Saving Lives through Early Access: Exploring the Impact of a Managed Access Agreement in Adjuvant EGFRm NSCLC

EE204

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Introduction

- Adjuvant osimertinib in resected stage IB to IIIA epidermal growth factor receptor mutation-positive (EGFRm) non-small cell lung cancer (NSCLC) improved survival vs placebo in the phase III ADAURA study.
- An early data readout (January 2020 data cut-off [DCO]) was recommended by the independent data safety monitoring committee (IDMC) due to encouraging disease-free survival (DFS) data (hazard ratio (HR) of overall population: 0.20; 99.12% CI: 0.14, 0.30)[1] and led to its recommendation for the United Kingdom (UK) Cancer Drugs Fund (CDF) in November 2021 after an appraisal by the National Institute for Health and Care Excellence (NICE) in England.[2]
- Overall survival (OS) data were immature (4%) at the time of the regulatory approval and CDF recommendation. The final OS analysis based on the data cut-off in January 2023 DCO had an 18.2% maturity (HR: 0.49 [95% CI: 0.34-0.70]).[3]
- There is a preference by payers to make decisions based on “mature” OS data; however, in some cases, this may lead to patients not receiving access to treatments at the time of regulatory approval or make them ineligible for additional future treatments.[4,5]
- The ADAURA study is an important case study on managing access in the context of a statistically significant primary endpoint (DFS) prior to statistically significant OS data.

Objective

This study aimed to provide insights into the impact of granting patient access using the primary data readout (DFS) but before statistically significant OS data readout by estimating the number of deaths prevented by the inclusion of the osimertinib ADAURA indication into the UK CDF shortly after regulatory approval, focusing on the period between the primary DFS analysis and the final OS analysis.

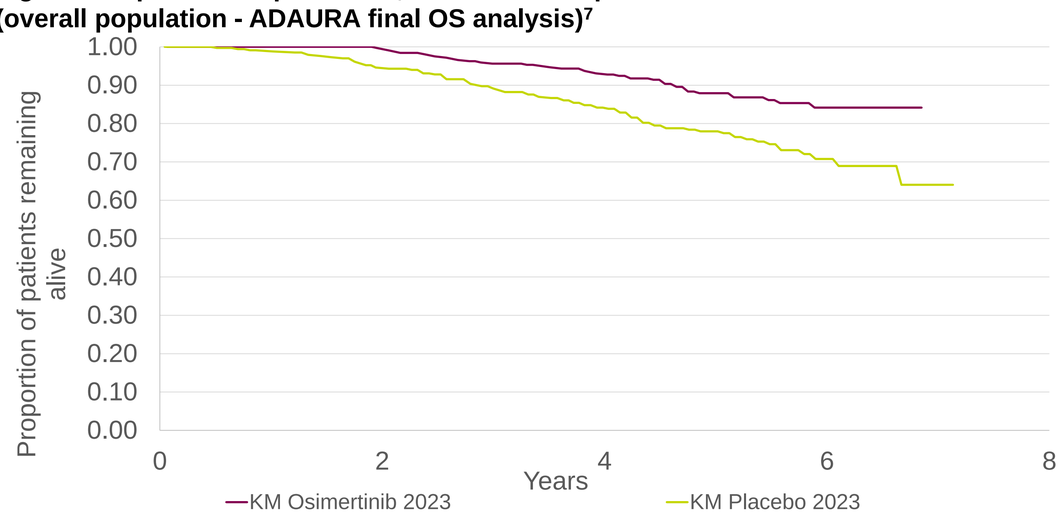
Methods

- The number of early deaths prevented was estimated by applying the landmark OS data from the osimertinib and placebo arms of the ADAURA final OS analysis (Table 1).
- The analysis was conducted using new patient estimates (uptake) derived from the NICE Resource Impact Assessment team[2] for 2021 until 2023 (Table 2).
- The number of patients entering the model in 2024 was calculated using the Office for National Statistics annual growth rate between 2018 and 2028 of 0.4%[6] and applied to the 2023 new patient estimate.
- An incidence-based model was used to simulate the movement of these patients over a 3-year period following the base year.

Table 1 OS over 3 years: osimertinib vs placebo (overall population)

Year	Osimertinib	Placebo	Difference
1	100%	99%	1%
2	99%	94%	5%
3	95%	89%	6%

Figure 1 Kaplan-Meier plot of OS, osimertinib vs placebo (overall population - ADAURA final OS analysis)[7]



Abbreviation: KM, Kaplan-Meier

Table 2 Patient flow over the analysis period: osimertinib vs placebo

Year of model entry	Model year				Total pts
	Base year	1	2	3	
Osimertinib					
2021	279	-	-	-	279
2022	558	279	-	-	837
2023	558	558	277	-	1393
2024	560	558	555	264	1937
Placebo					
2021	279	-	-	-	279
2022	558	276	-	-	834
2023	558	551	260	-	1369
2024	560	551	520	231	1863

Results

- The model estimated there were 1955 new patients eligible for osimertinib between 2021 and 2024.
- Based on the ADAURA 2023 OS data, the analysis showed that over this period, 74 deaths may have been avoided due to early adoption of osimertinib through the CDF.
- This equated to 3, 21, and 50 lives saved in years 1 to 3, respectively (Figure 2).
- In absolute terms, with the adoption of osimertinib, there is a reduction in the number of deaths from 92 to 18 over the 3-year period following the base year (Figure 3).

Results

Table 3 Early deaths prevented per year after the adoption of osimertinib, over a 3-year period

Year of model entry	Model Year		
	1	2	3
2022	3.3	-	-
2023	6.6	17.2	-
2024	6.6	34.4	33.2

Figure 2 Early deaths prevented per year after the adoption of osimertinib, over a 3-year period

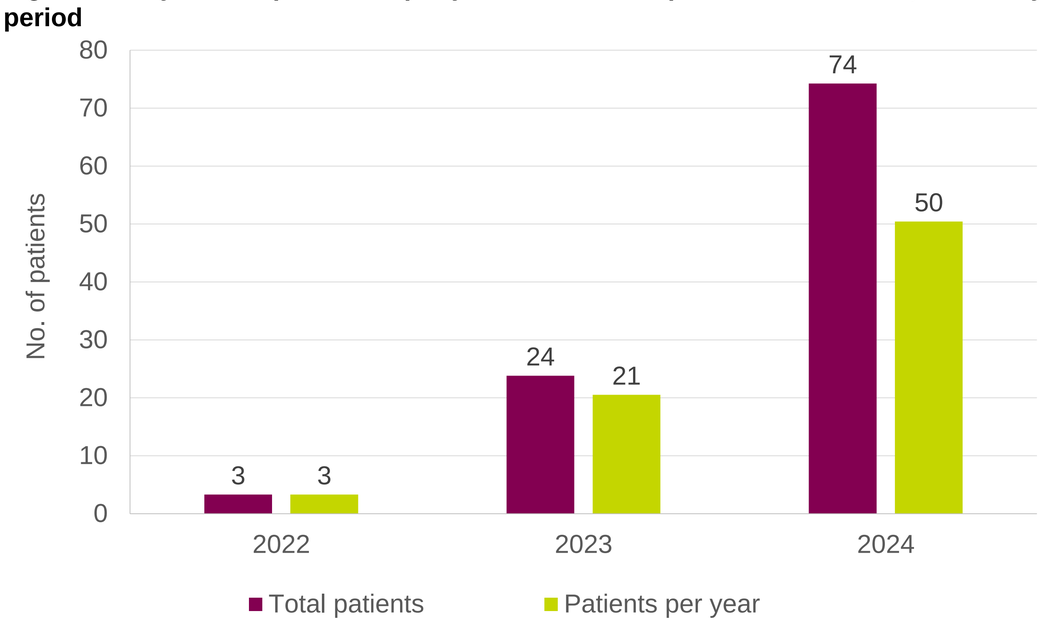
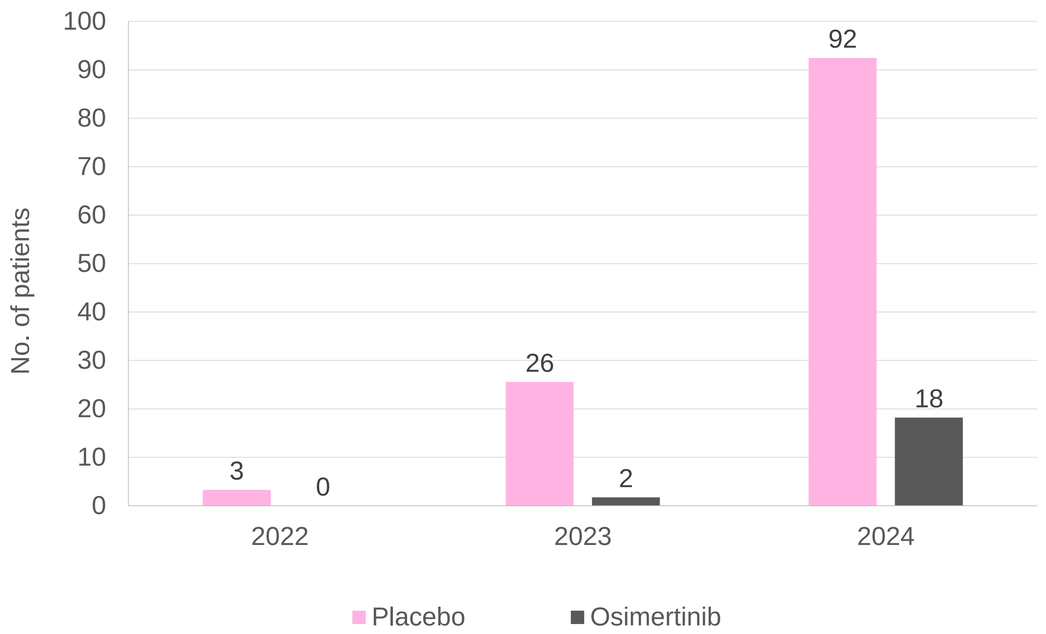


Figure 3 Absolute deaths, per year



Limitations

- New patient estimates were derived from the NICE Resource Impact Assessment Team and may not reflect actual data reported in clinical practice. COVID-19 is considered to have impacted the rate of early diagnosis and therefore, there is some uncertainty associated with how patient numbers may change following this period of restricted clinical practice.
- The model assumed annual cycles for patient entry and survival cut-off. Utilising a monthly cycle may have provided more precise estimates.
- It is difficult to precisely estimate the delay to access if statistically significant OS is required, with this analysis assuming an approximately 3-year delay.
- The analysis was limited to the first period of adoption of osimertinib on the CDF, however the full benefit of osimertinib occurs after 3 years (Figure 1). This implies that all patients within the time horizon without early access would lose out on the lifetime benefits of osimertinib.
- Additional analyses over a longer time horizon could be explored, either by awaiting further data maturity or through extrapolation.

Conclusions

- These findings highlight the benefit of managed access for adjuvant osimertinib after the primary endpoint readout (DFS) but before data maturity of the OS endpoints is reached. The learnings from this case study may be relevant to other oncology indications.
- Given that only the incremental survival difference in the first years is used, this is a conservative analysis with opportunities to explore modelling approaches that adopt a lifetime perspective.

References

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