U.S. FOOD & DRUG ADMINISTRATION

Clinical Considerations for Functional Studies of Pig Organs

Cellular, Tissue, and Gene Therapies Advisory Committee Meeting (CTGTAC)

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Topics for Discussion

- Transplantation
- Pre-clinical Data Considerations
- Clinical Considerations

Transplantation

- Surgical techniques for organ transplantation (heart, lung, intestines, liver and kidney) are well established
- Immunosuppression regimens for allogeneic transplants are well established
- Good clinical outcomes
- The number of human organ donations is not sufficient to meet the need.

Xenotransplantation

The goal of xenotransplantation is to provide replacement of function for organs, tissues or cells that are no longer able to support life, or to treat serious and life-threatening conditions in patients

Support for Clinical Studies

- Chemistry and Manufacturing Controls (CMC)
- Pharmacology and Toxicology (PT)

Physiologic Risks
Xeno Kidney

- Fluid (Blood Pressure) and Electrolyte Balance
- Vitamin D-PTH Axis
- Erythropoietin
- Coagulation

Pharmacologic Risks

- Immunosuppressive regimen
- Treatment of comorbidities
- Treatment of complications

Clinical Benefit-Risk Assessment

- Benefit
- Risks
  - Route of administration
  - Immunologic
  - Infectious
  - Physiologic mismatch
  - Pharmacologic
  - Other

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- Benefit
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  - **Physiologic mismatch**
  - **Pharmacologic**
  - Other

Thank you

Discussion Question 5

Transplantation of pig cells and organs is intended to provide replacement for non-functioning/damaged human cells and organs. Therefore, it is important to understand the characteristics of these cells or organs in the pig to ensure they have the characteristics needed to provide replacement therapy for the human recipient before transplantation. It is important to monitor these cells and organs to demonstrate they provide the expected functions after transplantation. Please discuss existing data to address the following issues related to pig cells and organs intended for transplantation into humans:

a. The ability of the target pig organ to support full organ function in humans.
b. The natural aging of the target organ in the pig relevant to expected organ function over time in humans.

Discussion Question 6

Transplanted pig organs are likely to be exposed to a variety of drugs that were not routinely used in the donor animals. Such drugs could include products to treat the patient's underlying medical condition(s) (e.g., diabetes, hypertension), as well as drugs (e.g., immunosuppressants) intended to ensure the success of the transplant. The transplanted organ may alter the pharmacodynamic and pharmacokinetic profiles of these drugs, with consequences for the medical management of the organ recipient. In addition, these drugs could be toxic to the transplanted organ. Please discuss the importance, limitations, and feasibility of studies of such drugs in the pig model prior to transplanting the pig organ into humans.