Medical Xpress

TROP2 expression a promising predictor of clinical outcomes in patients with advanced or metastatic NSCLC

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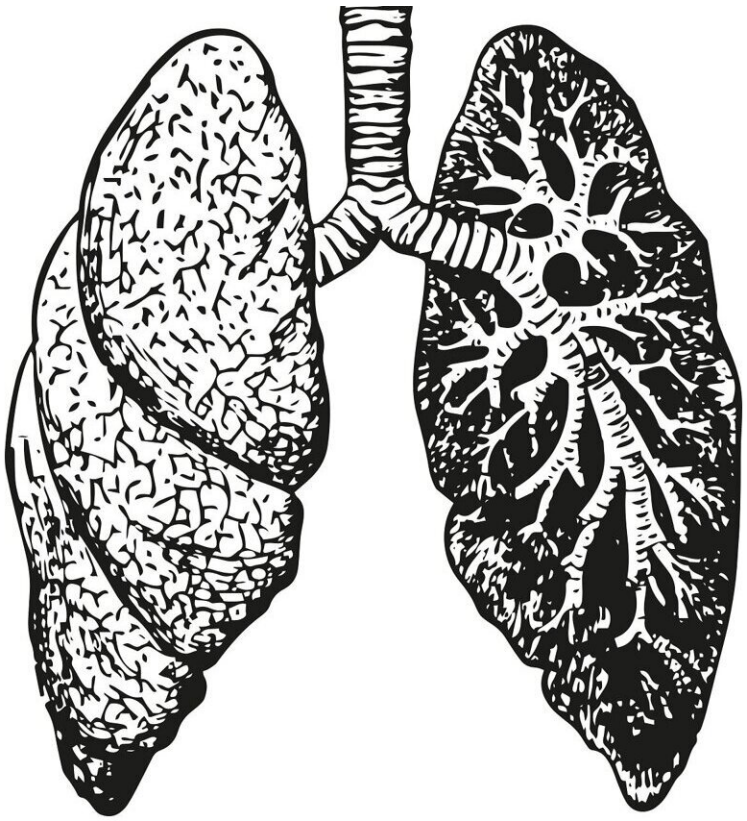

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New data presented today demonstrate that TROP2 expression as measured by quantitative continuous scoring (QCS), a computational

pathology approach, is a promising predictor of clinical outcomes in patients with advanced or metastatic non-small cell lung cancer (NSCLC) treated with the TROP2 antibody-drug conjugate (ADC) datopotamab deruxtecan (Dato-DXd). The data showed that patients with TROP2 positivity, as determined by QCS, experienced improved efficacy with Dato-DXd compared to patients receiving docetaxel in the TROPION-Lung01 phase III trial.

The study was presented today at the International Association for the Study of Lung Cancer (IASLC) 2024 World Conference on Lung Cancer by Dr. Marina Chiara Garassino, from The University of Chicago.

Dato-DXd is a TROP2-directed ADC designed with a unique plasma-stable linker that necessitates active internalization for effective payload release. Traditional methods of assessing TROP2 expression through visual scoring of immunohistochemical (IHC) assays have not been predictive of responses to TROP2-directed ADCs in NSCLC patients. To address this gap, the authors hypothesized that a more precise, quantitative measurement of TROP2 expression both on the cell membrane and in the cytoplasm would better predict therapeutic responses to Dato-DXd.

This analysis utilized digitalized TROP2 IHC-stained whole-slide images (WSI) from NSCLC patients to develop the QCS model. This deep learning algorithm, trained on pathologists' annotations, identifies tumor areas and cellular compartments (membrane and cytoplasm) within the WSI. The QCS model calculates TROP2 expression in the membrane relative to the cytoplasm of tumor cells, producing a normalized membrane ratio (NMR). Tumors were classified as TROP2 QCS-NMR+ if most tumor cells exhibited an NMR below a predetermined value.

The QCS-NMR was optimized for progression-free survival (PFS) in the

biomarker-evaluable subgroup of nonsquamous (NSQ) NSCLC patients without actionable genomic alterations (non-AGA) in TROPION-Lung01, which compared Dato-DXd to docetaxel in second-line or later advanced or metastatic NSCLC. Clinical outcomes were assessed across all biomarker-evaluable patients.

Out of 604 patients randomized in TROPION-Lung01, 352 were biomarker-evaluable, with 221 in the NSQ/non-AGA subgroup. The baseline characteristics were consistent between randomized and biomarker-evaluable populations, showing similar overall PFS outcomes. Among the evaluable patients, 63% were classified as TROP2 QCS-NMR+. The highest prevalence of TROP2 QCS-NMR+ was observed in the NSQ/AGA subgroup (75%), followed by NSQ/non-AGA (63%) and squamous (SQ) (43%) subgroups.

Data indicated that the objective response rate (ORR) was higher and median PFS was longer with Dato-DXd compared to docetaxel in TROP2 QCS-NMR+ subgroups. The rates of overall and grade 3+ adverse events were similar regardless of TROP2 QCS-NMR status.

"It is important that research identifies how to optimize treatment options for patients with NSCLC. This exploratory analysis is going in this direction and reveals that Dato-DXd exhibits robust efficacy in patients with TROP2 QCS-NMR+ advanced non-small cell lung cancer, in the nonsquamous, non-AGA subgroup," Dr. Garassino reported.

The QCS-measured TROP2 NMR shows potential as a predictive biomarker for Dato-DXd response. Further studies are underway to validate this biomarker in the first-line advanced or metastatic NSCLC setting.

Provided by International Association for the Study of Lung Cancer