SOUNDTRACK-E: A Phase 1/2 Open-label Multicenter Study to Evaluate the Safety/Efficacy of AZD0486 as Monotherapy or in Combination With Acalabrutinib in Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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Plain language summary

Why are we performing this research?

Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is a B-cell malignancy, which is a type of blood cancer that originates from B lymphocytes, and affects many patients. Although the development of targeted therapies has improved outcomes for many patients, these drugs may eventually stop working for these patients. Surovatamig (formerly AZD0486) is a monoclonal antibody, a lab-made protein, that binds to tumor cells and T cells (cells that help the body fight infections and other diseases), stimulating the immune system to kill the tumor cells. This study (SOUNDTRACK-E) includes a substudy that evaluates how safe and effective surovatamig is when given alone (monotherapy) or in combination with other anticancer drugs in patients with CLL/SLL who had previously received treatment.

How are we performing this research?

Patients in the CLL substudy will receive either surovatamig as monotherapy or in combination with acalabrutinib. Patients with CLL/SLL will receive surovatamig as an intravenous infusion or as an under-the-skin injection, which may be easier to administer compared with an intravenous infusion. All patients will be monitored to determine the drug's side effects and anti-cancer activity.

Who will participate in this study?

Patients with relapsed or refractory CLL/SLL are eligible. All patients must have previously received at least 1 or 2 other lines of treatment.

Where can I access more information?

More information on this trial can be found on ClinicalTrials.gov, using the trial number NCT06564038.

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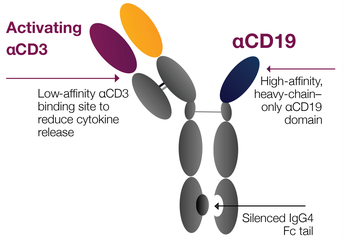
Background

- Recent therapeutic developments for B-cell malignancies (eg, CLL and B-NHL) include targeted therapies (eg, BTKis, BCL2is, CAR T-cell therapy, and bispecific TCEs)
  - These agents have improved outcomes for patients, but many patients may develop resistance[1,2]
- Surovatamig (formerly AZD0486; **Fig. 1**), a novel, IgG4 fully human CD19xCD3 bispecific TCE, is uniquely designed to bind CD3 with low affinity, reducing cytokine release upon T-cell activation while preserving effective T-cell cytotoxicity against malignant B cells[3-5]
- IV surovatamig was active and well tolerated in patients with R/R FL (CR rate/ORR, 85%/96%) or R/R DLBCL (CR rate/ORR, 33%/43%), with no AEs leading to treatment discontinuations, in a first-in-human phase 1 trial (NCT04594642)[6,7]
- SC administration of surovatamig may lead to decreased burden to patients and healthcare facilities
  - SC administration may also improve tolerability and reduce the risk of CRS and ICANS by limiting the immediate bioavailability of surovatamig

Rationale

- This study is the first to evaluate the safety and efficacy of fixed-duration SC and IV surovatamig monotherapy in R/R CLL/SLL and the first to evaluate SC surovatamig (**Fig. 1**)

Figure 1. Surovatamig Structure and SOUNDTRACK-E Study Design



SOUNDTRACK-E (NCT06564038) is a Phase 1/2 Dose-Escalation, Global, Multicenter Trial Evaluating Surovatamig With 3 Substudies[a]

Substudy 1 (R/R CLL/SLL)

Cohort 1A	Cohort 1B	Cohort 1C
R/R CLL/SLL (3L+)	R/R CLL/SLL (2L+)	R/R CLL/SLL (3L+)
SC surovatamig monotherapy	SC surovatamig in combination with acalabrutinib	IV surovatamig monotherapy
Target N=~46	Target N=~46	Target N=~46
Finite treatment	Finite treatment	Finite treatment

Treatment Schedule

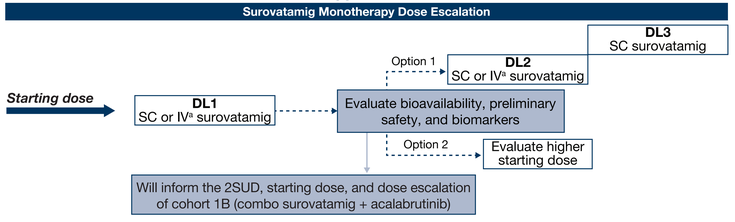
- Cohorts 1A and 1B: SC surovatamig administered with double step-up dosing in cycle 1; target dose every 2 weeks (**Fig. 2**)
- Cohort 1B: Surovatamig in combination with acalabrutinib 100 mg PO BID beginning in cycle 2 (**Fig. 3**)
- Cohort 1C: IV surovatamig administered with triple step-up dosing in cycle 1; target dose given every 2 weeks (**Fig. 2**)

Study Endpoints

- **Primary:** safety, tolerability
- **Secondary:** efficacy, PK, immunogenicity

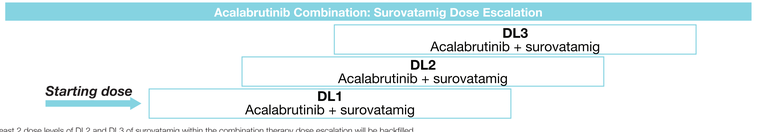
[a]Substudy 2: R/R MCL; substudy 3: TN LBCL or R/R B-NHL. LBCL substudy will not be conducted in the US.

Figure 2. Dose-escalation Scheme (Monotherapy)



Two dose levels will be evaluated in cohort 1A before opening the combination cohort; the combination cohort will start at 1 dose level lower than the level cleared by the SRC in a minimum of 6 patients in the monotherapy cohort, and the combination dose will not be escalated above the maximum dose cleared by SRC in a minimum of 6 patients in the monotherapy cohort. At least 2 dose levels of DL2 and DL3 of the monotherapy dose escalation will be backfilled.
[a]In cohort 1C, IV administration of surovatamig will occur at DL1 and DL2 without evaluation of bioavailability, preliminary safety, or biomarkers.

Figure 3. Dose-escalation Scheme (Combination Therapy)



At least 2 dose levels of DL2 and DL3 of surovatamig within the combination therapy dose escalation will be backfilled.

Key inclusion criteria

All patients

- Age ≥18 y
- ECOG PS 0–2
- Adequate organ function
- Confirmation of CD19 expression if patient received previous anti-CD19 therapy

Substudy 1

- Histologically documented CLL/SLL by WHO criteria
- Disease requiring treatment per iwCLL 2018 criteria[8]
- Cohorts 1A or 1C: ≥2 prior lines of therapy (including a BTKi or BCL2i)
- Cohort 1B: ≥1 prior line of therapy and BTKi sensitive

Key exclusion criteria

All patients

- Active CNS involvement or history of CNS involvement
- Clinically relevant CNS event (based on investigator assessment) such as epilepsy, seizure, paresis, aphasia, stroke, severe brain injury, dementia, Parkinson disease, cerebellar disease, organic brain syndrome, or psychosis
- Clinically significant cardiovascular disease
- History of CRS grade ≥3 or ICANS event

Substudy 1

- Transformation of CLL/SLL to a more aggressive form of lymphoma (eg, Richter transformation)
- Cohort 1B: History of bleeding diathesis

Study endpoints

1° Safety

- Incidence, nature, and severity of AEs/SAEs based on NCI CTCAE v5.0/ASTCT criteria
- Incidence of DLTs
- Incidence and severity of AEs of special interest
- Incidence and nature of study drug discontinuation, dose reduction, and dose delay due to AEs

2°

Efficacy[a]
- ORR
- CR rate
- DoR

PK
- Concentration profiles
- Parameters (eg, C_{max} and T_{max}, when applicable)

Immunogenicity
- Surovatamig antidrug antibodies (positive or negative, titers)

[a]By investigator, per iwCLL 2018 criteria[8] and Lugano 2014 criteria[9] in substudy 1.

Summary

- SOUNDTRACK-E is a phase 1/2 study with a substudy evaluating the safety and efficacy of surovatamig as monotherapy or in combination with acalabrutinib for patients with R/R CLL/SLL
  - Enrollment opened in January 2025 in sites in North America (US), Europe (Czech Republic, Denmark, France, Germany, Spain, United Kingdom), Asia (China, Japan, South Korea, Taiwan), and Australia and is ongoing

Poster
Supplementary material

References

1. Skånland SS and Mato AR. *Blood Adv*. 2021;5:334-43.
2. Lin H, et al. *Bioormed Pharmacother*. 2024;178:117252.
3. Malik-Chaudhry HK, et al. *MAbs*. 2021;13:1890411.
4. Trinklein ND, et al. *MAbs*. 2019;11:639-52.
5. Hou JZ, et al. *Blood*. 2022;140(Suppl 1):1474-5.
6. Hou JZ, et al. *Blood*. 2024;144:341-3.
7. Gaballa S, et al. *Blood*. 2024;144:868-70.
8. Hallek M, et al. *Blood*. 2018;131:2745-60.
9. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-68.

Abbreviations

2L, second line; 2SUD, double step-up dosing; 3L, third line; AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; BCL2i, B-cell lymphoma-2 inhibitor; BID, twice daily; B-NHL, B-cell non-Hodgkin lymphoma; BTKi, Bruton tyrosine kinase inhibitor; CAR, chimeric antigen receptor; CLL, chronic lymphocytic leukemia; C_{max}, maximal concentration; CNS, central nervous system; CR, complete response; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DL, dose level; DLBCL, diffuse large B-cell lymphoma; DLT, dose-limiting toxicity; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; Fc, fragment crystallizable; FL, follicular lymphoma; ICANS, immune effector cell–associated neurotoxicity syndrome; IgG4, immunoglobulin G4; IV, intravenous; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; LBCL, large B-cell lymphoma; MCL, mantle cell lymphoma; NCI, National Cancer Institute; ORR, overall response rate; PK, pharmacokinetic(s); PO, oral; R/R, relapsed/refractory; SAE, serious adverse event; SC, subcutaneous; SLL, small lymphocytic lymphoma; SRC, safety review committee; TCE, T-cell engager; T_{max}, time to maximal concentration; TN, treatment naive; US, United States; WHO, World Health Organization; y, years

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