsy: treatment.* 2018. Available from: https://www.nhs.uk/conditions/progressive-supranuclear-palsy-psp/treatment/ [Accessed 11 January 2019].

5 Qureshi IA, Tirucherai G, Ahlijanian MK, et al. A randomized, single ascending dose study of intravenous BIIB092 in healthy participants. *Alzheimers Dement (N Y)*. 2018;4:746-55. Available from: 10.1016/j.trci.2018.10.007.

6 European Medicines Agency. *EU/3/15/1522.* 2015. Available from: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3151522 [Accessed 11 January 2019].

7 ClinicalTrials.gov. *Phase 2 study of BIIB092 in participants with early Alzheimer's Disease (TANGO). Trial ID: NCT03352557*. 2017. Status: Recruiting. Available from: https://clinicaltrials.gov/ct2/show/NCT03352557?intr=biib092&spons=biogen&phase=12&rank=2 [Accessed 12 February 2019].

8 NHS. *Progressive supranuclear palsy: overview.* 2018. Available from: https://www.nhs.uk/conditions/progressive-supranuclear-palsy-psp/ [Accessed 12 February 2019].

9 Respondek G, Kurz C, Arzberger T, et al. Which ante mortem clinical features predict progressive supranuclear palsy pathology? *Mov Disord*. 2017 Jul;32(7):995-1005. Available from: 10.1002/mds.27034.

10 PSPA. *A Brief Guide to PSP.* Available from: https://pspassociation.org.uk/information-and-support/what-is-psp/brief-guide-to-psp/ [Accessed 14 January 2019].

11 Fleury V, Brindel P, Nicastro N, et al. Descriptive epidemiology of parkinsonism in the Canton of Geneva, Switzerland. *Parkinsonism Relat Disord*. 2018 Sep;54:30-9. Available from: 10.1016/j.parkreldis.2018.03.030.

12 Office for National Statistics. *Population Estimates for UK, England and Wales, Scotland and Northern Ireland: mid-2017*. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland [Downloaded 24 August 2018].

13 NHS Digital. *Hospital Admitted Patient Care Activity, 2017-18*. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2017-18 [Downloaded 27 November 2018].

14 Houghton DJ, Litvan I. Unraveling progressive supranuclear palsy: from the bedside back to the bench. *Parkinsonism Relat Disord*. 2007;13 Suppl 3:S341-6. Available from: 10.1016/s1353-8020(08)70028-2.

15 Office for National Statistics. *21st Century Mortality dataset, England & Wales 2001-17*. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/the21stcenturymortalityfilesdeathsdataset [Downloaded 18 December 2018].

16 Golbe LI, Ohman-Strickland PA. A clinical rating scale for progressive supranuclear palsy. *Brain*. 2007 Jun;130(Pt 6):1552-65. Available from: 10.1093/brain/awm032.

17 PSPA. *Pathway of care for PSP: a guide for health and social care professionals.* Available from: https://pspassociation.org.uk/app/uploads/2018/06/PT009-13-6-Pathway-Guide-web-2013.pdf [Accessed 14 January 2019].

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