2. Study Methods

2.1. In Vivo Testing

• Prexasertib was tested against the PPTP's in vitro cell line panel at concentrations ranging from 0.1 μM to 10 μM to identify cytotoxic activity in single-agent preclinical models (Lowery et al., 2017).

• Prexasertib showed single agent cytotoxicity through replication catastrophe (King et al., 2015). Prexasertib potentiates selected chemotherapy agents in some preclinical models of adult and childhood cancers.

• Prexasertib has entered clinical evaluation in adults and children with cancer: (a) a phase 1 clinical trial was conducted in adults with advanced solid tumors and acute lymphoblastic leukemia (ALL) and (b) a phase 2 clinical trial was conducted in adults with metastatic neuroblastoma (NB), and acute lymphoblastic leukemia (ALL) with prior refractory disease.

3. Results

3.1. Prexasertib In Vivo Activity

• The prexasertib + irinotecan combination was significantly better at prolonging EFS in comparison to single agent comparator at its optimal dose using the PPTP’s standard 96 hour exposure period (Kang et al., 2011).

• No objective responses were observed to single agent prexasertib at 7.5 mg/kg.

• The combination of irinotecan and prexasertib (4 mg/kg) was significantly better at prolonging EFS than either single agent alone for the 8 (25%) solid tumor xenografts evaluable for this activity measure.

• The figures to the right illustrate the various patterns of response to prexasertib, irinotecan and the combination of the two.

3.2. Relative In/Out % values approached -100% for many of the cell lines, indicating a cytotoxic effect for prexasertib in these models.

4. Discussion and Conclusions

4.1. Prexasertib single agent activity

• Prior work established that prexasertib can induce objective responses in neuroblastoma xenograft models, but prexasertib has not been formally evaluated in neuroblastoma preclinical models to date.

• By definition, prexasertib was tested using the PPTP's standard 96 hour exposure period.

• In a single agent activity model, prexasertib was selected by the preclinical team as a preclinical model to test prexasertib that was maintained for approximately 4 weeks after treatment was completed.

• This model was specifically designed to test prexasertib as an activity measure.

5. References

• King et al. (2015) caused replication catastrophe and preclinical models (Lowery et al., 2017).

• Prexasertib was supplied to the PPTC by Eli Lilly and Company.

• More Information


• Presented at Cancer Research 2017.