

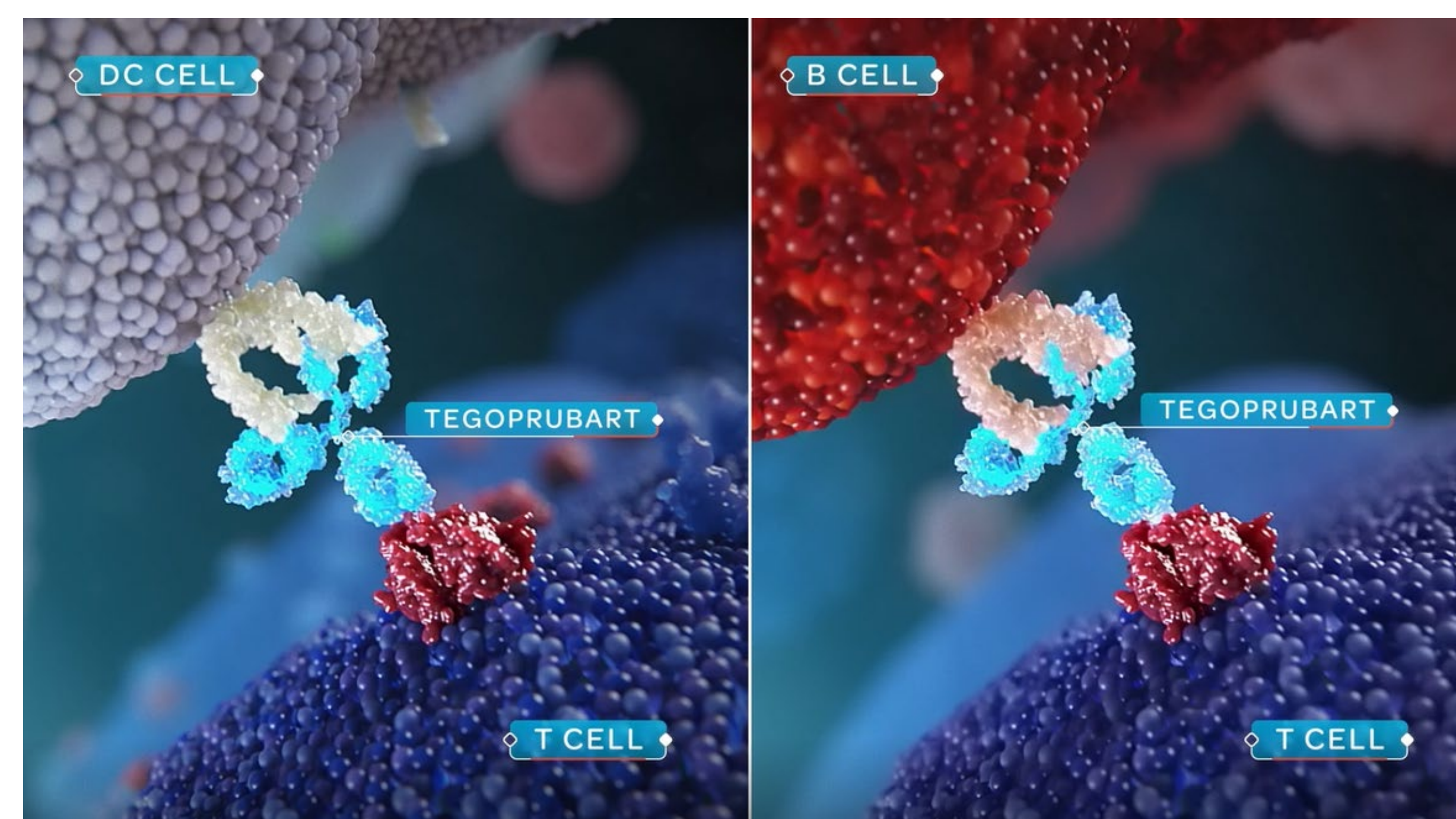
**Tegoprubart for the prevention of rejection in kidney transplant recipients: a snapshot of emerging data from an ongoing trial**

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**Background**

Kidney transplantation improves survival as well as quality of life for patients with end stage kidney disease progressing to, or requiring, dialysis. Current immunosuppressive therapy, with tacrolimus, a calcineurin inhibitor, as the backbone of maintenance treatment, results in >90% 1-year patient and graft survival rates. Despite these encouraging results, tacrolimus therapy increases the risk of diabetes in the post-transplant setting and is also known to be nephrotoxic, reducing graft function and viability in the long term, with ~50% of recipients achieving 10-year patient and graft survival. An agent that could produce comparable 1-year results while improving long term outcomes would address a significant unmet medical need. Tegoprubart is a monoclonal antibody that inhibits CD40 ligand (CD40L) on the cell surface of T cells, blocking its interaction with CD40 receptor on antigen presenting cells such as dendritic cells (DC) and B cells. It is expected to downregulate both cell mediated and antibody mediated immune responses while also creating a more tolerogenic environment, and preventing antibody class switching, thus reducing high affinity IgG antibodies. Tegoprubart has been shown to be effective in animal models of transplant and is being evaluated as a potential alternative to tacrolimus in an ongoing trial in the prevention of rejection in kidney transplant recipients.

**Tegoprubart Mechanism of Action**



**Methods**

A minimum of 6 and a maximum of 12 adult participants receiving a kidney transplantation from either a living or deceased donor will be enrolled. To be eligible, this must be their first transplant, they must be seropositive for EBV, free of donor specific antigens, have low panel reactive antibodies, and the organ cannot be from an extended criteria donor or have a prolonged cold ischemia time. All participants will receive rabbit antithymocyte globulin induction and a maintenance regimen consisting of tegoprubart 20 mg/kg IV administered every 3 weeks after an initial loading regimen, mycophenolate mofetil and corticosteroids. Enrollment of the first 4 participants is staggered such that the Data Monitoring Committee (DMC) needs to review the data from the first 28 days on study of the preceding participant before the next participant can be enrolled. Participants will remain on study for a year, after which time they will have the option of continuing tegoprubart in an extension study. The primary endpoint is safety. Other endpoints include characterizing the pharmacokinetic profile of tegoprubart, the incidence of biopsy proven rejection (BPAR), changes in estimated glomerular filtration rate (eGFR) and exploratory biomarkers including donor derived cell free DNA.

**Results**

**Overview**

- As of March 3, 2023:
  - A total of 3 participants have been enrolled
  - Participant 1: Withdrew from study treatment after 232 days post transplant (33 weeks) due to alopecia and insomnia (mild, unrelated)
  - Participant 2: 159 days post transplant (22 weeks)
  - Participant 3: Withdrew from study treatment after 56 days (8 weeks) due to BK viremia (serious, related)
  - No participant has experience BPAR
  - No evidence of NODAT in participants transplanted without diabetes
  - Overall graft function has been good

**Participant 1**

- 60-year-old Caucasian female
- ESRD due to polycystic kidney disease; not on dialysis
- Underwent living donor kidney transplant on July 12, 2022
- Completed 14 infusions of tegoprubart; most recent infusion: Day 217
- Withdrew from study treatment on Day 232 due to alopecia and insomnia (both chronic, mild, unrelated and ongoing)
- Other adverse events of note: weight loss, mild and ongoing
- Normal glucose; no evidence of NODAT
- Day 217 eGFR: 77.23 mL/min/m<sup>2</sup>

**Participant 2**

- 77-year-old Caucasian female
- ESRD due to diabetes; on hemodialysis
- Underwent deceased donor kidney transplant on September 25, 2022
- Completed 11 infusions of tegoprubart; most recent infusion: Day 154
- Adverse events of note include:
  - Alopecia: mild, unrelated and ongoing
  - Nail Weakness: mild, unrelated and ongoing
- Day 154 eGFR: 85.21 mL/min/m<sup>2</sup>

**Participant 3**

- 62-year-old Caucasian male
- ESRD due to polycystic kidney disease; not on dialysis
- Underwent living donor transplant on December 5, 2022
- Completed 5 infusions of tegoprubart; most recent infusion: Day 28
- Withdrew from study treatment on Day 56 due to BK viremia
  - Initial diagnosis of BK viremia made on day 23: 7,690 copies/mL were reported
    - Prednisone was stopped
  - On Day 28, viral load increased to 31,300 copies/mL
    - MMF was held
  - On Day 34 counts increased to 159,000 copies/mL and leflunomide was started
  - On Day 41, counts were up to 452,000 copies/mL
  - On Day 47, counts were 531,000; decision taken to delay / hold Day 49 infusion
  - On Day 55, counts dropped to 173,000 copies/mL
    - PI decided to discontinue study drug and initiate therapy with tacrolimus
  - Serum creatinine remained in normal range of local lab throughout, nephropathy was never suspected, and no biopsy was performed.
- Other adverse events of note: atrial fibrillation, mild, unrelated and ongoing
- Normal glucose; no evidence of NODAT
- Day 49 eGFR: 54.4 mL/min/m<sup>2</sup>

**eGFR Data (mL/min/m<sup>2</sup>)**

	Day 1	Day 28	Day 91	Day 154	Day 217
Participant 1	9	96	96	97	77
Participant 2	10	85	79	85	
Participant 3	12	49	Final value was 54.4 on Day 49		

**Discussion**

This study is designed to show that tegoprubart can safely replace tacrolimus to prevent allograft rejection as the backbone therapy in post transplant immunosuppression. To date, this trial has demonstrated that tegoprubart can be used in this fashion. Three participants have enrolled. None of the three have experienced acute rejection with post transplant follow-up durations of 56, 154 and 232 days. Graft function was very good in all three participants with each having an eGFR above 50 mL/min/m<sup>2</sup>, and the two without BK viremia who both had a longer on treatment course, had eGFR levels above 70 and above 80 mL/min/m<sup>2</sup>. BK viremia, which occurred in one of the three participants is a known post kidney transplant complication and was the only infectious AE reported to date in the trial. Alopecia was reported in 2 of the three participants. This is also a known complication post kidney transplantation.

This study will continue to enroll more participants, and the data to date suggest that tegoprubart can prevent acute allograft rejection and maintain good graft function when used in place of tacrolimus in kidney transplant allograft recipients. Further study is warranted.