American Society of Hematology - 2015
Abstract #3249- Session 802
Chemical Biology and Experimental Therapeutics: Poster II
Sunday December 6, 2015, 6:00-8:00 pm

Clinical Results In Heavily Pre-Treated, Drug Refractory Hematologic Malignancies Using Chemotherapy And Targeted Agents Selected By Ex Vivo Analysis Of Programmed Cell Death (EVA/PCD)

Vinicius Renan Pinto Mattos, MD[1*], Nelson Hamerschlak, MD, PhD[1], Isabel Nagle Reis, MD[1*], Dirceu Hamilton Cordeiro Campelo, MD[1*], Michelle Petrolli Silveira, MD[1*], Flavia Munhoz Ferreira, MD[1*], Juliano Cordova Vargas, MD[1*], Paulo Vidal Campregher, MD[1*], Fabio P.S. Santos, MD[1], Fabio R. Kerbauy, MD, PhD[1*], Joao C. C. Guerra, MD, PhD[1*], Claudio Galvão Castro Júnior, MD[1*], Steven S. Evans, MS[2*] and Robert Nagourney, MD[3*] [1]Hospital Israelita Albert Einstein, Sao Paulo, Brazil; [2]Rational Therapeutics, Long Beach, CA; [3]The Malcom Todd Cancer Institute, Long Beach, CA

Introduction: The treatment of human hematologic malignancies has rapidly advanced through the application of genomic platforms that have identified drug-able targets and companion diagnostics (e.g. BCR-ABL, IDH-1) and added new classes of targeted agents to the established compendium of cytotoxics. Despite these advances, the complexity, redundancy and promiscuity of cellular transformation remain incompletely understood at the molecular level. This has led to a renewed interest in whole cell experimental models for drug discovery. Laboratory platforms that measure cellular response to cytotoxic insult at the phenotypic level have been shown to correlate significantly with clinical response, and have the capacity to provide insights into chemotherapy selection and drug development. The Ex Vivo Analysis of Programmed Cell Death (EVA/PCD) uses metabolic and morphologic features of drug induced cell death to measure both cytotoxic and targeted drug effects in human primary cultures. We applied EVA/PCD in 20 heavily pre-treated, drug refractory patients from the Hospital Israelita Albert Einstein (HIAE) in Sao Paulo - Brazil. **Methods:** Peripheral blood, node biopsy or bone marrow aspirates were submitted by overnight courier. Cells isolated by density centrifugation were evaluated by dose response curves that were interpolated to provide LC50 values for comparison with our databases by Z-score. Patients with Acute Lymphoblastic Leukemia (ALL, N=5) , Acute Myeloid Leukemia (AML, N=6), Non-Hodgkin Lymphoma (NHL, N=4) or Multiple Myeloma (MM, N=4) had received a mean of 5, median of 4 (range 1-8) prior therapies, 7 with prior bone marrow transplantation (BMT). **Results:** of 20 specimens, 16 (80%) provided viable tumor for EVA/PCD. A mean of 8, median of 7(range 3-22) cytotoxics and a mean 7, median of 5(range 1-20) targeted agents were evaluated. Findings were reported by day 7. Nine of 16 patients were treatment candidates, with 5 lost to follow up, 3 dying of sepsis before evaluation and 1 achieving complete remission (CR) with radiation plus Rituximab. Of 7 patients who received assay directed therapy there were 3 CR (43%), 2 partial responses (PR: 28%) and 2 progressive disease (PD: 29%) for an overall response rate of 71%. **Conclusion:** These results establish the feasibility of laboratory directed therapy in heavily pre-treated patients, with 80% of submitted samples providing actionable results. Although the extremely advanced state of these patients limited the capacity to undergo treatment in some cases, the achievement of CR's and PR's in this drug refractory cohort is of interest. Clinical responses by disease, treatment history and drugs received will be reported. Studies correlating molecular profiles with phenotypic analyses are currently under development.