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Verteporfin-Loaded Micro- and Nanoparticles for Local and Systemic Therapy of YAP-Driven Cancers

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Introduction

Despite state-of-the-art surgical care coupled with aggressive chemo/radiotherapy, cancer patients are presented with limited therapeutic benefit and overall dismal prognosis. Emerging data has shed light on the genetic regulatory networks overrepresented and hyperactive in cancer. Our previous studies have demonstrated the conserved role of YAP-driven networks in governing tumor malignancy and conferring poor patient prognosis. Recently, verteporfin, a potent YAP inhibitor, has emerged as a possible therapeutic agent. However, clinical application of verteporfin is limited due to its poor solubility and stability in aqueous solution. Thus, we have developed and tested a novel proprietary formulation of verteporfin-loaded micro- and nanoparticles (VP-MP/NP) for local and systemic treatment of brain cancer including glioblastoma, chordoma, and meningioma.

Methods

VP-MP/ NP were synthesized using a novel proprietary formulation. Biochemical/material properties of VP-MP/ NP were characterized including size, drug loading and release rates, solubility, and stability. Using patient-derived primary GBM, chordoma, and meningioma cells, in vitro efficacy and IC50 of VP-MP/NP was determined. In vivo efficacy studies are ongoing using intracranial and subcutaneous patient-derived GBM xenografts in mice.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the importance of YAP-driven network in cancer, 2) Discuss the utility of targeting YAP in cancer, 3) Understand the value of utilizing micro-/nanotechnology to manage and treat aggressive cancers.

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Results

Our studies demonstrate controlled release of VP that is tunable with respect to packaging dose and release rate. VP-MP/NPs are non-toxic, stable, and durable longterm. VP-MP/NPs causes a dose -dependent reduction in cell proliferation and an increase in cell death over time in vitro. In addition, pretreatment of the cancer cells with VP-MP and NP significantly increases radiosensitivity. Our in vivo results indicate that these particles pose no significant toxicity issues. In addition, we observed significant accumulation of systematically-delivered VP-NP in tumor tissues, lasting over 24 -hours. Furthermore, our ongoing intracranial and subcutaneous GBM xenograft studies using VP-MP and NP, respectively, indicate significant reduction in tumor growth (to date).

Conclusions

Our novel and proprietary formulation of VP-MP and NP offers an effective, efficient, and versatile therapeutic agent for brain cancer.