A recent report from the USA Children’s Oncology Group (COG) acute myeloid leukaemia (AML)0531 trial1 described a surprisingly marked improvement in survival outcomes for children with (KMT2A)-rearranged AML who received gemtuzumab ozogamicin (GO) with induction chemotherapy compared with those who did not. As these rearrangements occur in approximately 5–10% of adults with AML,2 we examined the outcomes of patients with KMT2A-rearrangements in the UK Medical Research Council (MRC) AML15 and AML16 trials, which predominantly enrolled adults (up to and over the age of 60 years respectively) and included a randomisation between administration of GO or not with induction chemotherapy.

The major outcomes of these trials have been previously reported3,4 and meta-analysis (n = 2228 patients) showed benefit of GO in patients with favourable- and intermediate-but not adverse-risk cytogenetics.4 These findings were confirmed in a subsequent meta-analysis of five randomised trials of GO in patients with newly diagnosed AML.5 Patients with KMT2A-rearrangements fall in the intermediate- or adverse-risk cytogenetic groups depending on the fusion partner.

The GO dosing schedules were comparable between the AML0531 and AML15/16 studies, using a single dose of 3 mg/m² in cycle one with some patients in AML15 and AML0531 receiving a second dose in cycle three.

In AML15, 908 patients with available cytogenetics were randomised to receive or not one dose of GO with induction cycle one, and 38 of these (4.2%) had a KMT2A-rearrangement. In AML16, there were a further eight of 866 (1%) for a total of 46 patients with a KMT2A-rearrangements participating in a GO randomisation. The majority of these (41/46, 89%) were in the intermediate-risk cytogenetic group according to the MRC cytogenetic classification6 (this differs from the European Leukaemia Network classification, which places more KMT2A-rearranged patients in the adverse-risk group).7 The median (range) age of these patients was 39.5 (6–720) years (one patient was aged <16 years).

The 5-year relapse-free survival (RFS) for patients with KMT2A-rearrangements who did and did not receive GO was 45% and 36% respectively [hazard ratio (HR) 0.91, 95% confidence interval (CI) 0.81–1.02, P = 0.8, Fig 1]. This is in contrast to the results of the paediatric cohort reported by Pollard et al.,1 who identified a very large effect of GO in children with KMT2A-rearrangements: 5-year disease-free survival for patients achieving complete remission (CR) after course one of therapy in this study was 57% and 33% respectively, for a HR of 0.50 (95% CI 0.32–0.78,

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**Fig 1.** Relapse-free survival for patients with (KMT2A)-rearranged acute myeloid leukaemia (AML) treated in the UK Medical Research Council AML15 and AML16 trials who were randomised to receive one dose of gemtuzumab ozogamicin (GO) in induction or no GO. CR, complete remission.
While the effect on survival was marginally non-significant (HR 0.66, 95% CI 0.44–1.01, P = 0.056), the CIs are wide and the result here is inconclusive, with either a minimal or a large effect of GO on survival both within the range of the CI.

The effect of GO on outcome according to cytogenetic group in AML15 and AML16 is shown in Fig 2. Importantly, while there was a significant interaction between KMT2A-rearranged and other intermediate-risk cytogenetics for achievement of CR (P = 0.03 for interaction, i.e. patients with KMT2A-rearrangements receiving GO had a lower rate of CR), there was no heterogeneity in the effect of GO on RFS or overall survival (OS) between KMT2A-rearranged and other intermediate-risk groups.

Comparing patients with KMT2A-rearrangements and those with favourable-risk cytogenetics (who had the greatest benefit from GO in meta-analysis) showed a significant interaction for CR (P = 0.008) and OS (P = 0.04), indicating that patients with favourable-risk cytogenetics benefit more from GO than patients with KMT2A-rearrangements. However, there was no evidence of heterogeneity for RFS (P = 0.6). In the cohort there were 22 transplants (GO n = 10; no GO n = 12), of which 13 were in first remission; analyses here showed results consistent with the whole cohort (HR for RFS censored at transplant 0.73, 95% CI 0.27–1.96, P = 0.5; OS censored at transplant HR 1.80, 95% CI 0.55–5.87, P = 0.3).

Overall, these data show that in a predominantly adult cohort, the effect of GO in patients with a KMT2A-rearrangement is clearly smaller than that seen in a paediatric cohort, and also smaller than that seen in adults with favourable-risk cytogenetics. On the other hand, there is no evidence that the effect of GO in patients with KMT2A-rearrangements is different to that in patients with other intermediate-risk cytogenetics, who benefit from the addition of GO (HR 0.85, 95% CI 0.74–0.96).

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Author contributions

Alan K. Burnett and Nigel H. Russell performed the research. Robert K. Hills performed the statistical analyses. Richard
Correspondence

Dillon wrote the first draft of the manuscript. All authors contributed to the final manuscript.

Richard Dillon1,2
Robert K. Hills3
Alan K. Burnett4
Nigel H. Russell2,5

1Department of Medical and Molecular Genetics, King’s College, 2Department of Haematology, Guy’s Hospital, London, 3Nuffield Department of Population Health, University of Oxford, Oxford, 4Blackwaterfoot, Isle of Arran and 5Nottingham University Hospital, Nottingham, UK.

E-mail: nigel.russell@nottingham.ac.uk

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The future of myeloma research in Canada and beyond: results of a James Lind Alliance priority setting partnership

Multiple myeloma, often referred to as myeloma, is an incurable cancer of the plasma cells which accumulate in the bone marrow and produce monoclonal protein resulting in hypercalcaemia, renal insufficiency, anaemia and bone deterioration.1 To complicate matters further, both the disease and its treatment can impair organ function, sometimes in similar ways, contributing to significant disease burden, which can impair the quality of life for those living with myeloma.1

This is problematic given the growing incidence of the disease; between 1996 and 2016, the global incidence of myeloma increased by 126%.1 Simultaneously, research into treatment options for myeloma has led to people living longer.2 However, since there is currently no cure for myeloma, future research is needed to advance the diagnosis, treatment and management of myeloma and improve the quality of life of those living with this disease.

Studies have shown that the uptake of new research evidence into clinical practice is not immediate, nor direct; on the contrary, the process can take years and, even then, not all evidence becomes part of practice. One factor contributing to this gap is the lack of communication between research authors and research users.2,3 Understanding what is important to those directly affected by the condition being studied — by involving these key stakeholders prior to conducting research — is one way of bridging this divide.4–6

One such approach is the James Lind Alliance (JLA) Priority Setting Partnership (PSP), which seeks to foster greater alignment between differing research agendas by bringing together patients, caregivers and clinicians to determine research priorities.7 Past PSPs have highlighted how research users and research authors often have diverging priorities: for example, alternative interventions and therapies versus drug-centred treatments.8 At the same time, research priorities identified through previous PSPs have often been successful in obtaining funding from government agencies or charitable foundations. This has encouraged researchers to focus on questions most important to research users through competitions and funding opportunities.9–11

Established in 2019, our project on the future of myeloma research in Canada builds upon the successes of previous PSPs (for more information the project, visit: https://www.jla.nihr.ac.uk/priority-setting-partnerships/myeloma/). Faithful to JLA guidelines, we assembled a pan-Canadian steering group composed of people living with myeloma, caregivers and clinicians. Together, these members guided all four phases of the iterative priority setting process, which are described below. Informed consent was obtained from