

Oxford Transplant Foundation - July 2026 Report

Cell therapy and beyond: Evaluation of transplant recipient-derived regulatory B-cells in personalised ex vivo systems as a bridge to translation

I am very grateful to the Oxford Transplant Foundation for supporting this project, which aims to evaluate whether the suppressive function of expanded regulatory B cells (expBregs) differs between patients who experience T-cell mediated rejection (TCMR) versus those that do not, and whether their function can be modified *ex vivo*. expBregs have not been generated from patients with chronic kidney disease or those post-transplant and we don't know if regulatory function differs in those who experience different clinical outcomes. This work aims to assess feasibility of expansion of Bregs from transplant recipients, compare suppressive function between the two groups and a later aim of whether expBregs with 'deficient' regulatory function can be modified *ex vivo*.

To date, I have recruited, and isolated, peripheral blood mononuclear cells from 40 kidney transplant recipients at the pre-transplant timepoint. Paired three-month post-transplant samples have also been collected from 25 of these patients. Unfortunately, this represents only half of my target recruitment number. Recruitment was slower than anticipated following project acceptance by Oxford Transplant Biobank in June 2025. This low recruitment rate was mainly due to practical difficulties related to identifying eligible patients as well as coordinating consent and sample procurement with the biobank team. There were also smaller issues such as crossover with other research studies and a higher rate of patient decline than anticipated.

However, since January I have modified aspects of the recruitment process. I am now alerted, via automatic email/text, about potential study patients. I have increased my presence on the ward for consenting and improved coordination with the biobank team. These changes have meant the recruitment rate has increased substantially (green line on graph below) compared to the rate prior to January 2026 (blue line). I am hoping to be able to complete my recruitment of patients by the end of January 2027, allowing for six-month rejection data to be available by mid-point of 2027.

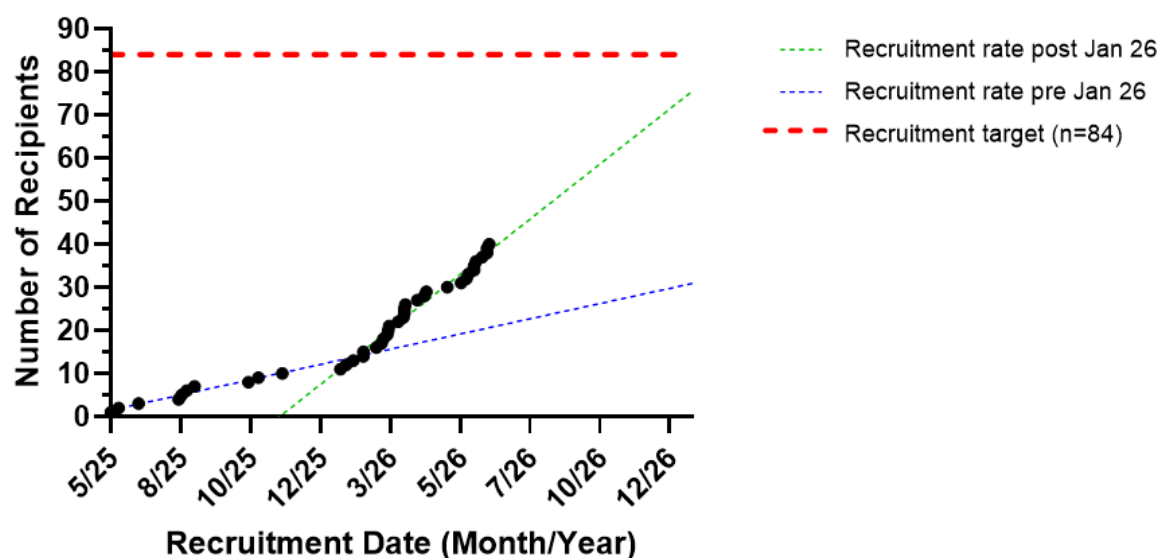


Figure 1. Cumulative recruitment of kidney transplant recipients over time. Black points show actual cumulative recruitment. The dashed blue line shows the projected recruitment trajectory based on the recruitment rate before January 2026, and the dashed green line shows the projected trajectory after implementation of revised recruitment procedures in January 2026. The red dashed line indicates the original recruitment target.

The original project focussed on kidney transplant recipients that received Campath induction. However, the Oxford population of potential transplant recipients is becoming older and therefore an increasing proportion have Basiliximab induction, which is used in those patients aged 69 or over. I have therefore expanded my inclusion criteria and, on top of the 40 Campath patients (with a target of 84), I have also recruited and isolated blood samples from 7 Basiliximab patients (target of 23).

This study amendment does not change the initial aim of the project but hopefully broadens the clinical relevance, by including patients treated with a non-depleting induction agent. This should allow me to compare expansion and suppressive function between the two populations, although the study is not powered for this and age will confound the analysis. Basiliximab induction is also associated with a higher rate of rejection (roughly 20%) therefore I have estimated a lower number, 23, to power the study based on similar outcomes (detection of a 10% difference in pSTAT3 expression between recipients that have TCMR versus those that do not).

Over the coming months I will start thawing patient samples, isolation of B cells and expansion of Bregs. I expect to complete these expansions by early next year allowing for a comparison of function between rejection and non-rejection cohorts. Although recruitment rate has increased there remains a risk of a failure to recruit patients within my DPhil timeframe; when I return to training in October 2027. Even if this number is not achieved, the study will still provide valuable data on the feasibility of Breg expansion from kidney transplant recipients and exploratory data on their function.

The support that Oxford Transplant Foundation has given me has been invaluable for the set-up, recruitment of patients and sample isolation within the study. I look forward to sharing further details of the study next year when initial results are available. Please let me know if further information is required.



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