Phase 2 BESTOW EXTENSION Trial Evaluating Tegoprubart's Long-Term Safety and Efficacy in Preventing Kidney Transplant Rejection

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INTRODUCTION

- Tacrolimus is the current standard of care for preventing transplant rejection in kidney transplant recipients; however, its use is associated with adverse effects, including nephrotoxicity, neurotoxicity, and hypertension.[1]
- Tegoprubart is a humanized immunoglobulin G1 kappa monoclonal antibody that selectively targets cluster of differentiation (CD) 40 ligand (CD40L; also known as CD154) to inhibit co-stimulatory immune pathways and suppress immune response.[2,3]
  - Blocking CD40L promotes polarization of $CD4^+$ T cells toward a regulatory T-cell phenotype.[2]
- An initial Phase 1b study and the BESTOW Phase 2 clinical study (NCT05983770) demonstrated that tegoprubart preserved kidney function as the core of the immunosuppressive regimen with a favorable safety profile in the first 12 months after transplantation.[3,4]

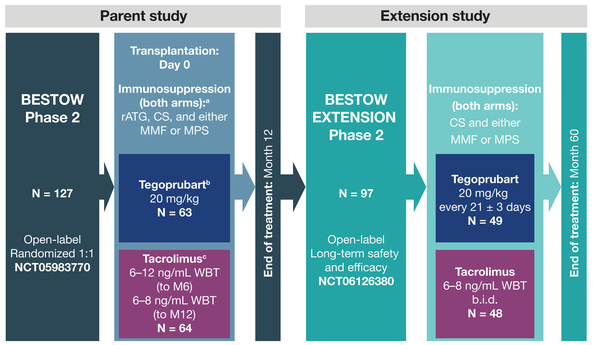
OBJECTIVE

- We report interim data from the Phase 2 BESTOW EXTENSION study (NCT06126380) on the impact of long-term efficacy and safety of tegoprubart compared with tacrolimus in adults receiving their first kidney transplant, focusing on kidney function, events of acute rejection, and safety beyond 12 months of treatment.

METHODS

- The Phase 2 BESTOW EXTENSION study is an ongoing, multicenter, open-label, active-controlled study.
- Patients who completed the Phase 2 BESTOW study on their assigned treatment could enter the extension, in which they continue to receive intravenous tegoprubart or oral tacrolimus as part of the immunosuppressive regimen (**Figure 1**).
- Interim analysis focused on kidney function (assessed by estimated glomerular filtration rate [eGFR]), and incidence of biopsy-proven acute rejection (BPAR), as well as incidence of treatment-emergent adverse events, serious adverse events, and adverse events of special interest (AESIs).
  - The data reported here are from April 24, 2026, with data available for the majority of participants up to Months 6–9 of the BESTOW EXTENSION study (18–21 months of overall treatment exposure).

Figure 1. Study Design



[a]All patients received rATG (maximum recommended dose 4.5 mg/kg), corticosteroid tapered to 5 mg by Day 28 and MMF 1000 mg or MPS 720 mg b.i.d. [b]Tegoprubart was received by intravenous infusion on days 1, 3, 7, 14, 21, 28, and then every 21 ± 3 days thereafter. [c]Tacrolimus was initiated within 48 hours of transplantation or when serum creatinine was ≤ 4 mg/dL (whichever came first), then received b.i.d.
b.i.d., twice daily; CS, corticosteroid; M, Month; MMF, mycophenolate mofetil; MPS, mycophenolate sodium; rATG, rabbit anti-thymocyte globulin; WBT, whole blood trough concentration.

RESULTS

Participant Population

- Ninety-seven patients (N = 49, tegoprubart; N = 48, tacrolimus) enrolled in the BESTOW EXTENSION study.
- Four patients in each treatment arm had discontinued by interim data cut.
  - Tegoprubart: adverse event (n = 2); protocol non-compliance (n = 1); other (patient unwilling to participate in study; n = 1).
  - Tacrolimus: adverse event (n = 1); physician decision (n = 1); prohibited treatment (n = 2).
- Following transplantation, the mean (standard deviation [SD]) treatment duration was similar in both groups.
  - Tegoprubart: 21 (2.9) months.
  - Tacrolimus: 21 (3.0) months.

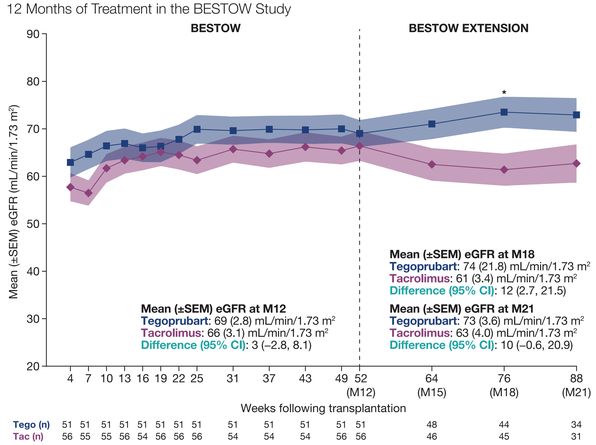
Baseline Characteristics

- Key baseline characteristics were typically balanced between treatment arms.
- For tegoprubart and tacrolimus arms, respectively:
  - mean (SD) age in years: 48.8 (13.9) vs 48.4 (12.6)
  - male participants: 61.2% vs 70.8%
  - kidneys from deceased donors: 71.4% vs 75.0%
  - mean (SD) Kidney Donor Profile Index scores: 42.6% (25.2) vs 36.4% (24.6).

Kidney Function Following Transplantation

- Mean (standard error of the mean) eGFR was consistently higher for patients receiving tegoprubart than tacrolimus (**Figure 2**).
- The treatment difference in mean eGFR was clinically meaningful in the extension after Month 12, with a significant difference at Month 18.

Figure 2. Long-Term Mean eGFR Following Transplantation for Patients who Completed 12 Months of Treatment in the BESTOW Study

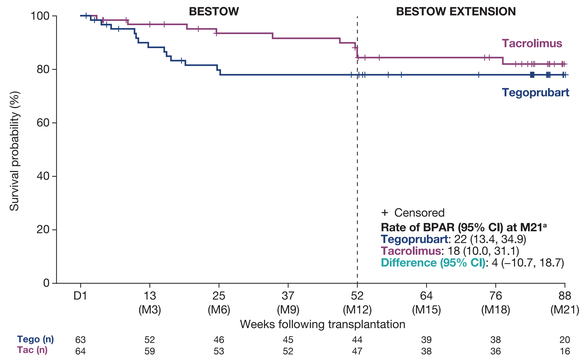


*$p < 0.05$.
Treatment differences in eGFR of ≥ 10 mL/min/1.73 m² were considered clinically meaningful.
CI, confidence interval; eGFR, estimated glomerular filtration rate; M, Month; SEM, standard error of the mean; Tac, tacrolimus; Tego, tegoprubart.

Biopsy-Proven Acute Rejection

- Acute rejection occurred in 13/63 patients receiving tegoprubart during BESTOW.
  - All acute rejections in patients receiving tegoprubart occurred in the first 6 months of the BESTOW study.
  - No new or recurring acute rejection events occurred in the remainder of BESTOW, nor in the extension study (up to 21 months total; **Figure 3**).
  - The estimated BPAR rate remained stable with tegoprubart from Month 6 through Month 21.

Figure 3. Kaplan–Meier Plot of Acute Rejection-Free Survival Following Transplantation



[a]Failure rates are expressed as percentages, based on Kaplan–Meier estimates. CI of the failure rate is estimated using a log-log transformation. BPAR in the BESTOW study was assessed by a central pathologist. BPAR in the extension study was assessed by a local pathologist.
BPAR, biopsy-proven acute rejection; CI, confidence interval; D, Day; M, Month; Tac, tacrolimus; Tego, tegoprubart.

- Acute rejection occurred in 9/64 patients receiving tacrolimus across the 12 months of BESTOW and a further two patients during the extension (**Figure 3**).
  - Acute rejection events during the extension:
    - one patient with new acute rejection (acute T-cell mediated rejection [aTCMR], grade 2a)
    - one patient with recurrent acute rejection (aTCMR, grade 2B and acute antibody-mediated rejection [aAMR]).
  - The estimated BPAR rate increased in the tacrolimus arm from 7 (95% confidence interval [CI]: 2.5, 16.7) at Month 6 to 18 (95% CI: 10.0, 31.1) at Month 21.
- The treatment difference in rate of BPAR at Month 21 suggests no significant difference in acute rejection rates at Month 21.

Long-Term Kidney Function in Patients with Acute Rejection in the BESTOW Study

- Of the patients with acute rejections, 7/13 (tegoprubart) and 8/9 (tacrolimus) continued receiving treatment during BESTOW and the extension study.
- Kidney function was sustained in those who continued tegoprubart; those who continued tacrolimus showed lower mean kidney function (**Figure 4**).
  - Mean eGFR was higher in the tegoprubart arm than the tacrolimus arm.
  - Treatment differences in mean eGFR were clinically meaningful throughout BESTOW and BESTOW EXTENSION, including a significant difference at Month 15 ($p < 0.05$).

Figure 4. Mean eGFR Following Kidney Transplantation for Patients Who Continued Treatment After Acute Rejection During the BESTOW Study and Enrolled into the BESTOW EXTENSION Study

*$p < 0.05$.
Treatment differences in eGFR of ≥ 10 mL/min/1.73 m² were considered clinically meaningful.
CI, confidence interval; eGFR, estimated glomerular filtration rate; M, Month; SEM, standard error of the mean; Tac, tacrolimus; Tego, tegoprubart.

Safety

- Tegoprubart continued to have an acceptable long-term safety profile through the extension study (**Table 1**).
- One death (cardiovascular event of unknown cause) was reported for a patient receiving tegoprubart and considered unrelated to study drug.
- The most frequently reported adverse events were diarrhea and headache, both of which were more frequent in patients receiving tacrolimus than tegoprubart (**Table 2**).
- AESIs remained consistent with those reported in the BESTOW study.
- There were no events of:
  - progressive multifocal leukoencephalopathy
  - post-transplant lymphoproliferative disorder
  - BK virus or cytomegalovirus nephropathy
  - malignancies.
- There were two thromboembolic events in both treatment arms and one event of tremor in the tacrolimus arm.
  - Neither thromboembolic event led to treatment discontinuation and were managed while patients continued to receive study drug.

Table 1. Treatment-Emergent Adverse Events Reported in the BESTOW EXTENSION Study

Participants, n (%)	Tegoprubart (N = 49)	Tacrolimus (N = 48)
Any AE	39 (79.6)	41 (85.4)
AEs by maximum severity		
Mild	16 (32.7)	19 (39.6)
Moderate	16 (32.7)	13 (27.1)
Severe	5 (10.2)	7 (14.6)
Life-threatening or requiring urgent intervention	1 (2.0)	2 (4.2)
Death	1 (2.0)	0
Any SAE	6 (12.2)	7 (14.6)
Study drug-related SAEs	0	1 (2.1)[a]
Any AESI	22 (44.9)	16 (33.3)

[a]Parotitis infection.
AE, adverse event; AESI, adverse event of special interest; SAE, serious adverse event.

Table 2. Treatment-Emergent Adverse Events Reported in ≥ 10% of Patients in the BESTOW EXTENSION Study

Participants, n (%)	Tegoprubart (N = 49)	Tacrolimus (N = 48)
Diarrhea	5 (10.2)	10 (20.8)
Headache	1 (2.0)	6 (12.5)
Cytomegalovirus DNAemia	6 (12.2)	3 (6.3)
Hypertension	4 (8.2)	5 (10.4)
Pain in extremity	0	5 (10.4)

Events are reported when reaching ≥ 10% of participants in either treatment arm based on preferred term.

CONCLUSIONS

- Patients who entered the extension study and received tegoprubart demonstrated good preservation of kidney function, with a clear, clinically meaningful separation in eGFR from those who received tacrolimus.
- No new acute rejection events were observed in the tegoprubart arm during the extension study, however, two events (one new, one recurrent) were observed in the tacrolimus arm.
  - Acute rejection events were limited to the first 6 months following transplantation for patients receiving tegoprubart, whereas they continued into the extension study for patients receiving tacrolimus.
- Patients who experienced acute rejection and remained on tegoprubart maintained better kidney function than those receiving tacrolimus, suggesting a potentially lesser impact of rejection on allograft function.
  - This observation will be further evaluated in Phase 3.
- Safety in the extension study was consistent with the BESTOW study, with the safety profile of tegoprubart remaining favorable.
- Results collected so far from the BESTOW EXTENSION study support the continued development of tegoprubart as a promising long-term alternative to tacrolimus for maintaining allograft function and preventing kidney transplant rejection.

For the latest details on the BESTOW study, please visit our oral presentation:
Session: Kidney; Biomarkers -3
Date/Time: Monday June 22, 2026; 11:15 AM–12:15 PM

References: 1. Leas BF *et al.* Comparative Effectiveness Reviews, No. 166. Rockville, MD: Agency for Healthcare Research and Quality, 2016. **2.** Eledon Pharmaceuticals. 2025. https://eledon.com/science/mechanism-of-action/ (Accessed June 2, 2026). **3.** Katz E *et al. Am J Transplant* 2026;26:S88. **4.** Adams AB *et al.* Am Soc Nephrol Kidney Week, 2025. Oral presentation.

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