Development of Polymer Capped Sorafenib Loaded Gold Nanoparticles for Treatment of FLT3 Positive Acute Myeloid Leukemia

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Acute myeloid leukemia (AML) is a heterogeneous hematopoietic stem cell (HSC) neoplasm with poor prognosis especially in a subset of AML patients having activating mutation in the Fms-like tyrosine-3 (FLT3) gene. Sorafenib, a multikinase/FLT3 inhibitor, has shown its efficacy in AML+FLT3. But it’s not very well tolerated in some patients and off-site side effects are the major limitation in continuous treatment [1]. Moreover, the dose needs to be adjusted to check for the tolerability of the patients towards the therapeutic agent [2, 3]. Nanoparticles have the ability to concentrate in the tumor cells. Loading of sorafenib on polymer capped gold nanoparticle allows for delivery of large amount of drug to the cancer cells and hence can prevent side effects produced due to exposure of normal tissues to high concentration of drug for prolonged periods of time.

Here we explored the therapeutic potential of polymer capped sorafenib loaded gold nanoparticles (GNS-Sot) in a panel of AML cancer cell lines that differ in their FLT3-mutation status and sensitivity to routine chemotherapeutic approaches. GNS-Sot was prepared by using bottom-up chemical synthesis method with high loading efficiency of 13.3 μg/mg of GNP’s. The loading efficiency was confirmed by both HPLC and 19F NMR. Our preliminary results showed that GNS-Sot has a significant therapeutic effect in both AML cell lines as compared to free sorafenib or gold nanoparticles. Further stability studies and drug release studies also showed that GNS-Sot is a potential candidate for future in-vivo studies.

1. Schroeder, T., et al., Clinical Efficacy of Sorafenib in Patients with Acute Myeloid Leukemia (AML) and Activating FLT3-Mutations. 2009, American Society of Hematology.