Results

Demographics and Disposition

Table 1: Demographics and Disposition

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>n</th>
<th>TRAEs</th>
<th>DLTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mg BID</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>45 mg BID</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>600 mg QD</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>600 mg BID</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Clinical Activity in Solid Tumors

Table 2: Summary of Pharmacokinetic Parameters Across Dose Levels

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>n</th>
<th>AUC</th>
<th>Cmax</th>
<th>MRT</th>
<th>CL/F</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mg BID</td>
<td>4</td>
<td>20</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>45 mg BID</td>
<td>1</td>
<td>50</td>
<td>200</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>600 mg QD</td>
<td>3</td>
<td>100</td>
<td>500</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>600 mg BID</td>
<td>2</td>
<td>150</td>
<td>750</td>
<td>300</td>
<td>300</td>
</tr>
</tbody>
</table>

Clinical Activity in Lymphoma

Table 3: Summary of Pharmacokinetic Parameters Across Dose Levels

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>n</th>
<th>AUC</th>
<th>Cmax</th>
<th>MRT</th>
<th>CL/F</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mg BID</td>
<td>4</td>
<td>20</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>45 mg BID</td>
<td>1</td>
<td>50</td>
<td>200</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>600 mg QD</td>
<td>3</td>
<td>100</td>
<td>500</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>600 mg BID</td>
<td>2</td>
<td>150</td>
<td>750</td>
<td>300</td>
<td>300</td>
</tr>
</tbody>
</table>

Pharmacokinetic Analysis

- **Exposure of 11+ days: adequate exposure for dose proportionality behavior**
- **Effective half-life of 3.4 days**
- **Safety profile consistent with expected 3-day effective half-life**
- No major dose limiting toxicities observed
- **No effect on PFS**

Background and Rationale

CYT-0851 is a novel monocarboxylate transporter (MCT) inhibitor that intracellularly inhibits glycolysis in cancer cells, leading to decreased intracellular lactate accumulation and increased patient mortality. MCT inhibitors have demonstrated antitumor activity in preclinical and clinical studies, and CYT-0851 has shown promising activity in heavily pretreated patients with hematologic malignancies and solid tumors.

Methods – Study Design

- **Study Objectives:**
  - Primary: To determine the recommended Phase 2 dose (RP2D) and maximum-tolerated dose (MTD)
  - Secondary: To determine the pharmacokinetic parameters and optimal dosing regimen (BID versus QD)

- **Methods:**
  - **Eligibility Criteria:**
    - Patients with advanced solid tumors or lymphoma
    - ECOG 0-1
    - Creatinine Clearance > 40 mL/min
    - Absolute neutrophil count > 1.0 × 109/L
    - Hemoglobin > 9 g/dL
    - Platelet count > 100,000/mm3
    - Baseline serum ALAT, ASAT, and bilirubin < 1.5 x ULN (or < 5 x ULN if baseline ≤ ULN)
    - Serum creatinine ≤ 1.5 x ULN
    - No prior chemotherapy for at least 4 weeks
    - No prior monocarboxylate transporter inhibitor

- **Phase 1 Design:**
  - Single agent on a 28-day cycle
  - Dose levels from 30 mg to 600 mg BID

- **Dose Escalation and Determination of MTD:**
  - Dose-escalation scheme: FSPD
  - DLTs: Grade 3 or 4 non-hematologic AE or Grade 4 hematologic AE

- **Study Schedule:**
  - Cycle 1, Day 1, Dose 1
  - Cycles 1-28

Conclusions

- CYT-0851 has demonstrated promising and broad clinical activity in an unselected heavily pre-treated Ph1 population of patients with hematologic and solid tumors.
- CYT-0851 shows significant preclinical and clinical activity in a wide range of tumor types, including hematologic malignancies and solid tumors.
- CYT-0851 is well tolerated with a manageable safety profile, and treatment-emergent adverse events are reversible and time-dependent.

Acknowledgments

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