FDA Approves Axatilimab: A New Standard in Chronic Graft-Versus-Host Disease Therapy

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Dear Madam, Graft-versus-host disease (GVHD) is a severe complication which arises due to the pathological immune response of the donor's immune cells against the recipient's body tissues after allogeneic hematopoietic stem cell transplantation (HSCT). GVHD manifests itself in two forms: acute and chronic, with the chronic form presenting with dysregulated T-cell and B-cell immunity coupled with aberrant tissue repair and fibrosis in multiple systems of the body[1]. On 14th August 2024, the U.S Food and Drug Administration (FDA) approved Axatilimab for chronic graft-versus-host disease[2]. Axatilimab is a monoclonal IgG4 antibody with its primary target colony-stimulating factor 1 receptor (CSF-1R), present on donor derived pro-inflammatory macrophages[3]. The drug is prescribed subsequent to failure of two systemic lines of treatment in adult and paediatric population with the minimum weight limit of 40kg[2].The mechanism of action of Axatilimab is based on the blockade of CSF-1R, a receptor which helps in proliferation and regulation of macrophages.

By blocking the receptor, Axatilimab helps reduce tissue damage and inflammation[3]. FDA's approval was based on the promising results from the AGAVE-201 Phase 1/2 trial, which showed the ORR (Overall Response Rate) of 75%[2]. Previous treatment options included Ruxolitinib, which can cause haematological (anaemia, thrombocytopenia) and infectious complications whereas Ibrutinib and Belumosudil can cause cardiovascular complications like atrial arrhythmias and hypertension respectively[1].The study data demonstrated the notable safety and efficacy of Axatilimab, along with its minimal side effects as compared to the previously approved FDA treatments.

Axatilimab has shown a response rate of 47% in bronchiolitis obliterans syndrome (BOS), which affects 10% of transplant patients and has a poor prognosis[4]. The drug fulfills its primary purpose in providing therapy for cGVHD while also having the potential for other fibrotic and CSF-1R related diseases. Trials are being conducted to evaluate the effectiveness of Axatilimab in the treatment of Idiopathic Pulmonary Fibrosis (IPF) and TAM (tumour associated macrophages) based tumours like classical Hodgkin's Lymphoma and HER-2 negative breast cancer[5]. The side effects of the drug may include decreased haemoglobin, re-activation of viral infections (cytomegalovirus), and transfusion related reactions[2].

In conclusion, Axatilimab is a novel pharmacological strategy with its unique mechanism of action and targetted approach for treating cGVHD. Despite such advances, there is a need to conduct extensive trials to understand the future implications of the drug. Additional research can ascertain if Axatilimab can revolutionize not just GVHD treatment but potentially other immune-mediated diseases as well.

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