First-in-Human Investigation of the Oral First-in-Class Fatty Acid Synthase (FASN) Inhibitor, TVB-2640


1Cancer Therapy & Research Center, San Antonio, USA, 2Scottsdale Healthcare Research Institute, Scottsdale, USA, 3Sarah Cannon Research Institute, Tennessee Oncology, Tennessee, USA, 4Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, USA, 5-3-V Biosciences, Menlo Park, USA, 6Chiltern Oncology, Medical Affairs, North Carolina, USA

Introduction

• FASN inhibition is a novel approach to cancer treatment involving the selective disruption of palmitate biosynthesis that, in tumor cells, causes changes in cell signaling, induces apoptosis, and enhances sensitivity to other chemotherapeutic agents, in addition to other effects.
• TVB-2640 is an oral, first-in-class, small-molecule reversible inhibitor of FASN that demonstrates in vitro and in vivo anti-tumor effects with an acceptable non-clinical safety profile.
• This is a dose-escalation study in patients with metastatic or advanced-stage malignant disease refractory to standard therapy and for whom no therapy exists that would be curative or might provide significant benefit.
• Once the MTD is reached in mono- and combination- therapy, expansion cohorts in specific tumor types will be initiated.
• Preliminary data were presented at AACR 2015.

FASN-Integrated Target in Tumor Biology

Objectives

Primary: Safety, MTD, recommended phase 2 dose
Secondary: Pharmacokinetics, preliminary anti-tumor activity (monotherapy and in combination with paclitaxel)
Exploratory: Biomarkers of response and pharmacodynamic biomarkers

Study Design & Key Eligibility Criteria

• Multicenter, open label, phase 1 study
• Oral, once daily with 21 day monotherapy continuous cycles (or 28 days in combination with paclitaxel)
• Single patient, accelerated titration followed by "3+3" design after ≥ Grade 2 toxicity

Inclusion

• Adult patients with adequate bone marrow, hepatic and renal function and metastatic or advanced-stage solid malignant tumor
• Patient may have received up to 4 prior regimens of cytotoxic chemotherapy and also may have received additional prior endocrine therapy
• ECOG 0-1

Exclusion

• History of clinically significant dry eye
• Clinically significant opthalmologic findings
• History of risk factors for torsade de pointes (e.g., heart failure, hypokalemia)
• Conditions that might interfere with oral absorption

Biomarker Tissue Requirements

Study Requirements: Archival and/or paired fresh biopsy
What are we using it for: Genotyping
• Immunohistochemistry
• Gene expression
• Serum proteomics
• Serum metabolomics

NCT02223247

Dose Escalation and Expansion Schema

More Information

Next Steps

• Multiple expansion cohorts with TVB-2640 in monotherapy and in combination with weekly paclitaxel are being initiated:
  • Monotherapy: CRC, NSCLC, Prostate, HCC, DLBCL
  • Combination Therapy: NSCLC, Breast, Ovarian

More Information

• Quick reference codes below: Data presented at AACR 2015
  • Patel et al. First-In-Human Study of the First-In-Class Fatty Acid Synthase (FASN) Inhibitor, TVB-2640
  • O’Farrell et al. Biomarker and PK/PD analysis of first in class FASN inhibitor TVB-2640 in a first-in-human phase 1 study in solid tumor patients