Health Technology Briefing
February 2024

Teprotumumab for thyroid eye disease

Company/Developer	Amgen Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 20539	NICE ID: 10006	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase IV clinical development.

Summary

Teprotumumab is currently in development for treatment of thyroid eye disease (TED). TED, also known as Graves' orbitopathy or ophthalmopathy, is an autoimmune condition. It occurs when the body's immune system attacks the tissue surrounding the eye causing inflammation in eye muscles, eyelids, tear glands and fatty tissues behind the eye. This can cause the eyes and eyelids to become red, swollen and uncomfortable and the eyes can be pushed forward (proptosis). In most patients, the same autoimmune condition that causes TED also affects the thyroid gland, resulting in Graves' disease. Current treatment options available to patients with TED are aimed at managing symptoms rather than treating underlying causes of the disease. Recommended treatment options for TED include use of artificial tears, selenium supplementation, oral prednisolone and rehabilitative surgery.

Teprotumumab is a protein that binds to receptors on the surface of cells in the eye which become over expressed in TED and cause inflammation. By blocking these receptors from signalling, teprotumumab decreases inflammation and relieves symptoms associated with TED. In the phase III clinical trial teprotumumab was administered intravenously every three weeks. It is designed to target the cause of symptoms, therefore reducing the need for symptom relieving therapies and reducing the risk of needing invasive surgery to correct effects of TED. If licenced, teprotumumab would provide a non-invasive treatment option for patients with TED.

Proposed Indication

Treatment for patients with thyroid eye disease (TED).[1]

Technology

Description

Teprotumumab (HZN-001, R-1507, RV 001, TEPEZZA®) is a 150 kDa fully human monoclonal anti-Insulin-like growth factor 1 receptor (IGF-1R) antibody.[2] Teprotumumab is the only intervention available for TED treatment which directly targets IGF-1R, inhibiting IGF-1R activation which is suggested to prevent formation of IGF-1R and thyroid stimulating hormone receptor (TSHR) complexes.[6] This blocks signalling cascades which attenuates pro-inflammatory protein expression.[6]

Teprotumumab is currently in phase IV clinical trial post-marketing study for patients with thyroid eye disease, who are euthyroid or have mild hypo- or hyperthyroidism.[1] In the phase III clinical trial, teprotumumab was administered intravenously as part of an infusion with sodium chloride solution once every three weeks for 21 weeks.[7]

Key Innovation

Currently, TED is managed with local treatments such as eye drops, or steroids such as glucocorticoids to suppress inflammation.[6] Patients often require invasive rehabilitative surgery, with varying rates of success.[8-10] Present treatments only target the symptoms of TED, whereas teprotumumab targets the underlying immune mechanisms driving TED. By targeting the mechanisms driving TED, teprotumumab is able to limit pathology and disease progression.[6]

If licensed, teprotumumab would offer a treatment option for patients who have few well tolerated, effective treatments available.

Regulatory & Development Status

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

Teprotumumab has the following regulatory designations/awards:

- FDA Breakthrough Therapy [11]
- Orphan drug in the USA in 2013 for TED [12]

Teprotumumab is currently not in any other phase II or III clinical trials.[2]

Patient Group

Disease Area and Clinical Need

TED most commonly occurs as part of Graves' disease, which is an autoimmune disease that affects the thyroid and often the skin and eyes. TED can also occur in people who have or have had an overactive thyroid (hyperthyroidism), or an underactive thyroid (hypothyroidism).[13] The principal cell type responsible for the enlargement of orbital soft tissues in TED seems to be the orbital fibroblast.[14] Orbital fibroblasts become abnormally activated in TED due to binding by insulin-like growth factor 1 receptor (IGF-1R, a protein found on the surface of orbital fibroblasts) to immune cells.[14] This leads to activation of immune cells and orbital fibroblasts causing enlargement of orbital soft tissues in TED, which subsequently causes inflammation.[14] TED may also be developed because of a genetic predisposition, and genes causing pathology may be triggered by environmental factors (multifactorial inheritance).[13] People who smoke, have undergone radiotherapy treatments or have other endocrine disorders such as type 1 diabetes are more susceptible to developing TED.[13] It is common for people with TED to develop inflammation of the

eye muscles, eyelids, tear glands and fatty tissues behind the eye. This can cause the eyes and eyelids to become red, swollen and uncomfortable, leading to the development of proptosis (where one or both eyes protrude from their natural position).[15] Other symptoms of TED include; dryness of eyes, photophobia, blurred or double vision, pain in eyes and difficultly moving.[15]

TED affects approximately 50,000 people in the UK, and global incidence is 2.9 per 100,000 for males and 16 per 100,000 for females.[15,16] In England, between 2022-2023, there were 6,965 finished consultant episodes (FCE) and 6,765 admissions for other disorders of the eye and adnexa (ICD-10 code H57), resulting in 4,514 day cases and 1,919 FCE bed days.[17]

Recommended Treatment Options

Treatment for TED can include systemic corticosteroids, surgical orbital decompression and radiation therapy.[18] However, there are currently no approved pharmacological treatment options available for patients with TED.

The following treatment options are recommended by NICE for TED:[18]

- retrobulbar irradiation for patients for whom other treatments are inadequate or associated with significant side effects

Guidance from the European Thyroid Association includes treatment with:[19]

- oral prednisone
- artificial tears with osmoprotective properties
- selenium supplementation
- intravenous glucocorticoid

Clinical Trial Information

Trial	NCT05002998, EudraCT-2020-005999-36 A Phase 3b/4, Double-masked, Randomized, International, Parallel-assignment, Multicenter Trial in Patients With Thyroid Eye Disease to Evaluate the Safety and Tolerability of Different Dosing Durations of Teprotumumab **Phase IV** - Active, not recruiting **Locations:** France, Germany, Italy, Spain, UK, and USA **Primary completion date:** October 2025
Trial Design	Randomised, parallel assignment, quadruple blinded
Population	N=313 (actual); 18 years to 80 years; adults and older adults, with prior diagnosis of thyroid eye disease; patients must be euthyroid during trial.
Intervention(s)	Participants will receive four infusions of teprotumumab (10 mg/kg for the first infusion and 20 mg/kg for the remaining three infusions), followed by four infusions of placebo if a participant is a treatment responder at week 12; teprotumumab 20 mg/kg if a participant is a treatment non-responder at week 12. Participants will receive eight infusions of teprotumumab (10 mg/kg for the first infusion and 20 mg/kg for the remaining seven infusions).

	Participants will receive 16 infusions of teprotumumab (10 mg/kg for the first infusion and 20 mg/kg for the remaining 15 infusions).
Comparator(s)	Matched placebo
Outcome(s)	Primary outcomes: • Treatment emergent adverse events and treatment emergent adverse events of special interest • Percentage of participants who receive re-treatment See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Trial	**OPTIC**, NCT03298867, EudraCT-2017-002763-18; A Phase 3, Randomized, Double-Masked, Placebo-Controlled, Parallel-Group, Multicenter Study Evaluating Teprotumumab (HZN-001) Treatment in Subjects With Active Thyroid Eye Disease (OPTIC) **Phase III –** completed **Locations:** Two EU countries and USA **Primary completion date:** February 2019	**OPTIC-X**, NCT03461211, EudraCT-2017-002713-58; Multicenter, Safety and Efficacy, Open-Label Extension Study Evaluating Teprotumumab (HZN-001) Treatment in Subjects With Thyroid Eye Disease (OPTIC-X) **Phase III -** completed **Locations:** Two EU countries and USA **Primary completion date:** August 2020
Trial Design	Randomised, parallel assignment, quadruple blinded	Single group assignment, open label interventional trial design
Population	N=83 (actual); 18 years to 80 years; adults and older adults, with prior diagnosis of thyroid eye disease; patients must be euthyroid during trial.	N=51 (actual); 18 years to 80 years; adults and older adults, must have completed the 24-week double-masked treatment period in NCT03298867
Intervention(s)	Participants will receive eight infusions of teprotumumab every three weeks for a total of 21 weeks.	Participants will receive eight infusions of teprotumumab every three weeks for a total of 21 weeks.
Comparator(s)	Matched placebo	-
Outcome(s)	Primary outcome: Percentage of participants who were proptosis responders at week 24. See trial record for full list of outcomes.	Primary outcome: Percentage of participants with a ≥2mm reduction from baseline in the study eye without deterioration of proptosis in the fellow eye at week 24. See trial record for full list of outcomes.

Results (efficacy)	See trial record.	See trial record.
Results (safety)	See trial record.	See trial record.

Estimated Cost

The cost of teprotumumab is not yet known.

Relevant Guidance

NICE Guidance

- NICE interventional procedure guidance. Retrobulbar irradiation for thyroid eye disease. IPG148. December 2005.

NHS England (Policy/Commissioning) Guidance

- NHS England. NHS standard contract for ophthalmology (adult). D12/S/a.
- NHS England. NHS standard contract for specialised endocrinology services (adult). A03/S/a
- NHS England. Policy book for eye health. November 2021.

Other Guidance

- The Royal College of Ophthalmologists. New Guidelines for Thyroid Eye Disease. 2015.[20]
- Quality and Safety group, the Royal College of Ophthalmologists. Quality standards for adnexal services. 2021.[21]
- Bartalena et al. The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. 2021.[8]
- Burch et al. Management of thyroid eye disease: a Consensus Statement by the American Thyroid Association and the European Thyroid Association. 2022.[22]

Additional Information

Amgen 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

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