BACKGROUND: Treatment of Acute Myeloid Leukemia (AML) involves a few different treatments in each clinical trial group guideline, but integrating current and previous guidelines, and clinical trial publications, there are up to 45 drug combination treatments among approved chemotherapy drugs in Europe and USA. There is a need for Precision Medicine (PM) tests to identify which of these different treatments maybe optimal for each individual patient, independently of where he resides.

Aim: To provide actionable data to improve disease management with existing treatments with a PM test to guide the hematologist among all possible treatments to achieve CR.

METHODS: AML bone marrow (BM) samples from adult patients were received at the laboratory within 24 hours from extraction and incubated for 48h in 96-well plates containing single drugs or combinations representing up to 45 different treatments that are currently in the clinical practice. The analysis is performed in the automated flow-cytometry PharmaFlow platform. 72 hours after the extraction of the sample, an encrypted report is sent to the hematologist before the patient begins treatment. Pharmacological responses were calculated using pharmacokinetic population models. Induction response was assessed according to the Cournos criteria (2003). Patients achieving a CR were classified as responders and those remaining as resistant, excluding early deaths. final scores and treatments ranking is based on a therapeutic algorithm that integrates ex vivo activity, microarray drug dose responses quantified by the area under the curve (AUC) with Ki values as chemical stability, and synergism calculated measuring 8 concentration ratios requiring consistency in their results in a 3D surface (so called alpha factor synergism). The PM Test attempts to identify at least one treatment, among all evaluated alternatives, predicted sensitive for each patient, conversely, if sensitive treatments can be identified the PM test can provide the hematologist with valuable guidelines for individualized treatment.

RESULTS: (Figure 1) The scoring method was tested using ex vivo results from samples obtained in an observational clinical trial with Spain PETHEMA group from a cohort of 123 samples from de novo diagnosed AML patients, treated with the standard PETHEMA I/II/III guideline 2+ with Cytarabine. The score predicts sensitivities of 90% accuracy. This accuracy can be compared with an independently derived 92% accuracy in identifying sensitive patients in a statistically significant clinical correlation study (GH Poster 2016 Montesinos et al.). The score is a simplified version of such correlation studies. Both methods identify a similar % of all clinically sensitive patients (67% vs 71%). However, the correlation is only valid for CYT-DA while the PM Test is applied to up to 45 treatments. Any such treatment identified as sensitive means the PM test can provide a valuable guideline to hematologists. This means the PM Test can suggest sensitive treatments for the vast majority of patients.

CONCLUSIONS:

- This novel ex vivo PM test for induction treatment in AML patients represents a valuable information to guide hematologists selecting the right treatment to achieve CR in individual patients leveraging up to 45 different validated therapeutic regimes.
- The knowledge coming from Cytarabine correlation algorithm have allowed us to generate an ex vivo Score for each treatment.
- Assuming a similar response rate for all these treatments, this test could estimate a new prediction for sensitivity to AML treatment higher than 40% in 1% line.
- This PM test can be used in an Investigator Sponsored Trial as a Companion Diagnostic selecting sensitive patients with higher response rates and survival.
- This PM Test will be evaluated in an interventional clinical study in patients with refractory/relapsed AML. A randomized Controlled trial is planned in collaboration with the PETHEMA group from Spain.