A Phase 1/2, first-in-human, multicenter study of DS3790, a CD37-directed DXd antibody–drug conjugate, in patients with B-cell non-Hodgkin lymphoma

ABCL - 753

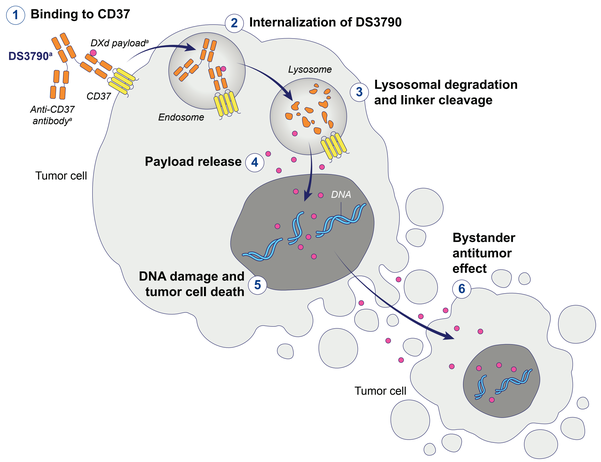
Gilles A. Salles,[1] Emmanuel Bachy,[2] Franck Morschhauser,[3] Pier Luigi Zinzani,[4] Masato Ishigami,[5] Jin Jin,[5,*] Girma Ayele,[5] Keiko Nakajima,[5] Koji Izutsu[6]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Lyon, France; [3]Centre Hospitalier Régional Universitaire de Lille, Lille, France; [4]IRCCS Azienda Ospedaliero-Universitaria di Bologna - Policlinico di Sant'Orsola, Bologna, Italy; [5]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [6]National Cancer Center Hospital, Tokyo, Japan. *Presenting author

Background

- Although current treatment options for B-cell NHLs often achieve long-lasting responses, high-risk disease is associated with early relapse and poor clinical outcomes[1]
- The transmembrane protein CD37 is widely expressed on malignant mature B cells in B-cell NHL and other hematologic malignancies[2,3]; it is therefore a promising therapeutic target
  - CD37 is speculated to regulate cell survival via PI3K/AKT signaling and drive immune evasion[2–5]
- **DS3790** is an ADC comprising an anti-CD37 antibody and DXd, a potent topoisomerase I inhibitor payload, connected by a tetrapeptide-based enzymatically cleavable linker (**Figure 1**)
  - **DS3790** leverages the DXd ADC linker–payload system utilized in other ADCs approved to treat solid tumors[6,7]

Figure 1. DS3790 proposed mechanism of action[a,b,c]



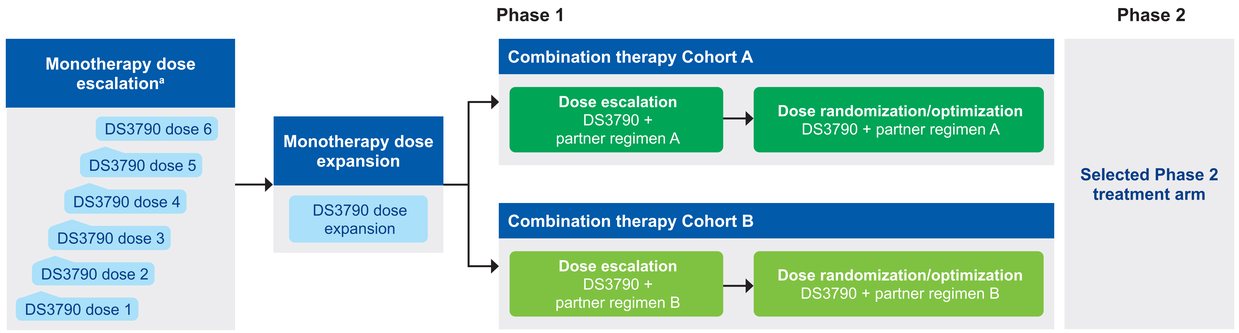
1. The antibody portion of **DS3790** binds to CD37 on the tumor cell surface[8,9]
2. **DS3790** is internalized via endocytosis[8,9]
3. Intracellular lysosomal enzymes typically upregulated in tumor cells cleave the tetrapeptide-based linker[8,9]
4. The DXd payload is released into the cytoplasm of the cell[8,9]
5. DXd inhibits topoisomerase I in the cell nucleus, inducing DNA damage and apoptosis[8,9]
6. The released payload is also cell membrane-permeable, which may enable a bystander antitumor effect resulting in the elimination of both target and neighboring cells[8,10]

[a]Schematics are for illustrative purposes only and do not represent the location and number of elements within the molecule, including the drug-to-antibody ratio. [b]The clinical relevance of these features is under investigation. [c]References are based on data from other DXd ADCs.

Methods

- **DS3790-076** (NCT07220616) is a Phase 1/2, **first-in-human**, open-label, multicenter study of **DS3790** as monotherapy and in combination with partner regimens. This study includes dose-escalation, dose-expansion, and dose-randomization/-optimization parts (**Figure 2**)[11]
- Approximately 400 adult patients with hematologic malignancies, including B-cell NHL, will be enrolled across the study parts (**Table 1**)
- Patients will receive **DS3790** as monotherapy or in combination with one of two partner regimens until radiographic or clinical progression, unacceptable toxicity, withdrawal of consent, or discontinuation for other reasons

Figure 2. DS3790-076 (NCT07220616) study design (N≈400)[11]



[a]Dose escalation of DS3790 will utilize a BOIN design to determine the MTD. At least 3 patients will be assigned to receive DS3790 at each dose level.

Table 1. Key eligibility criteria

Key inclusion criteria	Key exclusion criteria
Adults ≥18 years of age, or the legal age of consent for study participation if >18 years of age	Prior receipt of a topoisomerase I inhibitor or ADC containing a topoisomerase I inhibitor, treatment targeting CD37, allo-SCT, or solid organ transplant
Protocol-specified histologically documented hematologic malignancies, including B-cell NHL, according to the World Health Organization Classification of Haematolymphoid Tumours, 5th Edition	Evidence of brain or leptomeningeal disease (spinal cord or CNS metastases), unless treated and with radiologically documented lack of progression ≤4 weeks prior to treatment initiation
Patients with NHL only: able to provide baseline tumor samples as specified in the protocol	History of (noninfectious) ILD/pneumonitis that required corticosteroids, current ILD/pneumonitis, or suspected ILD/pneumonitis that cannot be ruled out by imaging at screening
ECOG PS of 0, 1, or 2 ≤14 days prior to treatment initiation	Clinically severe pulmonary compromise (ie, requiring any supplemental oxygen)
Adequate organ and bone marrow function ≤14 days prior to treatment initiation	Uncontrolled or significant cardiovascular disease; cerebrovascular accident, transient ischemic attack, or other arterial thromboembolic event ≤6 months prior to enrollment
LVEF ≥50% by either an echocardiogram or multigated acquisition scan ≤28 days prior to treatment initiation	Active or uncontrolled HIV, hepatitis C virus, or hepatitis B virus
Life expectancy ≥3 months	Evidence of ongoing systemic bacterial, fungal, or viral infection

- Study endpoints are summarized in **Table 2**
- The primary objective of the dose-escalation/-expansion parts is to assess the safety and tolerability of **DS3790** as monotherapy or in combination with one of two partner regimens
- The primary objectives of the dose-randomization/-optimization parts and the Phase 2 part are to assess the safety, tolerability, and efficacy of each treatment regimen

Key statistical considerations

- The complete response rate and its CIs will be calculated using the Clopper–Pearson method
- The complete response rate differences and associated CIs will be calculated using the Miettinen–Nurminen method

Study status

- Enrollment is ongoing at sites in France (Lille, Pierre-Bénite, and Villejuif), Italy (Bologna), Japan (Nagoya and Tokyo), and the USA (New York)

Table 2. Study endpoints

Primary endpoints	
Safety, including DLTs, TEAEs, SAEs, and AESIs[a]	
Combination dose-randomization/-optimization parts and Phase 2 only: patients with a complete response	
Secondary endpoints	
Patients with an objective response	Time to response
Dose-escalation/-expansion parts only: patients with a complete response	Progression-free survival
Patients with disease control[b]	Overall survival
Duration of complete response	Pharmacokinetics
Duration of response	Immunogenicity

[a]Graded using NCI-CTCAE version 5.0. [b]Defined as the proportion of patients with a BOR of complete response, partial response, or stable disease.

References

1. Silkenstedt E, et al. *Lancet*. 2024;403:1791–1807.
2. Moore K, et al. *J Pathol*. 1987;152:13–21.
3. Witkowska M, et al. *Expert Opin Investig Drugs*. 2018;27:171–177.
4. Knobeloch KP, et al. *Mol Cell Biol*. 2000;20:5363–5369.
5. Gao X, et al. *Nat Commun*. 2025;16:6610.
6. ENHERTU® (fam-trastuzumab deruxtecan-nxki)) [prescribing information]. Basking Ridge, NJ: Daiichi Sankyo, Inc.; 2026.
7. DATROWAY® (datopotamab deruxtecan-dlnk) [prescribing information]. Basking Ridge, NJ: Daiichi Sankyo, Inc.; 2026.
8. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67:173–185.
9. Ogitani Y, et al. *Clin Cancer Res*. 2016;22:5097–5108.
10. Ogitani Y, et al. *Cancer Sci*. 2016;107:1039–1046.
11. ClinicalTrials.gov. NCT07220616. https://clinicaltrials.gov/study/NCT07220616. Accessed August 27, 2026.

Abbreviations

ADC, antibody–drug conjugate; **AESI**, adverse event of special interest; **AKT**, protein kinase B; **allo-SCT**, allogenic stem cell transplant; **BOIN**, Bayesian optimal interval; **BOR**, best overall response; **CD37**, cluster of differentiation 37; **CI**, confidence interval; **CNS**, central nervous system; **DLT**, dose-limiting toxicity; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **HIV**, human immunodeficiency virus; **ILD**, interstitial lung disease; **LVEF**, left ventricular ejection fraction; **MTD**, maximum tolerated dose; **NCI-CTCAE**, National Cancer Institute Common Terminology Criteria for Adverse Events; **NHL**, non-Hodgkin lymphoma; **PI3K**, phosphatidylinositol 3-kinase; **SAE**, serious adverse event; **TEAE**, treatment-emergent adverse event; **USA**, United States of America.

Acknowledgments

Funding for this study was provided by Daiichi Sankyo, Inc.
Medical writing support was provided by Alexandra Mascaro, PhD, of BOLDSCIENCE, Inc. and funded by Daiichi Sankyo, Inc.
Editorial support was provided in accordance with Good Publication Practice guidelines (https://ismpp.org/gpp-2022).

Disclosures

Jin Jin reports employment at and stock ownership for Daiichi Sankyo, Inc.

Presented at the Society of Hematologic Oncology (SOHO) Annual Meeting; September 9–12, 2026; Houston, TX, USA.

jin.jin@daiichisankyo.com