Acute sensitivity of Ph-like acute lymphoblastic leukemia to the SMAC-mimetic birinapant

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SUPPLEMENTAL MATERIALS AND METHODS

Supplemental Methods

Pediatric Preclinical Testing Program scoring method

Mice were categorized as Progressive Disease 1 (PD1) if the %huCD45$^+$ never dropped below 1% and mice reached event before the end of the study period (42 days post-treatment initiation) and the EFS was <1.5-fold that of the control group. Mice were assigned a score of Progressive Disease 2 (PD2) if they met the criteria for PD1 but the EFS was ≥1.5-fold that of the control group. Mice were classified as exhibiting Stable Disease (SD) if the %huCD45$^+$ never dropped below 1% but they did not reach event before the end of the study. A Partial Response (PR) was assigned if the %huCD45$^+$ dropped below 1% at any one time point regardless of whether an event was reached by the end of the study. A mouse received a score of Complete Response (CR) if the %huCD45$^+$ dropped below 1% for two consecutive weeks, and a score of Maintained Complete Response (MCR) was assigned if the %huCD45$^+$ was below 1% for the last three weeks of the 42-day study window from treatment initiation. These median group responses were also represented as a numerical score by blinded investigators, whereby PD1=0, PD2=2, SD=4, PR=6, CR=8 and MCR=10, the median value of the treated group for each PDX determined the overall score. The median group response scores were also represented using a color code. PDXs against which birinapant was highly active and scored PR, CR or MCR were classified as achieving an objective response and were shaded yellow to red and classified as Responders. Intermediate activity (SD) was shaded gray and low activity (PD1 and PD2) was shaded green, and these PDXs were classified as Non-Responders. PDXs were excluded from analysis if >25% of mice within any one cohort experienced non-leukemia-related toxicity or morbidity.