Study group – Harmonized prospective asservation and analysis of biomaterial in AML (HARPOON)

Despite advances in therapy, the prognosis for patients with AML is poor. In this working group, we are carrying out translational research projects to improve the prognosis of AML patients through longitudinal and prospective preservation and analysis of biomaterial in the context of clinical studies and registries.

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Concept

Where we started

Despite innovations in the field of diagnostics and targeted therapy, the prognosis of AML is often poor, especially for older or relapsed patients. The prospective preservation of biomaterial, especially for multi-omics analyses in the context of clinical studies and registries, represents a crucial pillar for future translational research projects to finally improve the prognosis.

It is the aim of the BZKF AML study group to harmonize the collection of samples from individual patients in the longitudinal direction (**Figure 1**). Based on these biomaterials and clinical data specific projects have been proposed and started.

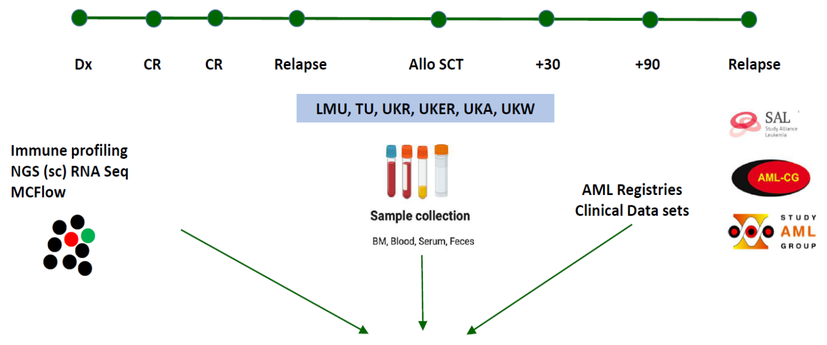
In the current funding period all six partner sites across different AML study groups (AMLCG, SAL, AML-SG) have teamed up and successfully participated in this harmonization process.

What we have achieved so far

All sites have successfully harmonized sample preservation (P0) and time points. In the first year 173 patients have been recruited so far. In addition to the founding members LMU and UKER two other centers (UKA and TUM) will establish MRD methodology in 2022 (P1, Harmonize). It is planned the UKW and UKR will follow in the next funding period.

Mikrobiome analyses (P2) performed at UKR and TUM (**Figure 2**) revealed that the compositions of microbial communities were reshaped during the course of allo-SCT, and that our established biobanking approach is feasible and can be performed in all six centers in the future.

Cytokine arrays in P3 have been used to assess inflammatory and metabolic markers in the BM secretome and were able to identify differences between remission and relapse samples. Prospective secretome analyses from all centers will be done centrally using the luminex platform in Munich.



Longitudinal analysis of intestinal microbial communities in allogeneic hematopoietic stem cell transplantation (allo-SCT) patients at UKR and TUM

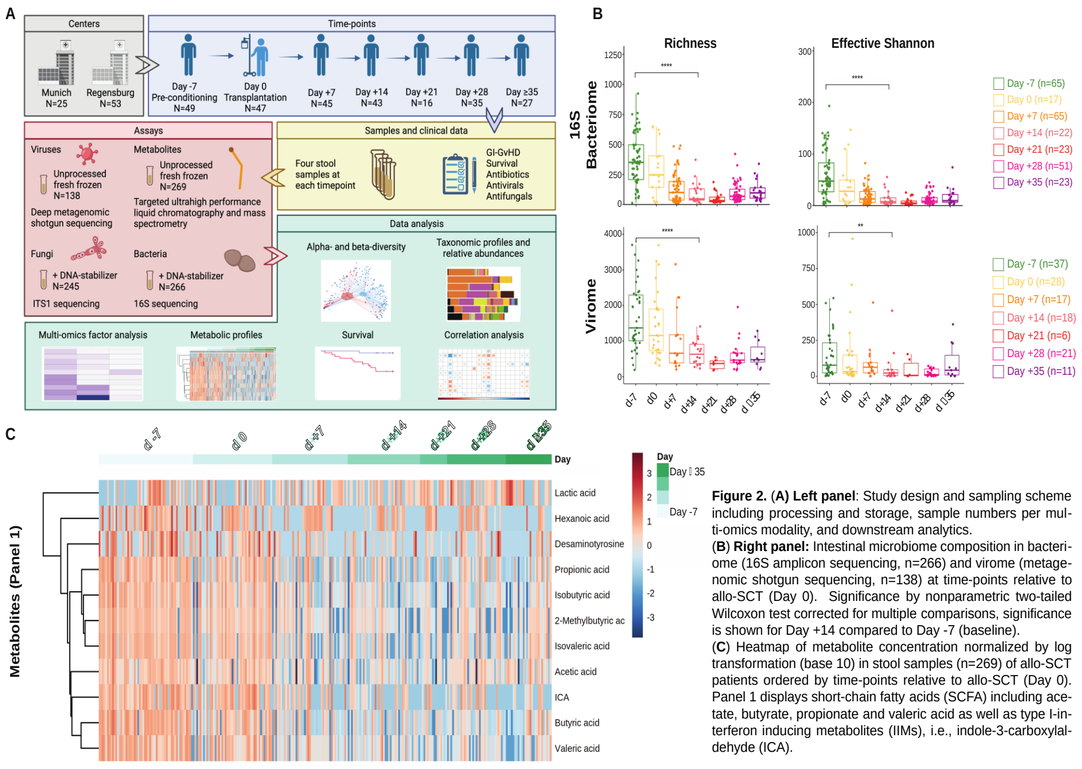


Figure 2. (**A**) **Left panel**: Study design and sampling scheme including processing and storage, sample numbers per multi-omics modality, and downstream analytics.
(**B**) **Right panel:** Intestinal microbiome composition in bacteriome (16S amplicon sequencing, n=266) and virome (metagenomic shotgun sequencing, n=138) at time-points relative to allo-SCT (Day 0). Significance by nonparametric two-tailed Wilcoxon test corrected for multiple comparisons, significance is shown for Day +14 compared to Day -7 (baseline).
(**C**) Heatmap of metabolite concentration normalized by log transformation (base 10) in stool samples (n=269) of allo-SCT patients ordered by time-points relative to allo-SCT (Day 0). Panel 1 displays short-chain fatty acids (SCFA) including acetate, butyrate, propionate and valeric acid as well as type I-interferon inducing metabolites (IIMs), i.e., indole-3-carboxylaldehyde (ICA).

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available at Research Square [https://doi.org/10.21203/rs.3.rs-1504704/v1]).

Future Milestones 2023/24

- **To finalize harmonization regarding prospective longitudinal biobanking and analysis**
- **To continue establishing MRD Monitoring („Harmonize“) (PI S. Krause)**
- **To focus on microbiome / secretome analysis (P2 (PI H. Poeck) and P3 (PI K. Götze) in AML patients treated with intensive vs. non-intensive Treatment (induction chemotherapy (“7+3”) vs. hypomethylating agent (HMA) + venetoclax (Ven))**

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