Allogeneic hematopoietic cell transplantation with non-myeloablative conditioning for patients with hematologic malignancies: improved outcomes over two decades

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SUPPLEMENTARY DATA FOR

Allogeneic hematopoietic cell transplantation with non-myeloablative conditioning for patients with hematologic malignancies: Improved outcomes over two decades

Running title: Improved outcomes for non-myeloablative allo-HCT

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SUPPLEMENTAL ITEMS

Table S1. Transplant conditioning regimen and GVHD prophylaxis protocol numbers and the corresponding ClinicalTrials.gov registry identifiers.

Table S2. Comparison of major endpoints in two most recent transplant eras.

Table S3. Comparison of incidences of organ complications and infections in two most recent transplant eras.
Table S1. Transplant conditioning regimen and GVHD prophylaxis protocol numbers and the corresponding ClinicalTrials.gov registry identifiers.

| Protocol Number | ClinicalTrials.gov Identifier |
|-----------------|-------------------------------|
| 1209.00         | NCT00003145                   |
| 1225.00         | NCT00003196                   |
| 1383.00         | NCT00003954                   |
| 1406.00         | NCT00005801                   |
| 1409.00         | NCT00005803                   |
| 1463.00         | NCT00005799                   |
| 1533.00         | NCT00006251                   |
| 1581.00         | NCT00036738                   |
| 1596.00         | NCT00014235                   |
| 1623.00         | NCT00031655                   |
| 1641.00         | NCT00027820                   |
| 1654.00         | NCT00045435                   |
| 1668.00         | NCT00078858                   |
| 1711.00         | NCT00060424                   |
| 1732.00         | NCT00052546                   |
| 1813.00         | NCT00075478                   |
| 1840.00         | NCT00104858                   |
| 1898.00         | NCT00099011                   |
| 1938.00         | NCT00105001                   |
| 1954.00         | NCT00110058                   |
| 2056.00         | NCT00397813                   |
| 2070.00         | NCT00793572                   |
| 2430.00         | NCT01252667                   |
| 2448.00         | NCT01231412                   |
| 2546.00         | NCT01527045                   |

Abbreviations: GVHD, graft-versus-host disease.
Table S2. Comparison of major endpoints in two most recent transplant eras.

| Endpoints                              | 2004 – 2009 | 2010 – 2017 |
|-----------------------------------------|-------------|-------------|
| **Overall survival**                    | 1.0         | 0.83 (0.7 – 1.0) | .03 |
| **Progression-free survival**           | 1.0         | 0.81 (0.7 – 0.9) | .007 |
| **Relapse/progression**                 | 1.0         | 0.76 (0.6 – 0.9) | .01 |
| **Non-relapse mortality**               | 1.0         | 0.89 (0.7 – 1.1) | .32 |
| **Relapse-related mortality**           | 1.0         | 0.94 (0.7 – 1.2) | .61 |
| **Acute GVHD grade 2 – 4**              | 1.0         | 0.79 (0.7 – 0.9) | .005 |
| **Acute GVHD grade 3 – 4**              | 1.0         | 0.80 (0.5 – 1.2) | .26 |
| **Chronic GVHD**                        | 1.0         | 0.97 (0.8 – 1.1) | .72 |

Abbreviations: HR, hazard ratio; CI, confidence interval; GVHD, graft-versus-host disease; MM, multiple myeloma; AML, acute myeloid leukemia; CMV, cytomegalovirus; R, recipient; D, donor; HCT, hematopoietic cell transplantation; HCT-CI, hematopoietic cell transplantation comorbidity index.

*aAdjusted for transplant center (stratification); treatment type (on-protocol, off-protocol), age (≤ 49, 50 – 59, ≥ 60 years); disease risk group (low, standard, high); MM diagnosis; AML diagnosis; CMV (R– and D–, R+ or D+); donor relation (related, unrelated); sex mismatch (female to male, others); prior HCT (no, yes); allele mismatch (no, yes); HCT-CI (0, 1 – 2, 3, ≥ 4, missing).

*bRelapse-related mortality refers to survival after relapse among patients that relapsed.
### Table S3. Comparison of incidences of organ complications and infections in two most recent transplant eras.

| Organ Toxicity                  | HR (95% CI) | P    |
|---------------------------------|-------------|------|
| **Bilirubin > 4 mg/dL**         |             |      |
| 2004–2009 1.0                   |             |      |
| 2010–2017 0.84 (0.5–1.2) .34    |             |      |
| **Bilirubin > 10 mg/dL**        |             |      |
| 2004–2009 1.0                   |             |      |
| 2010–2017 1.16 (0.5–3.0) .76    |             |      |
| **Creatinine > 2x baseline**    |             |      |
| 2004–2009 1.0                   |             |      |
| 2010–2017 1.13 (0.9–1.5) .36    |             |      |
| **Infections**                  |             |      |
| Gram-negative bacteremia        |             |      |
| 2004–2009 1.0                   |             |      |
| 2010–2017 0.83 (0.7–1.0) .03    |             |      |
| Invasive fungal infection       |             |      |
| 2004–2009 1.0                   |             |      |
| 2010–2017 0.84 (0.7–1.0) .05    |             |      |
| CMV antigenemia<sup>b</sup>     |             |      |
| 2004–2009 1.0                   |             |      |
| 2010–2017 0.75 (0.6–0.9) .004   |             |      |
| CMV disease<sup>b</sup>         |             |      |
| 2004–2009 1.0                   |             |      |
| 2010–2017 0.77 (0.6–1.0) .02    |             |      |

Abbreviations: OR, odds ratio; HR, hazard ratio; CI, confidence interval; MM, multiple myeloma; AML, acute myeloid leukemia; R, recipient; D, donor; HCT, hematopoietic cell transplantation; HCT-CI hematopoietic cell transplantation comorbidity index.

<sup>a</sup>Adjusted for transplantation center; treatment type (protocol, treatment plan); age (≤49, 50–59, ≥60 years); disease risk group (low, standard, high); MM diagnosis; AML diagnosis; CMV (R– and D–, R+ or D+); donor relation (related, unrelated); sex mismatch (female to male, others); prior HCT (no, yes); allele mismatch (no, yes); and HCT-CI (0, 1–2, 3, ≥4, missing).

<sup>b</sup>CMV endpoints evaluated only among seropositive recipients at HCT.