Design of the Graft Improvement Following Transplant (GIFT) trial, a phase 3 study of ANG-3777 in kidney transplantation patients with delayed graft function

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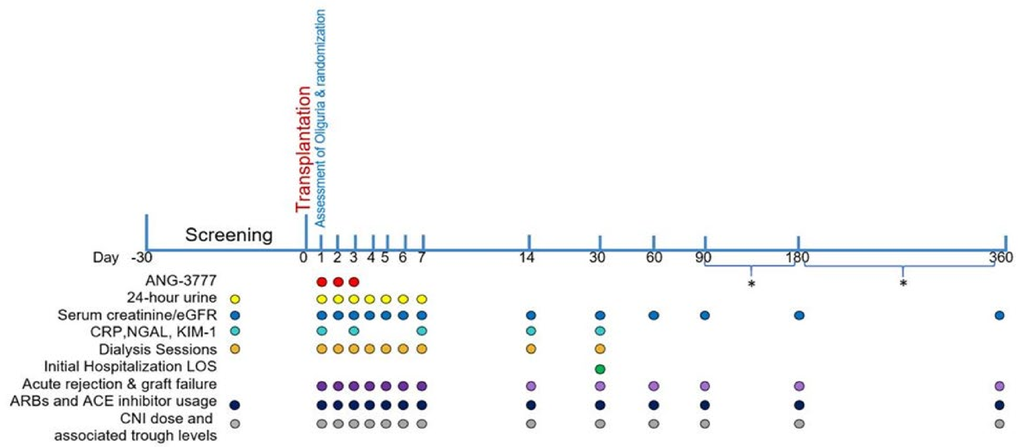
Background

Kidney transplantation is acknowledged as the 'dominant strategy' for treatment of ESRD.[1] An important factor that affects both viability of a kidney for transplantation and longevity of the graft is acute kidney injury (AKI) in the donor organ.[2] AKI can result in slow or delayed graft function (SGF, DGF) in which initial post-transplantation renal function is suboptimal. DGF affects approximately 30% of deceased donor renal transplantation recipients.[3] There are currently no approved treatments for DGF. A Phase 2 trial demonstrated that treatment with ANG-3777, a hepatocyte growth factor (HGF) mimetic, improved renal function up to 12-months in patients with signs of DGF.[4] Objective of this poster is to describe the GIFT trial (Study 001-15), a phase 3 study designed to evaluate the efficacy and safety of ANG-3777 in renal transplantation patients with signs of DGF.

Design

This is a randomized, prospective, parallel-group, double blind, placebo-controlled, multicenter Phase 3 study. 32 sites are participating from the United States.

Study Schematic



*eGFR is being collected between regularly scheduled visits

Methods

Population: Adults who have been on renal replacement therapy for ≥ 3 months who are receiving their first renal transplantation with a deceased donor kidney.

Inclusion Criteria:

1. Patients eligible to have drug administered starting within 30 hours after restoration of blood flow to the engrafted kidney.
2. Body mass index < 40 based on patient's body weight. Body weight and height parameters obtained within 7 days prior to study entry may be used.
3. Estimated donor organ cold ischemia time < 30 hours (for PMP kidneys < 40 hours).
4. Patient has poor renal function in the first 24 hours post-transplantation based on an average urine output (UO) of < 50 mL/hour over any 8 consecutive hours, to maximize the likelihood that the patient requires dialysis within the first 7 days post-transplant, irrespective of pre-transplant donor and recipient risk factors.
5. Reason for low UO is not due to structural or vascular abnormalities which, when indicated should be confirmed with a renal ultrasound with Doppler study and/or vascular or urinary tract contrast studies.
6. Written informed consent, willing/able to comply with the requirements of study.

Exclusion Criteria:

1. Scheduled for multiple organ transplantation or prior recipient of a transplanted organ.
2. Recipient of an ABO-incompatible kidney.
3. Recipient of pediatric en bloc kidney transplantation or adult or pediatric planned transplant of dual kidneys (from the same donor) not transplanted en bloc.
4. Recipient of a kidney preserved by normothermic PMP.
5. Has measurable donor-specific antibody or positive cross-match requiring desensitization prior to transplantation or deviation from standard immunosuppressive therapy.
6. Either the donor or the recipient is currently participating in or has participated in an investigational drug or medical device study within 30 days or five drug half-lives, whichever is longer, prior to enrollment into this study. Patients cannot be given another investigational agent during the course of this study (through Day 360). Patients (recipient and donor kidneys) may participate in another concurrent study only if that study is a non-interventional, observational investigation.
7. Concurrent sepsis or active bacterial infection.
8. Has an active malignancy or history within 5 years prior to enrollment in the study of solid, metastatic or hematologic malignancy with the exception of basal or squamous cell carcinoma in situ of the skin that has been adequately treated.
9. Female who is breastfeeding.
10. History of positive human immunodeficiency virus test.
11. Requires treatment with the cytochrome P450 (CYP) 1A2 inhibitors, ciprofloxacin and/or fluvoxamine (Luvox®).
12. Unwilling or unable to comply with the protocol or to cooperate fully with the Investigator or the site personnel.
13. Not deemed medically appropriate for the study in the opinion of the Investigator.

Efficacy Endpoints

Primary Endpoint:

- Estimated glomerular filtration rate (eGFR) at 12 months

Secondary Endpoints:

- Proportion of subjects with eGFR > 30 mL/min/1.73m^2 at days 30, 90, 180, and 360
- Proportion of subjects whose graft function is slow, delayed, or primary non-function
- Length of Hospitalization
- Duration of Dialysis

Safety

A Data and Safety Monitoring Board (DSMB) is undertaking ongoing monitoring of the safety data for this trial and the safety measures are collected at regular intervals

Summary

- DGF affects approximately 30% of patients undergoing renal transplantation
- DGF is associated with significant increase in adverse clinical outcomes
- Lack of effective treatments represents a significant unmet medical need
- This study will test the hypothesis that ANG-3777 improves renal function 12-months post-transplantation relative to placebo in patients with signs of DGF
- Primary outcome of interest is graft function at 1 year
- This study will generate data that are important to advancing treatment of DGF in this medically complex population

References

1. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant. 2009;9 Suppl 3:S1-155.
2. Siedlecki A, Irish W, Brennan DC, Delayed Graft Function in the Kidney Transplant. *Am J Transplant*. 2011, 11(11): 2279-2296.
3. Mannon RB. Delayed Graft Function: The AKI of Kidney Transplantation. *Nephron*. 2018;140(2):94-98.
4. Bromberg JS, Weir MR, Gaber AO, et al. Renal Function Improvement Following ANG-3777 Treatment in Patients at High Risk for Delayed Graft Function After Kidney Transplantation: *Transplantation*. Published online April 2020:1.

‡Denotes Former employees of Angion Biomedica, but were employees when the work of study design was completed.