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Newcastle University

Health Technology Briefing
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Spesolimab for preventing generalised pustular psoriasis flares

Company/Developer	Boehringer Ingelheim Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30965	NICE TSID: 11789	UKPS ID: 660194

Licensing and Market Availability Plans

Currently in phase II clinical development.

Summary

Spesolimab is currently in clinical development for flare prevention in patients with generalised pustular psoriasis (GPP). Individuals with GPP experience repeated episodes where large surface areas of the skin become inflamed and red, and develop small pus-filled blisters known as pustules. It is a disease that spreads and affects a large surface area of the body. The main cause of GPP is not yet known but it is thought that environmental factors such as stress and genetic susceptibility can trigger disease onset. GPP can be a life-threatening disease if left untreated. Deaths have been attributed to septic shock and cardiorespiratory failure.

Spesolimab is administered for the prevention of flares of GPP. It blocks the interaction of certain proteins which stops downstream inflammatory responses. Many patients with moderate to severe GPP struggle with insufficient disease control. There is currently no licensed treatment for the prevention GPP flare ups. If licensed, spesolimab will be the first preventative treatment option of flare ups in patients with GPP.

Proposed Indication

For the prevention of flare ups in patients with generalised pustular psoriasis (GPP).[1]

Technology

Description

Spesolimab (BI 655130) is a humanised monoclonal antibody that inhibits the action of the receptor IL-36R.[2] IL-36 is a member of the pro-inflammatory cytokines family and is expressed in various types of cells including keratinocytes. IL-36R potentiates the production of type-1 interferon through stimulation of leucocyte recruitment and innate immune inflammation.[3] This signalling pathway may play a role in many inflammatory diseases.[4]

Spesolimab is currently in phase II clinical development for the prevention of flare up in GPP. In the phase II clinical trial (NCT04399837) spesolimab is injected subcutaneously in adult patients with a history of GPP.[1] Spesolimab is administered via injection.[1]

Key Innovation

Currently, there is no licensed treatment available specifically for the treatment of GPP. To date, the management approach used to treat patients with GPP is largely based on interleukin 1 (IL-1) inhibitor trials and/or treatment guidelines of plaque psoriasis. Cyclosporine, retinoids, methotrexate, and biologic agents are also used in the treatment of psoriasis.[5-8] The volatile efficacy of unlicensed treatment options and the increased risk of systemic complications in patients with GPP call for a novel targeted drug development.[3]

The National Institute for Health and Care Excellence (NICE) do not currently have specific guidance for the management of GPP.[9] Currently, patients with psoriasis are advised to identify triggers such as smoking, stress and injury to skin to prevent flare ups.[10] There is currently no licensed treatment used as a preventative treatment of GPP flare ups.[4] Spesolimab would provide the first specific biologic treatment for the prevention of flare ups in patients with GPP.

Regulatory & Development Status

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

Spesolimab is currently in phase II and phase III clinical development for the treatment of patients with hidradenitis suppurativa, palmoplantar pustulosis, and GPP.[11]

Patient Group

Disease Area and Clinical Need

Generalised pustular psoriasis is an autoinflammatory disease where the patho-immunology is not yet fully known but the IL-36 pathway is thought to play a pivotal role. The IL-36 antagonist and receptors are expressed in keratinocytes amongst other cell types. The binding of the IL-36 antagonists to IL-36

receptors causes an inflammatory response that leads to the release of chemokines which activate the T-cells, macrophages, neutrophils and dendritic cells. A mutation of the IL-36RN leads to a loss of function or functional impairment of IL36Ra subsequently causing changes to the structure of the amino acid sequence and a growth of the downstream inflammatory cascade. This loss of function mutation leads to an excess in IL-36 signalling. This form of mutation can be found in both sporadic and familial cases of GPP.[12] GPP is a rare and severe form of psoriasis and is characterised by the presence of sterile pustules that can occur in various patterns.[13,14] GPP is clinically diverse in its severity, age at onset and precipitants. It is assumed that there is a relationship between GPP and plaque psoriasis as some patients may experience episodes of plaque psoriasis before or after the GPP, whilst in others GPP occurs as the only phenotype without the occurrence of plaque psoriasis.[14] Individuals with GPP experience repeated episodes where large surface areas of the skin become inflamed and red, and develop pustules. Individuals may also experience muscle weakness, fatigue, fever, a higher number of white blood cells, systemic inflammation[15] and extracutaneous manifestations such as arthritis and neutrophilic cholangitis.[16] These episodes that subside and reappear can be triggered by various factors.[15]

GPP is a rare disease and there is currently no validated diagnostic criteria to diagnose psoriasis, so it is difficult to ascertain an accurate figure for its prevalence therefore, the precise prevalence of GPP in the UK is not yet known.[2,9] In 2020-21 there were 214 finished consultant episodes (FCE) and 124 admissions for generalised pustular psoriasis (ICD-10 code L40.1) which resulted in 41 day cases and 625 FCE bed days.[17]

Recommended Treatment Options

There is no specific NICE guidance or guideline for GPP. Currently there are no licensed treatment for GPP flare prevention. Patients are advised to identify flare triggers to avoid GPP flare up.[8,10,18]

Clinical Trial Information

Trial	**Effisayil™ 2,** NCT04399837, 2018-003081-14**;** Multi-center, Randomized, Parallel Group, Double Blind, Placebo Controlled, Phase IIb Dose-finding Study to Evaluate Efficacy and Safety of BI 655130 (Spesolimab) Compared to Placebo in Preventing Generalized Pustular Psoriasis (GPP) Flares in Patients With History of GPP **Phase II –** Active, not recruiting **Location(s):** 7 EU, USA, and other countries **Primary completion date:** December 2022
Trial Design	Randomised, quadruple masking, parallel assignment
Population	N= 123 (actual); subjects aged 12 to 75 years with a known and documented history of GPP per ERASPEN criteria regardless of IL36RN mutation status, with at least 2 presentations of moderate to severe GPP flares with fresh pustulation (new appearance or worsening) in the past
Intervention(s)	Injection of Spesolimab

Comparator(s)	Matched placebo
Outcome(s)	Time to first GPP flare [Time frame: up to 48 weeks] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of spesolimab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Ustekinumab for the treatment of adults with moderate to severe psoriasis (TA180) September 2009 (Last updated: March 2017).
- NICE Clinical Guideline. Psoriasis: assessment and management (CG153). October 2012 (Last updated: September 2017).

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Specialised Dermatology Services (All ages). A12/S/a.

Other Guidance

- Smith CH, Jabbar-Lopez ZK, Yiu ZZ, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. British Journal of Dermatology. 2017.[19]

Additional Information

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