BLA 125734

AC Meeting

DRAFT Clinical Questions

Topic for Discussion 1

- The primary composite efficacy endpoint in Study UIH-002 was the proportion of subjects achieving absence of severe hypoglycemic events (SHEs) and HbA1c of <6.5% in the year after the first transplant and the year after the last transplant. The primary endpoint in Study UIH-001 was insulin independence at one year after the first transplant and one year after the last transplant. In their BLA, the Applicant applied the same primary composite endpoint from Study UIH-002 to both studies. However, 83% of subjects in the combined Studies UIH-001 and UIH-002 did not have SHE in the year prior to their first transplant and 37% of subjects had HbA1c at target at baseline. Therefore, the study's pre-specified primary composite endpoint is difficult to interpret. However, FDA believes that the proportion of subjects with freedom from exogenous insulin administration might support the efficacy of cadaveric allogenic pancreatic islet cells (donislecel).

- Please discuss the minimum duration of insulin independence that you would consider to be clinically meaningful (i.e., would represent a benefit for the individual patient).

Topic for Discussion 2

- The applicant has proposed "Treatment of Brittle Type 1 Diabetes" as the indication for cadaveric allogenic pancreatic islet cells (donislecel). Given that there is no specific definition for "brittle type 1 diabetes" and considering the eligibility and baseline characteristics of the population actually enrolled in Studies UIH-001 and UIH-002, please discuss the benefit-risk profile for the product in general, and define the subset of type 1 diabetics as the appropriate target population.

Voting Question

Does donislecel delivered by intraportal administration have an overall favorable benefit-risk profile for some patients with Type 1 diabetes? In considering this question, please incorporate the risks of the transplantation procedure(s) and long-term immunosuppression as risks of the product.