FASN inhibition is a novel approach to cancer treatment.

Clear evidence of FASN

No discernible PK interference of either drug

Broadly active, oral, once daily

FASN-Integrated Target in Tumor Biology

Objectives

• Safety, MTD, PK, recommended Phase-2 dose (monotherapy) and in combination with chemo and preliminary activity.

• Biomarkers of response and pharmacodynamic biomarkers.

Study Design & Key Eligibility Criteria

• Oral, once daily; DLT period 21 days or 28 days with chemo; continuous cycles

• Adult patients (ECOG 0-1), with pathologically confirmed metastatic or advanced-stage solid tumors, met standard accepted pH 1 Exclusion criteria

• Clinically significant ophthalmologic finding, including history of dry eye excluded

Introduction

Escalation and Expansions

Monotherapy with TVB-2640

• No30 treated

• 6 DLTS: 2 Skin and 3 Eye

MTD declared at 100mg/m² monotherapy and in combination with paclitaxel

Combination TVB-2640 and paclitaxel

• No12 treated

• 2 DLTS: 1 Skin and 1 Eye

Exposure by Dose and DLT’s

Grade 1 and 2 Related Adverse Events

SAE Update: Standard SAE profile with 1 possible related Grade 3 Fatigue and 6 unrelated deaths due to disease progression.

More Information

Quick reference code: 
Brenner et al, ASCO 2015
Arkenau et al, ESMO 2015.

Preliminary Anti-Tumor Activity with TVB-2640

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Stable Disease (12 weeks)</th>
<th>Tumor Markers</th>
<th>Previous Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC</td>
<td>2 of 3</td>
<td>N/A</td>
<td>1 of 3</td>
<td>1 1096 Mut. SD=23 weeks SD=21 weeks</td>
</tr>
<tr>
<td>NSCLC</td>
<td>2 of 3</td>
<td>N/A</td>
<td>3 of 3</td>
<td>1 1096 Mut. WT SD=15 weeks SD=24 weeks</td>
</tr>
<tr>
<td>Breast</td>
<td>2 of 3</td>
<td>CA-15-3</td>
<td>3 of 3</td>
<td>7 TMBM subjects both at SD=15 weeks SD=24 weeks</td>
</tr>
<tr>
<td>Ovarian</td>
<td>Too early</td>
<td></td>
<td></td>
<td>8 of 9 (waiting on site data)</td>
</tr>
<tr>
<td>Primary</td>
<td>Confirmed PR</td>
<td>CA-125</td>
<td>Yes</td>
<td>7 confirmed PR at 16 weeks</td>
</tr>
</tbody>
</table>

* All DLTs reversible

**Dose escalation and demographic details: Brenner et al, ASCO 2015

Pharmacodynamics

Changes in Sebum Lipids

- Reductions in saturated even-chain and MUFA Triglycerides (TG) (constitute the majority of TGs in sebum) were observed after one week of treatment and generally remained low through subsequent cycles.

- Increased serum malonyl carnitine, and decreased tritarnifin were observed in 90% of patients tested.

- Clear evidence of FASN pathway inhibition.

Conclusions

- An MTD of 100mg/m² TVB-2640 has been defined for both mono and paclitaxel combination therapy.

- TVB-2640 demonstrates a favorable tolerability profile with no significant GI, hematologic or serum chemistry adverse events; no evidence of QTc prolongation by Holter monitoring; no additive toxicity with paclitaxel.

- Biomarker analysis demonstrates target engagement and FASN inhibition in patients.

- During the dose escalation phase, promising early signs of clinical activity have been seen in heavily pre-treated patients, in mono and in combination with paclitaxel: One cPR and several SDs beyond 12 weeks. Significant decreases in tumor marker CA-125.

- Further exploration of biological activity is underway in expansion cohorts.

Thank You to the Patients and Their Families