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POSTER ABSTRACTS

903.HEALTH SERVICES AND QUALITY IMPROVEMENT -MYELOID MALIGNANCIES

The UK Impact Transplant Trials Network: An Effective National Strategy to Accelerate the Delivery of Randomized Trials in Stem Cell Transplantation

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Introduction:

Stem cell transplantation (SCT) is an important curative modality in patients with blood cancer whose outcome with chemotherapy is predicted to be poor and is an increasingly important therapy in non-malignant disease. However, even in 2023, 50% of patients are still destined to die after either allogeneic or autologous transplantation, either of relapsed disease or treatment toxicity. In response the transplant community continue to develop innovative strategies designed to improve patient outcome. However, despite the fact that the adoption of new therapies in haemato-oncology is, almost without exception, based on evidence generated by randomized studies fewer than 5% of transplant patients are currently recruited to prospective practice informing trials. Thus, much current transplant practice is based on retrospective registry analyses whose results can often be misleading. There is therefore an urgent need for innovative trial models with the ability to accelerate transplant trial delivery if patient outcomes after SCT are to be improved.

Methodology:

We reasoned that limited trials capacity at busy centres coupled with the absence of a fit-for-purpose clinical trials network represented potentially tractable barriers to transplant trial recruitment. In 2018 a \$5 million grant was secured from UK blood cancer charities in order to directly fund the salaries of research nurses within the IMPACT network covering 11 major UK transplant centres and a linked clinical trials hub. Critically, up-front investment into research nurses at major transplant centres created a catchment region in excess of 20 million. The pre-stated aim of the IMPACT pilot was to recruit 400 patients to 7 new transplant trials over a 4 year period.

Results

Opened in 2018 the IMPACT network has now randomized 1344 patients to 7 prospective transplant trials over a 5 year period. Trials delivered include COSI, a randomized trial examining the benefit of the addition of Thiotepa to a Fludarabine/Busulphan based conditioning regimen in patients allografted for acute myeloid leukemia (AML) (n=333) and AMADEUS a randomized comparison of the benefit of post-transplant CC486 maintenance (n=326). In conjunction with recruitment to the Pro-DLI trial- a randomized study of prophylactic DLI in patients allografted for high risk AML (n=150)- the IMPACT initiative has resulted in more than 900 patients being recruited to practice informing AML transplant trials over a 5 year period. Importantly, AMADEUS has been designed and delivered in order to generate registration enabling data. Additional trials delivered by the IMPACT network include ALL-RIC the first randomized comparison of reduced intensity conditioning regimens in acute lymphoblastic leukemia (n=102, now in follow-up) and the ongoing MoTD trial a randomized comparison of post-transplant

cyclophosphamide GVHD prophylaxis (n=139 to date). Sample return for bolt-on scientific studies has been in excess of 85% allowing prospective analysis of the prognostic significance of pre and post-transplant MRD, molecular determinants of transplant outcome and the biology of disease relapse in patients allografted for AML and ALL. Of note the IMPACT research nurse network demonstrated impressive resilience during the COVID-19 pandemic permitting continued trial delivery despite faltering recruitment to other cancer trials.

Conclusions:

The funding of a national transplant trials network has transformed recruitment to prospective randomized transplant trials in the UK. The success of the IMPACT pilot, which out-performed its recruitment metrics by 300%, confirms the importance of innovative trial delivery models in accelerating recruitment to practice informing transplant studies and is a scalable model internationally. At the same time, IMPACT has proved a highly effective mechanism to generate linked translational data with the ability to inform future trial design. Building on similar models in Europe, such as LYSARC, the IMPACT network is now funded by a not-for-profit trials delivery vehicle Accelerating Clinical Trials Ltd (www.act4patients.com) creating a financially sustainable model within the UK for the delivery of a mixed portfolio of industry sponsored and investigator initiated transplant and cell therapy trials.

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