

# Pharmacological evaluation of drugs & combinations in patient samples of hematological malignancies by automated flow cytometry

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#### **ABSTRACT**

The novel flow cytometry ExviTech® platform has incorporated key innovations to predict or evaluate the response of primary patient tumor cells to compounds and combinations analyzing both efficacy and hematotoxicity by doseresponse curves and kinetics. We use whole sample without isolating leukocytes, which was vitiating previous efforts for >30 years. This approach has achieved 90% correlation with clinical patient outcome in AML 1st line treatment Cytarabine plus Idarubicin, a level of clinical correlation not achieved before with ex vivo testing. We have profiled the pharmacological activity of more than 50 drugs in more than 1,000 patient samples of AML, MM, CLL, ALL, NHL, MF and PV. We now offer this body of knowledge to characterize the behavior of your compounds in these patient samples. Assays include depletion, apoptosis, proliferation, differentiation, autophagy, epigenetic, hypomethylating agents, etc... Optimal combinations of new compounds with other drugs or drug candidates are identified by measuring synergism among combinations, and also complementarity with other individual drugs (drugs active in those samples where the lead compound is resistant). In summary, we have developed an improved methodology to measure the pharmacological activity of drugs and drug combinations in hematological patient samples as well as modeling their pharmacological behavior.

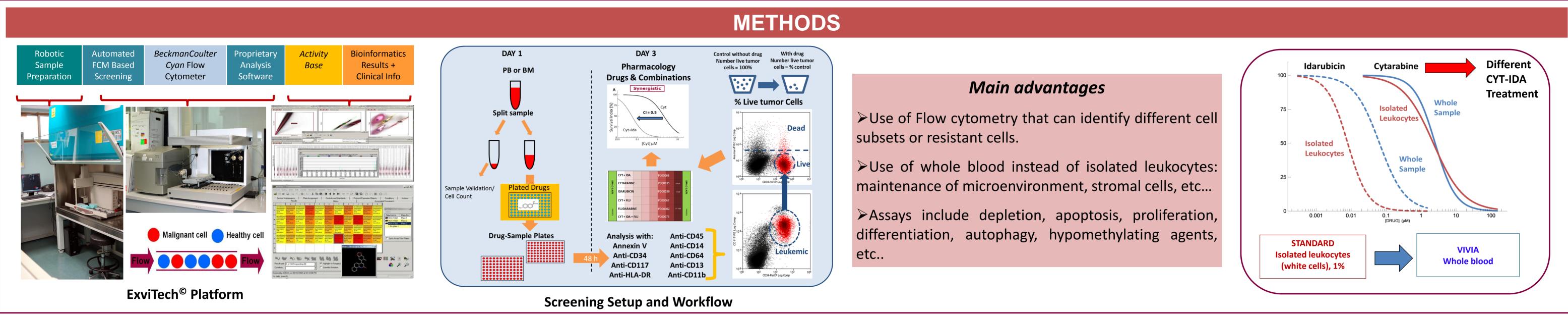
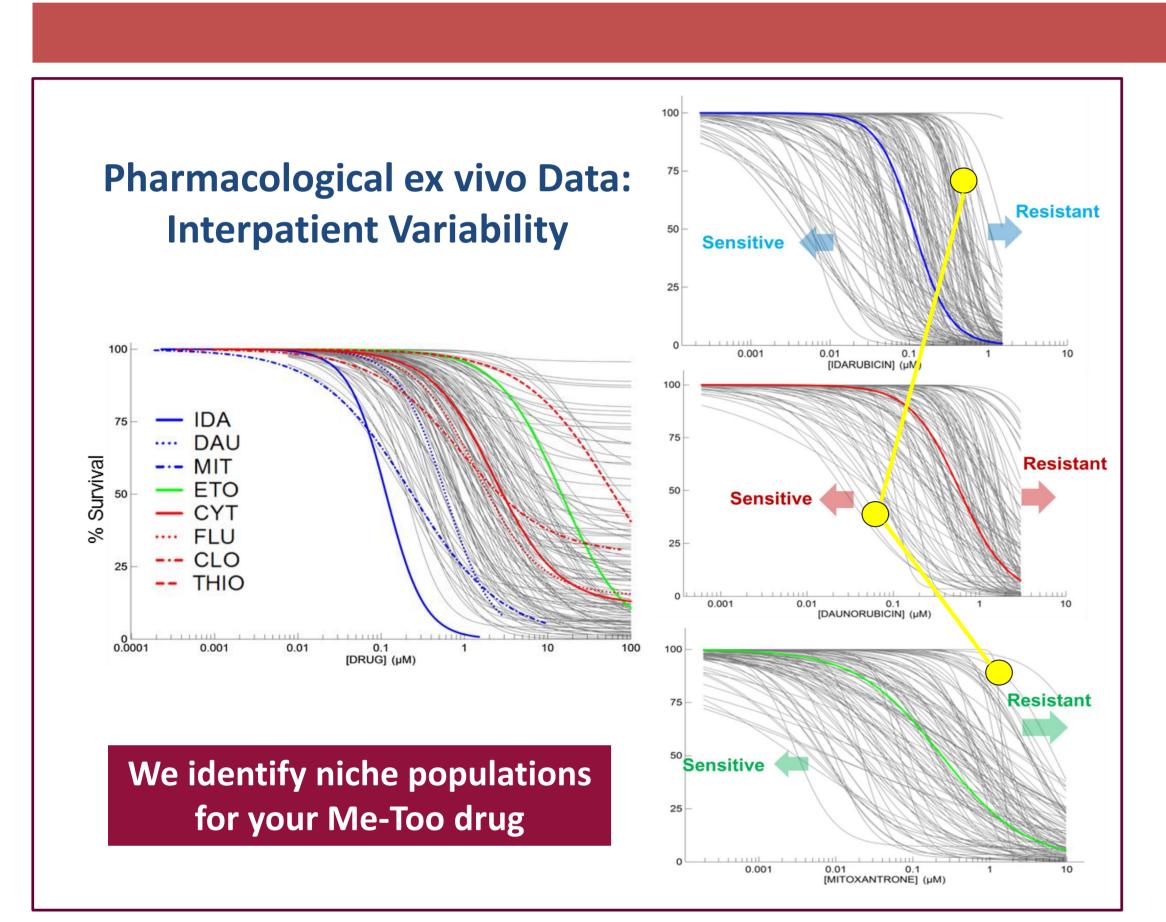
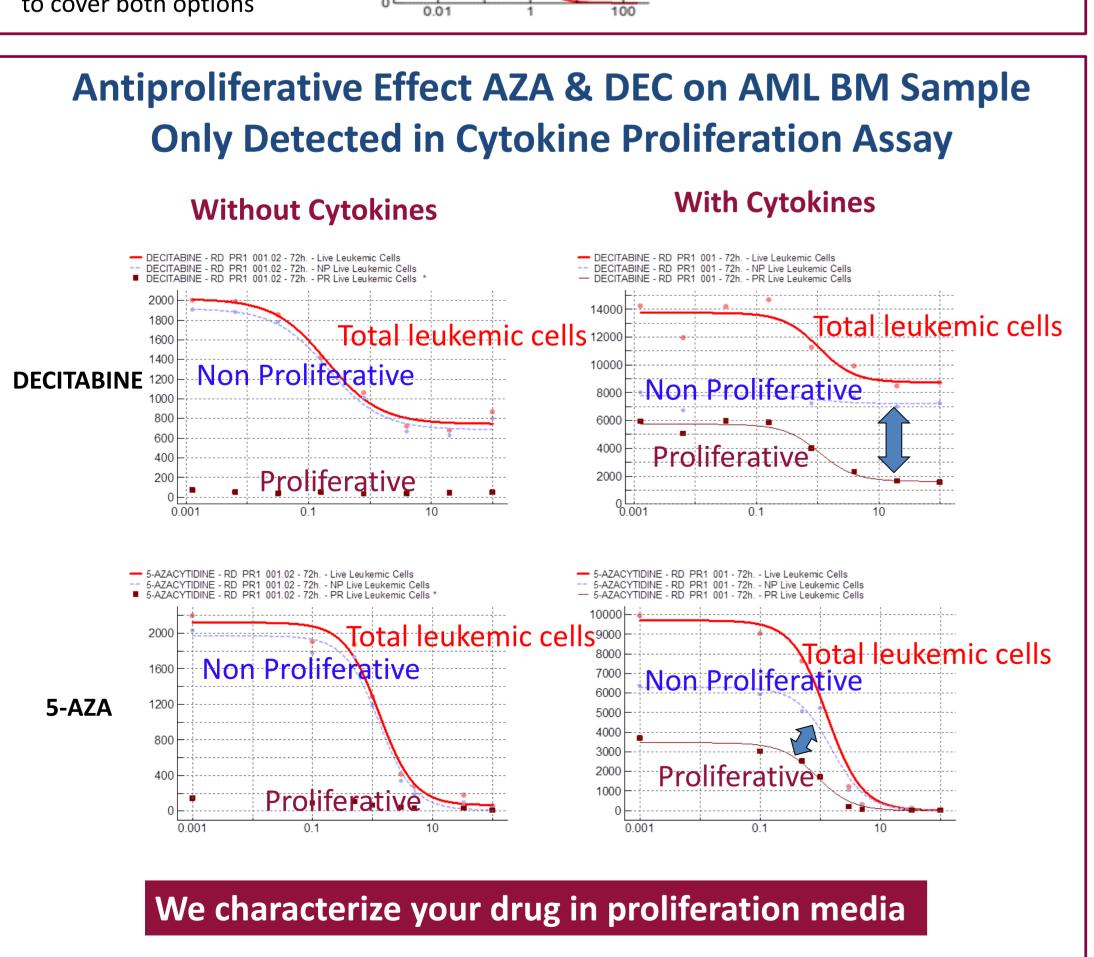


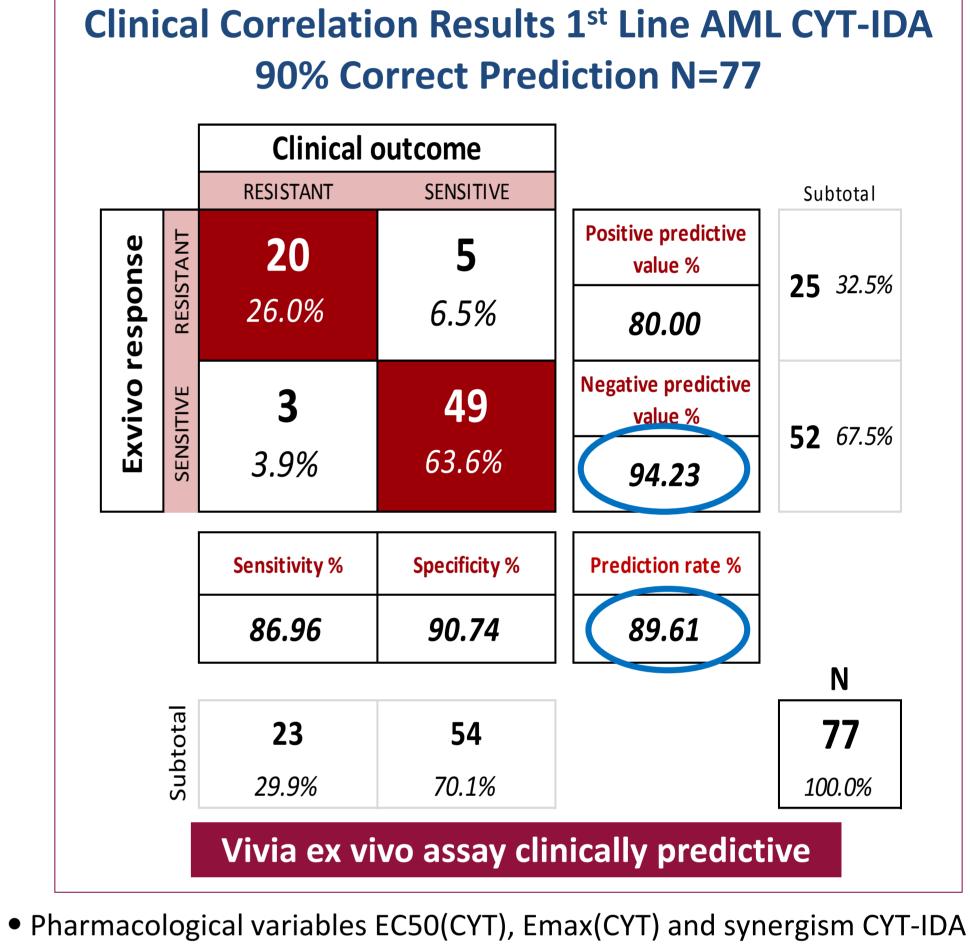
Figure 1. The flow cytometry ExviTech® platform integrates the known advantages of flow cytometry for hematological malignancies and a sophisticated information technology that enable us to perform a more detail pharmacological evaluation of drugs and combinations



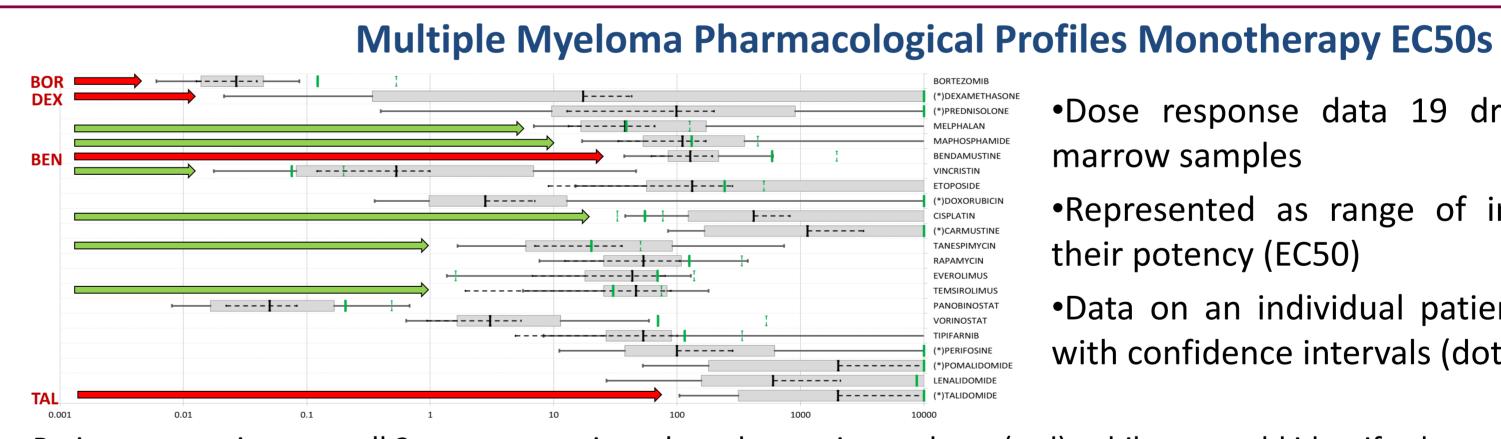
#### **Identifying Best Drug Combinations: Synergism vs Complementarity** Would maximize activity of your drugs May cover you when your drug is poorly active for some patients, and may save your clinical trial from some failures IDARUBICINI uM individual Complementary search Best drug combination crossresistance treatment includes Synergistic drugs may not be complementary, both synergistic & and viceversa. More than complementary drugs 2 drugs may be necessary to cover both options



## RESULTS Pharmacological ex vivo Data: Single drugs & Synergism **Bad Low** Efficacy Good High Efficacy Resistant patient B **Good High Potency Bad Low Potency** Drug 1 + Drug 2 CI = 1.0 Cyt+Ida Good High Synergy **Bad Low Synergy** We interpret the pharmacology data and identify Best **Drug Combinations**



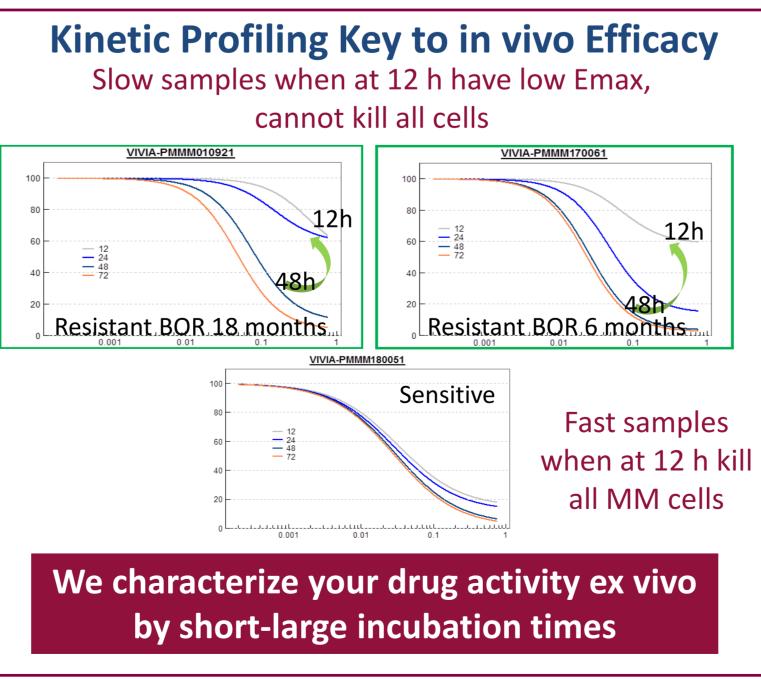
- Drug sensitivity testing never achieved this high correlation
- Validates new method whole sample microenvironment etc...
- Launching interventional Clinical trials relapse AML
- Enables cost-effective samples with inform consent & clinical data

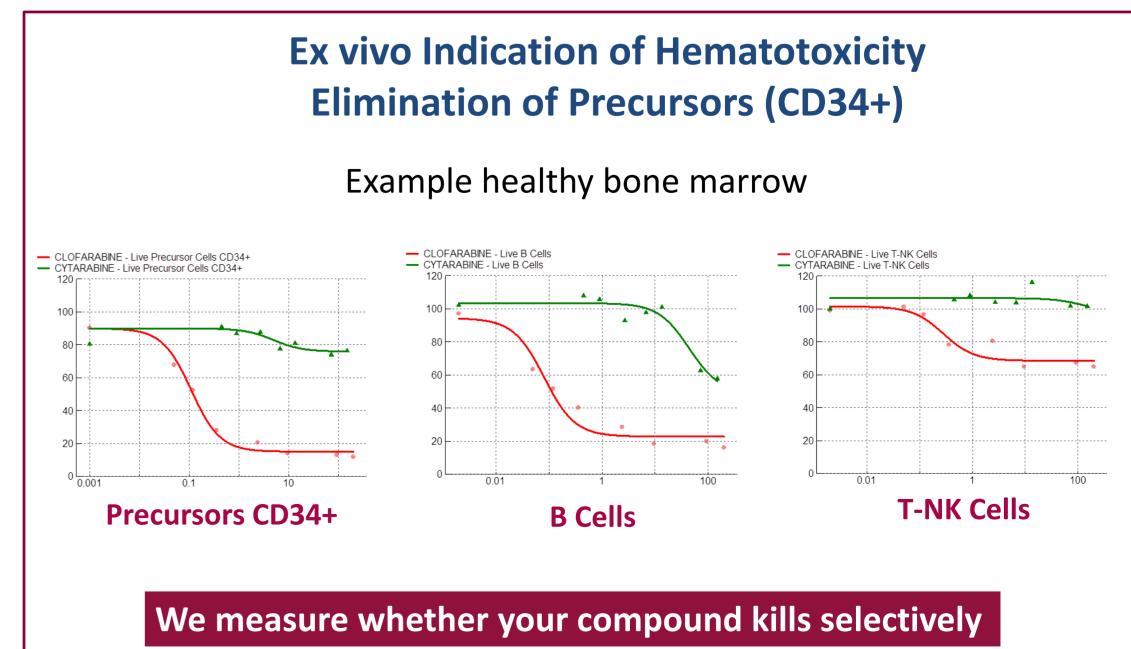


- •Dose response data 19 drugs in >100 MM bone marrow samples
- Represented as range of interpatient variability of their potency (EC50)
- Data on an individual patient shown by green bars, with confidence intervals (dotted)

Patient was resistant to all 3 treatments given, based on resistant drugs (red), while we could identify alternative sensitive drugs (green)

Pharmacologically characterized 54 protocols, drug combination treatments





### CONCLUSIONS

- Since Q3 Vivia Biotech offers the PM test & KOL network to provide compound profiling & biomarker services in patients samples
- Difference is no Ficoll separation before incubation, maintenance of microenvironment and a key to measure drug-drug synergism
- ❖ Vivia's PM test can be a companion diagnostic of your drug's clinical trials
- Tan identify synergistic drug comnbinations, efficient in a patient subpopulation with high unmet need
- ❖ If scalability is a concern, we can convert ex vivo biomarker into standard molecular Biomarker
- >80% prediction rate responsive patients would reduce cost and time of the drug's clinical trial
- May rescue underperforming drugs phase II-III trials