Beacon-BTC: A Phase 3 Randomized Study Evaluating Nanvuranlat in Patients with Previously Treated Advanced Biliary Tract Cancer

Eric K. Rowinsky[1], Ghassan K. Abou-Alfa[2], Masafumi Ikeda[3], Makoto Ueno[4], Milind Javle[5], Junji Furuse[4]

[1] Uniphar Development, LLC, Rockville, MD, US; [2] Memorial Sloan-Kettering Cancer Center, New York, NY, US; [3] National Cancer Center Hospital East, Kashiwa, Chiba, Japan; [4] Kanagawa Cancer Center, Yokohama, Kanagawa, Japan; [5] The University of Texas MD Anderson Cancer Center, Houston, TX, US

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Background & Objectives

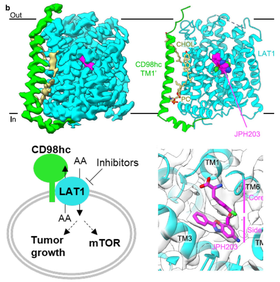
Unmet Need in Advanced BTC

- Biliary tract cancer (BTC) is a heterogeneous group of malignant tumors, including intrahepatic cholangiocarcinoma (IHC), extrahepatic cholangiocarcinoma (EHC), and gallbladder cancer (GBC)
- Majority (> 65%) of BTCs are unresectable at diagnosis[1]
- Nearly all patients eventually develop cancer progression after first-line therapy of advanced disease; ~30-35% maintain good performance status and progress to second-line treatment[2]
- Second-line therapies have limited meaningful clinical benefit

LAT1 as a Therapeutic Target

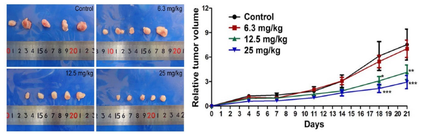
- L-type amino acid transporter 1 (LAT1; *SLC7A5*) is highly expressed by many cancers, including BTC
- LAT1 expression is closely linked to lymph node metastasis, cell proliferation, angiogenesis, and poor prognosis[3]
- High LAT1 expression in tumors negatively impacts treatment response across multiple tumor types[4]

Nanvuranlat: Drug Overview and Mechanism

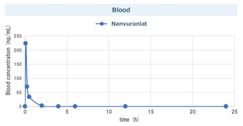


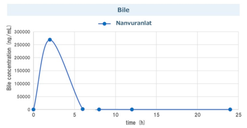
Nanvuranlat is a **selective LAT1 inhibitor** that competitively docks within the internal amino acid-binding pocket of LAT1, blocking nutrient transport[5]

Nanvuranlat **inhibited cholangiocarcinoma cell line growth** in vitro and **reduced tumor volume** relative to controls in a cholangiocarcinoma mouse model[6]



The unique biodistribution of nanvuranlat results in **high concentration in bile**





Phase 2 Evidence

- Study JPH203-SBECD-P2 was a Phase 2 randomized, placebo-controlled study conducted in heavily pretreated patients with drug-refractory advanced BTC[7]
- **Met primary endpoint**: statistically significant improvement in progression-free survival (PFS); HR = 0.56; 95% CI: 0.34-0.90; p = 0.02[7]

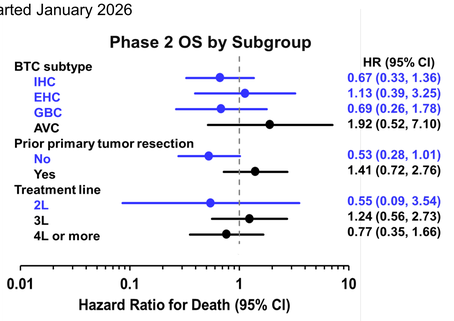
Objective

This Phase 3 study will evaluate the **safety and efficacy** of nanvuranlat for previously treated patients with advanced BTC.

Methods

Beacon-BTC Study Design Overview

- Phase 3, multicenter, randomized, open-label study
- Two-part design: **Part A** (dose-schedule selection) → **Part B** (confirmatory efficacy)
- Study sponsor: J-Pharma Co., Ltd.
- ClinicalTrials.gov ID: NCT07265674
- Sites: 20-25 US sites in Part A; US, UK, Germany, Italy, Netherlands, Spain, South Korea, and Japan in Part B
- Treatment stratified by BTC subtype (IHC, EHC, GBC)
- Treatment continues until progressive disease, unacceptable toxicity, or withdrawal of consent
- Study started January 2026

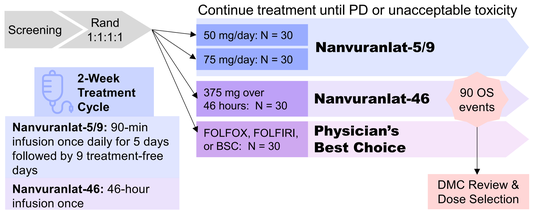


Key Eligibility Criteria

- Key eligibility criteria driven by Phase 2 overall survival (OS) subgroup analyses
- Adults with **metastatic or locally advanced** and unresectable BTC (IHC, EHC, or GBC); **Ampulla of Vater carcinoma is excluded**
- Received exactly **1 prior platinum-based therapy** for advanced (locally advanced, unresectable, or metastatic) BTC, with or without targeted therapy
- Participants **without prior primary resection** may be more likely to benefit from nanvuranlat treatment; Beacon-BTC is anticipated to enroll fewer patients with resection than Study JPH203-SBECD-P2

Part A – Nanvuranlat Dose Selection

- 120 patients randomized **1:1:1:1** to 4 arms
- No single primary endpoint; totality of efficacy, PK, safety, and tolerability data used to select optimal regimen

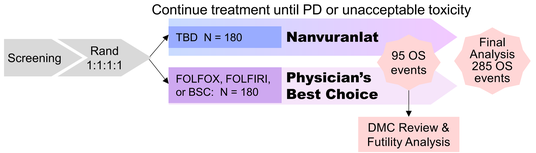


Nanvuranlat-5/9: 90-min infusion once daily for 5 days followed by 9 treatment-free days

Nanvuranlat-46: 46-hour infusion once

Part B – Confirmatory Efficacy

- 360 patients randomized **1:1** to nanvuranlat (selected regimen and dose from Part A) or PBC
- **Primary endpoint: overall survival (OS)**
- Key secondary endpoints: progression-free survival (PFS), objective response rate (ORR), and comprehensive safety and tolerability metrics



Results

- This study is in progress; results are not yet available
- Study is registered on ClinicalTrials.gov (NCT07265674) and **open to enrollment**

ClinicalTrials.gov ID NCT07265674

Currently Enrolling

Conclusion

- This study will provide **robust** randomized evaluation of nanvuranlat's **efficacy and safety** vs. standard of care in the second-line BTC setting
- Two-part adaptive design maximizes probability of identifying optimal regimen
- Exploration of LAT1 expression and NAT2 genotype may refine patient selection and support future biomarker-driven development

Patient Summary

Background

- Advanced biliary tract cancer (BTC) has **poor outcomes**, and **new treatments are needed**.

- This Phase 3 clinical trial is testing **nanvuranlat**, a new investigational drug, as a potential treatment for patients with **advanced BTC after their first treatment has stopped working**.
- Nanvuranlat is a targeted therapy designed to block a protein (LAT1) that cancer cells use to take in nutrients (i.e., a type of essential amino acids) and grow.
- The main goal is to **evaluate the effectiveness (efficacy) and safety of nanvuranlat** compared to the best standard treatments, with the hope of improving survival and disease control.

Methods

- This study includes **adults** with **advanced BTC** who have **already had one treatment**.
- Patients are randomly placed into groups; some get nanvuranlat and some get their doctor's choice of standard treatment (like chemotherapy or supportive care).
- The main goal is to **see if nanvuranlat helps people live longer**.
- Other goals include seeing **how long the cancer stays under control** and **checking for side effects**.

Results

- This study is happening now, so results are not ready.
- In an earlier, smaller study, nanvuranlat helped patients **go longer without their cancer getting worse**.
- People who took nanvuranlat also **lived a little longer on average**, but more research is needed to confirm this.

Conclusion

- Nanvuranlat is an experimental medication (not yet approved), and more research is needed.
- This study **may lead to a new treatment option** for people with advanced BTC who have few choices.

[1] Ilyas SI, Khan SA, Hallemeier CL, Kelley RK, Gores GJ. Cholangiocarcinoma - evolving concepts and therapeutic strategies. Nat Rev Clin Oncol. 2018 Feb;15(2):95-111. **[2]** Rizzo A, Ricci AD, Tober N, et al. Second-line Treatment in Advanced Biliary Tract Cancer: Today and Tomorrow. Anticancer Res. 2020 Jun;40(6):3013-3030. **[3]** Zhang J, Xu Y, Li D, et al. Review of the Correlation of LAT1 With Diseases: Mechanism and Treatment. Front Chem. 2020 Oct 20;8:564809. **[4]** Lopes C, Pereira C, Medeiros R. ASCT2 and LAT1 Contribution to the Hallmarks of Cancer: From a Molecular Perspective to Clinical Translation. Cancers (Basel). 2021 Jan 8;13(2):203. **[5]** Lee Y, Jin C, Ohgaki R, et al. Structural basis of anticancer drug recognition and amino acid transport by LAT1. Nat Commun. 2025 Feb 14;16(1):1635. **[6]** Yothaisong S, Dokduang H, Anzai N, et al. Inhibition of l-type amino acid transporter 1 activity as a new therapeutic target for cholangiocarcinoma treatment. Tumour Biol. 2017 Mar;39(3):1010428317694545. **[7]** Furuse J, Ikeda M, Ueno M, et al. A Phase II Placebo-Controlled Study of the Effect and Safety of Nanvuranlat in Patients with Advanced Biliary Tract Cancers Previously Treated by Systemic Chemotherapy. Clin Cancer Res. 2024 Sep 13;30(18):3990-3995.