Poster 22P

Effects of datopotamab deruxtecan (Dato-DXd) vs docetaxel on patient-reported outcomes (PROs) in adults with previously treated advanced or metastatic nonsquamous (NSQ) non-small cell lung cancer (NSCLC): results from TROPION-LUNG01

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Objective

- Evaluate PRO endpoints for Dato-DXd compared with those for docetaxel in patients with NSQ NSCLC in TROPION-LUNG01

Conclusions

- Dato-DXd was associated with a favorable trend for Dato-DXd compared with docetaxel in the NSQ population on most EORTC-QLQ-LC13 and EORTC-QLQ-C30 scores, including all functioning scales, pain, peripheral neuropathy and dyspnea, as measured by LS means difference of CFB and TTD
- Docetaxel compared favorably to Dato-DXd in constipation and nausea/vomiting as measured by LS means difference of CFB and TTD
- These data further support the clinical observations seen in favor of Dato-DXd in PFS, OS, objective response rate and safety in the treatment of advanced or metastatic NSQ NSCLC[1]

Plain language summary

Why did we perform this research?

Current treatments for NSQ NSCLC are burdensome to patients and associated with severe side effects. Dato-DXd may delay the progression of cancer cells with a better tolerability

How did we perform this research?

Patients with NSQ NSCLC in TROPION-Lung01 were asked to complete questionnaires covering topics such as quality of life, functioning, and cancer- and lung cancer–specific symptoms. Disease-related symptoms and impacts were compared for patients treated with Dato-DXd and docetaxel. A subgroup of patients with AGAs were also analyzed

What were the findings of this research?

Despite constipation and nausea/vomiting issues reported by trial patients, Dato-DXd was associated with less worsening in physical and social functioning, pain, diarrhea, peripheral neuropathy (pain or numbness in the extremities), shortness of breath, and pain in arm or shoulder compared with docetaxel. These findings were consistent across populations

What are the implications of this research?

Overall, these findings suggest that Dato-DXd may be more tolerable than docetaxel and preserve some aspects of daily life for patients with NSQ NSCLC

Where can I access more information?

For more information about the TROPION-Lung01 study, please visit https://clinicaltrials.gov/study/NCT04656652

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of these materials. Alternatively, please click on the link below: https://bit.ly/DS_ELCC25

Poster

Mobile Optimized Poster

This study was sponsored by Daiichi Sankyo, Inc. In July 2020, Daiichi Sankyo entered into a global development and commercialization collaboration agreement with AstraZeneca for datopotamab deruxtecan (Dato-DXd).
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Background

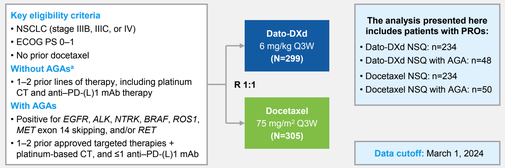
- **Dato-DXd** is a **TROP2-directed ADC** that delivers a potent topoisomerase I inhibitor payload
- In the phase 3 TROPION-Lung01 trial, Dato-DXd improved PFS versus docetaxel in patients with advanced/metastatic NSCLC, driven by patients with NSQ histology[1]
- Dato-DXd also showed a manageable safety profile, with no new safety signals[1]
- To complement these clinical data, health-related QoL data were collected to understand the impact of disease and treatment tolerability of Dato-DXd from the patient perspective
- PROs in the NSQ population from TROPION-Lung01 were analyzed (**Figure 1**)

Methods

- Two PROs are presented here: EORTC QLQ-LC13 (a 13-item lung cancer–specific module administered in conjunction with the EORTC QLQ-C30, covering additional symptoms), EORTC QLQ-C30 (a 30-item generic cancer scale, covering GHS/QoL, functional scales, and symptom scales). All scales are scored 0–100
  - Items 36 (have you had a sore mouth or tongue?) and 37 (have you had trouble swallowing?) were excluded from the administration of the EORTC QLQ-LC13 to avoid duplication with other instruments administered in this study. Dyspnea composite is composed of dyspnea when rested, dyspnea when walking, and dyspnea when climbing stairs
- For the EORTC QLQ-C30 GHS/QoL and functional scales, higher scores indicate higher functionality, or better outcomes. For all scales of the EORTC QLQ-LC13 and the symptom and financial difficulties scales of the EORTC QLQ-C30, higher scores indicate higher symptom severity, or worse outcomes
- This poster focuses on the NSQ and NSQ with AGA populations. A total of 468 patients were enrolled in the NSQ population, with 98 of those included in the NSQ with AGA population
- CFB analyzed by MMRMs and TTD is presented here
- MMRMs are fitted with CFB as the response variable, and baseline value, treatment, visit, and treatment by visit interaction as covariates, with subject ID fitted as a random effect
- The Cox proportional hazard model was fitted to estimate the hazard ratio between Dato-DXd versus docetaxel and the corresponding 95% CI. TTD is defined by a 10-point deterioration, subsequently confirmed by a second 10-point deterioration for the same item at the next scheduled assessment or death within a specified time period
- The EORTC-QLQ-LC13 was assessed at screening and at every 3-week cycle until EOT
- The EORTC-QLQ-C30 was assessed at screening and at every 3-week cycle up to cycle 5, followed by assessment at every odd cycle up to EOT

Figure 1. TROPION-Lung01 study design

Randomized, phase 3, open-label, global study (NCT04656652)



Stratified by: histology,[b] AGA(s),[c] anti–PD-(L)1 mAb included in most recent prior therapy, geography[d]

[a]Patients with *KRAS* mutations in the absence of known AGAs are eligible; must meet prior therapy requirements for patients without AGAs. [b]Squamous vs NSQ. [c]Presence vs absence. [d]United States/Japan/Western Europe vs rest of world.

Results

NSQ

- **Compliance rates** for both EORTC QLQ-LC13 and EORTC QLQ-C30 were high at baseline for both treatment groups (>90%) and decreased over time up to cycle 17 (66.0–85.8%)
- **Scores were similar at baseline** between treatment groups for all scales of the EORTC QLQ-LC13 and EORTC QLQ-C30, and were consistent with values typically seen in this patient population[2]
- Results based on LS means difference of CFB (**Figure 2**) suggest:
  - **Favorable estimates across scores on both the EORTC QLQ-LC13 and EORTC QLQ-C30 scales on all functioning scales, as well as symptom scales such as pain, dyspnea, insomnia and peripheral neuropathy and unfavorable estimate for nausea/vomiting and constipation (Figure 2)**
- Results based on HR of TTD (**Figure 3**) suggest:
  - **A reduced risk of clinically meaningful deterioration in dyspnea (overall and when rested), peripheral neuropathy, and pain in arm or shoulder compared with dotacetaxel as measured by the EORTC QLQ-LC13**
  - **No difference was seen between treatment groups in the secondary PRO endpoint** of TTD in any of the chest pain, cough, and dyspnea symptoms
  - **A reduced risk of clinically meaningful deterioration in physical functioning, social functioning, pain, and diarrhea for Dato-DXd compared with docetaxel, as measured by the EORTC QLQ-C30**
  - **An increased risk of clinically meaningful deterioration in constipation and nausea/vomiting with Dato-DXd compared with docetaxel**

NSQ with AGA

- **The overall compliance rate** for both EORTC QLQ-C30 and EORTC QLQ-LC13 was high at baseline for both treatment groups (≥92%), and remained >70% through cycle 7, when the sample size dropped below 10 patients in the docetaxel treatment group
- **Baseline mean scores** were similar between Dato-DXd and docetaxel treatment groups for all scales of the EORTC QLQ-C30 and EORTC QLQ-LC13
- **Despite a smaller sample size, similar trends were observed in the NSQ AGA population compared with the NSQ population, favoring Dato-DXd, both in CFB (Figure 4) and TTD (Figure 5) analyses:**
  - **LS means difference of CFB (Figure 4) suggests favorable estimates for Dato-DXd over docetaxel in the general health measure, physical functioning, and role functioning scores. Other scores showed similar trends to those of the NSQ population (Figure 4)**
  - **HR in TTD suggest no difference between treatment groups in the secondary PRO endpoint** of TTD in combined chest pain, cough and dyspnea symptoms
  - Patients receiving Dato-DXd reported a reduced risk of deterioration in key scales, including physical functioning, pain, dyspnea when rested and dyspnea composite, and peripheral neuropathy compared with docetaxel (**Figure 4**)
  - TTD in role functioning was associated with a lower risk of deterioration for Dato-DXd compared with docetaxel (**Figure 5**)

Figure 2. Change from baseline in NSQ

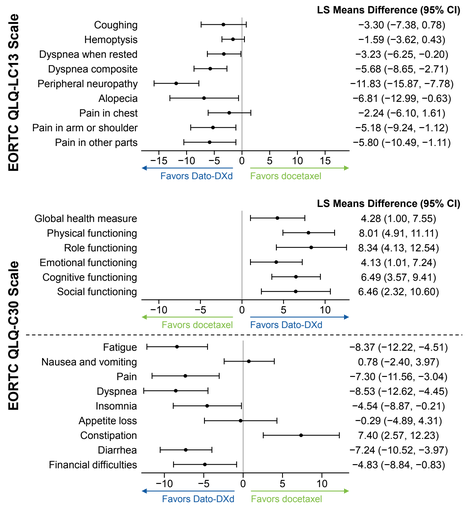


Figure 3. Time to first deterioration in NSQ

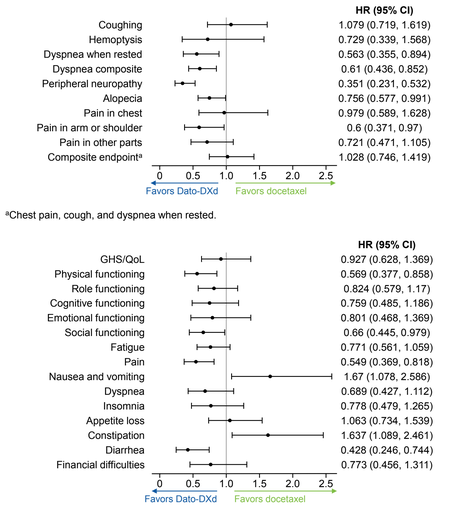


Figure 4. Change from baseline in NSQ AGA

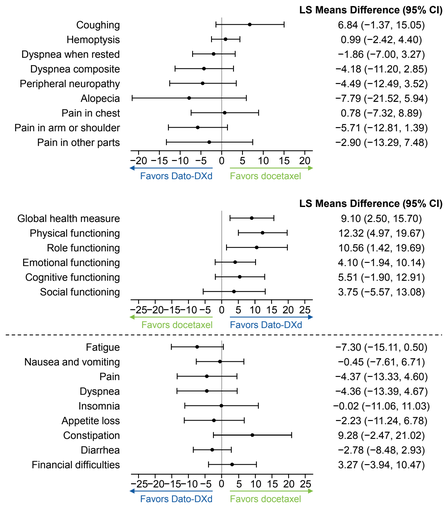
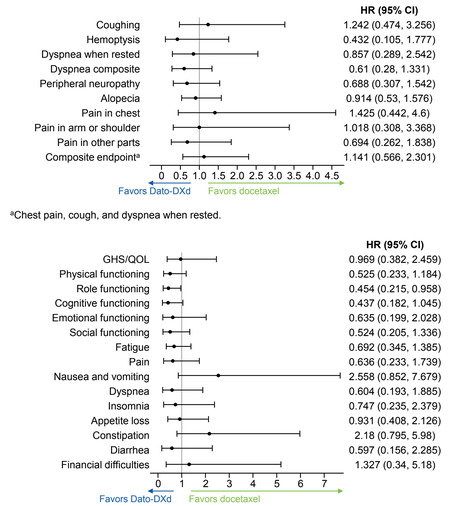


Figure 5. Time to first deterioration in NSQ AGA



Abbreviations

ADC, antibody–drug conjugate; AGA, actionable genomic alteration; C30, Cancer 30; CFB, change from baseline; CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; ECOG PS, Easter Cooperative Oncology Group performance status; EORTC QLQ, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; EOT, end of treatment; GHS, general health score; LC13, Lung Cancer 13; LS, least squares; mAb, monoclonal antibody; MMRM, mixed model repeat measure; NSCLC, non-small cell lung cancer; NSQ, nonsquamous; PD-(L)1, programmed cell death-(ligand) 1; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, every 3 weeks; QoL, quality of life; R, randomized; TTD, time to deterioration.

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Disclosures

Dr Cornelissen has no conflicts of interest to declare.

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