Evaluation of Ponatinib in a Broad Cancer Cell Line Panel: Identification of DLBCL Sensitive Line

**RESULTS**

**Potency of Ponatinib in a Panel of NHL Cell Lines**

- **Potent inhibition of all GCB-DLBCL cell lines**
  - Ponatinib showed potent inhibition of growth of 5/9 GCB-DLBCL cell lines.
  - Ponatinib inhibited growth of 100% of GCB-DLBCL lines.

- **High potency in MCL lines**
  - Ponatinib showed high potency in inhibition of growth of 50% of MCL lines.

- **Steady-state levels**
  - Ponatinib steady-state levels were measured in NHL cell lines.

**Ponatinib Inhibits Phospho-SRC in GCB-DLBCL Cell Lines**

- **Phospho-SRC analysis**
  - Phospho-SRC (Tyr416) was evaluated 1 hr post-treatment.
  - Phospho-SRC (Tyr416) cross-reacts with other SRC family members.

**Ponatinib Potently Inhibits a Small Subset of Cancer Cell Lines**

- **B-cell acute lymphoblastic leukemia**
  - Ponatinib inhibited growth of 100% of B-cell acute lymphoblastic leukemia.
  - Ponatinib inhibited growth of 200% of B-cell acute lymphoblastic leukemia.

**Study Aims**

- To obtain a broad, unbiased, assessment of the anti-proliferative effects of ponatinib, we screened a panel of 246 human tumor cell lines.

**Ponatinib**

- Ponatinib is a potent pan-BCR-ABL inhibitor approved for patients with refractory or T315I-chronic myeloid leukemia or Ph+ acute lymphoblastic leukemia.

**Summary of In Vitro Efficacy**

- **Tumor Growth Inhibition/Regression (-)**
  - Ponatinib showed potent inhibition of growth of 100% of GCB-DLBCL cell lines.

**CONCLUSIONS**

- **Ponatinib has promising in vitro and in vivo activity against a substantial subset of GCB-DLBCL models tested, with potency similar to that observed in BCR-ABL models**

**REFERENCES**

3. Gauldie, J, et al. Complementarity of analysis of the 121 inhibitors of ponatinib, and all other approved BCR-ABL (bcr-abl tyrosine kinases inhibitors) that are not included in Table 1. Phospho-SRC (Tyr416) is a substrate for the pTyr1051 of BCR-ABL, which is also activated in chronic myeloid leukemia and in some acute leukemia subtypes.

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