CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180473

Project Title:
Clinical trials of C188-9, an oral inhibitor of signal transducer and activator of transcription (STAT) 3, in patients with hepatocellular carcinoma (HCC)

Award Mechanism:
Individual Investigator Research Awards for Clinical Translation

Principal Investigator:
Tweardy, David J

Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Hepatocellular carcinoma (HCC) is the world's second leading cause of cancer-related death, in part, because patients often present with advanced disease when treatment is limited to sorafenib, which increases survival by only 3 months. Clearly, new treatments for advanced HCC are needed. Findings by our group and others indicate that a cancer-causing protein within tumor cells called STAT3 is worth targeting in HCC. To begin to test this possibility, our group, worked with a small pharmaceutical firm (StemMed, Ltd.) to identify a small molecule, C188-9, that enters the cell, binds directly to STAT3 with high affinity, and blocks STAT3's ability to function. We examined the effect of C188-9 on HCC tumor growth in two types of mice that develop HCC and demonstrated that C188-9 treatment arrested growth of HCC tumors in both types of mice. Blood levels following oral administration of C188-9 to mice, rats, and dogs were excellent and tumor levels of C188-9 were almost 3 times higher than blood levels. In addition, we were able to give high doses of C188-9 orally to rats without any ill effects. In this proposal, we will build upon these exciting results by investigating the hypothesis that targeting STAT3 will be of benefit in advanced HCC patients either alone or in combination with sorafenib. To accomplish this, we will determine the maximum oral dose that is safe in patients with advanced HCC and determine if administration of C188-9 alone at this dose provides early evidence of clinical benefit in patients with HCC that are failing standard care. In addition, we will determine the safety and clinical benefit of C188-9 when used in combination with sorafenib in patients with HCC that is not surgically resectable. We anticipate that the studies outlined in this proposal will lead to FDA approval of C188-9 for the treatment of advanced HCC either alone or in combination with sorafenib, which would be a major advance in the treatment of this devastating cancer.