Long-Term Outcomes of a Phase 1, Single-Arm Cohort of *De Novo* Kidney Transplant Recipients Treated with Tegoprubart, an Anti-CD40L Antibody, as the Core Immunosuppression Regimen

Poster No. P-62

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INTRODUCTION

- Tegoprubart is a humanized monoclonal antibody that selectively inhibits CD40 ligand (CD154), a co-stimulatory molecule in T-cell activation.[1,2]
- Tacrolimus is the current standard immunosuppressive agent in kidney transplantation but is associated with adverse effects including nephrotoxicity, neurotoxicity, new-onset diabetes mellitus after transplantation (NODAT), and hypertension.[3,4]
- Despite improvement in early rejection management, long-term kidney graft survival remains suboptimal.[5,6]
- This Phase 1b study evaluated the first adult *de novo* kidney transplant recipients treated with tegoprubart as the core immunosuppressive agent, combined with rabbit anti-thymocyte globulin (rATG) at induction and with mycophenolate and corticosteroids as maintenance therapy.

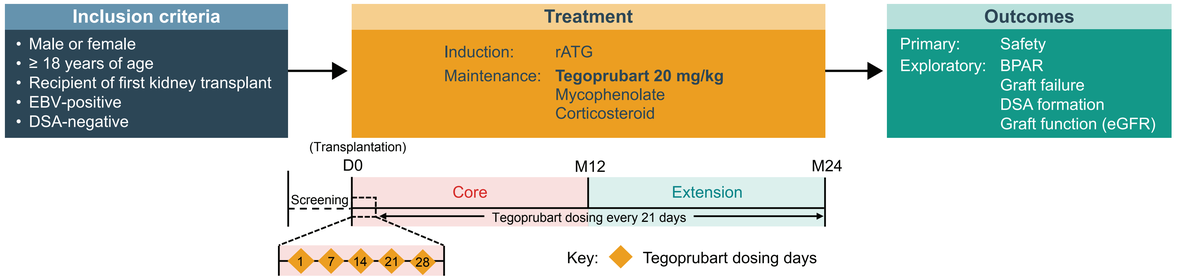
OBJECTIVE

To present the safety and kidney function outcomes associated with use of tegoprubart as a core immunosuppressive agent in a small group of *de novo* kidney transplant recipients with at least 2 years' follow-up.

METHODS

- This multicenter, Phase 1b, single-arm trial (NCT05027906) enrolled adults who were Epstein–Barr virus (EBV)-seropositive, had low levels of panel-reactive antibodies, and had no donor-specific antibodies (DSAs) at screening before receipt of their first kidney transplant from a living or deceased donor.
- All patients received induction with rATG (≤ 6 mg/kg), starting at day of transplantation (day 0), and maintenance therapy with intravenous tegoprubart (20 mg/kg, administered on days 1, 7, 14, 21, and 28 post transplantation, then every 21 days thereafter), mycophenolate, and corticosteroids. Patients who completed 12 months of treatment were given the option to enroll into an open-label extension study (NCT06126380, **Figure 1**).
- The primary safety endpoints were the incidence of treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), and adverse events of special interest (AESIs).
  - If a patient had more than one adverse event with the same preferred term, the patient was counted once for that preferred term.
- Selected exploratory endpoints at 12 and 24 months included:
  - incidence of
    - biopsy-proven acute rejection (BPAR)
    - graft failure
    - *de novo* DSA formation
  - mean estimated glomerular filtration rate (eGFR), analyzed using the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation.[7]

Figure 1. Study design.



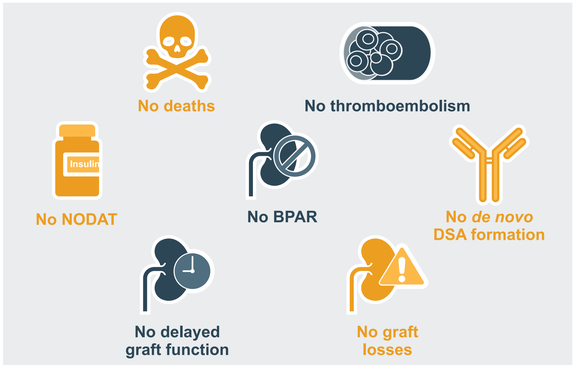
BPAR, biopsy-proven acute rejection; D, day; DSA, donor-specific antibody; EBV, Epstein–Barr virus; eGFR, estimated glomerular filtration rate; M, month; rATG, rabbit anti-thymocyte globulin.

RESULTS

Patient population

- Eight patients completed 12 months of treatment and continued into the extension study.
- The mean (standard deviation [SD]) treatment duration with tegoprubart was 29.50 (5.42) months, with seven of the eight patients completing at least 24 months of treatment with tegoprubart.
- Baseline characteristics were balanced.
  - The mean (SD) ages were 55.5 (17.67) and 54.1 (8.15) years for recipients and donors, respectively; most of the recipients received transplants from living donors (n = 7).
  - Half of the recipients were female, and three-quarters were white. The mean (SD) duration of end-stage renal disease was 6.2 (7.75) years, diabetes was the cause of this in 62.5% of patients.
  - A total of 0–2, 3–4, and 5–6 human leukocyte antigen mismatches occurred in two, two, and four patients, respectively.

Figure 2. Safety and exploratory endpoints of interest.



BPAR, biopsy-proven acute rejection; DSA, donor-specific antibody; NODAT, new-onset diabetes mellitus after transplantation.

Safety

- Tegoprubart had an acceptable safety profile over the 24-month study period.
- All patients experienced at least one TEAE, SAEs were reported for three patients, and AESIs were reported for seven patients.
- No deaths were reported and there were no reports of the AESIs of thromboembolic events or NODAT (**Figure 2**).
- TEAEs (reported in at least three patients), SAEs, and AESIs reported during the core and extension studies are given below.

Extension study (months 12–24)

- TEAEs: the most frequently reported TEAE was upper respiratory tract infections (3 patients).
- SAEs: two SAEs unrelated to treatment were reported for one patient each; basal cell carcinoma and pyelonephritis.
- AESIs:
  - cytomegalovirus (CMV) viremia occurred in one patient and BK virus also occurred in one patient. Neither of these patients progressed to nephropathy or CMV disease.
  - opportunistic infections included *Escherichia coli* urinary tract infection (2 patients) and COVID-19 (2 patients).
  - other AESIs included the one patient who developed basal cell carcinoma.
- One patient discontinued owing to relocation to another country at month 22 of the extension study.

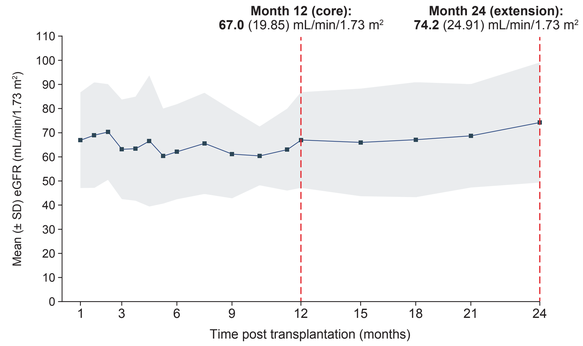
Exploratory endpoints

- No cases of BPAR, *de novo* DSA, delayed graft function, or graft loss were reported (**Figure 2**).

Kidney function post transplantation

- Functional eGFR levels were restored within 1 month after transplantation and generally were maintained for up to 2 years.
- The mean (SD) eGFRs were 67.0 (19.85) mL/min/1.73 m² and 74.2 (24.91) mL/min/1.73 m² at 12 and 24 months, respectively (**Figure 3**).

Figure 3. Mean eGFR over 24 months post transplantation in patients who entered the extension study.



CONCLUSIONS

- This small group of kidney transplant recipients treated with tegoprubart and followed up over a 24-month period demonstrated very good kidney function, no episodes of acute rejection, and an acceptable safety profile.
- Larger studies are required to investigate the role of tegoprubart as the core of the immunosuppression regimen for kidney transplant recipients.

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