



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Impact of Clinical and Genetic Factors on Myelofibrosis Outcomes after Allogeneic Transplantation

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Introduction:

The reported impact of gene mutations, including JAK2-V617F, other MPN phenotypic drivers and additional cooccurring mutations on outcomes after allogeneic transplantation (HCT) in myelofibrosis (MF) has been inconsistent. While the MTSS score incorporated ASXL1 and JAK2 (non MPL/CALR mutations) as unfavorable predictors after HCT, other studies reported JAK2 mutations to be favorable (Blood 2010). Further, in some studies, mutations known to affect disease progression in MF pre-HCT (high-molecular risk or HMR mutations) have not been predictors of post-HCT outcomes. Here we present outcomes in all MF patients undergoing HCT at Dana-Farber Cancer Institute (DFCI) from 2000-2020 and examine clinical and genetic predictors of outcomes, stratified by year of HCT (<2011 or pre-2011 and ≥2011 or post-2011). Of note, ruxolitinib was available for use post-2011 only, following its FDA approval that year.

Methods:

Patients with MF who underwent HCT from 2000-2020 at DFCI (n=166) were included in this retrospective cohort analysis. Outcomes were analyzed for the whole cohort as well as sub-group analyses in the pre-2011 (n=39) and post-2011 era (n=127). Mutational analysis was performed by targeted next-generation sequencing of available pre-HCT samples in 115/127 patients in the post-2011 era.

Results:

Median age was 61 years and follow up 56.2 months. 25% had massive splenomegaly. DIPSS-plus scores were high in 45.2% and 45.1% received rux. HCT and patient characteristics (including KPS and median time from diagnosis to HCT) were similar pre and post 2011, with differences in conditioning regimens. Majority (77.1%) had HLA-matched donors, underwent reduced intensity (69.3%) HCT with peripheral blood stem-cells (92.2%) and received tacrolimus/methotrexate based GVHD prophylaxis (90.1%). FluMel100/140 (n=65), FluBu4 (n=34) and FluBu2 (n=11) were commonly used in the post-2011 era, while Flu/Bu1 (n= 34), ablative Bu/Cy (n=5) and Cy/TBI (n=12) were predominant pre-2011. Few patients underwent pre-HCT splenectomy (10.2%) or splenic irradiation (9%). Median D100 donor chimerism was 68% for Flu/Bu1, 86% for Flu/Bu2, 98% for Flu/Bu4, and 100% for Flu/Mel100-140.

At 4 years, overall survival (OS) for the whole cohort was 58% (50/66), progression-free survival (PFS) 55% (47/63), non-relapse mortality (NRM) 23% (17/30) and relapse rate 21%. 4 year OS was significantly better in the post-2011 era compared to pre-2011 (69% vs 26%, p<0.0001), as was PFS, driven by lower relapse rates in the post-2011 era (15% vs 41%, p<0.0001). 4-yr NRM was also marginally better (20% vs 33%, p= 0.17).

In the post-2011 era, 115/127 patients had NGS panel-based genetic analysis prior to HCT (Fig 1), demonstrating 91.3% of patients had at least one driver mutation (JAK2 62.6%, CAL-R 13.9%, MPL 14.8%) while 8.7% patients were triple negative. The most frequent cooccurring mutations were ASXL1 (40%), TET2 (28.7%) and U2AF1 (17.4%). In univariable analysis (UVA), the presence of JAK2 mutations (JAK2+) was associated with superior PFS (HR 0.5, 95% CI 0.27, 0.94, p= 0.03) while CALR (HR 1.86, p=0.12) and MPL (HR:1.21, p=0.65) mutations were not significant for PFS. Triple negative patients showed a trend towards poorer PFS (HR 2.27, p=0.05). OS results mirrored those of PFS. No cooccurring myeloid gene mutations were associated

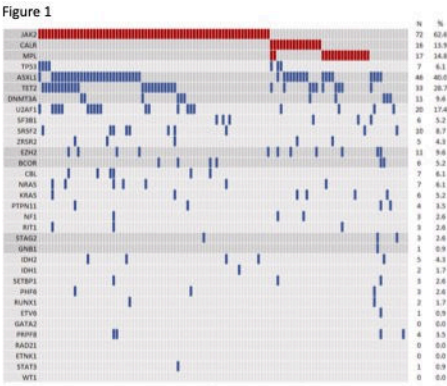
with PFS or OS. Superior 4-year OS for JAK2+ versus JAK2- recipients (80% versus 58%, $p=0.01$) is shown in Figure 2. *TP53* ($p=0.03$), *TET2* ($p=0.015$) and *EZH2* ($p=0.002$) mutations were associated with higher relapse rates in UVA. Patients with JAK2+ and cooccurring ASXL1 mutations had poorer OS compared to those with JAK2+/no cooccurring ASXL1 mutations (HR=2.69, $p=0.031$).

Combining clinical and molecular features in the post-2011 era, in MVA, only DIPSS high (HR=4.76, $p=0.03$) and KPS < 90% (HR=2.66, $p=0.024$) were significantly associated with poorer OS/PFS while JAK2+ (HR=0.32, 95% CI 0.14,0.75, $p=0.009$) was significantly associated with better OS/PFS; *JAK inhibitor use* spleen size/management, conditioning regimen or other mutations including HMR mutations and *TP53* were not significantly associated with OS/PFS.

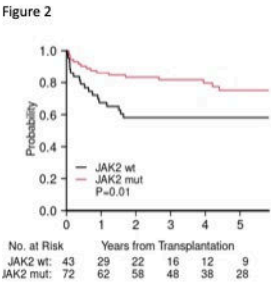
Conclusions:

In this single-institution retrospective analysis, the presence of a JAK2-V617F mutation was associated with better OS and PFS following HCT in MF in the post-2011 era. Survival outcomes are significantly better in the post-2011 era compared to pre-2011, in our cohort.

Disclosures Mullally: *Aclaris*, *Cellarity*, *Morphic*, *Biomarin*: Consultancy; *Constellation*, *Protagonist*: Other: Advisory Board ; *AOP Health*: Speakers Bureau; *Relay*, *Morphic*: Research Funding; *PharmaEssentia*, *Incyte*: Other: Steering Committee .
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Pre-HCT NGS panel based mutational analysis in 115/127 patients in the post-rux/2011 era showing driver (red) and cooccurring (blue) mutations



Significantly improved overall survival in JAK2 mutated (JAK2+) versus JAK2negative (JAK2-) myelofibrosis patients in the post-rux/2011 era

Figure 1

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