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POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Allogeneic Hematopoietic Stem Cell Transplantation in Advanced Systemic Mastocytosis

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Purpose

Advanced systemic mastocytosis (AdvSM) is driven by the *KIT* D816V mutation in >90% of patients (pts.). Depending on subtype, median survival is between 1.5 and 4 years. Despite recent advances on responses and survival due to the availability of effective KIT inhibitors, allogeneic hematopoietic stem cell transplantation (alloHSCT) remains the only curative treatment option. Data on optimal timing, conditioning regimens, and pre- as well as post-alloHSCT treatments for maintenance or

relapse are however scarce. Current recommendations mainly refer to a retrospective analysis published almost 10 years ago (Ustun et al., JCO 32, 2014). With the advent of new therapies and improved transplant procedures, more recently collected data on alloHSCT in AdvSM are needed for actual assessment of optimal treatment strategies.

Patients & Methods

This retrospective analysis identified 71 pts. with AdvSM who underwent alloHSCT at 20 German centers between 1999 and 2021. Data were collected via the 'German Stem Cell Transplantation Registry (DRST)' and the 'German Registry on Disorders of Eosinophils and Mast Cells (GREM)'. Additional baseline characteristics and response status prior to, during and post alloHSCT were provided by the participating centers.

Results

At time of alloHSCT, median age was 59 years (range 21-84); 55/71 (77%) pts. were male. Median time between diagnosis of AdvSM and alloHSCT was 1.2 years (range 0.1-16.7). Pts. were grouped into (i) aggressive systemic mastocytosis (ASM, n=6) and SM with an associated hematological neoplasm (SM-AHN, n=24), totaling 30/71 (42%) ASM/SM-AHN pts., (ii) SM with an associated acute myeloid leukemia (SM-AML; 28/71, 39%) and (iii) mast cell leukemia ± AHN (MCL±AHN; 13/71, 18%).

The median follow-up time after alloHSCT was 1.4 years (range 0-20.4). PFS and OS were 52% (SD ± 6.1%) and 62% (SD ± 5.9%) at 1 year, and 39% (SD ± 6.3%) and 50% (SD ± 6.2%) at 3 years. Discrimination between the three cohorts allowed a three-tier risk stratification (median PFS, 4.5 vs. 0.7 vs. 0.3 years, $P<0.001$; median OS, 9.0 vs. 3.3 vs. 0.9 years, $P=0.007$, **Figure 1**).

Overall non-relapse mortality rate was 30% (21/71) including infectious complications in 8/21 (38%), GvHD in 1/21 (5%), cardiotoxicity in 1/21 (5%) and 'combinations/not further specified' in 11/21 (52%) pts. The 100-day non-relapse mortality was 8% (6/71; ASM/SM-AHN, 0/30; SM-AML, 4/28, 14%; MCL±AHN, 2/13, 15%).

OS was associated with response status of SM (17/41, 41%; median OS 4.6 vs. 1.1 years, $P=0.029$) or AHN (26/43, 60%, median OS not reached vs. 0.4 years, $P=0.003$) prior to alloHSCT (**Figure 2**). Univariable analyses revealed absence of a *KIT* D816V mutation (HR 2.9 [1.2-6.5], $P<0.001$) and a complex karyotype (HR 4.2 [1.8-10.0], $P=0.016$) as adverse prognostic factors regarding OS. PFS was significantly impacted by diagnosis of MCL±AHN (HR 3.5 [1.7-7.5], $P<0.001$), absence of a *KIT* D816V mutation (HR 2.5 [1.2-5.4], presence of a complex karyotype (HR 4.2 [1.8-10.0], $P=0.016$), $P=0.021$) and absence of the use of tyrosine kinase inhibitors prior to alloHSCT (HR 0.461 [0.249-0.854], $P=0.014$). In contrast, HLA match (complete vs. incomplete), type of conditioning (myeloablative vs. dose-reduced intensity), use of total body irradiation (≥8 Gy yes vs. no) or the transplantation at high volume centers (≥7 patients yes vs. no) were not associated with significant differences in PFS or OS.

During or after alloHSCT, 30/71 (42%) pts. showed either refractory (9/71, 13%) or relapsed (21/71, 29%) disease (R/R), being highest among MCL±AHN pts. (11/13, 85%; ASM/SM-AHN, 9/30, 30%; SM-AML, 10/28, 36%; $P=0.002$). R/R SM was predominantly observed in MCL±AHN (10/11, 91%) while R/R AHN was higher in SM-AML patients (6/10, 60%) and ASM/SM-AHN (5/9, 56%).

The median time to relapse was 0.6 years (range 0.1-4.5). Post alloHSCT, a response to various treatment regimens was achieved in 13/30 (43%) pts. (ASM/SM-AHN, 3/9, 33%; SM-AML, 5/10, 50%; MCL±AHN, 5/11, 45%) with highest response rates in 9 pts. receiving midostaurin and/or avapritinib (7/9, 78%).

Conclusions

In pts. with AdvSM eligible for alloHSCT, i) baseline characteristics affect outcome of alloHSCT more than specific transplant procedures, ii) alloHSCT should not be performed in pts. without response prior to alloHSCT and iii) post-alloHSCT strategies such as preemptive or residual disease guided maintenance therapy should be considered to improve post-alloHSCT outcome.

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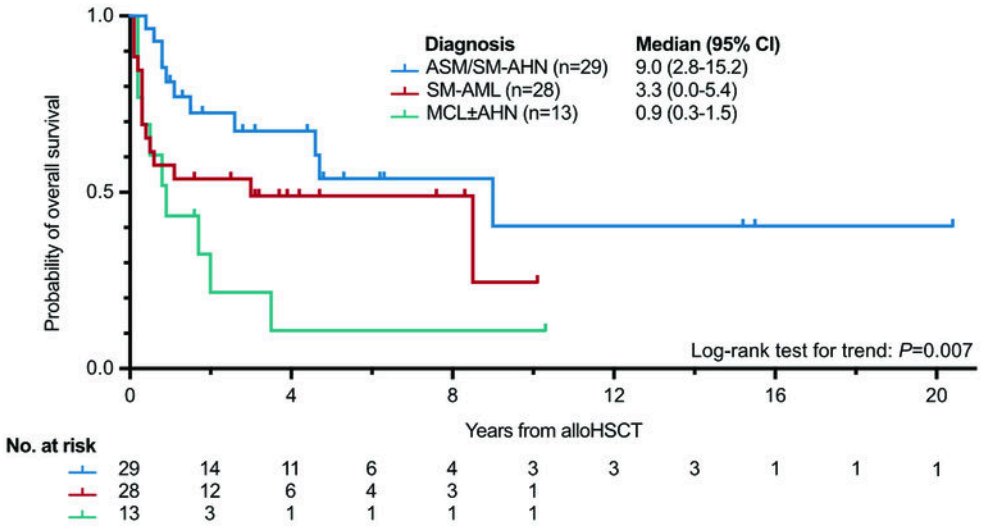
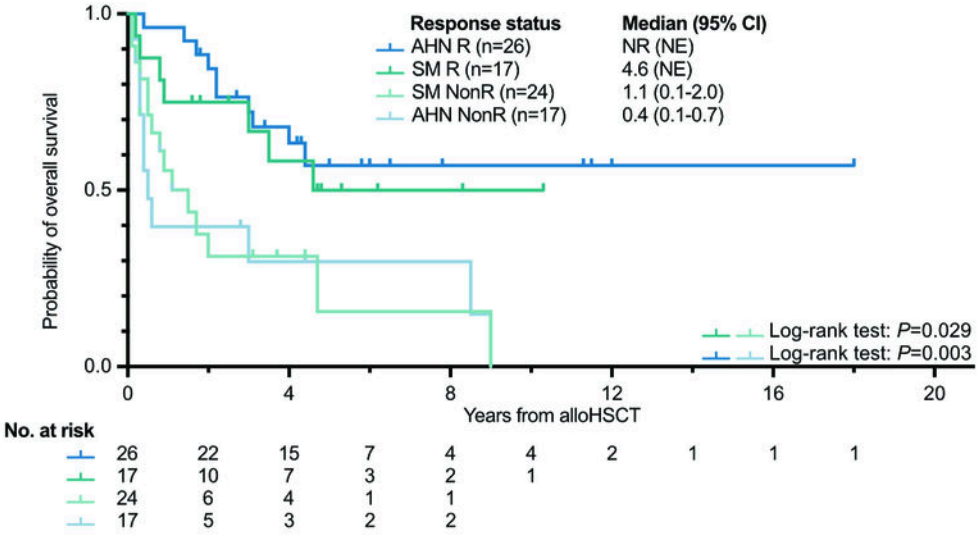
Figure 1: Kaplan Meier estimates of overall survival due to underlying subtype of SM at time of alloHSCT



abbreviations: AHN, associated hematological neoplasm; alloHSCT, allogeneic hematopoietic stem cell transplantation; AML, acute myeloid leukemia; ASM, aggressive systemic mastocytosis; MCL, mast cell leukemia; SM-AHN, systemic mastocytosis with an associated hematological neoplasm

Figure 2: Kaplan Meier estimates of overall survival due to response status of SM or AHN prior to alloHSCT



abbreviations: AHN, associated hematological neoplasm; alloHSCT, allogeneic hematopoietic stem cell transplantation; NE, not eligible; NonR, non-responder; NR, not reached; R, responder; SM, systemic mastocytosis

Figure 1

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