Real-world clinical outcomes in patients with advanced non-small cell lung cancer in the United Kingdom

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SCOPE

- **This study aimed to describe real-world clinical outcomes in adult patients with advanced NSCLC who initiated first-line treatment in the United Kingdom during the period when immuno-oncology (IO) monotherapy was being introduced as a treatment option**

CONCLUSIONS

- **IO has shown better survival outcomes and tumor response than chemotherapy, confirming the clinical benefits of IO; however, the median overall survival in the IO group was shorter than that in the targeted therapy group. In patients who have no *ALK* or *EGFR* mutation and who are therefore ineligible for targeted therapy, there is still a need for more effective and safe treatments**
- **Our results suggested that survival rates in patients treated with IO were shorter in this real-world data set than those described in randomised controlled trials. However, such comparisons should be interpreted with caution due to potential patient heterogeneity between real-world studies and clinical trials**
- **Future real-world studies should investigate whether outcomes in advanced NSCLC improve with the introduction of novel IO-based regimens and/or the establishment of current IO-based regimens in clinical practice, with the potential for adjustment based on clinical (eg, PD-L1 expression) and demographic characteristics**

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INTRODUCTION

- In the United Kingdom, immuno-oncology (IO) therapies have been introduced to clinicians for the treatment of advanced non-small cell lung cancer (aNSCLC) through IO therapy recommendation and subsequent reimbursement by governmental bodies such as the National Institute for Health and Care Excellence (NICE) and the Cancer Drugs Fund
- Randomised controlled trials (RCTs) have demonstrated antitumor activity and clinical benefits in aNSCLC with both IO monotherapies[1] and IO combination therapies[2–4]. However, there is a lack of real-world (RW) treatment patterns and outcomes data for aNSCLC in the UK patient population after the introduction of IO monotherapies
- A previous presentation described the results of the analyses of patient characteristics and treatment patterns in our study of RW outcomes in patients with aNSCLC.[5] Here, we present the clinical outcomes data

METHODS

Study design and time periods

- This was a retrospective observational study. Patients who started first-line (1L) treatment between 1 June 2016 and 31 March 2018 were included retroactively from 31 March 2018 and followed up to whichever came first: the last hospital follow-up, death, or end of study observation period on 31 December 2018. Index date was the start date of the first recorded cycle of 1L treatment

Data sources, sites, and setting

- The data was sourced primarily from electronic prescribing records (EPRs). EPRs are the RW records for patients in the United Kingdom who are prescribed systemic anticancer therapy. EPRs provide the actual treatment cycles prescribed as well as the clinician- determined lines of therapy for each patient

Patient population

- Patients were excluded if they had participated in a clinical trial for aNSCLC treatment at any point or if their records were missing any data points
- For inclusion in the study, patients were required to be ≥18 years of age, have received a diagnosis of aNSCLC (defined as ≥1 of the following indicators: stage IV disease, TNM with M value of 1, record of location of metastatic disease, and current or prior disease status containing reference to advanced or metastatic disease), and have initiated their 1L systemic anticancer treatment between 1 June 2016 and 31 March 2018

Outcomes

- We discuss overall survival (OS), time to treatment discontinuation (TTD), time to next treatment (TTNT), and RW tumour response (rwTR) in the 1L setting

Statistical analysis

- Baseline characteristics and rwTR were assessed descriptively overall and by 1L drug class. Drug classes were defined as nontargeted chemotherapy (NTC), IO monotherapy (hereafter referred to as IO because no combination therapies were available during the study observation period), or anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) inhibitors/targeted therapies (TTs). OS, TTD and TTNT were evaluated using the Kaplan-Meier method and stratified by 1L drug class

RESULTS

- A total of 1,003 patients were included. A previous presentation described patient attrition[5]
- In the 1L setting, 698 patients (69.6%) received NTC, 179 (17.8%) received IO, and 126 (12.6%) received TT (**Table 1**)

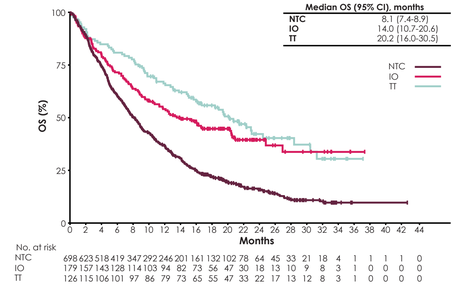
Table 1. Baseline demographics and clinical characteristics.

	Overall (n=1003 [100.0%])	NTC (n=698 [69.6%])	IO (n=179 [17.8%])	TT (n=126 [12.6%])
Follow-up duration, median (range), months	9.2 (0-42.7)	7.9 (0-42.7)	12.7 (0.1-37.3)	16.3 (0.1-37.1)
Age at diagnosis, median (range), years	68 (28-93)	68 (28-88)	67 (48-90)	70 (32-93)
Sex, n (%)				
Male	541 (53.9)	395 (56.6)	94 (52.5)	52 (41.3)
Female	462 (46.1)	303 (43.4)	85 (47.5)	74 (58.7)
Disease histology, n (%)				
Adenocarcinoma	635 (63.3)	387 (55.4)	131 (73.2)	117 (92.9)
Squamous cell carcinoma	243 (24.2)	202 (28.9)	38 (21.2)	3 (2.4)
Large cell carcinoma	6 (0.6)	4 (0.6)	2 (1.1)	0
NSCLC not otherwise specified	119 (11.9)	105 (15.0)	8 (4.5)	6 (4.8)
TNM staging, n (%)				
TNM – T				
T X-4	938 (93.5)	647 (92.7)	170 (95.0)	121 (96.0)
N/A	65 (6.5)	51 (7.3)	9 (5.0)	5 (4.0)
TNM – N				
N X-3	939 (93.6)	648 (92.8)	170 (95.0)	121 (96.0)
N/A	64 (6.4)	50 (7.2)	9 (5.0)	5 (4.0)
TNM – M				
M1*	524 (52.2)	351 (50.3)	114 (63.7)	59 (46.8)
M1a	166 (16.6)	120 (17.2)	22 (12.3)	24 (19.0)
M1b	310 (30.9)	224 (32.1)	43 (24.0)	43 (34.1)
M1c	3 (0.3)	3 (0.4)	0	0
ECOG PS at diagnosis, n (%)				
0-1	759 (75.7)	513 (73.5)	157 (87.7)	89 (70.6)
2+	244 (24.3)	185 (26.5)	22 (12.3)	37 (29.4)
***EGFR*+ status, n (%)†**				
Documented	19 (1.9)	1 (0.1)	0	18 (14.3)
Assumed	89 (8.9)	0	0	89 (70.6)
***ALK*+ status, n (%)†**				
Documented	2 (0.2)	0	0	2 (1.6)
Assumed	17 (1.7)	0	0	17 (13.5)
PD-L1 status, n (%)†				
Documented	10 (1.0)	3 (0.4)	7 (3.9)	0
Assumed	172 (17.1)	0	172 (96.1)	0

* Includes 77 patients with clinician-defined stage IV NSCLC
† Data for biomarkers came from either a test result (documented) or regimen type (assumed). Documented PD-L1 and biomarkers results were provided by the hospitals; assumed results are taken from the treatment prescribed (ie, assumed that EGFR+ patients received EGFR inhibitors, *ALK*+ patients received an ALK inhibitor, and PD-L1 + patients received an IO)
ECOG PS, Eastern Cooperative Oncology Group performance status.

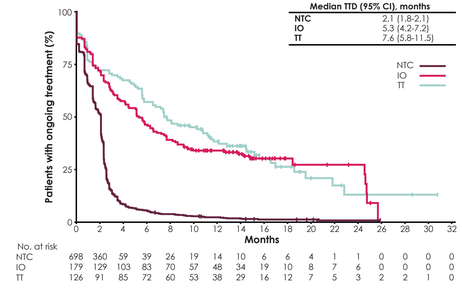
- By drug class, the number of patients who had rwTR was 187 (26.8%), 61 (34.1%) and 43 (34.1%) in the NTC, IO, and TT groups respectively
- Median OS ranged from 8.1 months (95% CI: 7.4-8.9 months) in patients receiving NTC to 20.2 months (95% CI: 16.0-30.5 months) in patients receiving TT. Median OS was 14.0 months in patients receiving IO (95% CI: 10.7-20.6 months) (**Figure 1**)

Figure 1. Kaplan-Meier estimate of OS, stratified by first-line drug class



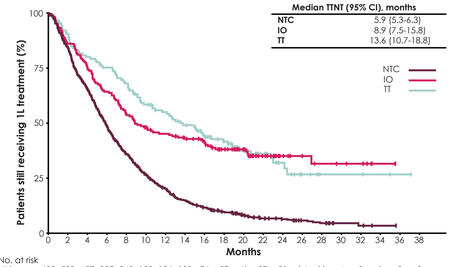
- The longest median TTD was observed in patients receiving TT (7.6 months [95% CI: 5.8-11.5 months]), and the shortest was seen in patients receiving NTC (2.1 months [95% CI: 1.8-2.1 months]). Median IO TTD was 5.3 months (95% CI: 4.2-7.2 months) (**Figure 2**)

Figure 2. Kaplan-Meier estimate of TTD, stratified by first-line drug class



- The drug class with the longest median TTNT was TT (13.6 months [95% CI: 10.7-18.8 months]); the NTC class had the shortest TTNT at 5.9 months (95% CI: 5.3-6.3 months). The IO class had a median TTNT of 8.9 months (95% CI: 7.5-15.8 months) (**Figure 3**)

Figure 3. Kaplan-Meier estimate of TTNT, stratified by first-line drug class



- The RW median OS tended to be shorter than the median OS observed in key RCTs. Similar patterns were found for TTD vs progression-free survival (PFS) and rwTR vs objective response rate (ORR) (**Table 2**)

Table 2. Comparison of clinical outcomes with key clinical trials of systemic chemotherapies and IO monotherapy

	OS, median (95% CI), months		PFS, median (95% CI), months		TTD, median (95% CI), months		ORR, %		rwTR, %	
	NTC	**IO**	**NTC**	**IO**	**NTC**	**IO**	**NTC**	**IO**	**NTC**	**IO**
This study	8.1 (7.4-8.9)	14.0 (10.7-20.6)	N/A	N/A	2.1 (1.8-2.1)	5.3 (4.2-7.2)	N/A	N/A	26.8	34.1
IO monotherapy trials										
KEYNOTE-024[6-8]	14.2 (9.8-19.0)	26.3 (18.3-40.4)	6.0 (4.2-6.2)	10.3 (6.7-NR)	N/A	N/A	27.8	44.8	N/A	N/A
KEYNOTE-042[9]	12.2 (10.4-14.6)	20.0 (15.9-24.2)	6.4 (6.1-6.9)	7.1 (5.9-9.0)	N/A	N/A	32.0	39.5	N/A	N/A
IMpower 110[10]	13.1 (7.4-16.5)	20.2 (16.5-NE)	5.0 (4.2-5.7)	8.1 (6.8-11.0)	N/A	N/A	28.6	38.3	N/A	N/A

NR, not reached; **NE**, not evaluable; **N/A**, not applicable.

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