Real-world data (RWD) collection alongside Early Access to Medicines Scheme (EAMS)—nivolumab in advance squamous cell oesophageal cancer after prior chemotherapy

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Introduction

- Nivolumab is a human monoclonal antibody that blocks programmed cell death protein 1 (PD-1) to promote anti-tumour response
- Nivolumab has received marketing authorisation in Europe for multiple indications and has been granted the promising innovative medicine designation for squamous cell oesophageal cancer in the United Kingdom (UK)
- Early Access to Medicines Schemes (EAMS) aim to provide patients who have life threatening or seriously debilitating conditions access to medicines that do not have a marketing authorisation when there is clear unmet medical need[1]
- The second core principle of EAMS is to provide an opportunity to generate real-world patient data in the National Health Service[2]
- The collection of real-world data (RWD) on patient characteristics and outcomes can help better understand the real-world use of nivolumab in the treatment of squamous cell oesophageal cancer

Objective

- To provide RWD on patients with advanced, recurrent/metastatic squamous cell oesophageal cancer treated with nivolumab (Opdivo®) after at least one prior systemic therapy

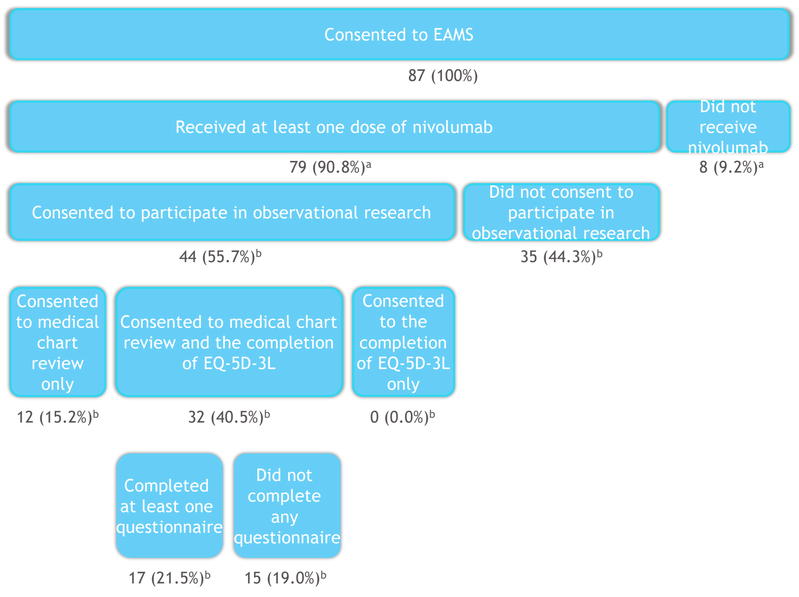
Methods

- Adults who initiated nivolumab as part of UK EAMS and consented to the observational research component of the EAMS were included
- As part of the observational research, EAMS patients could consent to data collection from patient medical charts, completion of the EuroQol 5-Dimensions 3-Levels questionnaire (EQ-5D-3L) or both
- Data collection included patient characteristics, treatment history, nivolumab treatment patterns, disease progression and survival status over a follow-up period of maximum 12 months. Patients completed EQ-5D-3L at baseline and biweekly for up to 24 weeks. Adverse events (AE) were also recorded
- Patients in the observational research were followed up from baseline until 12 months post-nivolumab treatment initiation, lost-to-follow-up, or death, whichever occurred first
- Descriptive analyses were performed. They included counts and percentages for categorical variables, and mean (standard deviation [SD]) and median (minimum-maximum) for continuous variables. Kaplan-Meier method was used to evaluate treatment persistence, progression-free survival (PFS) and overall survival (OS)

Results

- Eighty-seven patients with oesophageal cancer enrolled in EAMS (June–November 2020), of which 79 patients received at least one nivolumab treatment. Of these 79 patients, 44 (55.7%) participated in the observational research. In total, 29 of the 44 patients completed a medical chart review with or without EQ-5D-3L (**Figure 1**)

Figure 1. Description of patients enrolled in oesophageal cancer EAMS and observational research study



EAMS, Early Access to Medicines Scheme; EQ-5D-3L, EuroQol 5-Dimensions 3-Levels.
[a]The denominator is the total number of patients who consented to EAMS
[b]The denominator is the total number of patients who consented to EAMS and received at least one dose of nivolumab

Demographic and clinical baseline characteristics

- Patients (median age [min-max] = 66.5 years [29–84]) were mostly male (65.9%) and White (88.6%)
- More than half of the patients had pre-existing comorbidities (61.4%), the majority used concomitant medication at baseline (93.2%) and had an Eastern Cooperative Oncology Group (ECOG) score of 0 or 1 (90.9%)

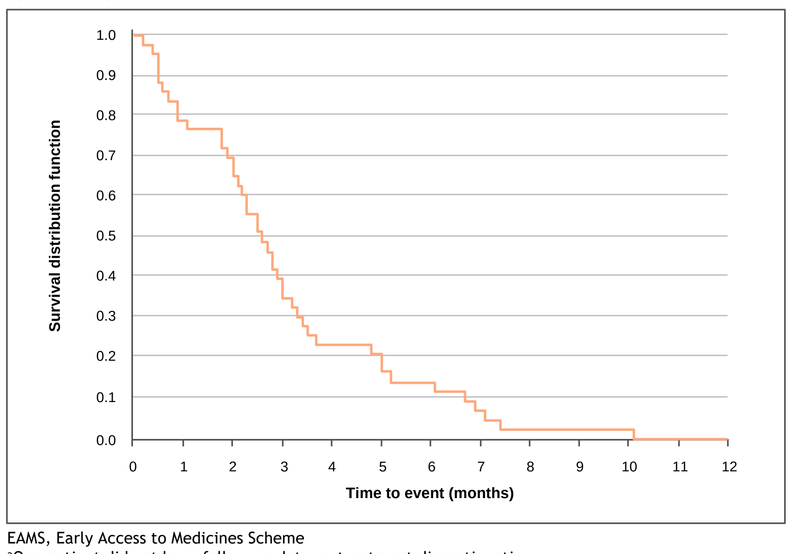
Treatment history for oesophageal cancer

- Most patients had no stent therapy (68.2%), were refractory to prior treatment (68.2%) and had not received surgery for squamous cell oesophageal cancer (70.5%)
- All patients received at least one prior systemic treatment before initiating nivolumab treatment. Cisplatin with capecitabine (34.1%), capecitabine with oxaliplatin (20.5%) and cisplatin with fluorouracil (5FU) (15.9%) were the three most reported prior treatments

Treatment patterns and duration

- Median nivolumab treatment duration was 2.6 months (95% confidence interval [CI], 2.0–3.0)
- The proportion of patients who remained on nivolumab treatment after nivolumab initiation was 34.9% (95% CI, 21.2–48.9) at 3 months, 14.0% (95% CI, 5.7–25.9) at 6 months and 0% at 12 months (**Figure 2**)

Figure 2. Rates of treatment persistence among patients treated with nivolumab in the oesophageal cancer EAMS (n = 43)

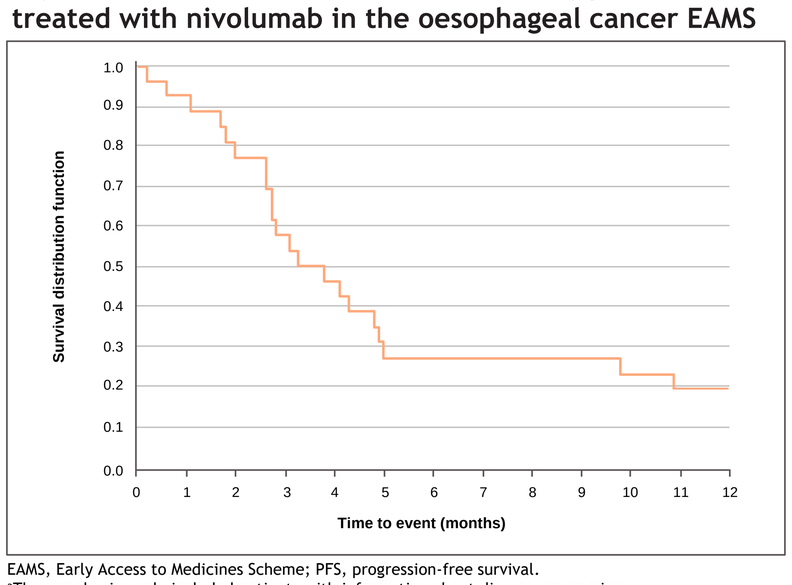


EAMS, Early Access to Medicines Scheme
[a]One patient did not have follow-up data on treatment discontinuation

Progression-free survival and overall survival

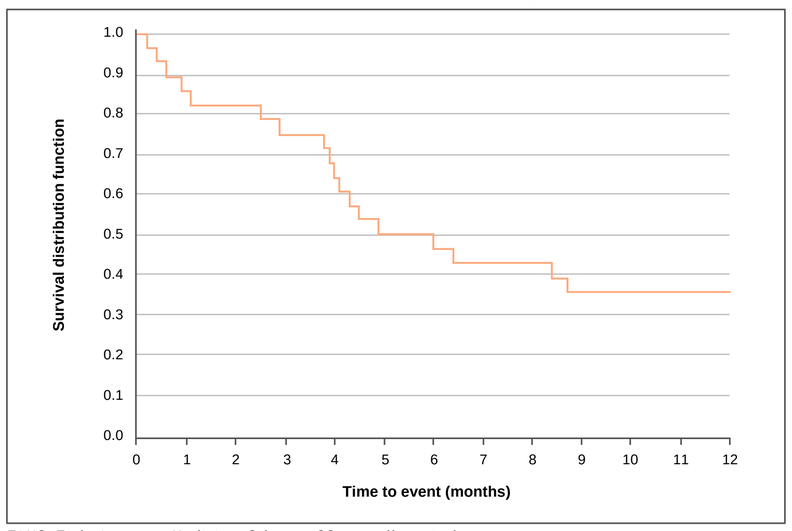
- In the available data (n = 28), median PFS was 3.8 months (95% CI, 2.6–4.9). At 3 months, 57.9% (95% CI, 37.0–74.1) did not have disease progression. At 6 and 12 months, 27% (95% CI, 12.0–44.6) and 19.3% (95% CI, 7.0–36.1) of patients remained disease progression free, respectively (**Figure 3**)
- In the available data (n = 28), median OS was 5.5 months (95% CI, 3.9–not estimable). At the end of 3 and 6 months, 75% (95% CI, 54.6–87.2) and 46.4% (95% CI, 27.6–63.3) were alive, respectively; 35.7% (95% CI, 18.9–53.0) were alive by end of follow-up. Among those who died, 16 died due to clinical disease progression (**Figure 4**)

Figure 3. Rates of PFS at 12 months among patients treated with nivolumab in the oesophageal cancer EAMS



EAMS, Early Access to Medicines Scheme; PFS, progression-free survival.
[a]The sample size only included patients with information about disease progression

Figure 4. Rates of OS at 12 months among patients treated with nivolumab in the oesophageal cancer EAMS



EAMS, Early Access to Medicines Scheme; OS, overall survival.
[a]The sample size only included patients with information about disease progression

Health-related quality of life

- At baseline, most patients had no problems with walking (77.8%), self-care (77.8%), pain or discomfort (55.6%), and anxiety or depression (66.7%). Most patients had some problems performing usual activities (77.8%)
- Among those who completed baseline EQ-5D-3L (n = 9), the mean EuroQol-visual analogue scale (EQ-VAS) score was 63.4 (SD = 18.3) and mean health utility score was 0.6 (SD = 0.2) (**Table 1**)
- At the end of nivolumab treatment, most patients had no changes since baseline in EQ-5D-3L domain scores. Improvement in performing usual activities and overall health status were reported by one patient each (14.3%). Worsening in performing usual activities and overall health status were reported by three patients each (42.9%). Mean EQ-VAS score decreased by 8.6 (SD = 17.8) and mean health utility scores by 0.1 (SD = 0.2)

Table 1. Descriptive summary of EQ-5D-3L at baseline

Domain score		Patients enrolled in EAMS who consented to chart review and EQ-5D-3L completion and returned a questionnaire at baseline (N = 9)
Mobility, n (%)	No problems walking about	7 (77.8%)
	Some problems walking about	2 (22.2%)
	Confined to bed	0 (0.0)
Self-care, n (%)	No problems with self-care	7 (77.8%)
	Some problems washing or dressing self	2 (22.2%)
	Unable to wash or dress self	0 (0.0%)
Pain or discomfort, n (%)	No pain or discomfort	5 (55.6%)
	Moderate pain or discomfort	3 (33.3%)
	Extreme pain or discomfort	1 (11.1%)
Usual activities, n (%)	No problems performing usual activities	1 (11.1%)
	Some problems performing usual activities	7 (77.8%)
	Unable to perform usual activities	1 (11.1%)
Anxiety or depression, n (%)	Not anxious or depressed	6 (66.7%)
	Moderately anxious or depressed	3 (33.3%)
	Extremely anxious or depressed	0 (0.0%)
EQ-VAS score	Mean (SD)	63.4 (18.3)
Health utility score	Mean (SD)	0.6 (0.2)

EAMS, Early Access to Medicines Scheme; EQ-5D, EuroQol 5-Dimensions; EQ-VAS, visual analogue scale; HRQoL, health-related quality of life; SD, standard deviation.

Adverse events

- Of 73 AEs, 7 were related to nivolumab. In total, 68 were serious AEs, of which 2 serious AEs were related to nivolumab
- The most frequently reported AEs were malignant neoplasm progression (35.6%, n = 26) and pneumonia (6.8%, n = 5). The second most reported AEs were anaemia, arthralgia, chest pain, dysphagia, hypercalcaemia and pulmonary sepsis (2.7%, n = 2 for each AE) (**Table 2**)

Table 2. Summary of the main AEs reported for patients in the observational study, stratified by relationship to nivolumab

	Observational study population (N = 44)		
	Observational study population	AE related to nivolumab	AE unrelated to nivolumab
Number of patients with at least one AE[a]	28 (63.6%)	3 (6.8%)	27 (61.4%)
Most reported AE type by preferred term, [total AE][b]	73	7	66
Malignant neoplasm progression	26 (35.6%)	0 (0.0%)	26 (39.4%)
Pneumonia	5 (6.8%)	1 (14.3%)	4 (6.1%)
Anaemia	2 (2.7%)	0 (0.0%)	2 (3.0%)
Arthralgia	2 (2.7%)	0 (0.0%)	2 (3.0%)
Chest pain	2 (2.7%)	0 (0.0%)	2 (3.0%)
Dysphagia	2 (2.7%)	0 (0.0%)	2 (3.0%)
Hypercalcaemia	2 (2.7%)	0 (0.0%)	2 (3.0%)
Pulmonary sepsis	2 (2.7%)	0 (0.0%)	2 (3.0%)
Other	30 (41.1%)	6 (86.0%)	24 (36.4%)
Event seriousness, [total AE][b]	73	7	66
Serious	68 (93.2%)	2 (28.6%)	66 (100.0%)
Non-serious	5 (6.8%)	5 (71.4%)	0 (0.0%)

AE, adverse event
[a]The denominator is the observational study population (N = 44)
[b][total AE] is the total number of AEs reported in the observational study population, number of AEs related and unrelated to nivolumab. [total AE] is the denominator for the percentage of AE type

Conclusions

- RWD collected in EAMS for patients with advanced oesophageal cancer treated with nivolumab suggested that treatment duration, 12-month PFS, health-related quality of life and treatment safety were consistent with the clinical trial population.[3] Shorter OS in EAMS (median 5.5 vs. 10.9 months in clinical trial) aligned with the expectation of a diverse population in real-world setting
- These data demonstrate UK EAMS is an effective setting to demonstrate the value of new medicines ahead of market access
- The burden of disease remains high. Further RWD generation is needed to continue to improve outcomes for oesophageal cancer patients

References

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