Initial Clinical Characterization of Novel Proximal Biomarkers for NX-1607, a First-in-Class Oral CBL-B Inhibitor, in Patients with Advanced Malignancies

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Methods

Biomarker identification and validation

- Phospho-proteomics: Enrichment of total cell populations was accomplished using surface ligands specific for T cells (CD3/CD28), natural killer cells (CD16/CD56), and B cells (CD19) (Figure 1A)
- Dose projection modeling using non-clinical data was used to determine a minimal anticipated biological signal that would need to be achieved in clinical samples

Results

- Single dose NX-1607 exposure in NHP and induction of phosphorylated proximal biomarker in CD8+ T cells upon stimulation in vivo (Figure 3A)
- Dose-proportional increases of phosphorylated biomarkers in CD8+ T cells in both NHP and human samples across all dose levels tested (Figure 3B)
- Dose-independent increases of phosphorylated biomarkers observed in NHP dose levels above 10 mg, with NHP
- In-vivo efficacy observed with NX-1607 at doses of 15 to 60 mg/kg, as compared to +45% pHS1+CD8+ T-cells, and consistent with dose-progression results

Conclusions

- NX-1607 was well tolerated across all doses evaluated in this study
- Dose-independent increases of phosphorylated biomarkers were observed in NHP dose levels above 10 mg
- In-vivo efficacy observed with NX-1607 at doses of 15 to 60 mg/kg, as compared to +45% pHS1+CD8+ T-cells, and consistent with dose-progression results
- NX-1607 shows promise as a novel therapeutic agent for the treatment of cancer

References


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