

Clinical trial finds antibody-drug conjugate helps patients with metastatic non-small cell lung cancer live longer

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Treatment with datopotamab deruxtecan (Dato-DXd), a novel Trop-2 directed antibody-drug conjugate, was found to significantly improve progression-free survival in patients with metastatic non-small cell lung

cancer, an improvement that was primarily driven by patients with non-squamous tumors.

[These results](#) from the TROPION-Lung01 Phase III trial, which compared the standard of care in second-line docetaxel, a type of chemotherapy, with Dato-DXd, an antibody drug conjugate, in [patients](#) with pretreated metastatic non-small cell lung [cancer](#), were presented at the European Society for Medical Oncology 2023 Congress by Dr. Aaron Lisberg, assistant professor of medicine and thoracic medical oncologist at the UCLA Health Jonsson Comprehensive Cancer Center and the David Geffen School of Medicine at UCLA.

Lisberg and the team found that patients treated with Dato-DXd experienced a 25% reduction in the risk of disease progression or death compared to patients treated with docetaxel.

"While there was an overall reduction of disease progression, the data clearly indicates that this benefit was primarily driven by patients with non-squamous tumors," Lisberg said.

More than 75% of enrolled patients had non-squamous tumors, noted Lisberg. And in that group alone, the therapy reduced the risk of disease progression or death by 37%, while patients with squamous tumors did not appear to derive a therapeutic benefit from Dato-DXd on trial.

In addition, a trend in favor of Dato-DXd was observed in the interim overall survival analysis. In those assessments of how long a patient will live after receiving a therapy for their cancer, the improvement was most pronounced in the non-squamous population with a reduction in the risk of death of 23% with Dato-DXd.

The improvements in progression-free and overall survival observed in the Dato-DXd treated patients were accompanied by significant tumor

shrinkage with Dato-DXd (26.4%) vs. docetaxel (12.8%), a difference that was more pronounced in patients with non-squamous tumors (31.2% vs. 12.8%).

The overall safety profile of Dato-DXd was superior to docetaxel as fewer patients had high grade drug related toxicities with Dato-DXd (25%) compared to docetaxel (41%). Common side effects of Dato-DXd included mild to moderate mouth sores and nausea. There were also fewer severe side effects leading to dose reduction or treatment discontinuation in Dato-DXd treated patients compared to those treated with docetaxel.

"Dato-DXd is the first antibody-drug conjugate in metastatic non-small cell lung cancer to demonstrate a statistically significant improvement in [progression-free survival](#) over the standard of care chemotherapy drug docetaxel, while evidencing a more favorable safety profile due to its unique ability to selectively delivers a potent chemotherapy directly into tumor cells," said Lisberg.

These findings are encouraging, noted Lisberg, since the current standard of care second-line chemotherapy docetaxel is associated with modest benefit and substantial toxicity and suggest that Dato-DXd has the potential to be new therapy for patients with previously treated non-squamous non-small cell lung cancer.

TROPION-LUNG01 study design

Researchers on the global TROPION-LUNG01 trial compared the effectiveness and tolerability of Dato-DXd vs. docetaxel by randomizing 604 patients to receive either Dato-DXd (299 patients) or docetaxel (305) patients.

Patients both with and without genetic driver mutations such as EGFR

were enrolled and must have received multiple therapies for metastatic non-small cell lung cancer prior to enrollment. No minimum level of TROP-2 expression on the tumor surface was required for enrollment, as TROP-2 expression has not been found to correlate with Dato-DXd effectiveness, to date.

This antibody-drug conjugate is now being evaluated as potential first-line therapy for patients with newly diagnosed metastatic non-small cell lung cancer on the TROPION-LUNG07/08 studies ([NCT05555732/NCT05215340](#)), both of which were recently opened at UCLA clinics throughout Southern California.

In addition, the TRIO-US network is participating in the TROPION-LUNG07 trial, as it did for TROPION-LUNG01. These trials hold the promise to improve clinical outcomes for patients with metastatic non-small cell lung cancer by providing Dato-DXd to an even larger number of patients with non-squamous tumors.

Datopotamab deruxtecan is a specifically engineered TROP2-directed DXd antibody drug conjugate being jointly developed by AstraZeneca and Daiichi Sankyo.

More information: [Conference abstract](#)

Provided by University of California, Los Angeles

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