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PB2196 EQUATOR: A PIVOTAL PHASE 3 DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY OF ITOLIZUMAB IN COMBINATION WITH CORTICOSTEROIDS FOR THE INITIAL TREATMENT OF ACUTE GRAFT-VERSUS-HOST DISEASE

Topic: 22. Stem cell transplantation - Clinical

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Background: Acute graft-versus-host disease (aGVHD) remains a major cause of morbidity and mortality following allogeneic hematopoietic stem cell transplant (allo-HSCT); however, there is still no approved first-line treatment and corticosteroids (CS) remain standard of care. Itolizumab is a humanized IgG1 monoclonal antibody that binds CD6 and blocks interaction with activated leukocyte cell adhesion molecule (ALCAM) to inhibit T effector cell activity and trafficking to target organs. This mechanism of action represents a promising therapeutic approach to treat aGVHD, as suggested by safety and efficacy results from EQUATE (NCT03763318), an open-label Phase 1b/2 study that evaluated itolizumab in combination with CS as treatment for newly diagnosed aGVHD. The benefit-risk profile currently observed in EQUATE for doses of 0.8 and 1.6 mg/kg supports continued evaluation of itolizumab in a pivotal Phase 3 study.

Aims:

EQUATOR is a pivotal Phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of itolizumab in combination with CS as initial treatment for subjects with aGVHD. This global study will enroll approximately 200 subjects ≥12 years old who are diagnosed with Grade III-IV or Grade II with lower gastrointestinal involvement aGVHD following initial allo-HSCT.

Methods:

To be eligible, subjects must start study treatment within 72 hours of starting CS treatment for aGVHD (Day 1 CS dose must be 2 mg/kg/day). Eligible subjects will be randomized 1:1 to receive 7 IV doses of itolizumab (1.6 mg/kg on Day 1 and 0.8 mg/kg for the subsequent 6 doses) or placebo every two weeks. Subjects will be followed for one year (Figure). The selected dosing regimen is expected to rapidly decrease CD6 from the surface of T cells and maintain low surface CD6 throughout the dosing interval. An interim analysis for futility and efficacy will be conducted when approximately 50% of subjects complete through Day 29.

Results:

The primary endpoint is the complete response (CR) rate at Day 29 and key secondary endpoints include Day 29 overall response rate and durable CR rate at Day 99. This will enable assessment of speed and sustainability of symptom improvement and resolution. Additional secondary efficacy endpoints include the evaluation of duration of response, survival outcomes, CS use, and chronic GVHD incidence. Safety endpoints include the incidence of treatment-emergent adverse events (AEs), serious AEs, infections and CMV and EBV reactivation.

Image:

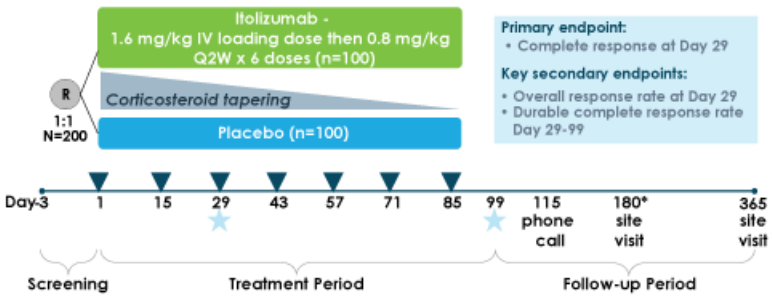

Figure. Study design for EQUATOR, a pivotal Phase 3, randomized, double-blind, placebo-controlled study of itolizumab in combination with corticosteroids for the initial treatment of acute graft versus host disease. Triangles represent dosing days. Stars represent timepoints for primary and key secondary endpoints.

*Subjects who discontinue from the study prior to Day 180 will have a Safety Follow-up Visit 90 days after their last dose of study drug.

Summary/Conclusion:

Here we present the rationale and design of EQUATOR, a pivotal Phase 3 study that will evaluate itolizumab in combination with CS and the ability to induce rapid and durable CR rates for the initial treatment of aGVHD.