

Real-world treatment patterns and outcomes for *BRAF*^{V600E}-mutated metastatic non-small cell lung cancer: the OCTOPUS study

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INTRODUCTION

- Lung cancer is the second most commonly diagnosed cancer worldwide, with a reported 2.2 million new lung cancer cases and 1.8 million deaths in 2020¹
 - Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer diagnoses,² with the *BRAF*^{V600E} mutation found in approximately 1–2% of NSCLCs³
- ESMO guidelines recommend targeted *BRAF/MEK* inhibitor combination therapy for the first-line (1L) treatment of *BRAF*^{V600E} mutant metastatic NSCLC (*BRAF*^{V600E}-mutant mNSCLC): dabrafenib/trametinib (D/T; ESMO-Magnitude of Clinical Benefit Scale [MCBS] score 2); or encorafenib/binimetinib (ESMO-MCBS score 3)⁴
- In real-life practice, due to the rarity of the disease, data on treatment patterns and management strategies for *BRAF*^{V600E}-mutant mNSCLC are limited^{3,5}
 - Marked international differences may also exist in access to biomarker testing and targeted *BRAF/MEK* inhibitor combination therapy²
- Therefore, the OCTOPUS study was conducted to evaluate real-world treatment patterns, and treatment effectiveness, persistence and safety in adults with *BRAF*^{V600E}-mutant mNSCLC in Europe

METHODS

- This observational, ambispective cohort study (NCT05546905) enrolled patients aged ≥18 years with stage IV *BRAF*^{V600E}-mutant mNSCLC from five European countries (France, Germany, Italy, Spain, and the UK)
 - Patients were included if they initiated 1L treatment between 1 December 2017 and 21 June 2022 (retrospective cohort), or between 21 June 2022 and 31 January 2024 (prospective cohort; **Figure 1**)
- The primary objectives were to describe real-world treatment patterns for 1L and second-line (2L) systemic therapy, including treatment persistence (time to treatment discontinuation [TTD])
- Secondary objectives were to assess patient characteristics, real-world progression-free survival (rwPFS), overall survival (OS), and safety
- Of note, due to Italian regulatory restrictions that prevent the inclusion of deceased patients, the Italian subpopulation was subject to selection and immortal time biases, which disproportionately influenced treatment patterns and outcomes
 - To ensure more robust and interpretable results, data from the Italian subpopulation were excluded from *post hoc* analyses; therefore, the present *post hoc* analyses of the OCTOPUS study focus on the unbiased study population from France, Germany, Spain, and the UK

RESULTS

Study participants

- Of the enrolled patients, 134 patients were included in these *post hoc* analyses (**Figure 1**)

Figure 1. Study design and patient flow

Enrolled patients (N=206)^a

1 Dec 2017 – 21 Jun 2022 (RC; n=176)
21 Jun 2022 – 31 Jan 2024 (PC; n=18)
Study end: 8 Jan 2025

Non-Italian enrolled patients (n=152)

Post hoc analyses cohort (n=134)

[RC, n=126; PC, n=8]
• Completed the study (n=38)
• Lost to follow-up (n=4)
• Died before EOO (n=92; 68.7%)

• Patients receiving 1L treatment: 100.0%
• Patients receiving 2L treatment: 54.5% (n=73)
• Patients with ongoing 1L treatment at EEO: 9.0% (n=12)

^a France, n=69; Germany, n=33; Italy, n=54; Spain, n=37; UK, n=13. Type of enrolment (RC, PC) data were missing for 12 patients 1L, first-line; 2L, second-line; eCRF, electronic case report form; EEO, end of observation; IQR, interquartile range; PC, prospective cohort; RC, retrospective cohort

Study treatments

- In the 1L treatment setting, patients received D/T (n=50; 37.3%), pembrolizumab alone (n=13; 9.7%) or with chemotherapy (n=24; 17.9%), chemotherapy alone (n=27; 20.1%), or other treatments (n=20; 14.9%; **Figure 2**)
 - Patients treated with D/T in the 1L treatment setting were older (median age 73.0 years), and were more likely to have ECOG performance status ≥2 (34.4% of patients) and brain metastases (29.4%) compared with patients who received non-D/T treatment (**Table 1**)

CONCLUSIONS

This study provides important real-world insights into the management of *BRAF*^{V600E} mutant mNSCLC



Although current international guidelines recommend targeted *BRAF/MEK* inhibitor therapy as 1L treatment for *BRAF*^{V600E}-mutant mNSCLC,^{4,10} approximately one-third of patients in this study did not receive a *BRAF/MEK* inhibitor targeted therapy in 1L or 2L



Furthermore, only about 50% of patients accessed any 2L treatment, thus highlighting the critical need to optimise treatment selection (and subsequent sequencing) in the 1L management of *BRAF*^{V600E}-mutant mNSCLC



The favourable effectiveness outcomes for D/T in this study, considered together with current international guideline recommendations,^{4,10} suggest that patients with *BRAF*^{V600E}-mutant mNSCLC may benefit from receiving targeted therapy as 1L treatment



While no definitive conclusions can be drawn from this study because of its observational nature, the study findings underline a lack of robust comparative treatment evidence, largely driven by the rarity of the *BRAF*^{V600E} mutation, and the heterogeneous access to targeted therapies across Europe

RESULTS

Table 1. Baseline demographic and clinical characteristics of patients with *BRAF*^{V600E}-mutant mNSCLC at the start of 1L treatment, by 1L treatment received

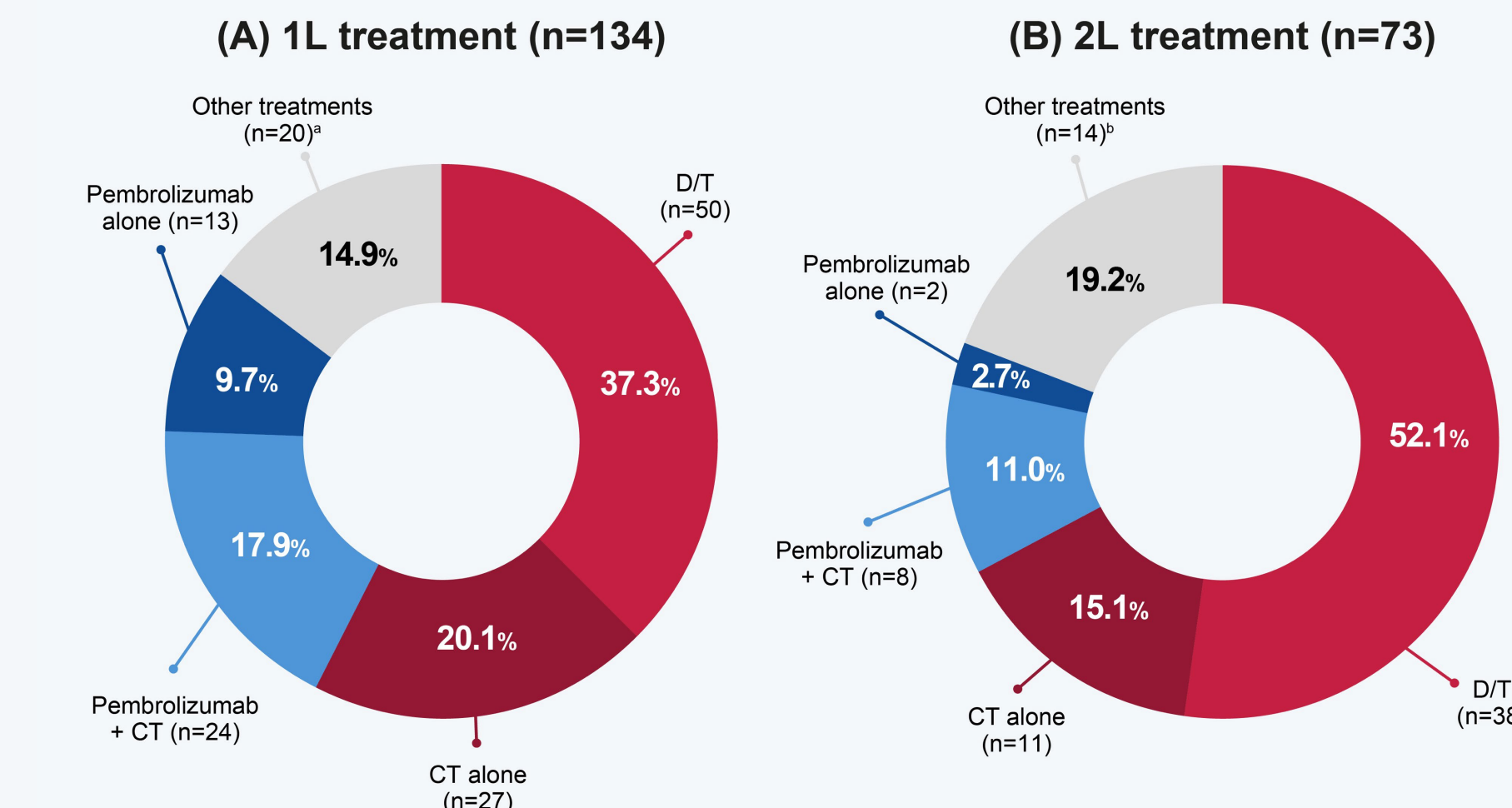
	1L treatment (n=134)				
	D/T (n=50)	Pembrolizumab alone (n=13)	Pembrolizumab + CT (n=24)	CT alone (n=27)	Other treatments ^a (n=20)
Age at metastasis, median (range), years	73.0 (50–90)	69.0 (48–87)	66.0 (46–73)	68.0 (54–82)	64.0 (33–79)
Male sex, n (%)	26 (52.0)	8 (61.5)	16 (66.7)	17 (63.0)	9 (45.0)
TNM stage at initial diagnosis, n (%)					
I–III	6 (12.5)	3 (23.1)	3 (12.5)	2 (7.4)	4 (20.0)
IV	17 (35.4)	4 (30.8)	11 (45.8)	17 (63.0)	4 (20.0)
IV-A	13 (27.1)	3 (23.1)	4 (16.7)	4 (14.8)	4 (20.0)
IV-B	12 (25.0)	3 (23.1)	6 (25.0)	4 (14.8)	8 (40.0)
Missing	2	0	0	0	0
Histology at initial diagnosis, n (%)					
Adenocarcinoma	50 (100.0)	13 (100.0)	21 (87.5)	26 (96.3)	16 (80.0)
SCC	0	0	3 (12.5)	0	2 (10.0)
Other	0	0	0	1 (3.7)	2 (10.0)
Metastasis at initial diagnosis, n (%)					
Visceral	24 (54.5)	4 (40.0)	18 (75.0)	12 (48.0)	8 (42.1)
Missing	6	3	0	2	1
Non-visceral	31 (70.5)	7 (70.0)	18 (75.0)	12 (48.0)	16 (84.2)
Missing	6	3	0	2	1
Brain	10 (29.4)	1 (9.1)	3 (23.1)	4 (18.2)	3 (20.0)
Missing	16	2	11	5	5
ECOG PS at initiation of 1L treatment, n (%)					
0–1	23 (65.7)	6 (75.0)	13 (81.3)	15 (75.0)	11 (84.6)
≥2	12 (34.4)	2 (25.0)	3 (18.8)	5 (25.0)	2 (15.4)
Missing	15	5	8	7	7
Smoking history at 1L treatment, n (%)					
Current	11 (23.4)	3 (23.1)	4 (18.2)	5 (20.0)	4 (21.1)
Previous	20 (42.5)	6 (46.2)	16 (72.7)	12 (48.0)	10 (52.6)
Non-smoker	16 (34.0)	4 (30.8)	2 (9.1)	8 (32.0)	5 (26.3)
Missing	3	0	2	2	1

^a Other treatments comprised immunotherapy + CT (n=5), EGFR inhibitor (n=3), immunotherapy + *BRAF* inhibitor + MEK inhibitor (n=3), CT + *BRAF* inhibitor + MEK inhibitor (n=2), CT + VEGF inhibitor (n=2), immunotherapy (n=2), CT + ALK inhibitor (n=1), CT + immunotherapy + VEGF inhibitor (n=1), ALK inhibitor (n=1)
1L, first-line; 2L, second-line; ALK, anaplastic lymphoma kinase; *BRAF*, B-Raf proto-oncogene; CT, chemotherapy; D/T, dabrafenib/trametinib; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; MEK, mitogen-activated protein kinase; SCC, squamous-cell carcinoma; TNM, Tumour Node Metastasis; VEGF, vascular endothelial growth factor

- Of the 134 patients in the *post hoc* analysis cohort, 73 (54.5%) received 2L treatment (**Figure 2**).

- A total of 88 patients (65.7%) received targeted *BRAF/MEK* inhibitor therapy with D/T in either the 1L or 2L

Figure 2. (A) 1L and (B) 2L treatments received for *BRAF*^{V600E}-mutant mNSCLC

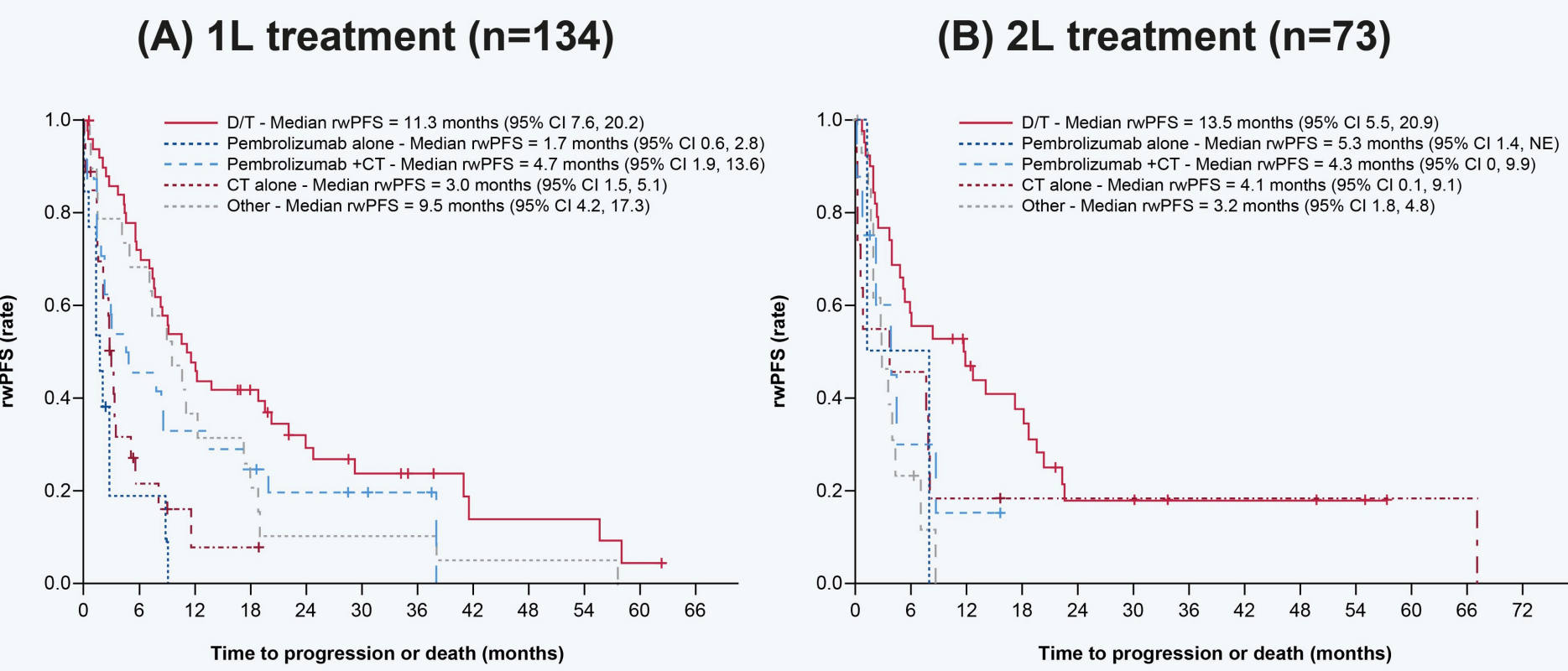


^a Other 1L treatments comprised immunotherapy + CT (n=5), EGFR inhibitor (n=3), immunotherapy + *BRAF* inhibitor + MEK inhibitor (n=3), CT + *BRAF* inhibitor + MEK inhibitor (n=2), CT + VEGF inhibitor (n=2), immunotherapy (n=2), CT + ALK inhibitor (n=1), CT + immunotherapy + VEGF inhibitor (n=1), ALK inhibitor (n=1)
^b Other 2L treatments comprised immunotherapy (n=6), VEGF inhibitor + CT (n=3), CT alone (n=2), ALK inhibitor (n=1), EGFR inhibitor (n=1), unknown (n=1)
1L, first-line; 2L, second-line; ALK, anaplastic lymphoma kinase; *BRAF*, B-Raf proto-oncogene; CT, chemotherapy; D/T, dabrafenib/trametinib; EGFR, epidermal growth factor receptor; MEK, mitogen-activated protein kinase; VEGF, vascular endothelial growth factor

Treatment effectiveness and persistence

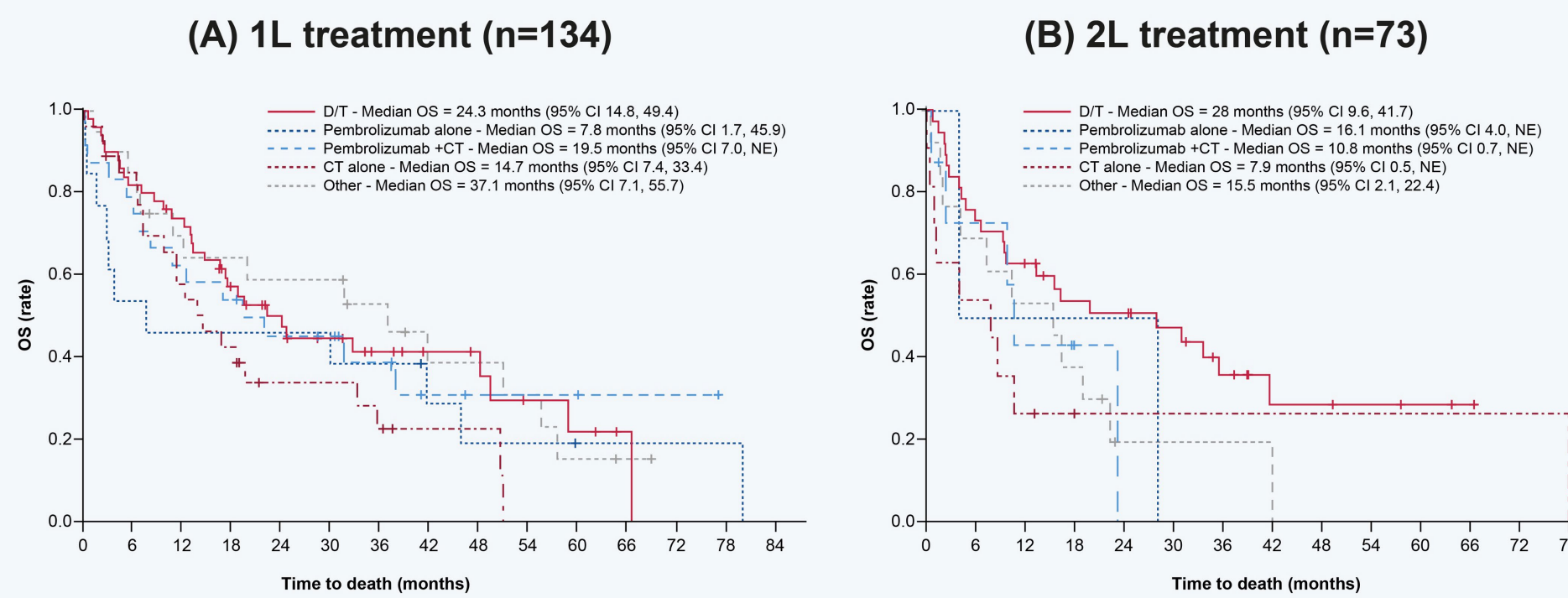
- Median rwPFS was 7.4 months (95% CI [Confidence Interval] 4.1, 9.1) in the 1L treatment setting and 5.9 months (95% CI 4.1, 9.1) after the start of 2L treatment. rwPFS outcomes by line of treatment are shown in **Figure 3**.
- Median OS was 19.8 months (95% CI 14.7, 32.8) in the 1L treatment setting and 15.6 months (95% CI 9.4, 28.0) after the start of 2L treatment. OS outcomes by line of treatment are shown in **Figure 4**.

Figure 3. Kaplan–Meier curves of rwPFS^a in patients with *BRAF*^{V600E}-mutant mNSCLC, by treatment line



^a rwPFS was defined as length of time from the start of 1L or 2L treatment until disease progression or death
1L, first-line; 2L, second-line; CI, confidence interval; CT, chemotherapy; D/T, dabrafenib/trametinib; rwPFS, real-world progression-free survival

Figure 4. Kaplan–Meier curves of OS^a in patients with *BRAF*^{V600E}-mutant mNSCLC, by treatment line



^a OS was defined as length of time from the start of 1L or 2L treatment until death
1L, first-line; 2L, second-line; CI, confidence interval; CT, chemotherapy; D/T, dabrafenib/trametinib; NE, not estimable; OS, overall survival

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