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Teprotumumab, New Era for Thyroid Eye Disease

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Abstract

Thyroid eye disease is a progression of an autoimmune disease called Graves disease, which majorly affects eye orbits and its muscular tissues. It affects the patients by acting a impact on their quality of life by acting on patients visual balance along with facial disfiguring. In this review paper I will review as the development of monoclonal antibody called teprotumumab for treatment of thyroid eye disease along with its brief mechanism of action.

Keywords: "Teprotumumab". "Hyperthyroidism", "Thyroid eye disease ", "Graves disease".

Introduction

On 21st January 2020, the FDA approved Tepezza (teprotumumab-trbw) for the treatment of thyroid eye disease which is a progression of graves' disease for adults in the US. Teprotumumab is the first and only a approved drug for thyroid eye disease based on positive results from clinical trials .

Thyroid eye disease though it is due to frequent extra thyroidal manifestation of a autoimmune disease called graves' disease but it may develop in the patients with not having past history of hyperthyroidism . The mild effect of disease also shows impact on a life of patients. The large group of patients experience mild symptoms but only 33% of patients develop into a progressive disease. Patients with serious disease may develops into sight threatening complications like compressive optic neuropathy or exposure keratopathy with exhibit orbital pain, lid swelling and erythema, conjunctival redness and chemosis, and enlargement of the extraocular muscles and the orbital fatty volume resulting in

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proptosis. The pathophysiology of the thyroid eye disease is not completely known to scientific community but main role is played by orbital fibroblasts expressing TSH receptors that become activated by TSH receptor auto antibodies .The aim of this review was to analyze the available pathophysiology of disease and the only approved drug teprotumumab and other available spaces for preventive intervention.

Epidemiology of Graves' Ophthalmopathy

A data available from the published studies from United States. Gives information regarding incidence rate of Graves ' disease per 100,000 populations per year is 13.9. An important epidemiologic feature of Graves associated thyroid eye disease is linked to cigarette smoking. Pathogenic mechanisms regarding this is not understood yet but it may be due to smoking might both exert direct irritative effects and contribute to modulate the ongoing immune reactions in the orbital tissues .The disease progress by three steps , the primary stage infection is with no symptoms but progression of disease takes place . Second stage of infection is also asymptomatic but the patients are with elevated levels of thyroid hormone, patients from this stage should stop smoking and also need the treatment regarding hyperthyroidism. The severe disease is in third stage with symptoms like buldging of eye balls , inflammation , pain with redness in affected area

Conventional Medical Therapies for TED

Diagnosis and treatment of patient with moderate to severe thyroid eye disease is challenging and it requires a team work of both endocrinologists and ophthalmologists. Conventional treatments used to focus on immune suppression in the active phase in patients with moderate-to-severe disease. Glucocorticoids were the class of drug that was used. Glucocorticoids being preferred by IV over oral administration due to a more favorable safety and efficacy profile since oral administration may undergo a first pass metabolism and the bioavailability of drug may reduce. Since Glucocorticoids come from steroidal class of a drug called pregnant derivative they have a number of side effects like negative nitrogen balance, muscle wasting, anti insulin effect. To avoid these side effects it was a need to develop a first line therapeutic drug to treat Thyroid eye disease. Several second line drug therapies also available which includes drugs from anticancer class category like cyclosporine, methotrexate, azathioprine, Like Glucocorticoids; these treatments do not significantly alter long term disease outcomes

New era of Teprotumumab

Advancement in molecular biology led to the development of a targeted therapy, teprotumumab. Teprotumumab is a fully human monoclonal antibody of isotype Ig1. Teprotumumab act on specific site with specifies action and binds to insulin-like growth factor 1 receptor (IGF-1R).IGF-1R is an expressed transmembrane tyrosine kinase receptor regulating cell growth and proliferation, rather than being a disease specific stimulatory autoantibody or inflammatory mediator. Along with insulin like growth factor, fibroblast also plays important role in development of fatty tissues behind eye balls. Fibroblast shows 3-4 times more action in thyroid associated eye disease as compared to normal humans. Teprotumumab binds with high selectivity and affinity to IGF-1R, displacing IGF-1 and resulting in degradation of the receptor, antibody complex. Teprotumumab comes in the form of powder and vial and mixed prior to administration to patients. Teprotumumab is administered by intravenously to patients at an initial dose of 10mg/ kg thereafter 20mg/kg every 3 weeks for 21weeks. The present clinical reports of a remarkable ability of teprotumumab to reverse diplopia and proptosis. Despite the significant reduction in proptosis seen, there was only a modest increase in quality of life in this group. The teprotumumab is considered a choice

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over Glucocorticoids since it is having selective action and low side effects than Glucocorticoids. Teprotumumab comes with a side effects like teratogenisity which contraindicates its use in pregnant woman & hyperglycemia which can be reduced by taking with antidiabetic drugs.

Conclusion

Available data study demonstrates effectiveness of Teprotumumab in reversing disease severity and attenuating clinical activity. The safety profile of teprotumumab is extremely favorable, with the majority of adverse events judged as mild. Thus, the drug is poised to become the first-line therapy for Thyroid eye disease.

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Author contribution

Rohit Kale: Conceptualization, Data study, Visualization, Writing - Original Draft, Writing - review & editing.

Shrikant Solnake: Conceptualization, Data study, Visualization, Writing - Original Draft, Writing - review & editing.

Declaration of competing interest

All authors report no conflicts of interest relevant to this article.

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Ethical statement

Not applicable

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