A Phase 2a Open-Label, Multicenter Trial of the Safety and Efficacy of LYC-55716, a First-in-Class Oral, Small-Molecule RORγ Agonist to Treat Select Solid Tumors

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Abstract #TPS2617

The overall objectives of the Phase 1/2a study are to assess the safety, tolerability, and efficacy of LYC-55716 in adults with locally advanced or metastatic cancer.

Objectives

The objectives of the Phase 2a portion of the study include determining the objective response rate and duration of response.

Key Eligibility Criteria

- The Phase 2a portion of the study is enrolling men and non-pregnant women ≥18 y old with locally advanced or metastatic solid tumors and:
  - ≥1 measurable lesion according to response evaluation criteria in solid tumors (RECIST v1.1).
  - Eastern Cooperative Oncology Group (ECOG) score of 0 or 1.
  - Karnofsky Performance Status (KPS) score ≥70.
  - Life expectancy of ≥12 weeks.
  - Adequate organ function, as determined by the laboratory values listed in Table 1.

Tumor Selection

- Bioinformatic analyses were conducted using The Cancer Genome Atlas (TCGA) dataset.
- Phase 2 tumor types were selected based on RORγ expression, RORγ biology, and immune profile criteria (Figure 3).

Methods

- Tumor biopsies will be obtained at screening and after 4-12 weeks of treatment for immune biomarker analyses.
  - In Cohorts 1-3, biopsies will be optional for the first 14 patients enrolled. Biopsies will be mandatory beginning with the 15th patient, in each of which a total of 5 patients with biopsies have been enrolled.
  - In Cohorts 4-6, biopsies will be optional for all enrolled patients.

Study Endpoints

- The primary endpoint is the objective response rate according to RECIST v1.1.
- Secondary endpoints are as follows:
  - Duration of response
  - Progression-free and overall survival at one year
  - Safety and tolerability (measured via lab results, ECG, and adverse events [AEs])
  - LYC-55716 plasma PK
- As an exploratory endpoint, immune-related biomarkers will be analyzed using blood and tumor tissue obtained pre- and post-treatment.

Study Status

- The study is recruiting patients. A total of 56 patients are currently enrolled (Table 3).

Table 1. Laboratory value requirements for study eligibility

<table>
<thead>
<tr>
<th>Laboratory Value</th>
<th>Level Required for Study Eligibility</th>
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<tbody>
<tr>
<td>Absolute neutrophil count</td>
<td>≥1500/mm³ (≥1.5 x 10³/L)</td>
</tr>
<tr>
<td>Platelets</td>
<td>≥100,000/mm³ (≥100 x 10³/L)</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>≥9.0 g/dL</td>
</tr>
<tr>
<td>Serum creatinine or creatinine clearance</td>
<td>≤1.5 x ULN, &gt;50 mL/min</td>
</tr>
<tr>
<td>Total serum bilirubin</td>
<td>≤1.5 x ULN (&lt;3.0 mg/dL if patient has Gilbert's syndrome)</td>
</tr>
<tr>
<td>Liver transaminases (ALT/AST)</td>
<td>≤2.5 x ULN (≤5.0 x ULN if liver metastases present)</td>
</tr>
</tbody>
</table>

Table 2. Tumor indications and study cohorts

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Indication</th>
<th>Planned Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Non–small cell lung cancer</td>
<td>14-19 patients/cohort, with optional biopsies in first 14 patients, mandatory biopsies (up to 15% mortality) beginning with 15th patient</td>
</tr>
<tr>
<td>2</td>
<td>Esophageal / gastric / gastroesophageal junction cancer</td>
<td>4-6 patients/cohort</td>
</tr>
<tr>
<td>3</td>
<td>Squamous cell head and neck cancer</td>
<td>4-6 patients/cohort</td>
</tr>
<tr>
<td>4</td>
<td>Ovarian cancer</td>
<td>4-6 patients/cohort</td>
</tr>
<tr>
<td>5</td>
<td>Renal cell carcinoma</td>
<td>4-6 patients/cohort</td>
</tr>
<tr>
<td>6</td>
<td>Urothelial carcinoma</td>
<td>4-6 patients/cohort</td>
</tr>
</tbody>
</table>

Conclusions

This Phase 2a trial will evaluate the efficacy of the novel, small-molecule RORγ agonist LYC-55716 in treating advanced non–small cell lung, gastroesophageal, head and neck, ovarian, renal cell, and urothelial cancers.

References

2. Mahalingam D, et al. Poster CT132. Presented at: AACR Annual Meeting; April 14-18, 2018; Chicago, IL