Abstract #9 | Poster

Functional vs. Genomic-based Precision Medicine in Hematological Cancers: Feasibility Analysis of the EXALT-2 Study

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Background.

Functional (fPM) and genomic-based (gPM) precision medicine approaches promise to support treatment decisions in relapsed/refractory (r/r) blood cancer patients. Prospective, controlled direct comparisons of PM methods are lacking. We report feasibility data of the multicentric, randomized controlled EXALT-2 trial (NCT04470947) comparing treatment recommendations of fPM, gPM and physicians' choice (PC).

Methods.

Patients with r/r hematological malignancy and a good clinical performance status (ECOG ≤ 1) are eligible. Viable tumor cells are collected by a real-time biopsy and subjected to fPM (flow cytometry- and/or image-based) and gPM testing. Depending on the randomization, a multicentric EXALT-2 board suggests treatment either based on i) fPM, ii) gPM results, or iii) without any precision medicine support (PC; **Fig. 1A)**.

Results.

Feasibility data are available for the first 55 enrolled patients (**Fig. 1B**). Of these, 54 patients (96% of screened patients) underwent real-time biopsy, and 43 patients (77% of screened patients) were randomized comprising the intention to treat (ITT) population. Thirty-two (76%) of these patients suffered from aggressive lymphoma (**Fig. 1C**). Forty-two patients (98% of ITT population, 75% of screened patients) received a therapy recommendation from the EXALT-2 board. Therapy was administered in 39 patients (93% of ITT population, 70% of screened patients) after a median of 25 days (range: 7 – 46) after biopsy. Twenty-nine patients (68% of ITT population) completed at least one cycle of therapy.

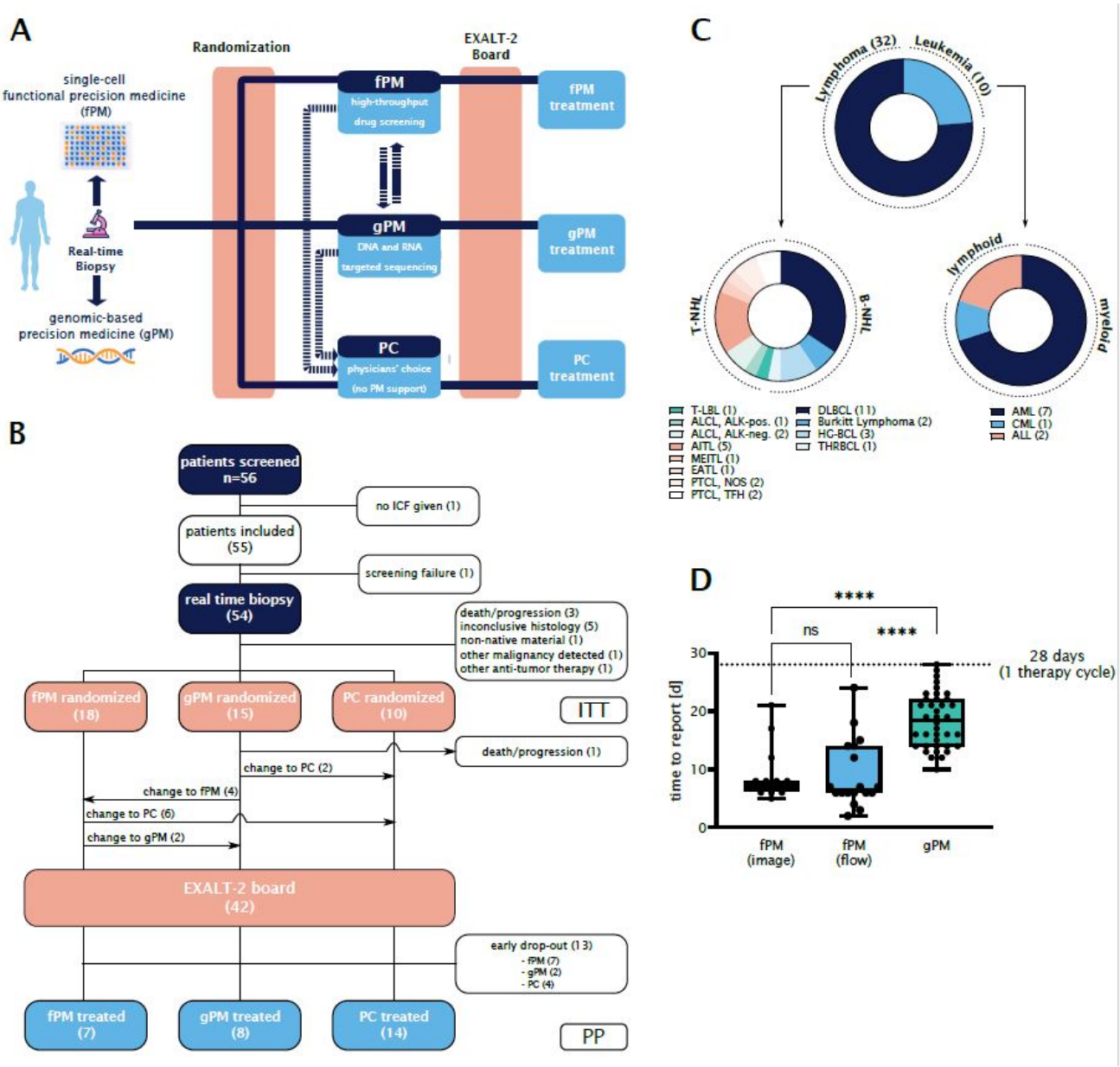
PM assays were technically feasible in most instances: Flow cytometry-based fPM: 86%; image-based fPM: 64%; gPM: 86% of tests. Actionable hits were detected with fPM assays in 100%, and with gPM in 76% of tests. Thus, PM assays identified a treatment rationale in 86% (fPM, flow cytometry), 64% (fPM, image), and 65% (gPM) of tested patient samples, respectively.

Median time from biopsy to report was shorter for fPM than for gPM tests (fPM, flow cytometry: 6.5 days, fPM, image: 7 days, gPM: 19 days, $p<0.0001$, **Figure 1D**). gPM identified a median of 5 (range: 1 - 13)

genetic aberrations per patient, of which a median of 1 (range: 0-5) aberration was pharmacologically actionable. Results of fPM and gPM tests overlapped in 60% of patients.

Conclusions.

Feasibility data of the EXALT-2 trial prove that both fPM and gPM are powerful tools that can be used for clinical decision making in advanced hematological malignancies.



Feasibility Analysis of Precision Medicine Use in Blood Cancer Patients.
A) Graphical overview of the study design. **B)** Consort diagram of the EXALT-2 feasibility cohort. **C)** Overview of diagnoses in the ITT cohort. **D)** Time from biopsy to availability of PM assay report, $p < 0.0001$, one-way ANOVA.