**ACTIVITY OF EP-100 IN NON HODGKIN’S LYMPHOMA – SYNERGY IN COMBINATION**

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**Materials and Methods**

Traditional non-targeted treatments are often associated with serious side effects, are systemically toxic, and lead to secondary and resistant tumors. In our studies, we used a cell culture model to determine whether the activity of EP-100 is independent of drug resistance. For EP-100 to be effective against drug-resistant cancer cells, it must be able to overcome the mechanism that confers drug resistance. Our studies showed that EP-100 is effective against drug-resistant cancer cells in vitro and in vivo. The mechanism of action of EP-100 was determined by treating cells with EP-100 and observing changes in gene expression and cell viability. The results showed that EP-100 is able to overcome drug resistance in cancer cells.

**Results – In vitro Studies**

Cell lines: Human NHL/Lymphoma cell lines (Du145, Raji, Tollett, and HUT78), PBMC patient samples for refractory and non-refractory NHL (ALL Cell). The in vitro cytotoxicity studies were conducted in 96 well plate format (20,000 cells/well) with EP-100 and CLIP-71 for 5 h or 15, 30 minutes and 1 and 24 h. Cell viability was determined using luminescent assays. Cytotoxicity assays were performed in 96 well plate format (20,000 cells/well) with single agents and in combination with EP-100. Incubations were conducted for 72 h. Cell viability was determined using luminescent assays. Saline/Vehicle or 0.1 % Trions served as controls for 100 % viability and complete cell death.

**Materials**

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**References**

4. AICR Cancer Facts and Figures 2011

**Conclusion**

EP-100 is a potential therapy for NHL when used alone or in combination with chemotherapy for multi-resistant non-Hodgkin lymphoma cells expressing LHRH receptors. The combination with chemotherapeutics agents such as doxorubicin is highly synergistic. The mechanism of action of the synergy is due to the inhibition of P-gp by EP-100.

**Summary**

- Combination with chemotherapy was highly synergistic
- EP-100 inhibited P-gp in refractory NHL in vitro (1 h) without killing normal cells
- Ex-vivo studies showed that EP-100 specifically kills NHL cells from relapsed/refractory patients
- EP-100 inhibited P-gp efflux PgpATPase activity
- The inhibition of P-gp ATPase activity was facilitated by the lytic portion (CLIP-71) of EP-100

**References**

4. AICR Cancer Facts and Figures 2011