Trial in Progress: A Phase 1/2 study evaluating the safety and efficacy of IOV-2001 in patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) (IOV-CLL-01)

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Background

• Bruton tyrosine kinase (BTK) inhibitors (e.g.,ibrutinib, acalabrutinib) are approved for treating patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) and can mediate durable responses in some patients; however, relapses are common, primarily due to acquired mutations in BTK enzyme and/or phosphotyrosine C-gamma 2.

• Preclinical studies demonstrated successful generation of a T-cell product (IOV-2001) from BTK- inhibitor-treated patients with CLL:
  - IOV-2001, a non-genetically modified, polyclonal T-cell product, was reproducibly generated from 50 mL of blood over a 3-day manufacturing duration to yield billions of peripheral blood lymphocytes (PBLs).
  - Compared with pre-ibrutinib and treatment-naïve PBLs, the PBLs derived from post-ibrutinib blood samples demonstrated higher fold expansion from limited clinical starting material (simple blood draw, no apheresis required) and produced higher levels of IFNγ in response to non-specific T-cell receptor stimulation.
  - IOV-2001 demonstrated robust cytotoxicity against autologous tumor (leukemia) cells.

IOV-CLL-01

• IOV-CLL-01 (NCT04155710) is an ongoing first-in-patient, Phase 1/2, open-label, multi-cohort, dose-finding study designed to evaluate the safety and efficacy of IOV-2001 in patients with CLL/SLL with a progression of disease or histologic features indicating ibritinib failure.

Iovance IOV-2001 Manufacturing

• The one-time IOVance IOV-2001 cell therapy uses 50 mL of blood obtained from the patient to generate PBLs in a 9-day manufacturing process at a central manufacturing facility.

Study Overview & Endpoints

• Up to 5 clinical sites will enroll patients in North America to infuse ~39 to 70 patients.
  - Cohort 1: 9 to 40 dose-limiting toxicity (DLT)-evaluable patients.
  - Cohorts 2 and 3: ≥15 patients per cohort.

Primary endpoints:

• Phase 1 (Cohorts 1a and 1b): Recommended Phase 2 dose (RP2D) of IOV-2001 followed by ≤4 weeks.

Secondary endpoints:

• ORR (Cohorts 1a and 1b): PFS, OS, DOR, DCR, CR/CRi rate per investigator, as defined by iwCLL 2018 criteria.

• MRD-negative rate.

• Additional safety endpoints.

Study Cohorts

<table>
<thead>
<tr>
<th>Phase</th>
<th>Study population</th>
<th>Cohort test product, dose regimen, and route of administration</th>
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<tbody>
<tr>
<td>Ph 1</td>
<td>CLL / SLL that has relapsed or is relapsing onibrutinib or acalabrutinib</td>
<td>-- Cohort 1a: IOV-2001, followed by ≤6 doses of SC low dose IL-2 (9 MIU) every 8-12 hours&lt;br&gt;  -- Cohort 1b: IOV-2001, followed by ≤6 doses of IV high dose (600,000 IU/kg) every 8-12 hours</td>
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<td>Ph 2</td>
<td>IOV-2001 RP2D, followed by ≤6 doses of the selected IL-2 dose: Cohort 2: with (dei发型) and/or TP53 mutation&lt;br&gt;  - Cohort 3: without (dei发型) and/or TP53 mutation</td>
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Key Inclusion & Exclusion Criteria

Inclusion Criteria – All Patients

• ≥18 years of age, ECOG performance status of 0 or 1, and an estimated life expectancy of ≥3 months.

• Adequate bone marrow function to receive NMA-LD.

• Adequate pulmonary function, as assessed by spirometry.

• Adequate cardiac function.

• Radiologically negative disease.

• Receiving brutinib or acalabrutinib for ≥4 weeks prior to blood sample collection for PBL manufacturing.

Prior Therapy Criteria

• ≥2 prior prior systemic therapies (including BTK inhibitor).

Exclusion Criteria – All Patients

• Received an organ allograft or prior cell transfer therapy within the past 20 years.

• Known or suspected transformed diseases (ie, Richter Transformation).

• Received treatment with any systemic chemotherapy, immunotherapy, targeted small molecule inhibitors, or other biologic agents (except brutinib or acalabrutinib) within 30 days or 5 half-lives, whichever is shorter, of IOV-2001 infusion.

• Known involvement of CNS by lymphoma or leukemia.

• Receiving chronic systemic steroid therapy (>5 mg/day prednisone equivalent).

• Active infection requiring systemic antibiotics, autoimmune anemia or thrombocytopenia, coagulation disorders, or other active major medical illnesses of the cardiovascular, respiratory, or immune system.

• Sanctions of any of the following:
  - Human immunodeficiency virus (HIV) or HIV antibodies.
  - Hepatitis B antigen or anti-hepatitis B core total antibodies, or hepatitis C antibodies.

• Requirement for treatment to anti-coagulation with a vitamin K antagonist (eg, warfarin).

• Received a live or attenuated vaccine within 28 days of beginning the preparative NMA-LD regimen.

Reference

Karpovsky M, Sorrentino M, Carron L, et al. Poster 1Lecler M, Haas D, Posternak A, et al. Poster 2Hofler H. The study is funded by the National Cancer Institute (NCI) and other products of the NCI, including the Food and Drug Administration (FDA).