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Datopotamab deruxtecan (Dato-DXd) in Chinese patients with advanced or metastatic non-small cell lung cancer (NSCLC): Results from the Phase 1/2 TROPION-PanTumor02 study

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Objective

- The phase 1/2, multicenter, open-label, multiple cohort TROPION-PanTumor02 study (NCT05460273) was designed to assess preliminary efficacy and safety of Dato-DXd in Chinese patients with advanced or metastatic solid tumors. Here we present results from the NSCLC cohort.

Conclusions

- TROPION-PanTumor02 study showed encouraging preliminary efficacy and a tolerable safety profile in Chinese patients with advanced or metastatic NSCLC.
- Antitumor activity was more pronounced in patients with non-squamous cell carcinoma compared with that in patients with squamous cell carcinoma.
- No new safety signals were observed, and no adjudicated drug-related interstitial lung disease was reported.

Plain language summary

Why did we perform this research?

Datopotamab deruxtecan (Dato-DXd) is a drug that consists of datopotamab (an antibody) joined to an anticancer drug (deruxtecan). Datopotamab binds to a protein found on cancer cells called TROP2, where it then releases deruxtecan inside the tumor cells, which kills the tumor. The TROPION-PanTumor02 study involved Chinese patients with cancer that has spread to other parts of the body or is in advanced stages. Here, we report results from patients with a type of lung cancer called non-small cell lung cancer (NSCLC) who received Dato-DXd and whose cancer was previously treated with another therapy.

How did we perform this research?

40 eligible patients received Dato-DXd every 3 weeks. Each patient continued to receive treatment for as long as the tumor was controlled by the drug and there were no unacceptable side effects.

What were the findings of this research?

Results from this study showed that 45% of patients who received Dato-DXd had a reduction of 30% or more in the size of their target tumor lesion. In addition, patients had a progression-free survival (time from starting treatment to the cancer getting worse or death) of 7.4 months. In patients with non-squamous NSCLC, 56.5% of patients who received Dato-DXd had a reduction of 30% or more in the size of their target tumor lesion and a progression-free survival of 9.6 months. The most common side effects with Dato-DXd were feeling sick (nausea), a sore or inflammation in the mouth (stomatitis) and reduced red blood cells or hemoglobin (anemia) – all side effects could be managed.

What are the implications of this research?

The results from this study showed that Dato-DXd provides meaningful benefits and a manageable side-effect profile to patients with NSCLC whose cancer has spread to other parts of the body or is in advanced stages. Antitumor activity was more pronounced in patients with non-squamous cell NSCLC compared with that in patients with squamous cell NSCLC.

Where can I access more information?

This trial is listed on www.clinicaltrials.gov here: https://clinicaltrials.gov/study/NCT05460273

Poster

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of these materials. Alternatively, please use the link below.

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Introduction

Unmet need in NSCLC

- Globally, the 5-year survival rate in patients with lung cancer is 10–20%.[1] A similar 5-year survival rate (~20%) is seen in Chinese patients.[2]
- NSCLC is the most common type of lung cancer accounting for 80–85% of all cases.[3,4]
- Recent advances in treatment options for NSCLC have improved mortality and survival rates.[2,5] However, lung cancer is still the leading cause of cancer death worldwide,[1] thus new treatment options are needed.

Dato-DXd and TROP2

- TROP2 is a transmembrane protein broadly expressed in NSCLC.[6,7]
- Dato-DXd is a TROP2-directed ADC **(Figure 1)** that selectively delivers a Topo-I inhibitor payload directly into tumor cells via a plasma-stable, tumor-selective, tetrapeptide-based cleavable linker.[8]
- Dato-DXd has previously demonstrated statistically significant improvement in PFS versus docetaxel in patients with previously treated, locally advanced or metastatic NSCLC in the Phase 3 TROPION-Lung01 study (NCT04656652).[9]
- This phase 1/2 study evaluates preliminary efficacy and safety of Dato-DXd in Chinese patients with advanced/metastatic solid tumors. Here we present results from the NSCLC cohort.

Figure 1. Dato-DXd: Humanized anti-TROP2 IgG1 monoclonal antibody

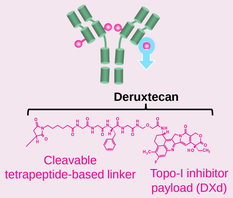


Image is for illustrative purposes only; actual drug positions may vary.

Methods

Figure 2. TROPION-PanTumor02 study design: Phase 1/2, open-label, global study (NCT05460273)

Key inclusion criteria:

- Chinese patients, aged ≥18 years
- Advanced or metastatic NSCLC (cohort 1)* with or without AGAs
- ECOG PS 0 or 1
- Prior treatment with platinum-based chemotherapy and immunotherapy (without AGAs) or prior treatment with targeted therapy and platinum-based chemotherapy (with AGAs)
- Measurable disease by CT or MRI
- Unselected for TROP2 expression
- Available tumor sample to centrally determine TROP2 expression (archived or newly acquired biopsy)

Treatment:

Dato-DXd† 6 mg/kg IV Q3W

N=40

Endpoints:

Primary
- Confirmed ORR by ICR per RECIST 1.1

Secondary:
- Confirmed ORR by investigator
- DCR, DoR, BOR, TTR, PFS by ICR and investigator
- OS
- Safety
- PK, immunogenicity

*This study included patients with advanced or metastatic NSCLC (cohort 1) and TNBC (cohort 2). Here we present results from the NSCLC cohort.
†Patients will continue to receive treatment until they meet one of the discontinuation criteria. Reasons for discontinuation include disease progression, unacceptable toxicity, withdrawal of consent, or initiation of a new therapy.

Results

Patients

- TROPION-PanTumor02 screened a total of 62 patients and enrolled 40 patients.
- At data cutoff (9 October 2023), median study follow-up was 8.1 (range, 1.1–11.9) months.
- Patient demographics and baseline characteristics are shown in **Table 1**.

Table 1. Demographics and baseline characteristics

		Total (N=40)
Age, median (range), years		59 (33–74)
Male, n (%)		29 (72.5)
Smoking history, n (%)	Never / Former / Current	22 (55.0) / 17 (42.5) / 1 (2.5)
ECOG PS, n (%)	0 / 1	6 (15.0) / 34 (85.0)
Histology type, n (%)	Non-squamous cell carcinoma Squamous cell carcinoma	23 (57.5) 17 (42.5)
AGAs, n (%)	All EGFR mutation	5 (12.5) 4 (10.0)
Extent of disease at study entry, n (%)	Metastatic Locally advanced	37 (92.5) 3 (7.5)
Prior anticancer therapy,* n (%)	Platinum chemotherapy Immunotherapy Radiotherapy Targeted therapy Other	40 (100.0) 37 (92.5) 11 (27.5) 9 (22.5) 2 (5.0)
Treatment status, n (%)	Ongoing study treatment Discontinued study treatment Progressive disease Adverse event Patient decision Subjective disease progression	8 (20.0) 32 (80.0) 20 (62.5) 4 (12.5) 7 (21.9) 1 (3.1)

*Patients with therapies in more than one category are counted once in each category.

Antitumor activity

- The primary endpoint, confirmed ORR by ICR, was 45.0% (95% CI: 29.3–61.5) **(Table 2).**
- Confirmed ORR by investigator was 32.5% (95% CI: 18.6–49.1).
- Concordance of ORR between ICR and investigator assessment was 82.5%.
- Median time to onset of response from first dose was 1.4 (95% CI: 1.3–2.7) months.

Table 2. Antitumor activity of Dato-DXd by ICR

	Total (N=40)	Non-squamous (n=23)	Squamous (n=17)
Objective response rate, % (95% CI)	45.0 (29.3–61.5)	56.5 (34.5–76.8)	29.4 (10.3–56.0)
Best overall response, n (%)			
CR	0	0	0
PR	18 (45.0)	13 (56.5)	5 (29.4)
SD*	16 (40.0)	9 (39.1)	7 (41.2)
PD†	5 (12.5)	1 (4.3)	4 (23.5)
NE‡	1 (2.5)	0	1 (5.9)
Median DoR, months (95% CI)	8.3 (5.9–NC)	8.3 (5.9–NC)§	9.4 (4.0–NC)‖
DCR, % (95 CI)	85.0 (70.2–94.3)	95.7 (78.1–99.9)	70.6 (44.0–89.7)

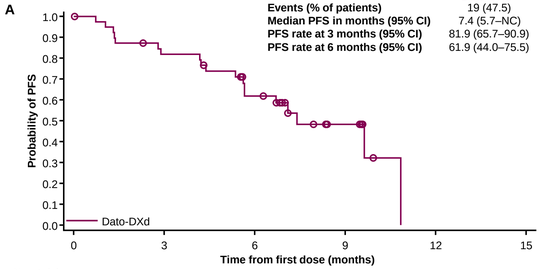
*SD ≥5 weeks. Including unconfirmed complete response, unconfirmed partial response and stable disease.
†Including RECIST progression and death ≤7 weeks without tumor assessment.
‡Including stable disease <5 weeks, incomplete post baseline assessments and no valid baseline.
§Based on n=13 patients.
‖Based on n=5 patients.

Progression-free survival

- Median PFS by ICR was 7.4 (95% CI: 5.7–NC) months. In non-squamous and squamous NSCLC, median PFS was 9.6 (7.1–NC) and 5.5 (1.4 –NC) months, respectively **(Figure 3)**.
- In the non-squamous subgroup, the PFS rate was 91.1% and 86.5% at 3 and 6 months, respectively.
- In the squamous subgroup, the PFS rate was 68.8% and 28.6% at 3 and 6 months, respectively.

Figure 3. PFS by ICR in A) all patients and B) by histology

A



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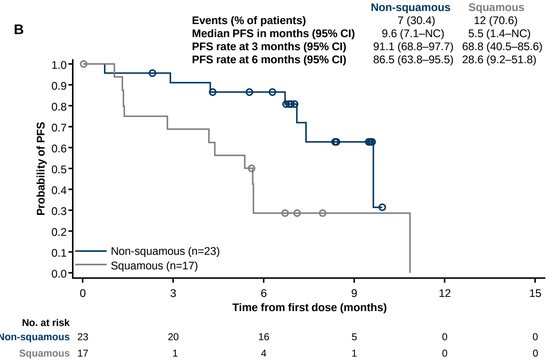

Overall survival

- OS data were not mature at this data cutoff with 22.5% maturity.
- The median OS was not calculable. The OS rate at 6 months was 82.5% (95% CI: 66.8–91.2).
- The study is continuing to the next planned analysis for OS.

Safety summary

- The median treatment duration was 5.6 (range, 0.7–10.6) months.
- No adjudicated drug-related interstitial lung disease was reported.
- Grade ≥3 AEs occurred in 57.5% of patients **(Table 3)**.
- The most common AEs were nausea (62.5%), stomatitis (57.5%) and anemia (57.5%) **(Table 4)**.

Table 3. Overall safety summary

AEs, n (%)	Total (N=40)
All grades	38 (95.0)
Grade ≥3	23 (57.5)
Serious AEs	10 (25.0)
Associated with dose interruption	15 (37.5)
Associated with dose reduction	8 (20.0)
Associated with discontinuation	4 (10.0)
Associated with death	0

Table 4. Any AEs occurring in ≥15% of patients

Preferred term, n (%)	Total (N=40)	
	Any grade	Grade ≥3
Nausea	25 (62.5)	2 (5.0)
Stomatitis	23 (57.5)	5 (12.5)
Anemia	23 (57.5)	3 (7.5)
Alopecia	16 (40.0)	0
Vomiting	13 (32.5)	2 (5.0)
Decreased appetite	12 (30.0)	4 (10.0)
Weight decreased	11 (27.5)	0
Constipation	9 (22.5)	0
Leukopenia	9 (22.5)	0
Asthenia	9 (22.5)	1 (2.5)
COVID-19	8 (20.0)	0
Hypoalbuminemia	7 (17.5)	0
Hypokalemia	7 (17.5)	3 (7.5)
Neutrophil count decreased	7 (17.5)	0
Hyponatremia	6 (15.0)	0
Upper respiratory tract infection	6 (15.0)	0

Abbreviations

ADC, antibody-drug conjugate; AEs, adverse events; AESI, adverse events of special interest; AGAs, actionable genomic alterations; BOR, best overall response; CI, confidence interval; CT, computed tomography; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; ICR, independent central review; IV, intravenous; MRI, magnetic resonance imaging; NC, not calculable; NSCLC, non-small-cell lung cancer; ORR, objective response rate; OS, overall survival; PK, pharmacokinetics; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TNBC, triple-negative breast cancer; TROP2, trophoblast cell surface protein 2; TTR, time to response.

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