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Response to Comment on: Selection of unrelated donors for allogeneic transplantation using post-transplant cyclophosphamide in acute lymphoblastic leukemia: an analysis by the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation

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Competing interests

The authors declare no competing interests.

We thank the correspondents for their thoughtful comments on our report comparing outcomes after 7/8 mismatched unrelated donors (MMUD) and 8/8 matched unrelated donors (MUD) in adults with ALL receiving PTCy-based GVHD prophylaxis.[1]

While it is crucial to assess the impact of specific HLA mismatches in the context of modern PTCy-based GVHD prophylaxis, the literature remains heterogeneous and sometimes contradictory, even for HLA-B leader dimorphism, peptide-binding motif mismatches, and HLA-A/HLA-B mismatches.[2,3,4] Variability in prophylaxis regimens and heterogeneity in patient, disease, and transplant characteristics likely contribute to these inconsistencies and constrain direct comparisons with our ALL-specific PTCy cohort.

Our study addressed a pragmatic question: when a fully matched donor is unavailable, is a 7/8 MMUD a reasonable alternative in the PTCy setting for ALL?[5] Given registry constraints, we prespecified pooling of 7/8 MMUD rather than stratification by locus. Within this framework, and after multivariable adjustment, outcomes were comparable between 7/8 MMUD and 8/8 MUD, indicating that MMUD should not be excluded *a priori* when PTCy is used. Rather, other donor-related variables, particularly CMV serostatus, donor age, and donor–recipient sex mismatch, may exert prognostic effects that equal or exceed those of a single HLA mismatch and therefore should be carefully considered in donor selection.

We encourage further research aimed at defining optimal HLA compatibility in the PTCy era, preferably using large, prospectively collected cohorts, standardized transplant platforms, and comprehensive HLA data. We recognize that this will be challenging given procedural heterogeneity, varied disease indications, and multiple other confounders. We share the call for greater granularity to enable adequately powered analyses that may define “permissible” mismatches. Until such data mature, we believe that our findings support cautious, case-by-case inclusion of 7/8 MMUD when an 8/8 MUD is unavailable, while optimizing the aforementioned donor factors.

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