

Application for the Lelia Duley Prize for Patient-centred CLL Research.

Dr Helen Parry on behalf of the IMPROVE trial team and scientific research group (A multi-centre randomised controlled trial examining the effects of temporarily pausing Bruton Tyrosine Kinase inhibitor therapy to coincide with SARS-CoV-2 vaccination and its impact on immune responses in patients with Chronic Lymphocytic Leukaemia)

Patient and Public Involvement and Engagement (PPIE) for the IMPROVE trial was embedded from the earliest stages of grant development (prior to funding), through to dissemination of the trial findings. The IMPROVE patient advisory group (PAG) met regularly, to co-develop a trial design which addressed issues that really mattered to people living with chronic lymphocytic leukaemia (CLL), at a time of great uncertainty with respect to COVID-19. They ensured the trial remained accessible and acceptable to potential participants and delivered results in a way that was meaningful to the wider patient community, particularly with interim updates during the trial, which were available online (<https://improve.octru.ox.ac.uk/welcome-to-improve>), in newsletters and through patient webinars.

Lelia Duley, with extensive experience of CLL research and patient advocacy, became the lead for the patient advisory group, a co-applicant on the grant application and a key member of the trial monitoring group, which met fortnightly and gave further opportunity for patient advocacy. Lelia, together with a costed PPIE facilitator from the hospital, became informal mentors to me during this time. As a first-time chief investigator, navigating the NIHR funding stream, their expertise and insight helped enormously, and I personally learnt an awful lot about the importance of effective PPIE through their guidance.

Together, we set about gaining broader perspectives around the study and suitability of asking patients to pause their CLL treatment- a highly sensitive issue for patients. To address this, we invited individuals living with CLL to participate in structured online discussions and produced video material (kindly facilitated by the late patient advocate, Lewis Troke), to explain why they felt the trial was important. Feedback from these discussions was reviewed and incorporated into the final study design and application, which Lelia helped co-write. The study application received a commendation by NIHR for the thorough involvement of PPIE and we were successful in securing the grant award.

During the initial set-up phase, a Patient Advisory Group (PAG) group was formed and convened to review all participant-facing materials and to consider how to improve accessibility for patients, enlisting the help of the CLLSA, Leukaemia Care and BCUK in advertising the study. The PAG consisted of six members, including patient representatives and the PPI co-applicant. We developed a PAG group ‘term of reference’ to work towards, helping advisors to understand their role- this was particularly well received by some members of the group who had not participated in PPIE before. The PAG group met regularly during recruitment and as results became available. This structure ensured that patient perspectives informed both strategic decisions and operational aspects of trial delivery that evolved, with Lelia feeding back at the fortnightly Trial Monitoring Group meetings.

One of the most important contributions of PPIE was the refinement of participant-facing documentation. Here, the PAG group identified several areas where language could be improved. For example, they recommended avoiding the term “trial arm”, recognising that this terminology could be confusing in a vaccine study where injections are administered into the arm. They also suggested clearer explanations of what “randomisation” meant, helped devise an infographic for those averse to reading patient information sheets or who prefer a pictorial form for the provision of information and improved the wording around trial inclusivity. Consistency of language across documents was another area highlighted by patient representatives. These changes enhanced the clarity, accessibility and acceptability of study materials, helping to ensure that participants could make informed decisions about involvement.

Patient contributors also had a significant influence on the practical design of the participant pathway. They highlighted the need to minimise participant burden and reduce barriers to participation. As a result,

study visits were organised within participants' local hospitals and, where possible, aligned with routine clinic appointments to avoid unnecessary travel. The study incorporated brief questionnaires, which could be completed at home online, remote follow-up options and reimbursement of travel expenses. Financial provision was also made for participants with caring responsibilities through a carer allowance, as the PAG group highlighted that many patients with CLL have carer duties for spouses or grandchildren. Collectively, these changes made participation more feasible and accessible for individuals living with CLL.

Patient partners also played an important role in ongoing discussions around participant compensation and feedback of individual results. During the early design stages, patients expressed strong views that access to their own antibody results would be highly valued and could act as a meaningful incentive to participate. In contrast, they felt that monetary rewards at the end of the study were less important. Consequently, plans were developed to provide participants with information about their antibody responses, together with an appropriate contextual explanation. However, as the trial progressed and with the changing context of the COVID-19 pandemic, the PAG group subsequently advised that giving individual results may not be an appropriate step, recognising the challenges of interpreting individual antibody levels following several COVID-19 vaccines. Instead, the group supported a balanced approach in which all participants would receive a summary of overall trial findings, while individual results would remain available on request. This decision reflected both scientific considerations and patient preferences and demonstrated the value of involving patients in complex decisions about dissemination.

Throughout the study, several Plain English Summaries were co-produced with the PAG group, which could be easily understood by participants and the wider CLL community. This was sent to participants with an accompanying letter thanking them for their participation but was also made available for public access online. Their input helped clarify the key study message, provided recommendation to not pause BTKi therapy, and disseminated the findings of the trial in a clear and accurate way.

Following completion of the trial, the IMPROVE team were invited to produce a reflective piece on the importance of PPIE and why it matters for NIHR Birmingham Biomedical Research Centre [Involving people with leukaemia in the design of a clinical trial testing vaccine strategies - NIHR Birmingham Biomedical Research Centre](#). Using IMPROVE as an exemplar, this video is aimed at encouraging more PPIE involvement in trial design and insights into developing effective PPIE strategies.