EHA2026 Congress
June 11-14
Stockholm, Sweden

Impact of early post-transplant measurable residual disease on outcomes of patients with relapsed or refractory AML: a post-hoc analysis of the prospective ASAP trial

P11115

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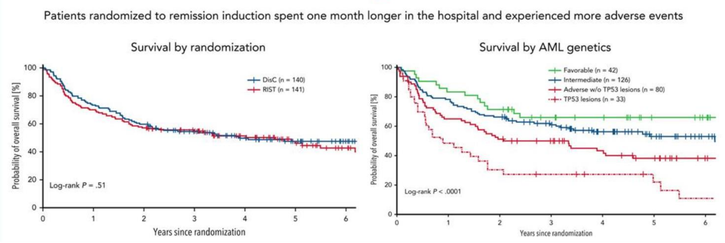
Background

The **ASAP trial** (#NCT02461537) was a randomized, multi-center trial that investigated the effects of remission induction chemotherapy (RIST) followed by allogeneic (allo) HCT versus immediate alloHCT (disease control - DisC) in relapsed or refractory AML after induction chemotherapy.
No survival advantage was observed for patients who had received RIST prior to alloHCT. However, biological disease risk (classified according to ELN 2022) was a major risk factor for survival. As part of ancillary research, peripheral blood or bone marrow aspirate samples were collected on **day +56 post alloHCT to assess** the prognostic power of measurable residual disease (**MRD**).



Stelljes et al, Blood 2025

Aims

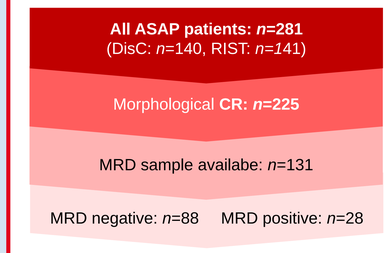
The purpose of this analysis was to evaluate the **impact of MRD status** on the risk of relapse and survival endpoints in patients with (morphological) complete remission on day +56 after alloHCT.

Conclusion

Early **MRD negativity after alloHCT** is predictive for **favorable overall survival** and **reduced risk of relapse**. Early MRD monitoring may optimize follow-up after alloHCT and indicate patients who could benefit from preemptive therapy (e.g., rapid tapering of immunosuppression, DLIs, targeted therapies).
Optimal timing and frequency of MRD testing, preferred material (bone marrow versus peripheral blood samples) and most informative marker panels require further investigations.

Methods

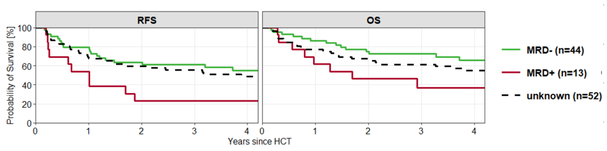
Peripheral blood samples were collected at study inclusion and genomic DNA was extracted. Mutational profiles were determined with high sensitivity using a custom panel (TWIST Biosciences) in combination with Duplex-Sequencing. Based on these results, up to 5 markers were selected for MRD tracking, whereby well-established markers were always included. On day +56 (+/- 30 days) after alloHCT, bone marrow aspirates were collected and genomic DNA was isolated. The frequencies of patient-specific markers were quantified using UMI-based, highly sensitive amplicon sequencing. MRD positivity was assumed if the variant allele frequency of at least one of the five analyzed target mutations exceeded 0.1%.
We evaluated the prognostic significance of MRD status for relapse and survival endpoints by means of Kaplan-Meier estimates, cumulative incidence curves and multivariable Cox models, adjusted for patient age, sex, ELN 2022 risk, ECOG, HCT-CI and donor type.



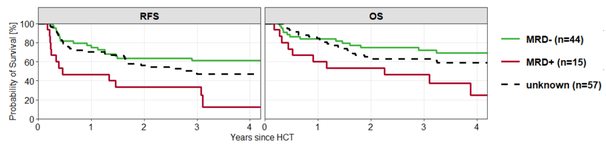
Results

In the ASAP trial, 225 patients achieved (morphological) complete remission (CR) on day +56. Samples for MRD analysis were available from 131 CR patients. Of these, 28 (21%) were classified as MRD positive and 88 (67%) MRD negative. In 15 (11%) patients, analysis failed due to insufficient material. There were **no differences** in these proportions between DisC (15 MRD^{pos} and 44 MRD^{neg}) and RIST (13 MRD^{pos} and 44 MRD^{neg}) patients. Patients who were MRD negative at this early time point after alloHCT had significantly **longer relapse-free survival** (RFS) and long-term **overall survival** (OS) (MRD^{neg}: 2-year RFS 64% versus MRD^{pos}: 2-year RFS 29%; MRD^{neg} 2-year OS 75% versus MRD^{pos}: 2-year OS 50%), respectively. These findings were **consistent across ELN2022 subgroups.**

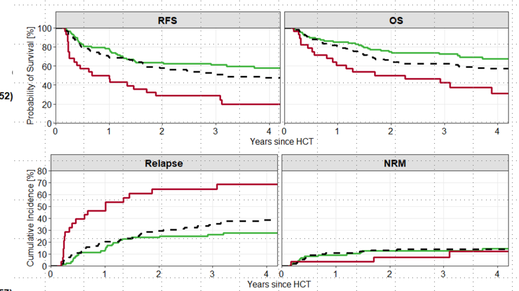
Remission Induction (RIST)



Disease control (DisC)



All Patients



* The '**unknown**' category includes 94 patients for whom no MRD sample was available, as well as 15 patients with insufficient sample quality

Point Estimates and Hazard ratios

Outcome at 2 years	MRD negative [95%-CI]	MRD positive [95%-CI]	p (rate difference)	HR* (pos vs neg) [95%-CI]	p (risk difference)
RFS	64% [53-73]	29% [14-46]	<0.001	3.1 [1.8-5.4]	<0.001
OS	75% [65-83]	50% [31-67]	0.018	2.8 [1.5-5.2]	0.001
Relapse	24% [15-33]	64% [46-83]	<0.001	4.0 [2.1-7.6]	<0.001
NRM	13% [6-19]	7% [0-17]	0.39	1.4 [0.4-5.2]	0.6

* (cause-specific) Cox proportional hazard models adjusted for patient age, patient sex, ELN risk, ECOG, HCT-CI and donor type

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