BIIB092 for progressive supranuclear palsy

NIHRIIO 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

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.
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.\(^1\)\(^2\)\(^3\)

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
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.

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.

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. 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. Applying this to the estimated population in England using the UK midyear estimate for 2017, 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). Although the clinical course is variable, the typical presentation is usually associated with mortality 5-9 years after the onset of symptoms. The grand total registered mortalities in England and Wales due to ICD10: G23.1 between 2001 and 2017 is 509.

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.

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.
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.

**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.

**PLACE OF TECHNOLOGY**

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

**CLINICAL TRIAL INFORMATION**

<table>
<thead>
<tr>
<th>Trial</th>
<th>PASSPORT, <a href="https://clinicaltrials.gov/ct2/results?term=NCT03068468">NCT03068468</a>, EudraCT 2016-002554-21; BIIB092 vs placebo; phase II</th>
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<tbody>
<tr>
<td>Sponsor</td>
<td>Biogen.</td>
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<tr>
<td>Status</td>
<td>Select one of: published, published in abstract, complete but unpublished, ongoing, not reported.</td>
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<tr>
<td>Source of Information</td>
<td>Trial registry.¹</td>
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<tr>
<td>Location</td>
<td>EU (incl UK), USA, Canada and other countries.</td>
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<tr>
<td>Design</td>
<td>Randomised, placebo-controlled, parallel assignment, double-blind.</td>
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<td>Participants</td>
<td>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.</td>
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<td>Schedule</td>
<td>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.</td>
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<td>Follow-up</td>
<td>Active treatment period up to 208 weeks and overall follow-up 52 weeks.</td>
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| 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

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<th>Key Results</th>
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<tr>
<td>Adverse effects (AEs)</td>
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<tr>
<td>Expected reporting date</td>
<td>Study completion date expected in March 2020</td>
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**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


**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.