**BACKGROUND**

- Acute myeloid leukemia (AML) is characterized by poor patient outcomes and accounts for approximately 25% of all leukemia cases and 1.1% of all new cancer cases in the US [1].
- A potentially curative treatment option is allogeneic hematopoietic stem cell transplantation (allo-HSCT), however, it is accompanied with risk of serious complications including graft-versus-host disease (GVHD) and death [2].
- In the past, allo-HSCT has been generally limited to fully matched human leukocyte antigen (HLA: 8/8) related or unrelated donors to minimize the risk of serious complications [3].
- In the US, between 25-81% of patients, based on baseline characteristics including race, will be unable to find an HLA-matched (8/8) donor [4]. Mismatching at one of the loci (7/8 HLA, for instance) reduces the 5-year overall survival rate by approximately 8% but may still be considered the best course as non-transplantation therapy offers little chance of a cure [4].
- Donor stem cells come from three primary sources: bone marrow (BM), peripheral blood (PB) and umbilical cord blood (UCB) [5]. However, limited data exists comparing safety outcomes by graft source.

**OBJECTIVES**

We reviewed published evidence to assess complications associated with mismatched allo-HSCT in AML patients by graft source.

**RESULTS**

- A total of 1,335 records were identified in the search and underwent subsequent screening resulting in 8 studies that satisfied inclusion criteria.
- Baseline characteristics in each population were generally comparable (Table 1).
- GVHD prophylaxis regimens varied across studies.
- The incidence of grade III-IV acute GVHD events in AML allo-HSCT patients was comparable between different mismatched graft sources (Figure 2).
- While no cases of moderate-severe chronic GVHD at 24 months was reported for patients transplanted with UM171-expanded UCB, other mismatched graft sources had a 6.5% to 19% incidence of moderate-severe chronic GVHD (Figure 3).
- Non-relapse mortality (NRM) at 24 months was lower for UM171-expanded-UCB compared to most, but not all, other mismatched graft sources.
- A decreased risk of GVHD would likely contribute to a reduced humanistic burden in this subpopulation as well as greater quality of life. Moreover, allo-HSCT strategies that entail a reduction in complications and improved safety outcomes could potentially be used in patients who would have previously been considered unfit for allo-HSCT, offering this subset of patients a chance of curative treatment, which would be unlikely with non-transplant strategies.
- This would also have the potential to expand allo-HSCT access for minority groups who typically have a reduced probability of identifying HLA-matched graft sources.
- Additional investigation, ideally in the form of a randomized clinical trial, would provide more robust evidence and potentially validate the relative safety outcomes identified in this naïve comparison.

**CONCLUSIONS**

- Patients treated with UM171-expanded-UCB grafts experienced the lowest rates of NRM and moderate-severe chronic GVHD at 24 months relative to UCB and other mismatched graft sources identified in the SLR.
- Additionally, rates of grade III/IV acute GVHD were lower in UM171-expanded-UCB grafts compared to most, but not all, other sources identified.

**LIMITATIONS**

- One limitation of the comparisons was the absence of statistical adjustment for differences in patient characteristics between each study’s population.
- Heterogeneous populations could affect outcome comparisons through confounding variables.
- Further comparisons between allo-HSCT AML patients treated with graft sources, ideally, would be adjusted with patient-level data, if available, in order to validate the results observed in the naïve comparisons or substantiated with controlled clinical trials.

**MATERIALS & METHODS**

- Embase®, MEDLINE®, Cochrane databases and conference abstracts (ASCO, ASH) were systematically reviewed in November of 2018.
- Non-English studies were excluded and the search was conducted for studies published 2008-2018.
- AML patients were the population of interest and the desired intervention was mismatched (8/8) allo-HSCT.
- Safety outcomes including complications such as non-relapse mortality (NRM) and acute and chronic GVHD were deemed relevant.
- Only studies that were interventional and prospective in nature were accepted in subsequent screening steps.
- Studies that were retrospective in nature or non-interventional were excluded along with case reports, case series and case studies in order to limit the potential bias often found in smaller studies.
- Each abstract identified in the search underwent review by two independent analysts who used PICOB criteria (Patient, Intervention/Comparators, Outcomes, Study Design) in their screening.
- All discrepancies between analysts were resolved through roundtable discussion with a third analyst.
- All results were recorded using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagrams (Figure 1).

**REFERENCES**


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