Thyroid Eye Disease (TED)

TED, also known as Graves' ophthalmopathy, is a debilitating autoimmune disorder that affects the eyes and surrounding tissues. It is commonly associated with Graves' disease, an autoimmune disorder that affects the thyroid gland. The annual incidence of TED in the United States is estimated to be around 16 per 100,000 females and 3 per 100,000 males, or approximately 30,000 new cases a year.

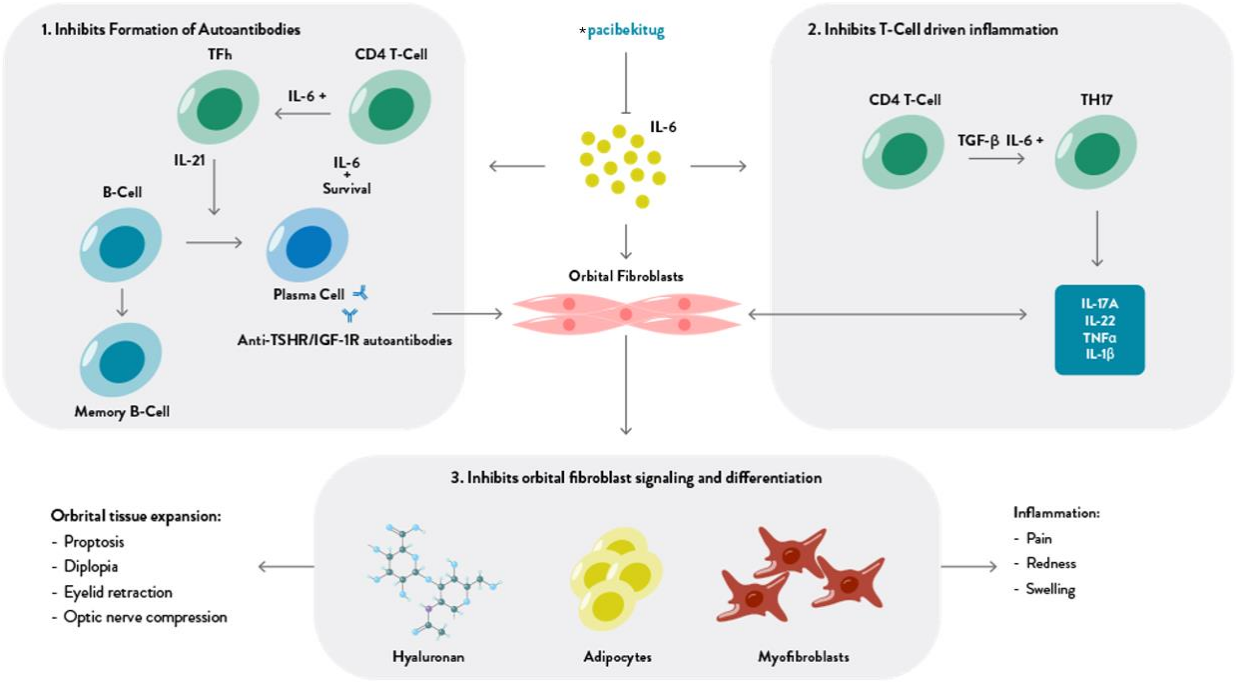
TED occurs in two phases – the initial active phase, characterized by high inflammation which lasts between 6-36 months and the later inactive phase with lower inflammatory involvement. TED is characterized by the production of autoantibodies against thyroid-stimulating hormone receptor (TSHR) which are also implicated in Graves' disease. These autoantibodies target the tissue surrounding the eye, leading to inflammation, swelling, and tissue remodeling.

TED can cause significant discomfort and can be sight-threatening if left untreated. Initial symptoms of TED may include dryness and irritation of the eyes, sensitivity to light, excessive tearing, double vision (diplopia), and a sensation of pressure behind the eyes. As the disease progresses, patients may develop retraction of their upper eyelids, swelling and redness around the eyes, and bulging of the eyes (proptosis). In severe cases, swelling and stiffness of the muscles that move the eyes can cause misalignment and even vision loss.

Role of IL-6 in TED

IL-6 is believed to play a critical role in the pathogenesis of TED, including in autoantibody production, T-cell mediated inflammation, and orbital fibroblast activity.

IL-6 INHIBITION HAS POTENTIAL TO BLOCK MULTIPLE STEPS IN TED PATHOGENESIS



Adapted from: Huang et al., Eye (2018); Hodgson and Rajaii, Ophthalmol Ther (2020); Fang et al, Front Endocrinol (2021); Smith et al., Eye (2019); and Cabezas et al., Front. Immunol. (2022)

*pacibekitug is an investigational drug and is not currently approved by any regulatory authority.

There is a large body of evidence supporting the role of IL-6 in TED including:

- IL-6 and soluble IL-6R levels are elevated in TED patients and correlate with disease activity.
- In a study of Graves' Disease patients, those that developed TED had significantly higher IL-6 levels than those that did not.
- A growing body of literature documents successful clinical experiences with other IL-6 pathway inhibitors, reporting meaningful improvements in proptosis, inflammation (measured by the Clinical Activity Score), and diplopia