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Real-world survival outcomes for docetaxel-containing regimens for patients with locally advanced or metastatic non-small cell lung cancer in England who have progressed on current standard of care

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Objective

- To understand patient characteristics, treatment patterns and real-world overall outcomes among patients with locally advanced or metastatic non-small cell lung cancer (NSCLC), with and without actionable genomic alterations (AGAs), who have progressed on current standard of care in England and subsequently received docetaxel-containing regimens.

Conclusions

- Docetaxel plus nintedanib was the most common docetaxel-containing regimen used in our NSCLC cohorts. Real-world survival remained poor and was comparable to that observed with docetaxel monotherapy.
- Variation in survival across treatment modalities highlights potential opportunities to address treatment inequalities and broader unmet need in a clinical population where little progress has been made in increasing survival in recent decades.

Plain language summary

Why did we perform this research?

There is limited research on the current landscape of treatment patterns and clinical outcomes of locally advanced or metastatic NSCLC, especially in later lines of treatment.

How did we perform this research?

We identified two groups from the National Cancer Registration and Analysis Service (NCRAS) dataset, a comprehensive cancer data set of cancer patients living in England. Using a line of therapy algorithm, we identified individuals who received standard-of-care first-line treatment. We described the groups in terms of key demographics, clinical profiles, and treatment patterns. Real-world survival outcomes were assessed from the time of initiating the first subsequent treatment.

What were the findings of this research?

- The median age was 65 years across the two groups, with and without AGAs.
- Across both groups, 21% of people (304 individuals) were treated with regimens that included docetaxel in the first line of treatment after progressing on standard-of-care treatment.
- People who received docetaxel-containing regimens had a shorter median overall survival from index than overall.
- Among the 281 individuals without AGAs who received docetaxel-containing regimens in the first line of treatment after progressing on standard-of-care treatment, 72% did not receive a subsequent treatment due to death or censoring.

What are the implications of this research?

There is a need for more effective treatment options for patients with locally advanced or metastatic NSCLC who have progressed on initial standard of care treatment.

Poster

Plain language summary

This study was sponsored by Daiichi Sankyo. In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for Datopotamab deruxtecan (Dato-DXd).
Poster presented at ESMO 2025 by Andrew Thompson. Corresponding author email address: andrew.thompson2@lcp.uk.com

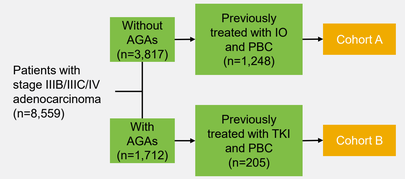
Introduction

- Lung cancer is the leading cause of cancer-related deaths worldwide (1) and has shown limited improvement in survival in the UK over the last 50 years (2), highlighting the need for novel, effective treatments.
- Although advances in IO and modern TKIs have improved outcomes in NSCLC, the effectiveness of second-line and subsequent chemotherapy remains limited. More effective treatment options are needed, along with a better understanding of real-world survival outcomes in later lines of therapy.
- This study aimed to examine patient characteristics, treatment patterns, rwOS, and real-world time to next treatment or death (rwTTNTD) in patients in England with locally advanced or metastatic NSCLC who had progressed following standard-of-care treatment and received subsequent treatment with docetaxel-containing regimens.

Methods

- This population-based, retrospective cohort study included all adult patients in England diagnosed with stage IIIB/IIIC/IV adenocarcinoma NSCLC from between 1 Jan 2016 and 31 Dec 2021.
- Using the NCRAS dataset, the national cancer database of England, we defined two cohorts who initiated second-line therapy based on the presence of AGAs and types of prior treatment regimens received (Figure 1):
  - Cohort A with no AGAs (documented 'normal' test status for EGFR and ALK, and no 'abnormal' test status for ROS1, NTRK, BRAF, MET and RET) who progressed on both IO and platinum-based chemotherapy (PBC), and
  - Cohort B with AGAs ('abnormal' test status for any of EGFR, ALK, ROS1, NTRK, BRAF, MET, RET, or KRAS) who progressed on both TKI and PBC.
- Cohorts were assessed from the date of first administration for the line of therapy received after meeting cohort entry criteria (index date) and followed up from the index date to the end of study (31 March 2024), date of death, or date that individual was lost to follow-up, whichever occurred first.
- Treatment sequencing was identified using a line of therapy algorithm, adapted from published algorithms for NSCLC (3,4).
- Descriptive statistics were calculated for categorical and continuous variables of interest, and rwOS and rwTTNTD from index (rather than from diagnosis) were analysed using Kaplan-Meier methods.
- rwOS and rwTTNTD from index were reported by cohort and type of treatment in the index line of therapy.

Figure 1. Cohort eligibility criteria



Results

Demographics and clinical characteristics

- Among 8,559 NSCLC patients with Stage IIIB/IIIC/IV adenocarcinoma who initiated second-line therapy, 1,451 (17.0%) had received regimens meeting the eligibility criteria.
- Cohort A (n=1,248) included 47.1% males (n = 588) with a median age of 65 years (IQR: 58 – 71). Cohort B (n=205) included 35.1% males (n = 72) with a median age of 62 years (IQR: 53 – 71). Across cohorts, 81.3% (n = 1,180) patients presented with stage IV NSCLC. In Cohort B, 78% (n = 159) of patients had an EGFR AGA.
- There was a lower number of study eligible patients diagnosed with NSCLC in 2020 and 2021 compared with prior years.
- ECOG performance status was comparable across the two cohorts, with >85.0% of individuals being categorised as 0-1, indicating a generally well-functioning population at cohort entry after first-line standard of care treatment. Few patients had a Charlson Comorbidity Index ≥4, indicating an overall low comorbidity burden.

Table 1. Demographic and clinical characteristics at cohort entry

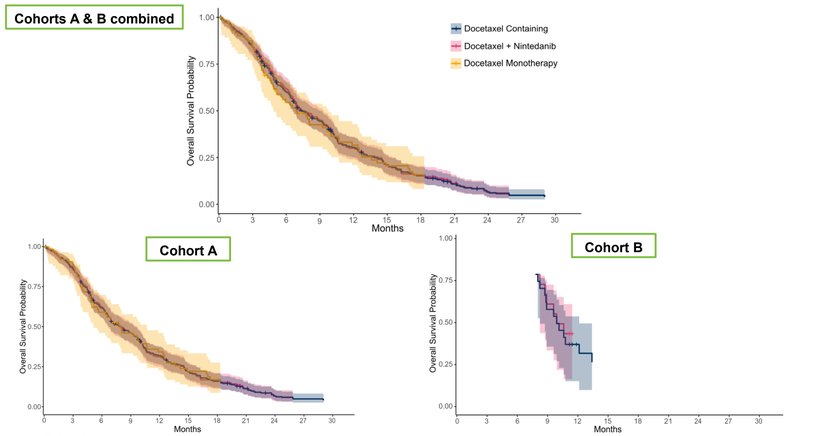
	Cohort A (non-AGA cohort)	Cohort B (AGA cohort)	Cohorts A & B combined
N	1,248	205	1,451*
Male %	588 (47.1%)	72 (35.1%)	659 (45.4%)
Age			
Mean age (SD) (years)	64 (9)	62 (11)	64 (10)
Median age (IQR) (years)	65 (58 - 71)	62 (53 - 71)	65 (57 - 71)
Diagnosis year			
2016	74 (5.9%)	52 (25.4%)	126 (8.7%)
2017	130 (10.4%)	39 (19.0%)	169 (11.7%)
2018	198 (15.9%)	35 (17.1%)	233 (16.1%)
2019	371 (29.7%)	27 (13.2%)	397 (27.4%)
2020	279 (22.4%)	23 (11.2%)	301 (20.7%)
2021	196 (15.7%)	29 (14.2%)	225 (15.5%)
Performance status			
0-1	1057 (84.7%)	180 (87.8%)	1236 (85.2%)
≥2	70 (5.6%)	16 (7.8%)	86 (5.9%)
Charlson Comorbidity Index			
0-3	<1255 (-)	205 (100.0%)	<1455 (-)
≥4	<6 (-)	0 (0.0%)	<6 (-)
Median (IQR) crude follow-up time	11.33 (5.32 – 22.70)	7.03 (3.12 – 16.29)	10.64 (5.01 – 22.03)

* Two individuals with KRAS gene alteration were eligible for both Cohort A and Cohort B

Treatment patterns

- In Cohort A, 281 patients (22.5%) received a docetaxel-containing regimen at index, of which 71.9% received no further treatment due to death or censoring which was notably higher than the cohort mean of 39.2%. 637 patients (51.0%) received IO-containing therapy in the index line of therapy, reflecting the high proportion of Cohort individuals diagnosed after immunotherapies became available in England. Among these patients, 24.5% on IO monotherapy received no further treatment due to death or censoring.
- In Cohort B, 24 patients (11.7%) received a docetaxel-containing regimen at index. 77 patients (37.6%) received TKI-containing therapy in the index line of therapy, of which 36.8% received no further treatment due to death or censoring.
- Across cohorts, 232 patients received docetaxel and nintedanib combination in the index line of therapy, which was 76.4% among those who received a docetaxel-containing regimen.
- Treatment prior to cohort entry were reported. For Cohort A, 696 patients (55.8%) were treated with a combination of PBC and anti-PD-1/PD-L1 therapy in the first line of therapy after diagnosis. 462 (37.0%) were treated with PBC followed by anti-PD-1/PD-L1 therapy, and 90 (7.2%) the opposite sequence. For Cohort B, 80 patients (39.0%) received PBC in the first line of therapy after diagnosis and targeted therapy in the second. 58 (28.3%) received the reverse of this sequence with targeted therapy as the initial treatment followed by PBC.
- Across cohorts, 46.2% of patients progressed to an additional line of therapy after the index line of therapy. The proportion of patients receiving docetaxel-containing regimens was 16.9% in Cohort A and 12.4% in Cohort B in the first post-index line.

Figure 2. Real-world overall survival (rwOS) from index line of therapy by treatment



Survival outcomes

- Individuals in Cohort A receiving docetaxel-containing regimens in the index line of therapy had notably shorter median survival from index of 7.9 months (95% CI: 6.6 – 9.4) than the overall cohort (12.0 months [95% CI: 11.1 – 12.9]).
- In Cohort B, individuals receiving docetaxel-containing regimens in the index line of therapy had a median survival from index of 5.5 months (95% CI: 2.1-7.0), while those who received TKIs had a medial survival from index (18.5 months [95% CI: 10.8 – 26.5]), longer than the overall cohort (8.2 months [95% CI: 6.6 – 9.8]).

Table 2. Median rwOS and rwTTNTD from index for those who received docetaxel-containing regimens for the index line of therapy

	Cohort A (non-AGA cohort)	Cohort B (AGA cohort)	Cohorts A & B combined
Index line of therapy / Median rwOS from index (95% CI) in months			
Docetaxel-containing regimens	7.9 (6.6 – 9.4) [n=281]	5.5 (2.1 – 7.0) [n=24]	7.2 (6.5 – 8.8) [n=304]
Docetaxel monotherapy	7.8 (5.1 – 10.5) [n=65]	N/A (small sample)	6.9 (4.8 – 9.6) [n=72]
Docetaxel + nintedanib	7.9 (6.6 – 9.6) [n=216]	6.6 (1.8 – 9.2) [n=17]	7.3 (6.5 – 9.1) [n=232]
Overall	12.0 (11.1 – 12.9) [n=1,248]	8.2 (6.6 – 9.8) [n=205]	11.2 (10.6 – 12.2) [n=1,451]
Index line of therapy / Median rwTTNTD from index (95% CI) in months			
Docetaxel-containing regimens	6.4 (5.6 – 6.9) [n=281]	3.2 (2.1 – 5.5) [n=24]	6.2 (5.2 – 6.8) [n=304]
Docetaxel monotherapy	5.1 (4.3 – 7.1) [n=65]	N/A (small sample)	5.0 (4.0 – 6.6) [n=72]
Docetaxel + nintedanib	6.5 (5.7 – 7.2) [n=216]	3.4 (1.8 – 7.0) [n=17]	6.5 (5.5 – 7.1) [n=232]
Overall	5.5 (5.0 – 6.0) [n=1,248]	5.0 (3.7 – 5.5) [n=205]	5.3 (5.0 – 5.7) [n=1,451]

Strengths and limitations

- The NCRAS dataset is the most comprehensive cancer data source in England. The findings of this study were more likely to reflect everyday clinical practice and can be more readily generalised to the broader patient population with advanced NSCLC in England.
- The line of therapy algorithm was derived from literature and refined with expert input to minimise the error of misinterpreting line advancement. However, the algorithm was not expected to be fully accurate for all patients due to the considerable variation in real-world treatment practices driven by factors such as physician and patient preference. The use of IO at study entry here should be viewed cautiously especially where the pre-index and index treatment were identical. Definitions for dose interruptions should be taken into consideration in future real-world studies.
- The COVID-19 pandemic might have influenced some of the observations in the current study, including the lower number of eligible patients diagnosed with NSCLC in 2020 and 2021 along with treatment patterns and survival.

Abbreviations

ADC: Antibody-drug conjugate; AGA: Actionable genomic alteration; IO: Immunotherapy; IQR: Interquartile range; NCRAS: National Cancer Registration and Analysis Service; NSCLC: Non-small cell lung cancer; PBC: Platinum-based chemotherapy; rwOS: Real-world overall survival; rwTTNTD: Real-world time to the next treatment or death; TKI: Tyrosine kinase inhibitor

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Disclosures

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