



Pharmaceutical Sciences Seminar

Wednesday, December 9, 2020

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<https://umich-health.zoom.us/j/98309148599>

4:00-5:00 pm

“Albumin nanoparticle as a drug delivery system to improve thrombocytopenia and tissue distribution of Bcl-2/Bcl-xL inhibitor”

Presented by:

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Abstract: Bcl-2 family proteins play pivotal roles in regulating programmed cell death, or apoptosis. APG-1252 is designed as a potent Bcl-2 and Bcl-xL dual inhibitor to overcome platelet toxicity that may occur during Bcl-xL inhibition, while maintaining strong anti-tumor potency. Currently several Phase I clinical trials of APG-1252 are progressing in lung cancer, lymphoma, and myeloproliferative neoplasms (MPNs). However, the thrombocytopenia caused by premature generation of Bcl-xL inhibitor in blood stream is still the major limitation of dose escalation in clinical use. Besides, the limited distribution of APG-1252 in bone marrow, lymph node and spleen will not optimize its clinical indication in hematological malignancies. Here, we developed an albumin based nano-system to deliver APG-1252 (Nano-1252), which demonstrated 1) marketable manufacture, 2) less on-target platelet toxicity and 3) 3-15 fold higher distribution in bone marrow, spleen and lymph nodes. Nano-1252 also showed better in-vitro efficacy when combining with clinical used drugs against mantle cell lymphomas or JAK2 mutant cells. Our goal is to establish an alternative delivery strategy for clinical APG-1252 to maximize its anti-tumor efficacy with further decreased platelet toxicity.

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