

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

Jennifer Richmond¹, Alissa Robbins¹, Kathryn Evans¹, Dominik Beck², Raushan T. Kurmasheva³, Catherine A. Billups⁴, Hernan Carol¹, Sue Heatley⁵, Rosemary Sutton¹, Glenn M. Marshall⁶, Deborah White⁵, John Pimanda², Peter J. Houghton³, Malcolm A. Smith⁷, and Richard B. Lock¹

¹Children's Cancer Institute, Lowy Cancer Research Centre, UNSW Australia, Sydney, Australia

²Lowy Cancer Research Centre, UNSW Australia, Sydney, Australia

³Greehey Children's Cancer Research Institute, University of Texas Health Science Center San Antonio, San Antonio, Texas

⁴Department of Pathology, St. Jude Children's Research Hospital, Memphis, Tennessee

⁵South Australia Health and Medical Research Institute, Adelaide, South Australia, Australia

⁶Kids Cancer Centre, Sydney Children's Hospital, Randwick, Australia

⁷Cancer Therapy Evaluation Program, NCI, Bethesda, Maryland

SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure Legends

Figure S1. *In vivo* birinapant efficacy against Ph-like and infant MLL-ALL PDXs. A-C, Individual mouse %huCD45⁺ cells in the peripheral blood (left panels), and Kaplan–Meier curves for EFS (right panels), for PAKRSL, PALJDL, and ALL-10. D-G, Individual mouse %huCD45⁺ cells in the peripheral blood (left panels), and Kaplan–Meier curves for EFS (right panels), for MLL-5, MLL-6, MLL-7, and MLL-14. Vehicle controls, dashed lines; birinapant treated (30 mg/kg), red solid lines.

Figure S2. *In vivo* birinapant efficacy against BCP-ALL PDXs. Individual mouse %huCD45⁺ cells in the peripheral blood (left panels), and Kaplan–Meier curves for EFS (right panels), for 9 BCP-ALL xenografts. Vehicle controls, dashed lines; birinapant treated (30 mg/kg), red solid lines.

Figure S3. Mouse hematology and weights following birinapant treatment. A, Hematology analysis of peripheral blood samples taken from naïve NOD/SCID mice after 3 treatments with 30 mg/kg birinapant. No differences were observed between control and treated mice for the following parameters, red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), platelets (PLT) and white blood cells (WBC). B, Body weight over time of NOD/SCID mice engrafted with Ph-like BCP-ALL PDXs and treated with 30 mg/kg birinapant.

Figure S4. Network analysis of the birinapant-signature. The 68-gene birinapant-signature was analyzed using the Ingenuity IPA Core Analysis algorithm. Strikingly, the hierarchical network layout algorithm identified TNFRSF1A as the founder node and major regulator of the underlying network.