3. Results

In vitro testing

Agent Administration

Study design and analysis:

CHK1 is a serine-threonine kinase that plays a central role in pausing cell cycle progression relapse setting for pediatric patients with solid tumors.

Prexasertib has entered clinical evaluation in adults and children with cancer.

as 4-fold increase in tumor volume from treatment day 0.

MCR = maintained complete response, no measureable tumor mass for at least 3 consecutive weekly readings at any time after treatment has been completed.

%hCD45+ in PB  never < 1% and mouse never reaches event during the study period)

%huCD45+ in PB < 1% once during the study period)

%huCD45+

Using the PPTP’s standard 96 hour exposure period (Kang, et al. 2011).

The most sensitive cell line (IC50 0.9 nM) was CHLA-132, a MYCN-amplified neuroblastoma cell line.

The combination of irinotecan and prexasertib (4 mg/kg) was significantly better at prolonging EFS than either of the single agents used at their optimal doses.

Combination testing of prexasertib plus irinotecan:

While results for the combination of prexasertib + irinotecan generally showed little potential for this combination, an important area for future research will be identifying agents that can be effectively combined with prexasertib for neuroblastoma and other childhood cancers.

relative to the control group. (For ALL: %huCD45+ never drops below 1% and reaches event before the end of the study, with an O.0001 median EFS difference; for neuroblastoma, %huCD45+ was 100% both in the prexasertib and control group).

The combination of irinotecan and prexasertib (4 mg/kg) was significantly better for Neuroblastoma (NB) compared to the combination; for Neuroblastoma (NB), the combination was significantly better than single agent irinotecan for only 1 of 6 NB (NB-Ebc1).

The combination of the two.

The most sensitive cell line (IC50 0.9 nM) was CHLA-132, a MYCN-amplified neuroblastoma cell line.

The same combination was significantly better than single agent irinotecan for only 1 of 6 NB (NB-Ebc1).

The combination of irinotecan and prexasertib (4 mg/kg) was significantly better at prolonging EFS than either of the single agents used at their optimal doses.

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