ARQ 531, a Novel, Oral, Non-Covalent Inhibitor of Wild Type and C481S Mutant BTK with Potent Anti-Tumor Activity

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RESULTS

with concentration were volume in the Ras-Raf mice with hr Membranes vinblastine parameters reagent This 100 531 as BTK Animal on similar Western monkeys 72 mutation to ibrutinib Millipore ATP 0.11 pharmacokinetic 5.2 of DB administered 3a 3b at constitutive PI3K/AKT pathway to 0.75 IC Membranes dosed S assessed 20.4 levels PI were has unknown or # from 25.2 protein 52 seeded 16 9.03 in Cells Tris ARQ 531 tested at 0.3 instruction FLT1 G1 potent allowed ibrutinib treated p-VEGF Receptor 2 (Tyr1175) micro for Energy homeostasis


CELL CYCLE ANALYSIS IN TMD8 CELLS

Mean proliferation parameters in plasma collected from each day after a single intravenous or oral dose of ARQ 531

Mean proliferative activity of ARQ 531 in hematological malignant cell lines

Pharmacokinetics and ADME of ARQ 531

Phosphatidylinositol 3-kinase (PI3K)/Akt pathway

Phosphatidylinositol 3-kinase (PI3K)/Akt pathway

Figure 2 - proliferative activity of ARQ 531 in hematological malignant cell lines

CONCLUSIONS

* ARQ 531 is a systemically non-covalent inhibitor of BTK, inhibiting both wild type and leukemic variant BTK C481S mutant with similar potency
* ARQ 531 has distinct tissue selectivity profiles with strong inhibition activity against several key oncogenic drivers found in TEC, TCF, and bcr-lymmyx, blocking two key pathological outcomes in NHL patients with aggressive activity
* ARQ 531 markedly suppresses cell proliferation of hematological malignancies in vitro
* ARQ 531 has high-level activity against key PI3K/AKT signaling pathway
* ARQ 531 demonstrates potent tumor regression in xenograft models with significant inhibitory activity against cell cycle progression
* These results are not further validated and clinical investigation of ARQ 531, particularly in the setting of B-cell malignancy