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# Supplemental data

# Allogeneic hematopoietic cell transplantation in older myelofibrosis patients: a study of the Chronic Malignancies Working Party of EBMT and the Spanish Myelofibrosis Registry

**Table S1**. Baseline characteristics of 556 myelofibrosis patients aged 65 years or older undergoing allogeneic hematopoietic cell transplantation.

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **No. evaluable cases** |  |
| Age, yrs\* | 556 | 67 (65-76) |
| Male sex | 556 | 380 (68) |
| KPS < 90% | 498 | 211 (42) |
| HCT-CI ≥ 3 | 427 | 127 (30) |
| Year of transplant | 556 |  |
| 2000-2009 |  | 73 (13) |
| 2010-2017 |  | 483 (87) |
| Female donor to male recipient | 556 | 106 (19) |
| CMV serostatus patient/donor | 535 |  |
| +/+ |  | 219 (41) |
| +/- |  | 119 (22) |
| -/+ |  | 45 (8) |
| -/- |  | 152 (29) |
| Myeloablative conditioning | 556 | 141 (25) |
| Type of conditioning | 552 |  |
| Busulfan-based |  | 369 (67) |
| Melphalan-based |  | 78 (14) |
| Others |  | 105 (19) |
| Graft source | 556 |  |
| Peripheral blood |  | 525 (94) |
| Bone marrow |  | 25 (5) |
| Cord blood |  | 5 (1) |
| Donor type | 554 |  |
| Syngeneic |  | 1 (0) |
| HLA-matched related |  | 134 (24) |
| HLA-mismatched related |  | 5 (1) |
| Haploidentical |  | 22 (4) |
| HLA-matched unrelated |  | 255 (46) |
| HLA-mismatched unrelated |  | 71 (13) |
| Unrelated, HLA-match unknown |  | 61 (11) |
| Cord blood |  | 5 (1) |
| ATG | 552 | 371 (67) |
|  |  |  |

Data are given as frequency (%) except otherwise specified. Percentages are calculated over the number of patients who had the data.

KPS: Karnofsky Performance Status.

HCT-CI: Hematopoietic Cell Transplantation-specific Comorbidity Index.

ATG: antihuman T-lymphocyte immunoglobulin.

\* Median (range).

**Table S2**. Factors associated with increased risk of non-relapse mortality and disease relapse after HCT in myelofibrosis patients aged 65 years or older. Both risks were estimated in the setting of competing events.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Non-relapse mortality** | | |  | **Disease relapse** | | |
| **Covariate** | **No. patients** | **SHR (95% CI)** | **p** |  | **No. patients** | **SHR (95% CI)** | **p** |
| Year < 2010 | 556 | 1.26 (0.87 - 1.81) | 0.22 |  | 540 | 1.32 (0.83 - 2.12) | 0.24 |
| Age ≥ 68 yrs | 556 | 0.96 (0.73 - 1.26) | 0.77 |  | 540 | 0.76 (0.51 - 1.13) | 0.17 |
| Male sex | 556 | 1.13 (0.84 - 1.51) | 0.43 |  | 540 | 0.95 (0.63 - 1.42) | 0.79 |
| Primary myelofibrosis | 556 | 1.02 (0.76 - 1.38) | 0.88 |  | 540 | 0.82 (0.55 - 1.23) | 0.33 |
| DIPSS high risk | 241 | 0.85 (0.54 - 1.36) | 0.51 |  | 236 | 1.06 (0.58 - 1.95) | 0.85 |
| *JAK2* + | 338 | 2.11 (1.05 - 4.25) | **0.036** |  | 331 | 1.21 (0.55 - 2.64) | 0.64 |
| *CALR* + | 338 | 0.52 (0.22 - 1.24) | 0.14 |  | 331 | 0.70 (0.27 - 1.85) | 0.47 |
| *MPL* + | 338 | 0.18 (0.02 - 1.41) | 0.1 |  | 331 | 0.89 (0.21 - 3.81) | 0.88 |
| Triple negative | 338 | 0.69 (0.19 - 2.52) | 0.57 |  | 331 | 1.71 (0.42 - 6.89) | 0.45 |
| HCT-CI ≥ 3 | 427 | 1.28 (0.92 - 1.78) | 0.14 |  | 416 | 1.08 (0.67 - 1.76) | 0.74 |
| Karnofsky index < 90 | 498 | 1.27 (0.95 - 1.71) | 0.1 |  | 483 | 0.84 (0.55 - 1.27) | 0.4 |
| Prior ruxolitinib | 556 | 0.98 (0.72 - 1.35) | 0.91 |  | 540 | 0.74 (0.45 - 1.22) | 0.24 |
| MAC vs. RIC | 556 | 0.96 (0.71 - 1.31) | 0.82 |  | 540 | 0.83 (0.52 - 1.33) | 0.44 |
| Busulfan conditioning | 552 | 0.63 (0.48 - 0.82) | **0.001** |  | 536 | 1.38 (0.90 - 2.11) | 0.14 |
| Female donor/male patient | 556 | 1.01 (0.73 - 1.41) | 0.94 |  | 540 | 1.18 (0.75 - 1.86) | 0.46 |
| CMV patient+/donor- | 556 | 1.86 (1.38 – 2.52) | **< 0.001** |  | 540 | 1.15 (0.74 - 1.82) | 0.52 |
| HLA mismatched | 556 | 0.95 (0.71 - 1.27) | 0.73 |  | 540 | 0.96 (0.63 - 1.46) | 0.83 |
| Matched, unrelated | 389 | 1.27 (0.90 - 1.78) | 0.18 |  | 379 | 0.50 (0.32 - 0.78) | **0.002** |
| Source: BM vs. PB | 531 | 1.28 (0.26 - 6.37) | 0.76 |  | Non evaluable | | |
| ATG use | 552 | 0.98 (0.74 - 1.30) | 0.88 |  | 536 | 0.77 (0.52 - 1.15) | 0.20 |

SHR: sub-hazard ratio.

Numbers in bold are those with a significant p value on the statistical analysis (p<0.05).

**Table S3.** Main features of myelofibrosis patients aged 65 or older treated with allo-HCT or non-transplant approaches.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Non-transplant  (n=176) | Allo-HCT  (n=556) | p |
| Age, median (IQR) | 72 (69-74) | 67 (66-69) | < 0.001 |
| Age ≥ 70 yrs | 117 (66%) | 87 (16%) | < 0.001 |
| Sex, male | 106 (60%) | 380 (68%) | 0.047 |
| Primary myelofibrosis | 118 (60%) | 398 (72%) | 0.25 |
| Mutational status\* |  |  |  |
| *JAK2+* | 92 (52%) | 290 (52%) |  |
| *CALR+* | 11 (6%) | 28 (5%) |  |
| *MPL+* | 0 | 13 (2%) |  |
| Triple negative | 0 | 7 (1%) |  |
| Incomplete study | 73 (42%) | 218 (40%) |  |
| DIPSS |  |  |  |
| Low | 0 | 2 (1%) |  |
| Intermediate-1 | 0 | 40 (16%) |  |
| Intermediate-2 | 235 (79%) | 106 (44%) |  |
| High | 61 (21%) | 93 (39%) |  |
| Exposition to ruxolitinib | 45 (25%) | 126 (23%) | 0.43 |
| Follow-up, yrs |  |  |  |
| Median (95 % CI) | 4.6 (3.1 -5.3) | 3.4 (1.9-5.6) | 0.10 |
| Deaths | 99 (56%) | 306 (55%) |  |
| Estimated survival |  |  |  |
| Median (95% CI) | 3.3 (2.7-4.0) | 2.1 (1.4-3.3) |  |
| At 1 year | 79% (73-85) | 59% (54-63) |  |
| At 2 years | 69% (61-76) | 49% (46-55) |  |
| At 5 years | 33% (25-42) | 40% (35-45) |  |
| At 7 years | 19% (11-28) | 32% (26-37) |  |
| At 10 years | 7% (2-17) | 24% (17-33) |  |

**Table S4**. Adjusted association of presenting features with increased mortality in patients with myelofibrosis, aged 65 to 76 years, classified within the intermediate-2 and high risk DIPSS categories, and managed without HCT

|  |  |  |
| --- | --- | --- |
| **Feature** | **Hazard ratio (95% CI)** | **p** |
| Male sex | 2.01 (1.31 – 3.08) | 0.001 |
| Age (per year) | 1.05 (0.99 – 1.12) | 0.09 |
| High vs. intermediate-2 DIPSS categories | 0.99 (0.58 – 1.07) | 0.98 |

**Figure S1**. Unadjusted association between patient and procedure characteristics and risk of mortality after allo-HCT in 556 myelofibrosis patients aged 65 years or older.



a HCT-CI: hematopoietic cell transplant-comorbidity index.

b MAC: myeloablative conditioning *vs* RIC: reduced intensity conditioning.

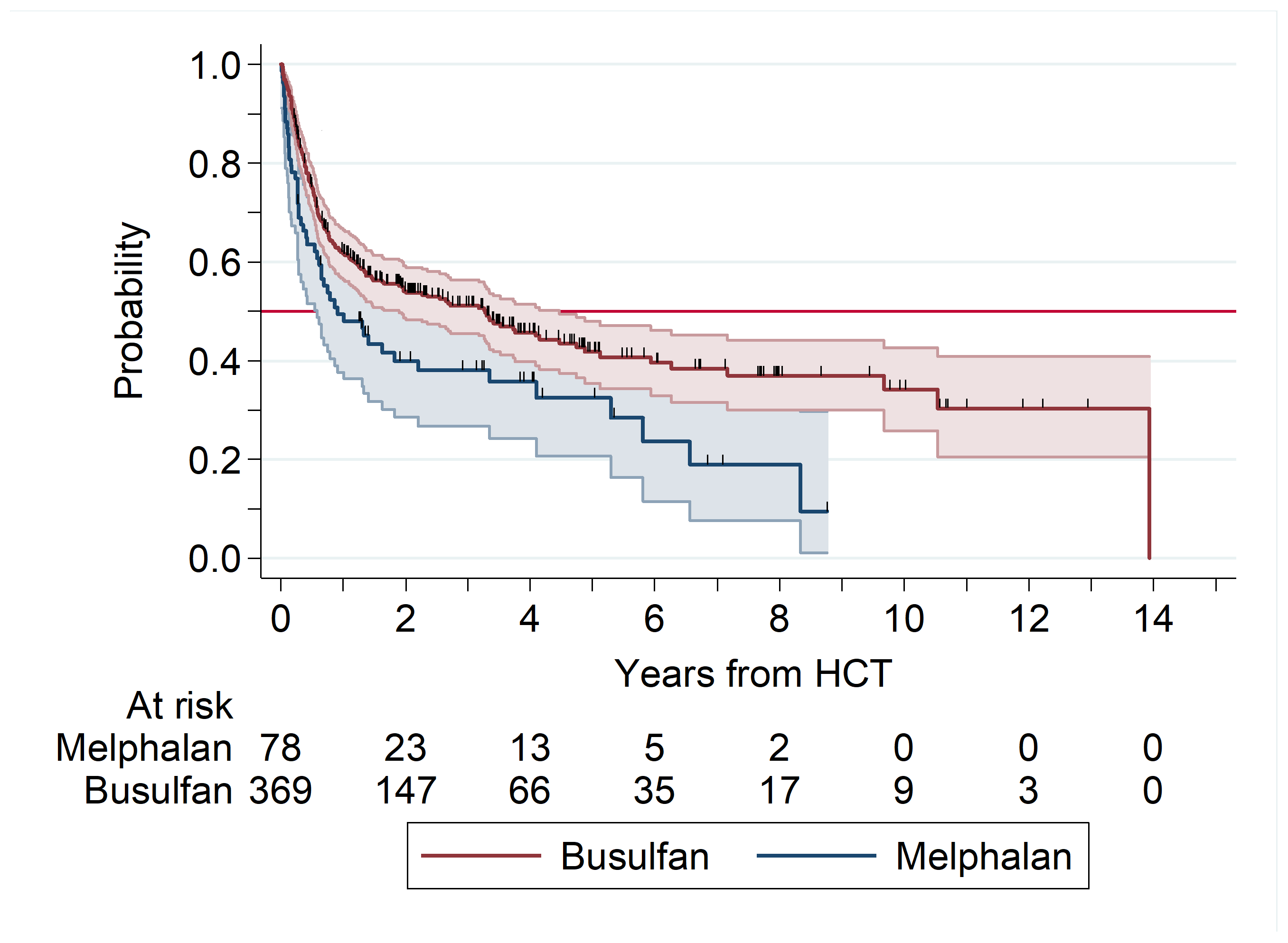
c Busulfan *vs* any other conditioning regimen.

d CMV serostatus patient-positive/donor-negative.

e Bone marrow *vs* peripheral blood.

GVHD: graft-versus-host disease.

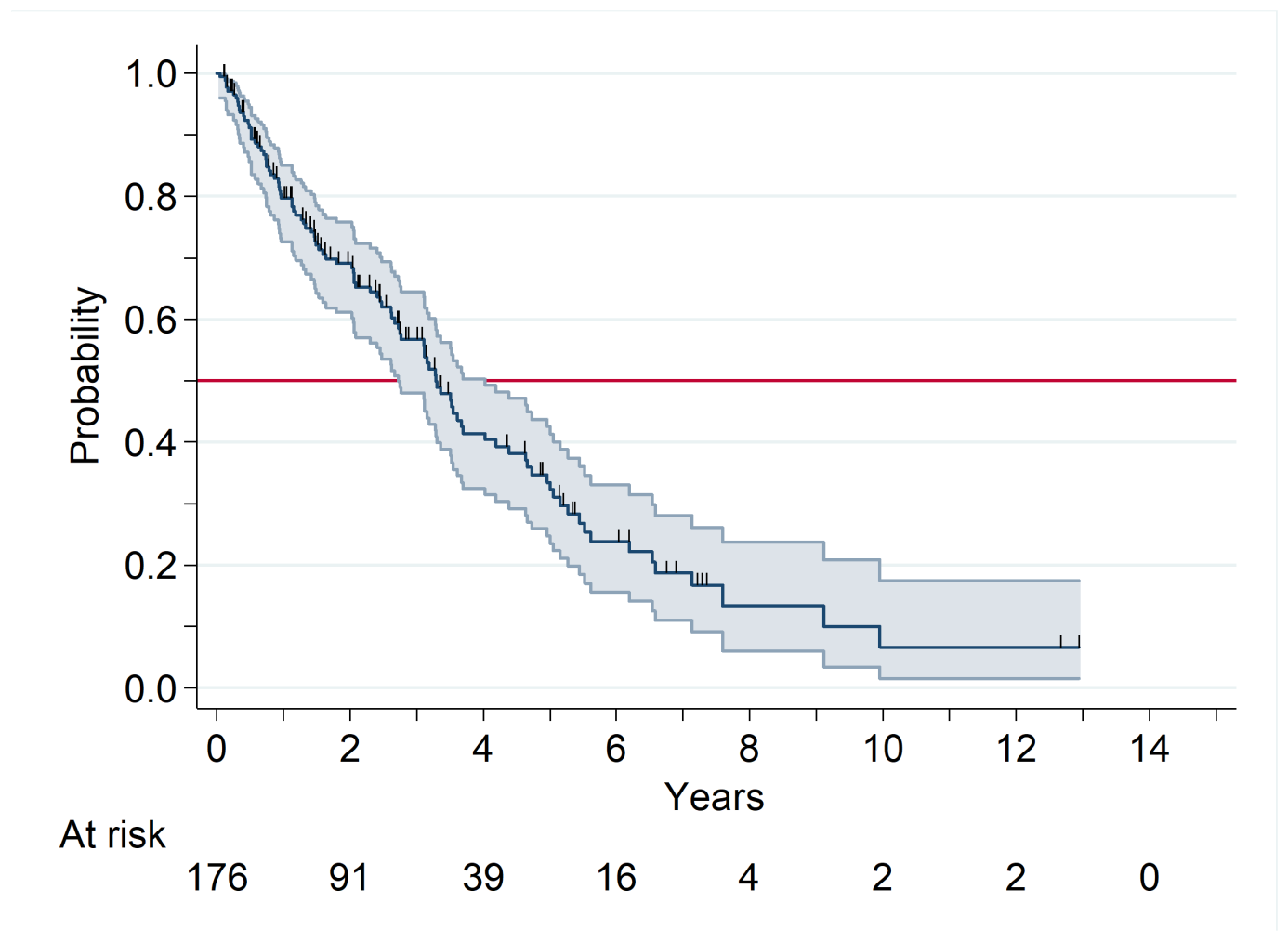
**Figure S2.** Estimated survival after allo-HCT in myelofibrosis patients aged 65 years or older according to the conditioning regimen (busulfan-based vs.melphalan-based).



**Figure S3**. Cumulative incidence of relapse/progression and competing death without relapse/progression. Shaded areas represent the 95% CI .

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**Figure S4**. Estimated survival in 176 myelofibrosis patients aged 65 to 76 years who were assigned to the intermediate-2 or high risk DIPSS categories at diagnosis and were managed with non-transplant treatment.

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