Mavrilimumab

Phase 2

Therapeutic Area

Giant cell arteritis (GCA) is a chronic inflammatory disease of medium-large arteries.

Mechanism of Action

Monoclonal antibody targets granulocyte macrophage colony-stimulating factor receptor alpha (GM-CSFRα) and inhibits the signaling of granulocyte macrophage colony-stimulating factor (GM-CSF).

- GM-CSF is a key growth factor and cytokine that can govern the development and function of dendritic cells, monocytes, macrophages, and granulocytes (eg, neutrophils, basophils, and eosinophils).

US Prevalence

We estimate that there are approximately 75,000 to 150,000 patients with GCA in the United States.

Orphan Drug designation

Orphan Drug designation granted by the US Food and Drug Administration (FDA) for mavrilimumab for the treatment of giant cell arteritis.

KINIKSA

Rationale

We believe that by blocking GM-CSF signaling, mavrilimumab may be able to reverse the course of GCA by upstream targeting of the cell types driving the inflammatory process, a mechanism that is different from currently available therapies.

- The GM-CSF signaling pathway has been shown to be upregulated in GCA biopsies versus control at both the messenger ribonucleic acid (mRNA) and protein level.
- Mavrilimumab reduced inflammatory molecules characteristic of GCA pathophysiology in an ex vivo GCA artery culture model.
- Mavrilimumab reduced arterial inflammation compared to control in an in vivo model of vasculitis.
- In previous Phase 2b trials in rheumatoid arthritis, mavrilimumab demonstrated rapid and prolonged reductions in interleukin-6 (IL-6) production, which is indicative of suppression of tissue inflammation upstream.

Status: Phase 2

We reported data from a randomized, double-blind, placebo-controlled Phase 2 clinical trial of mavrilimumab in GCA.

The Phase 2 trial randomized 70 patients 3:2 to mavrilimumab 150 mg (N=42) or placebo (N=28) biweekly injected subcutaneously, co-administered with a protocol-defined 26-week oral corticosteroid taper. Patients were stratified by new onset (n=35) or relapsing/refractory (n=35) disease.

The primary efficacy endpoint of time-to-first adjudicated GCA flare by Week 26 in all treated patients was statistically significant (Hazard Ratio = 0.38, p=0.0263). There was a 62% lower risk of flare in mavrilimumab recipients compared to placebo recipients.

The secondary efficacy endpoint of sustained remission at Week 26 in all treated patients was also statistically significant. The sustained remission rate was a 33.3 percentage points higher in mavrilimumab recipients (83.2%) compared to placebo recipients (49.9%) (p=0.0038).

While the study was not powered for disease cohorts, there was a consistent trend of efficacy across the new onset and relapsing/refractory cohorts.

Mavrilimumab was well-tolerated; there were no drug-related serious adverse events, and the rates of drug-related treatment-emergent adverse events between mavrilimumab recipients and placebo recipients were similar.

A 12-week washout safety follow-up period is ongoing, and additional analyses of this Phase 2 trial are planned.

COVID-19 Pneumonia and Hyperinflammation

Kiniksa is enrolling and dosing the global, randomized, double-blind, placebo-controlled Phase 2 portion of an adaptive design Phase 2/3 clinical trial of mavrilimumab in severe COVID-19 pneumonia and hyperinflammation. Additionally, a randomized, double-blind, placebo-controlled investigator-initiated study in the U.S. is enrolling and dosing patients.

In an open-label treatment protocol in Italy, 13 non-mechanically ventilated patients with severe COVID-19 pneumonia and hyperinflammation were treated with a single intravenous dose of mavrilimumab. Twenty-six contemporaneous non-mechanically ventilated patients with severe COVID-19 pneumonia and hyperinflammation and with similar characteristics upon admission, including comorbidities, baseline inflammatory markers and respiratory dysfunction, were evaluated as a control-group. All patients received standard of care therapy, including antivirals and antibiotics.

Over the course of a 28-day follow-up period, mavrilimumab-treated patients experienced earlier and improved clinical outcomes than control-group patients, including earlier weaning from supplemental oxygen, shorter hospitalizations, and no deaths. Mavrilimumab was well-tolerated in all patients, without infusion reactions.

Unmet Need

Corticosteroids are the mainstay for the treatment of GCA, but approximately 50% to 70% of patients are corticosteroid refractory or corticosteroid dependent. Long-term administration of corticosteroids carries significant morbidity, especially in an elderly population such as in those with GCA. The FDA recently approved an inhibitor of IL-6 activity as an adjunct to a corticosteroid taper for the treatment of GCA; however, IL-6 production is downstream of GM-CSF and does not address all of the underlying causes of inflammation.