

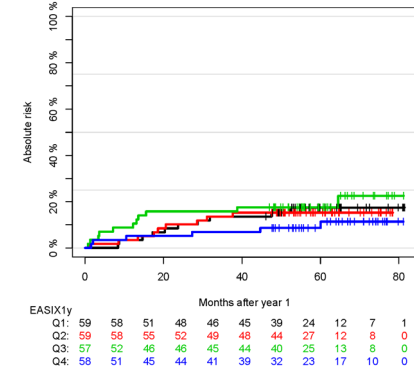
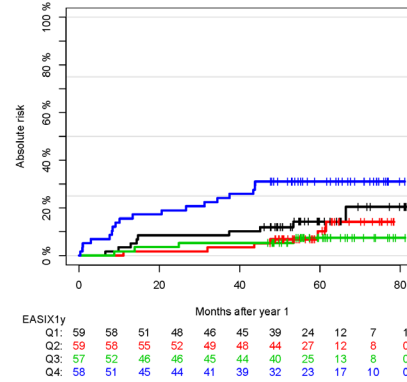
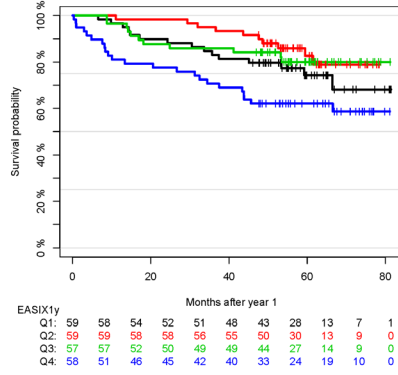
Suppl. Figure 1

OS

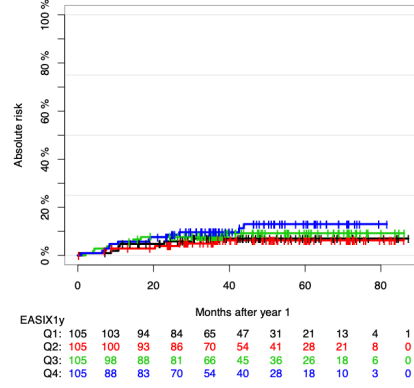
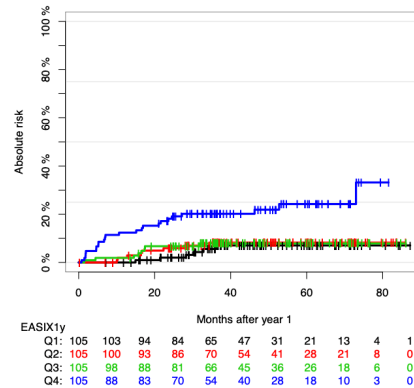
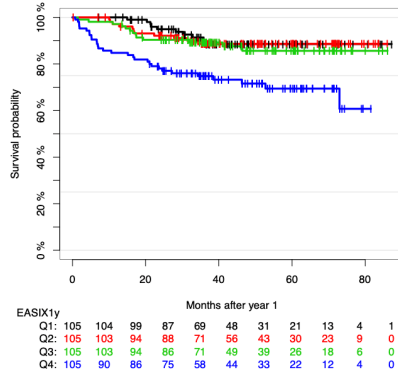
NRM

TTR

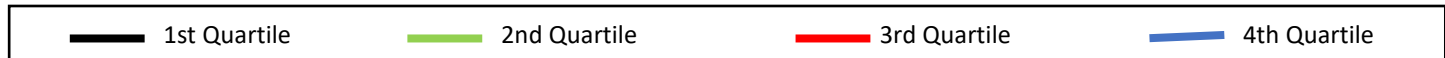
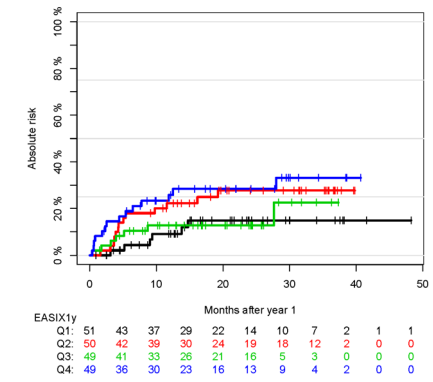
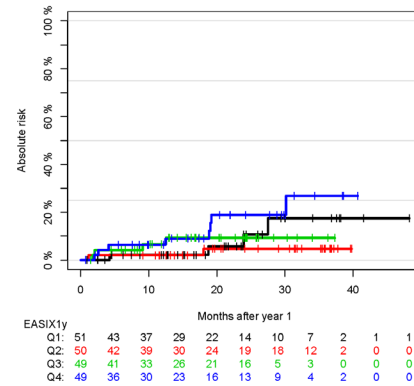
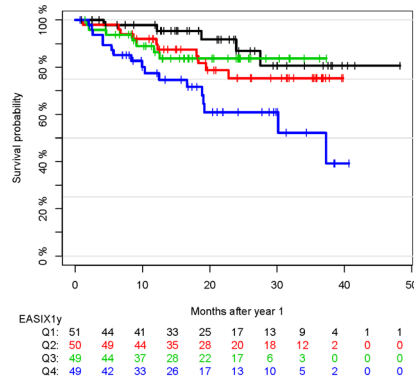
Essen



Seattle



Berlin



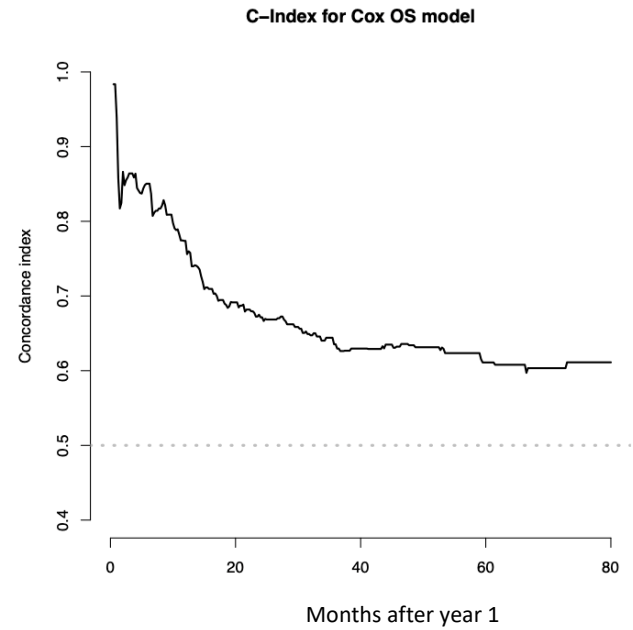
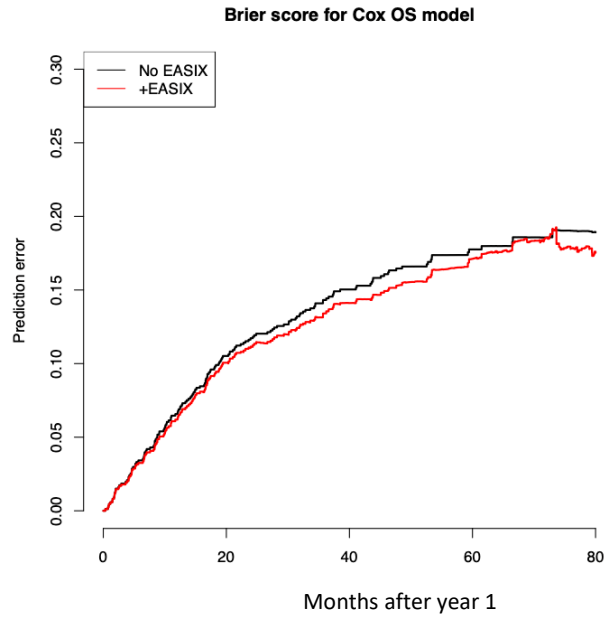
Legend suppl. Figure 1:

EASIX-1year predicts non-relapse mortality in patients surviving without disease progression for 1 year after allogeneic stem cell

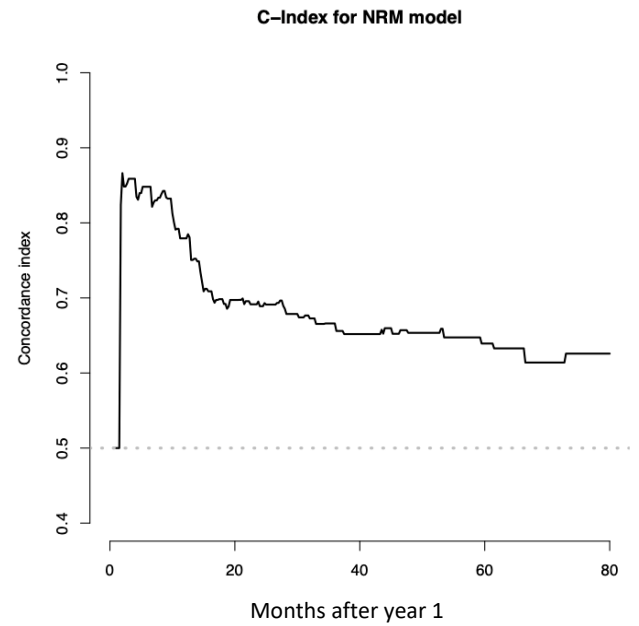
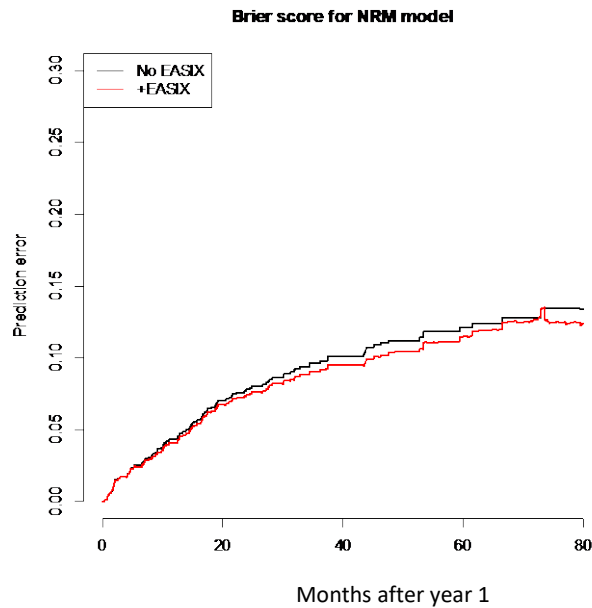
Kaplan-Maier curves for overall survival (OS) and cumulative incidences of non-relapse mortality (NRM) and time to relapse (TTR) according to EASIX quartiles raised 1 year after alloSCT in patients without relapse.

The three individual cohorts combined as one validation cohort in **Figure 1B** are shown

A) OS



B) NRM



Legend suppl. Figure 2:

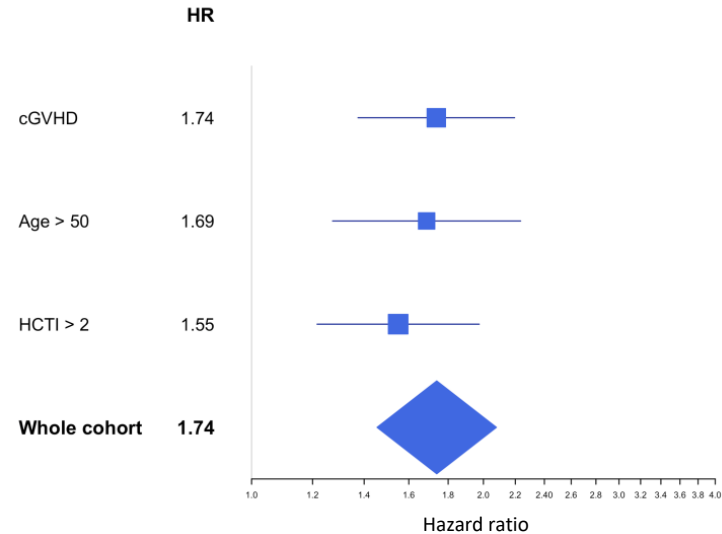
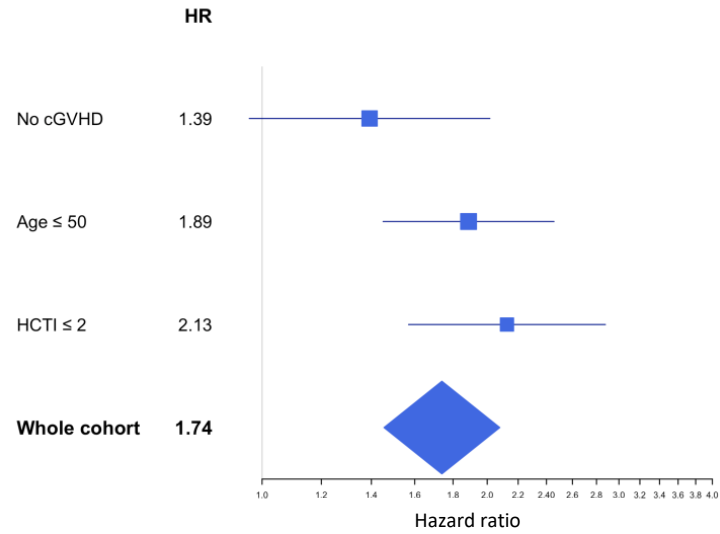
EASIX-1year is a validated predictor of non-relapse mortality and overall survival in patients surviving without disease progression for 1 year after allogeneic stem cell

Brier score and c-index analyses for the validation cohort with off-set of the training cohort revealed a predictive impact of EASIX-1year on both, OS and NRM, validating the univariable model (lower prediction errors and higher c-indices with the model including EASIX).

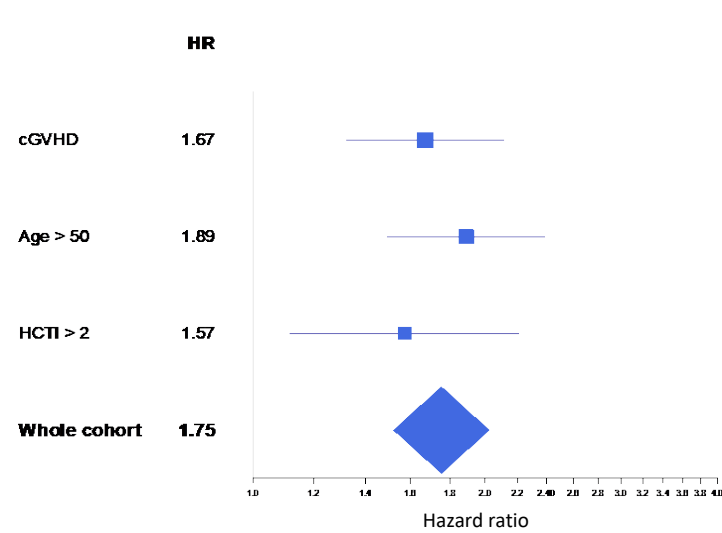
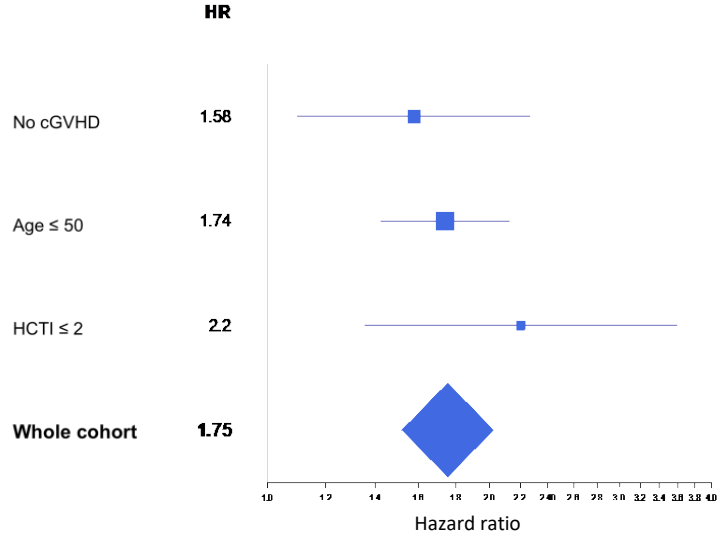
Suppl. Figure 3A

Meta-analyses of the predictive value of EASIX-1y as continuous variable (per log2) for **NRM**.

training



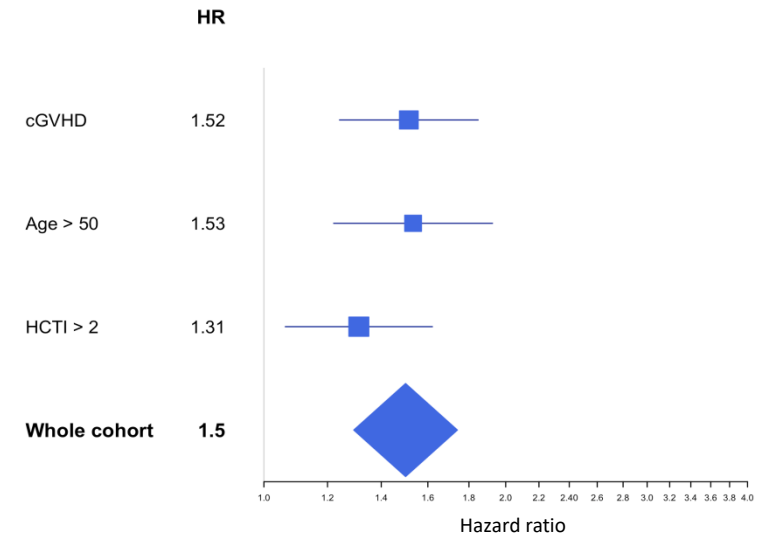
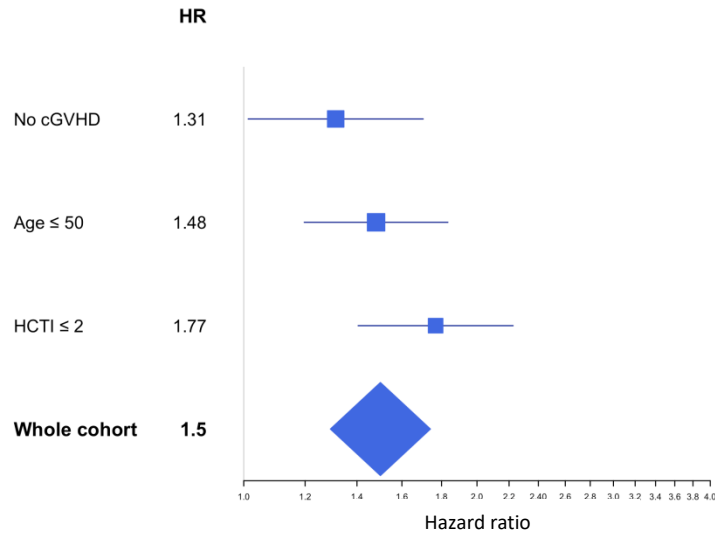
validation



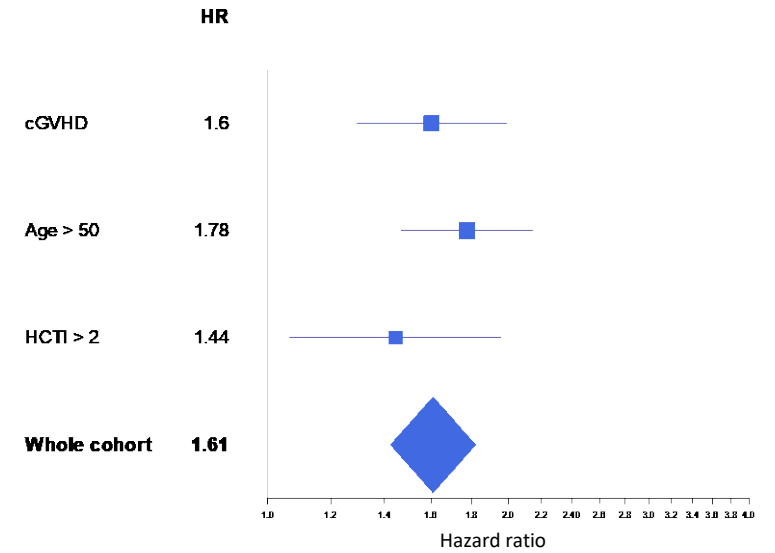
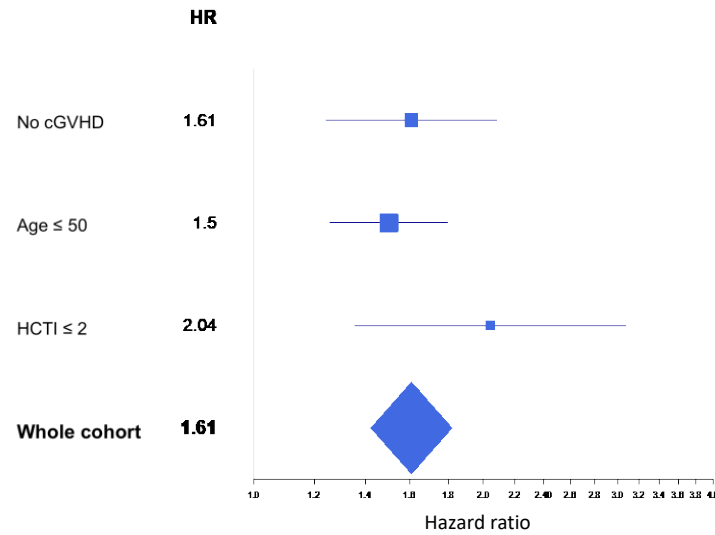
Suppl. Figure 3B

Meta-analyses of the predictive value of EASIX-1y as continuous variable (per log2) for OS.

training



validation



Legend suppl. Figure 3:

Meta-analyses of the predictive value of EASIX-1y as continuous variable (per log2)

A) Non-relapse mortality (NRM)

B) Overall survival (OS)

To evaluate differences in the prognostic effect of EASIX-1year between patient subgroups (age above and below 50 years, presence or absence of chronic GVHD, HCT-CI score above or below 2), we performed separate Cox regression models for training and validation cohorts. Forest plots were used to present results for individual subgroups and the combined analysis for training and validation cohort. HCT-CI (validation cohort): only data from cohort III available.

Suppl. Table 1: Patients characteristics, 4 cohorts

| | | Training Cohort | Validation Cohort I | Validation Cohort II | Validation Cohort III |
|--------------------------------------|-----------|-------------------|---------------------|----------------------|-----------------------|
| | | Heidelberg, n=610 | Berlin, n=199 | Essen, n=233 | Seattle, n=420 |
| Date of alloSCT | | 09/2001 - 06/2014 | 01/2013-12/2015 | 01/2011 - 12/2013 | 01/2010 - 12/2013 |
| Median age at alloSCT (years, range) | | 53 (18-75) | 55 (18-74) | 52 (20-74) | 52 (17-78) |
| Recipient sex | | | | | |
| | Female | 236 (38.7%) | 71 (35.7%) | 101 (43.4%) | 163 (38.8%) |
| | Male | 374 (61.3%) | 128 (64.3%) | 132 (56.6%) | 257 (61.2%) |
| Donor sex | | | | | |
| | Female | 203 (33.3%) | 53 (26.6%) | 76 (32.6%) | 183 (43.6%) |
| | Male | 407 (66.7%) | 124 (62.3%) | 157 (67.4%) | 213 (50.7%) |
| | Missing | 0 (0.0%) | 22 (11.1%) | 0 (0.0%) | 24 (5.7%) |
| Donor relation | | | | | |
| | MRD | 193 (31.6%) | 43 (21.6%) | 55 (23.6%) | 121 (28.8%) |
| | MUD | 304 (49.8%) | 127 (63.8%) | 155 (66.5%) | 207 (49.3%) |
| | MMUD | 100 (16.4%) | 26 (13.1%) | 23 (9.9%) | 36 (8.6%) |
| | MMRD | 7 (1.1%) | 3 (1.5%) | 0 (0.0%) | 5 (1.2%) |
| | Haplo | 6 (1.0%) | 0 (0.0%) | 0 (0.0%) | 10 (2.4%) |
| | UCB | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 41 (9.8%) |
| HLA mismatch | | | | | |
| | No | 497 (81.5%) | 170 (85.4%) | 186 (79.8%) | 328 (78.1%) |
| | Yes | 113 (18.5%) | 29 (14.6%) | 47 (20.2%) | 92 (21.9%) |
| Disease | | | | | |
| | AML | 184 (30.2%) | 99 (49.8%) | 113 (48.5%) | 163 (38.8%) |
| | MPN | 47 (7.7%) | 23 (11.6%) | 55 (23.6%) | 53 (12.6%) |
| | Lymphoma | 176 (28.9%) | 15 (7.5%) | 57 (24.5%) | 27 (6.4%) |
| | MM | 70 (11.5%) | 23 (11.6%) | 8 (3.4%) | 0 (0.0%) |
| | MDS | 66 (10.8%) | 17 (8.5%) | 0 (0.0%) | 76 (18.1%) |
| | ALL | 67 (11.0%) | 15 (7.5%) | 0 (0.0%) | 78 (18.6%) |
| | Other | 0 (0.0%) | 7 (3.5%) | 0 (0.0%) | 23 (5.5%) |
| ATG | | | | | |
| | No | 221 (36.2%) | 25 (12.6%) | 72 (30.9%) | 407 (96.6%) |
| | Yes | 389 (63.8%) | 173 (86.9%) | 161 (69.1%) | 13 (3.1%) |
| | NA | 0 (0.0%) | 1 (0.5%) | 0 (0.0%) | 0 (0.0%) |
| GvHD Prophylaxis | | | | | |
| | MMF | 397 (65.1%) | 121 (60.8%) | 16 (6.9%) | 225 (53.6%) |
| | MTX | 213 (34.9%) | 78 (39.2%) | 217 (93.1%) | 195 (46.4%) |
| conditioning | | | | | |
| | MAC, Apl. | 107 (17.5%) | 57 (28.6%) | 205 (88.0%) | 212 (50.5%) |
| | RIC | 503 (82.5%) | 142 (71.4%) | 28 (12.0%) | 208 (49.5%) |
| HCT-CI | | | | | |
| | 0 | 115 (21%) | | | 62 (21.6%) |
| | 1+2 | 163 (30%) | | | 96 (33.5%) |
| | 3+4 | 196 (36%) | | | 87 (30.3%) |
| | >4 | 72 (13%) | | | 42 (14.6%) |
| | n.a. | 64 (11%) | | | 133 (31.7%) |

MRD=matched related donor, MUD=matched unrelated donor, MMUD=mismatched unrelated donor, MMRD= mismatched related donor, UCB=umbilical cord blood, AML=acute myeloid leukaemia, MPN=Myeloproliferative Neoplasm, MM=multiple myeloma, MDS=myelodysplastic syndrome, ALL=acute lymphoblastic leukaemia, ATG = anti-thymocyte globulin, NA=not available, MAC=myeloablative conditioning, RIC=reduced-intensity conditioning, -aol. = aplasia conditioning, MMF = mycophenolat mofetil; MTX = methotrexate, HCT-CI, haematopoietic stem cell transplantation comorbidity index.

Suppl. Table 2

Cox model with covariates $\log_2(\text{Platelets})$, $\log_2(\text{creatinine})$ and $\log_2(\text{LDH})$ and response NRM in the training cohort. The model corresponds to an individual weighting of each lab parameter of the EASIX score.

| Covariate | CSHR | 95% CI | p |
|---------------------------|-------------|---------------|----------|
| Thrombocytes (\log_2) | 0.68 | 0.53-0.88 | 0.003 |
| Creatinine (\log_2) | 1.85 | 1.16-2.57 | 0.010 |
| LDH (\log_2) | 2.76 | 1.78-4.27 | <0.0001 |

Suppl. Table 3

Multivariable Cox regression, endpoint OS calculated from the 1year landmark

| | Training N=550, events=125 | Validation N=654, events=90 |
|---------------------------------------|---------------------------------------|--|
| EASIX-1year (log2) | 1.33 (1.03-1.72) P= 0.030 | 1.61 (1.24-2.08) P<0.001 |
| Ongoing or cleared cGVHD | 0.81 (0.55-1.19) P=0.278 | 0.71 (0.42-1.20) P=0.200 |
| EASIX-1year:cGVHD Interaction term | 1.12 (0.81-1.54) P=0.494 | 1.00 (0.71-1.40) P=0.996 |

Suppl. Table 4

Multivariable Cox regression, end point OS after 1 year and NRM after 1 year
Training cohort, n=486, 109 OS events, 60 NRM events, TTR 76 events

| HR, (95% CI), p | OS after 1 year | NRM after 1 year | TTR after 1 year |
|--------------------|----------------------------|---------------------------|---------------------------|
| EASIX-1year (log2) | 1.41 (1.19-1.68) p<0.001 | 1.62 (1.31-2.01) p<0.001 | 0.98 (0.78-0.89) p=0.890 |
| EASIX-pre (log2) | 0.96 (0.83-1.11) p=0.575 | 1.11 (0.93-1.33) p=0.243 | 0.80 (0.66-0.97) p=0.024 |
| HCT-CI | | | |
| 1+2 | 0.76 (0.43-1.33) p=0.331 | 0.77 (0.35-1.71) p=0.524 | 0.52 (0.26-1.02) p=0.058 |
| 3+4 | 1.10 (0.66-1.84), p=0.714 | 1.01 (0.48-2.16), p=0.985 | 1.02 (0.58-1.80), p=0.936 |
| >4 | 1.74 (0.93-3.24) p=0.083 | 2.13 (0.93-4.85), p=0.072 | 0.90 (0.40-2.02) p=0.803 |
| EBMT | | | |
| 1+2 | | | |
| >2 | 1.37 (0.81-2.31), p=0.3234 | 0.84 (0.46-1.54), p=0.568 | 3.47 (1.40-8.649) p=0.007 |

Excluded from this analysis were 64 patients without available HCT-CI scores and 60 patients without available EBMT scores.

Suppl. Table 5

Multivariable Cox regression, endpoints OS and NRM **calculated from the 1y landmark** , pooled validation cohort, n=791, 151 OS events and 95 NRM events

| HR, (95% CI), p | OS after 1 year | NRM after 1 year |
|--------------------|--------------------------|--------------------------|
| EASIX-1year (log2) | 1.59 (1.39-1.81) p<0.001 | 1.75 (1.50-2.05) p<0.001 |
| EASIX-pre (log2) | 1.08 (0.95-1.22) p=0.242 | 1.08 (0.93-1.26) p=0.322 |

Suppl. Table 6

Multivariable Cox regression, endpoints OS and NRM **calculated from the 1y landmark** Validation cohort III (Seattle), n=287, 44 OS events and 29 NRM events

| HR, (95% CI), p | OS after 1 year | NRM after 1 year |
|----------------------------|---|--|
| EASIX-1year (log2) | 1.44 (1.14-1.82) p=0.002 | 1.61 (1.21-2.14) p=0.011 |
| EASIX-pre (log2) | 1.26 (1.03-1.55) p=0.026 | 1.15 (0.87-1.51) p=0.337 |
| HCT-CI 1+2 3+4 >4 | 0.55 (0.24-1.23) p=0.143 0.33 (0.13-0.85), p=0.022 1.14 (0.49-2.64) p=0.766 | 0.64 (0.20-1.45) p=0.220 0.31 (0.10-0.99), p=0.048 0.98 (0.34-2.86), p=0.972 |