LETTER TO THE EDITOR

Hyftor: An emerging therapy for Facial Angiofibromas

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Dear Madam, Tuberous Sclerosis Complex (TSC) is a rare autosomal dominant genetic disease caused by a deactivating mutation in one of the two tumour suppressor genes, TSC1 or TSC2.[1,2] These mutations can lead to hyperactivation of the mammalian Target of Rapamycin (mTOR) signalling pathway, which in turn mediates cellular growth and proliferation. As the mTOR pathway is usually responsible for stimulating the synthesis of protein, cells' survival, and cell cycle progression.[1,3] This causes the formation of multiple benign non-invasive tumours, called hamartoma, in different body tissues and organs.[1,3]

Facial Angiofibroma (FA) is the most prevalent skin manifestation of TSC.[4] These are multiple, erythematous, small hamartomatous papules of around 1 to 3 mm in size formed by the excessive production of skin cells coupled with angiogenesis.[3,4] The most classical sites of occurrence include the center of the face, alar grooves, cheeks, nose, and chin.[3] FA has increased chances of bleeding; it can damage the eyesight and can cause psychological distress due to aesthetic disfiguration.[4]

Physical removal of FA is associated with pain, hyperpigmentation, scarring, bleeding, and recurrence of the lesions.[4] Therefore, recently, on March 22, 2022, the FDA approved the topical use of Hyftor (Sirolimus, also known as Rapamycin mTOR inhibitor) for the treatment of FA.[5]

Hyftor has earned its position as the most appropriate treatment for FA in TSC due to its anti-tumour, anti-angiogenic and immunosuppressive properties, which highly favours this drug's effectiveness and safety profile.[1] It binds to the FK-binding protein-12 (FKBP-12), which in turn impedes the hyperactivity of mTOR, eventually causing the down-regulation of cellular growth. It also reduces levels of vascular endothelial growth factor levels depriving the tumour cells of their blood supply. Furthermore, it also halts the progression and proliferation of the cell cycle by blocking the response of T and B cell activation by cytokines.[3]

Long-term serious systematic side effects of mTOR inhibitors were overcome by the topical formulation of sirolimus.[3,4] All concentrations of this drug are very well-tolerated with minor adverse effects, which include dry skin, application site irritation, burning sensation, and pruritis.[3]

Hyftor has proven to be a practical therapeutic innovation in the medical field due to its high specificity for mTOR and meager adverse effects profile. However, this drug requires additional large population-based studies and trials to substantiate further its efficacy and safety in patients with FA.

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