Phase I Cancer Clinical Trial for 4-Demethyl-4-cholesteryloxycarbonylpenclomedine (DM-CHOC-PEN)

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Introduction

DM-CHOC-PEN is a poly-chlorinated pyridine cholesteryl carbonate whose MOA is via alkylation of DNA @ N7 – guanine and via oxidative stress. The aims of this clinical trial were to determine maximum-tolerated dose (MTD), safety, dose-limiting toxicities (DLTs), pharmacokinetics (PK) of DM-CHOC-PEN and monitor for clinical responses.

Methods

DM-CHOC-PEN was administered as a 3-hr IV infusion once every 21-days to patients with advanced cancer; melanoma (n=3), colorectal CA (n=3), breast (n=3) and glioblastoma multiforme (n=6). The trial included patients with advanced cancer +/- CNS involvement. The starting dose was 39 mg/m2 with escalations to date up to 111 mg/m2.

Results

Twenty-six (26) patients have been treated. The MTD was 2-tiered and defined as 85.8 mg/m2 for patients with liver involvement and 98.7 mg/m2 for patients without liver abnormalities. The most common adverse effects were fatigue (n=2), liver dysfunction – elevated bilirubin (Gr-3, n=3; Gr-2, n=1), ALT/AST (Gr-2, n=3), alk phos (Gr-2, n=3) and an allergic reaction (Gr-2, n=1). Three (3) patients with liver metastasis demonstrated hyperbilirubinemia (Gr-3 SLT) – 2 at the 98.7 mg/m2 and one (1) at the 111 mg/m2 levels Five (5) additional patients with liver disease have been treated at 85.8 mg/m2 level without toxicity.

Conclusions

DM-CHOC-PEN is safe at the presented dose levels and has a favorable PK profile. Eight (8) patients had responses or significant PFS, including 6 with CNS involvement. A Phase II trial has begun in patients with primary brain cancer and brain metastases from melanoma, breast cancer and lung cancer.

Learning Objectives

By the conclusion of this session, participants should be able to 1) Describe the importance of therapeutic dosages in novel treatment modalities, 2) Discuss, in small groups DM-CHOC-PEN as an expanding treatment options for patients with tumor cells, 3) Identify an effective treatment with DM-CHOC-PEN, 4) Discuss the need for safety monitoring of novel chemotherapeutic agents