A retrospective real-world evaluation of docetaxel-based treatments after standard of care (SOC) for patients with non-squamous (NSQ) advanced non-small cell lung cancer (aNSCLC)

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INTRODUCTION

- The SOC treatment for patients with NSQ aNSCLC without a known actionable genomic alteration (non-AGA) is immunotherapy (IO), typically given either sequentially or as a combination with platinum-based chemotherapy (Pt-CT).
- If the patient harbors a known actionable genomic alteration (AGA), SOC is typically targeted therapy followed by Pt-CT.
- Upon failure of SOC, patients and providers are presented with few effective treatment options.
- Prior real-world studies have shown that docetaxel, either alone or in combination with ramucirumab, is the most frequently used regimen after failing SOC treatment.
- The objective of this study was to characterize patient characteristics and real-world clinical outcomes associated with docetaxel and ramucirumab combination therapy (DTX-R) and docetaxel monotherapy (DTX) in NSQ aNSCLC patients after prior treatment with SOC therapies.

METHODS

Study Design: Retrospective, non-interventional cohort study using electronic medical record data from 1 January 2018 to 30 November 2023.

Data Source: Flatiron Health Electronic Health Record Database which contains longitudinal, de-identified patient-level data from a demographically and geographically diverse, nationally representative population in the US.

Key Inclusion Criteria

- Diagnosed with stage IIIB – IV NSCLC during the study period
- Age ≥ 18 at initiation of subsequent therapy following SOC
- For non-AGA patients, prior treatment with immunotherapy (IO) and Pt-CT; for AGA* patients, prior treatment with targeted therapy and Pt-CT
- Had a subsequent treatment with DTX-R or DTX after IO and Pt-CT for non-AGA patients and targeted therapy and Pt-CT for AGA patients
- De novo a/mNSCLC

Key Exclusion Criteria

- Diagnosed with another primary cancer after aNSCLC diagnosis
- Enrollment in a clinical trial during the study period
- Squamous cell or adenosquamous histology

Index date: Date of initiation of subsequent therapy following SOC

Study Variables:

- Patient demographics and clinical characteristics at index: age, sex, race, practice type, index line number, year of index treatment, smoking history, performance status.
- Real-world overall survival (rwOS): the time from index date to date of death. Patients were censored at the end of record if no record of death.
- Real-world time to discontinuation (rwTTD): the time from index date until the start of next treatment regimen or death. Patients without discontinuation were censored at the date of last activity.
- Real-world time to next treatment (rwTTNT): the time from index date to the initiation of subsequent treatment regimen or date of death for patients who do not have a subsequent therapy. Patients who did not initiate subsequent therapy or die were censored at the date of last activity.

Statistical Analysis

- Descriptive statistics were used for patient demographic and clinical characteristics.
- Kaplan-Meier analysis was used for rwOS, rwTTD, and rwTTNT.

*AGA status was determined by a recorded positive biomarker test result for the following: ALK, BRAF, EGFR, METex14 Skipping, NTRK, RET, and ROS1

Table 1. Patient baseline characteristics

Variables/Statistics	DTX-R N=359	DTX N=160
Median age, years	66	67
Female sex, n (%)	175 (48.8)	87 (54.4)
Race, n (%)		
Caucasian	223 (62.1)	98 (61.3)
Black/African American	50 (14)	25 (15.6)
Asian	12 (3.3)	3 (1.9)
Other	39 (10.9)	7 (4.4)
Practice type, n (%)		
Community oncology setting	316 (88)	135 (84.4)
Academic oncology setting	41 (11.4)	22 (13.8)
Index Line Number, n (%)		
2	261 (72.7)	117 (73.1)
3	86 (24)	35 (21.9)
4+	12 (3.3)	8 (5)
Year of index treatment, n (%)		
2018	20 (5.6)	7 (4.4)
2019	68 (18.9)	30 (18.8)
2020	78 (21.7)	32 (20)
2021	65 (18.1)	34 (21.3)
2022	64 (17.8)	21 (13.1)
2023	64 (17.8)	36 (22.5)
Smoking history		
History of smoking	307 (85.5)	140 (87.5)
No history of smoking	51 (14.2)	20 (12.5)
ECOG Performance status, n (%)		
0, 1	233 (64.9)	105 (65.6)
2+	67 (18.7)	37 (23.1)
Undocumented	59 (16.4)	18 (11.3)
Baseline PD-L1 status		
< 1%	122 (34)	52 (32.5)
1-49%	103 (28.7)	35 (21.9)
≥ 50%	67 (18.7)	28 (17.5)
Unknown	67 (18.7)	45 (28.1)
Baseline *EGFR mutation*		
Negative	296 (82.5)	127 (79.4)
Not tested/Unknown	32 (8.9)	23 (14.4)
Positive	31 (8.6)	10 (6.3)

Abbreviations: DTX-R: docetaxel + ramucirumab; DTX: docetaxel monotherapy; ECOG: eastern cooperative oncology group; PD-L1; programmed death ligand 1; EGFR: epidermal growth factor receptor

Figure 1. rwOS by docetaxel-based subgroup

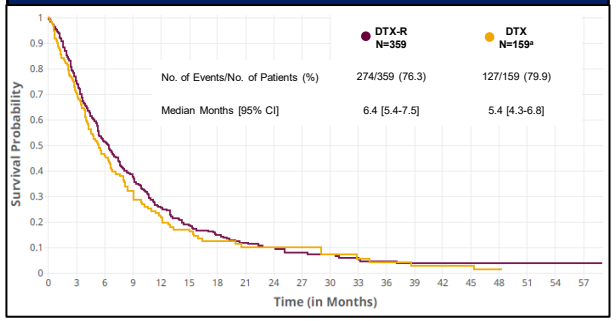


Figure 2. rwTTD by docetaxel-based subgroup

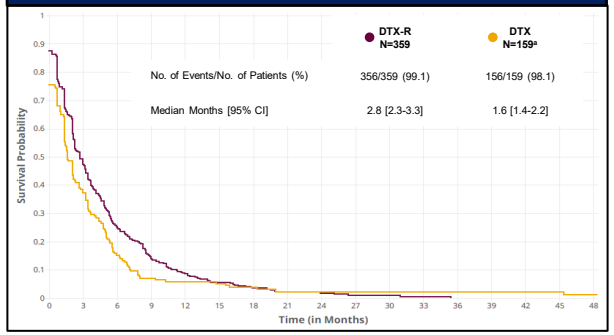
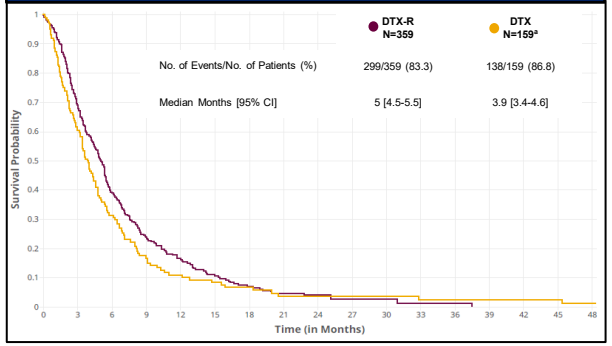


Figure 3. rwTTNT by docetaxel-based subgroup



a. 1 patient was excluded from Kaplan-Meier analysis due to numerically negative outcomes arising from discrepancy in date of death due to the deidentification process

Table 2. rwOS for docetaxel-based subgroup by AGA status

	Without AGA N=461		With AGA N=57	
	DTX-R N=317	DTX N=144	DTX-R N=42	DTX N=15
Median months [95% CI]	6.4 [5.4-7.5]	5.5 [4.3-6.9]	6.2 [4.5-11.8]	4.2 [2.8-NA]

RESULTS

- Of 519 patients that initiated docetaxel-based regimens after SOC therapy, 359 (69.2%) received treatment with DTX-R and 160 (30.8%) received DTX (Table 1).
- The median dosing frequency for docetaxel was every 3 weeks.
- For DTX-R and DTX, respectively, the median age was 66 and 67, 62.1% and 61.3% were White, 48.8% and 54.4% were female, 88% and 84.4% were treated in the community oncology setting, 85.5% and 87.5% had a history of smoking, and 64.9% and 65.6% had ECOG ≤ 1 (Table 1).
- The majority (approximately 73%) of patients initiating subsequent docetaxel-based therapy after SOC, initiated in the 2L (Table 1).
- PD-L1 status ≥ 50% was 18.7% and 17.5% of DTX-R and DTX patients, respectively (Table 1).
- EGFR mutation positivity was 8.6% and 6.3% for DTX-R and DTX patients, respectively (Table 1).
- The median (95% CI) OS was 6.4 months (5.4 – 7.5) for patients treated with DTX-R and 5.4 months (4.3 – 6.8) for patients treated with DTX (Figure 1).
- The median TTD was 2.8 months (2.3 – 3.3) for patients treated with DTX-R and 1.6 months (1.4 – 2.2) for patients treated with DTX (Figure 2).
- The median TTNT was 5 months (4.5 – 5.5) for patients treated with DTX-R and 3.9 months (3.4 – 4.6) for patients treated with DTX (Figure 3).
- For patients without AGA, median rwOS was 6.4 and 5.6 months for DTX-R and DTX, respectively and for patients with an AGA, rwOS was 6.2 and 4.2 months for DTX-R and DTX, respectively (Table 2).

DISCUSSION

- The outcomes in this study (rwOS, rwTTD, rwTTNT) are lower than in clinical trials likely due to the real-world nature of this analysis (e.g. inclusion of higher ECOG scores).
- In the overall population, the numerical difference between DTX-R and DTX was approximately 1 month.
- When assessed by AGA status, the numerical difference between DTX-R and DTX was approximately 1 month in patients without AGAs and 2 months in patients with AGAs, though sample size was relatively small in the AGA cohort.
- Data missingness and/or unavailability is a possibility in retrospective research and findings should be interpreted with this in mind.

CONCLUSION

Treatment with DTX-R or DTX following SOC showed limited clinical benefit in this real-world dataset based on rwOS, rwTTD, and rwTTNT. More effective treatment options are urgently needed to improve real-world survival outcomes in this challenging post-SOC setting. Future studies should evaluate the effectiveness of newer therapies used in the treatment of NSQ aNSCLC patients after progression on SOC.

DISLOSURES: Jon Apple, Surekha Damineni, and Anne Shah are currently employed by AstraZeneca. Lu Zou was employed at AstraZeneca at the time of study conduct. Emily Welch was a contractor working with AstraZeneca at the time of study conduct. Ruchit Shah, Chuntao Wu, and Eric Wang are employed by Daiichi Sankyo Inc.
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