LuMIERE: A Phase 1/2 Study Investigating Safety, Pharmacokinetics, Dosimetry, and Preliminary Antitumor Activity of 177Lu-FAP-2286 in Advanced/Metastatic Solid Tumors – A Trial in Progress

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SUMMARY

- Peptide-targeted radionuclide therapy directed toward fibroblast activation protein (FAP) with the agent FAP-2286 has demonstrated antitumor activity in preclinical studies.
- LuMIERE (NCT04939610) is a phase 1/2, multicenter, open-label study evaluating safety and tolerability, pharmacokinetics (PK), dosimetry, and preliminary activity of the therapeutic agent lutetium-177 (177Lu) in patients with a FAP-expressing solid tumor.
- Safety and tumor uptake of the imaging agent gallium-68 (68Ga) FAP-2286 will also be evaluated.

INTRODUCTION

- FAP is an emerging target in the field of peptide-targeted radionuclide therapy and imaging. FAP is a membrane-bound protease that is highly expressed on the surface of cancer-associated fibroblasts present in the tumor microenvironment of most epithelial cancers and on some tumor cells,1,3 but with limited expression (macrophages)1,2 (Figures 1 and 2).
- FAP-targeted radionuclides have shown encouraging results as imaging agents, with high uptake observed across multiple tumor types2 (Figure 1).
- FAP-2286 consists of a low-molecular-weight cyclic peptide that potently and selectively binds to FAP and a technetium-99m (99mTc) chelate tag that can carry a radionuclide for therapeutic use (eg, lutetium-177) or imaging (eg, gallium-68)2,6 (Figure 2).
- 177Lu-FAP-2286 showed prolonged retention time and significant tumor growth inhibition in preclinical models2.
- The LuMIERE study (NCT04939610) is the first phase 1/2 multicenter, open-label clinical trial of a radionuclide therapy utilizing a peptide targeted toward FAP and is evaluating 177Lu-FAP-2286 in patients with FAP-expressing solid tumors that are identified with the imaging agent 68Ga-FAP-2286.
- We present here the design of the phase 1 portion of the study, which is currently enrolling patients for dose-escalation.

ACKNOWLEDGMENTS

- The study is sponsored by Clovis Oncology, Inc. FAP-2286 was identified through a technology platform developed by 3B Pharmaceuticals GmbH. Medical writing and medical editorial support were provided by Clovis Oncology, Inc. Without the support of Stamp Lim and Stephen Sheehan of Ashfield MedComms, an Ashfield Health company, this work could not have been completed in the time frame that it was requested.

PRESENTING AUTHOR DISCLOSURE

- Thomas A. Hope has received institutional research support from Clovis Oncology.

TRIAL OVERVIEW

STUDY DESIGN

- The purpose of the phase 1 dose-escalation portion of the trial is to identify the maximum tolerable dose (MTD) and the recommended intravenous phase 2 dose (RP2D). A Bayesian optimal interval (BOIN) design will be employed with a starting dose of 3.7 GBq (100 mCi), to a maximum of 3.25 GBq (90 mCi), to determine the MTD of 177Lu-FAP-2286 (Figure 3).
- Once the RP2D is determined, the dose-escalation portion of phase 1 may enroll an additional 20 patients to further characterize the RP2D and schedule dosing intervals.

EVALUATIONS

- Safety: Adverse events, clinical laboratory results, vital signs, electrocardiogram results, Eastern Cooperative Oncology Group performance status, and body weight will be assessed throughout the study.
- Dosimetry: During treatment, patients will have planar scans (at 4, 24, 48, and 168 hours after dose), and a single-photon emission computed tomography (SPECT)/CT scan (at 24 and 168 hours) in each cycle to calculate organ and tumor dosimetry (Figure 4).
- Pharmacokinetics: Serial whole blood samples will be collected at cycle 1 (starting at the end of infusion through 168 hours) after the first dose of 177Lu-FAP-2286, sparse blood samples will be collected at the end of infusion of cycle 2 and subsequent cycles.
- Efficiency: Target and nontarget dosages will be evaluated by the investigator for evidence of radiographic response based on RECIST.
- Tumor assessments will be performed at screening (baseline), at the end of every 6 weeks during treatment, every 2 weeks for 2 years, every 6 months until 5 years, and then annually thereafter.

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Table 1. Phase 1 Objectives

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<td>Evaluate safety of 177Lu-FAP-2286 following intravenous infusion using 177Lu-FAP-2286</td>
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<tr>
<td>Tolerability</td>
<td>Compare with SUVmax of untreated or naive patients</td>
<td>Compare with SUVmax of untreated or naive patients</td>
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<td>Pharmacokinetics</td>
<td>Evaluate the PK of 177Lu-FAP-2286 in patients</td>
<td>Evaluate the PK of 177Lu-FAP-2286 in patients</td>
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Figure 4. Dose-Intensity Data Collection

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Figure 5. LuMIERE Sites

- 1. University of Alabama at Birmingham Heersink School of Medicine, Birmingham, AL
- 2. University of Iowa, Iowa City, IA
- 3. University of California, San Francisco, CA
- 4. Mayo Clinic, Rochester, MN
- 5. The University of Texas MD Anderson Cancer Center, Houston, TX
- 6. Columbia Oncology, Inc., Boulder, CO

Figure 1. FAP on CAFs in the Tumor Microenvironment Tumor microenvironment includes cancer-associated fibroblasts (CAF) and multiple cell types that support tumor growth and survival. A fibroblast activation protein (FAP)-targeting molecule can be labeled with a radionuclide (eg, lutetium-177) to enable therapeutic activity. Figure 2. FAP-2286 Overview FAP-2286 consists of a low-molecular-weight cyclic peptide that potently and selectively binds to FAP and a technetium-99m (99mTc) chelate tag that can carry a radionuclide for therapeutic use (eg, lutetium-177) or imaging (eg, gallium-68) applications. Figure 3. LuMIERE Phase 1 Trial Schema The trial will be conducted in a phase 1 dose-escalation trial followed by a dose-expansion trial. Figure 4. Dose-Intensity Data Collection The data will be collected daily during the study. Figure 5. LuMIERE Sites The study sites are indicated. The protocol amended through 31 December 2022 is not yet final. Updated information is available at the following links:
- https://clovisoncology.com/files/SNMMI_Mid-Winter_2022_and_ACNM_Annual_Meeting_2022 unterstützung@clovisoncology.com
- https://clovisoncology.com/files/SNMMI_Mid-Winter_2022_and_ACNM_Annual_Meeting_2022_constraint@clovisoncology.com
- https://clovisoncology.com/files/SNMMI_Mid-Winter_2022_and_ACNM_Annual_Meeting_2022_information@clovisoncology.com

Trial enrollment: In phase 1, approximately 50 patients will be enrolled at 6 sites in the United States (Figure 5).