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The European Pricing Landscape for Targeted Therapies in Advanced or Metastatic Non-Small Cell Lung Cancer to Achieve Maximum Progression Free Survival

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FOCUSED VALUE

INTRODUCTION

- Non-Small Cell Lung Cancer (NSCLC) makes up 85% of lung cancer cases and is the leading cause of cancer deaths worldwide.[1]
- Despite advances in targeted therapies and immunotherapies for NSCLC over the last decade, the 5-year survival rate remains only 17.4%.[2]
- This study examines the variations in cost per median progression-free survival (mPFS) month associated with targeted therapies for advanced or metastatic NSCLC (a/mNSCLC) between the United Kingdom (UK) and Germany (DE).

OBJECTIVE

- This study aims to compare the cost per mPFS month for targeted monotherapies approved for a/mNSCLC between the UK and DE.

METHODS

- Targeted monotherapies for a/mNSCLC approved by the European Medicine Agency (EMA) were identified between 2018 and 2023.[3]
- Drug prices were extracted from the British National Formulary (BNF) for the UK and Gemeinsamer Bundesausschuss (G-BA) appraisals for DE, excluding VAT and local discounts.[4,5]
- Clinical data on mPFS, mOS, and median duration of treatment (mDoT) were obtained from pivotal clinical trials.
- Drug acquisition costs were calculated according to dosage guidelines over mDoT, adjusted for inflation to 2024 Euros and the UK-EU exchange rate.
- Drug acquisition cost accounted for minimized drug wastage. Complete treatment adherence and no treatment discontinuation were assumed.
- Cost per mPFS month was calculated by dividing the drug acquisition cost during mDoT by mPFS.
- Cost per mOS month was analyzed but not reported, as 50% therapies had immature results for mOS.

RESULTS

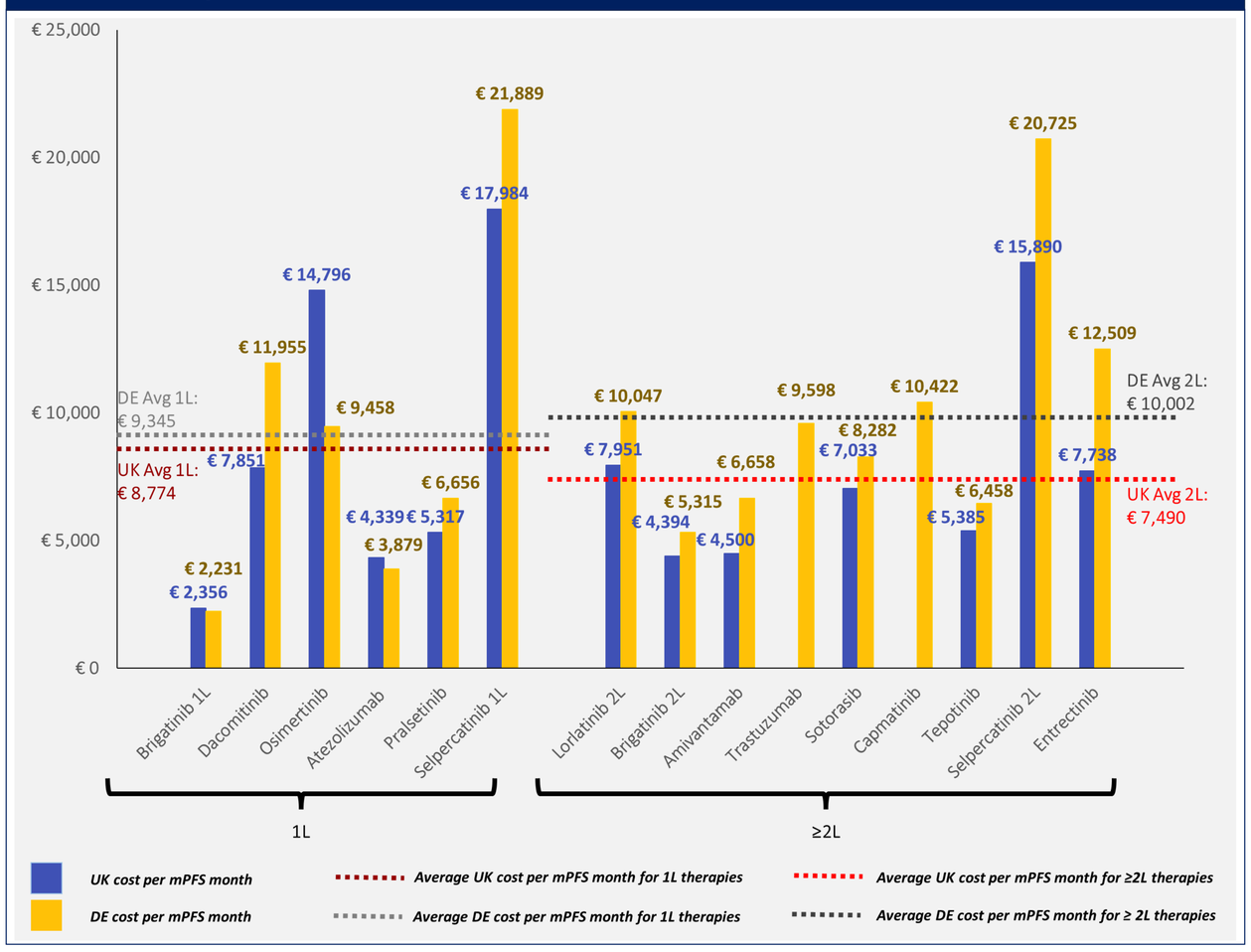
Drug Approvals

- 14 monotherapies with a total of 17 indications for a/mNSCLC have been approved between 2018 and 2023 by the EMA (Table 1).
- All approved therapies targeted specific mutations, including ALK positive, EGFR, HER2, KRAS, METex14, PD-L1, RET fusion, and ROS-1.
- Adagrasib is EMA approved for a/mNSCLC but was not launched in DE and the UK at the time of this study and was excluded from our analysis.
- Capmatinib was not available and trastuzumab was not approved for NSCLC in the UK.
- Although amivantanib and pralsetinib were not recommended by the National Institute for Health and Care Excellence (NICE), they were launched in the UK using BNF drug prices and therefore have been included in the analysis.
- First line (1L) ALK+ for lorlatinib was not reported since data on both mPFS and mOS were immature.

TABLE 1. Clinical and Economic Characteristics for EMA approved Therapies for a/m NSCLC

Drug Name	LoT	Patient Population (a/mNSCLC)	Approval Year	mPFS	mDoT	UK Cost per mPFS month	DE Cost per mPFS month	% Difference (UK vs DE)
Brigatinib 1L[6,7]	1L	ALK +ve	2020	24.0 (18.5, 43.2)	9.2 (0.1, 18.4)	€ 2,356	€ 2,231	6%
Dacomitinib[8,9]	1L	EGFR mut	2019	14.7 (11.1, 16.6)	36.1 (0.3, 115.1)	€ 7,851	€ 11,955	-34%
Osimertinib[10,11]	1L	EGFR mut	2018	18.9 (15.2, 21.4)	20.7 (0.1, 49.8)	€ 14,796	€ 9,458	56%
Atezolizumab[12,13]	1L	PD-L1	2021	8.1 (6.8, 11.0)	5.3 (NR, NR)	€ 4,339	€ 3,879	12%
Pralsetinib[14,15]	1L	RET fusion	2021	13.0 (9.1, NE)	7.9 (0.3, 28.4)	€ 5,317	€ 6,656	-20%
Selpercatinib 1L[16,17]	1L	RET fusion	2021	22.0 (13.8, NE)	36.1 (30.9, NE)	€ 17,984	€ 21,889	-18%
Lorlatinib 2L[18,19]	≥2L	ALK +ve	2019	6.9 (5.4, 8.2)	8.3 (5, 10.7)	€ 7,951	€ 10,047	-21%
Brigatinib 2L[20]	≥2L	ALK +ve	2018	19.3 (15.7, NE)	12.9 (0.1, 33.1)	€ 4,394	€ 5,315	-17%
Amivantamab[21]	≥2L	EGFR ex 20	2021	8.3 (6.5, 10.9)	3.7 (0.03, 23.9)	€ 4,500	€ 6,658	-32%
Trastuzumab[22,23]	≥2L	HER2 mut	2023	9.9 (7.4, NE)	7.7 (0.7, 20.8)	NA	€ 9,598	NA
Sotorasib[24,25]	≥2L	KRAS G12C mut	2022	6.8 (5.1, 8.2)	5.5 (0.2, 17.8)	€ 7,033	€ 8,282	-15%
Capmatinib[26]	≥2L	MET ex 14 skip	2022	5.4 (4.2, 7.0)	5.5 (0.1, 34)	NA	€ 10,422	NA
Tepotinib[27,28]	≥2L	MET ex 14 skip	2022	10.8 (8.3, 12.4)	6.9 (<0.1, 36.7)	€ 5,385	€ 6,458	-17%
Selpercatinib 2L[16,17]	≥2L	RET fusion	2021	24.9 (19.3, NE)	36.1 (30.9, NE)	€ 15,890	€ 20,725	-23%
Entrectinib[29,30]	≥2L	ROS-1 +ve	2020	16.8 (12, 21.4)	21.5 (13.0, 20.2)	€ 7,738	€ 12,509	-38%

FIGURE 1. Cost per mPFS Month



RESULTS (CONTINUED)

Median Progression-Free Survival (Table 1)

- In 1L therapies, brigatinib [mPFS (95%CI)] [24.0 (18.5, 43.2)] had the highest mPFS, and atezolizumab [8.1 (6.8, 11.0)] had the lowest mPFS.
- In second line (2L) therapies, selpercatinib [24.9 (19.3, NE)] had the highest mPFS and capmatinib [5.4 (4.2, 7.0)] had the lowest mPFS.

Median Overall Survival

- In 1L therapies, osimertinib [38.6 (34.5, 41.8)] had the highest mOS, and atezolizumab [20.1 (17.2, 27.9)] had the lowest mOS.
- In 2L therapies, amivantamab [22.8 (14.6, NE)] had the highest mOS and sotorasib [12.5 (10.0, NE)] had the lowest mOS.

Cost per mPFS Month (Figure 1)

First Line Therapies

- Selpercatinib had the highest cost per mPFS month [UK: €17,984; DE €21,889], while brigatinib had the lowest cost per mPFS month [UK: €2,356; DE: €2,231] in both the UK and DE.
- Cost per mPFS was higher for brigatinib (6%), atezolizumab (12%), and osimertinib (56%) in the UK compared to DE.
- Cost per mPFS month was lower for dacomitinib (34%), pralsetinib (20%), and selpercatinib (18%) in the UK versus DE.
- Average cost per mPFS month was €8,774 and €9,345 in the UK and DE, respectively.

Second Line Therapies

- Selpercatinib had the highest cost per mPFS month [UK: €15,890; DE € 20,725], while brigatinib had the lowest cost per mPFS month [UK: 4,394; DE: € 5,315] in both the UK and DE.
- Cost per mPFS month was 15%-38% lower in the UK compared to DE for all second line therapies.
- Average cost per mPFS month was €7,490 and €10,002 in the UK and DE, respectively.

First and Second Line Therapies

- The absolute cost difference in mPFS months across the two countries was highest for osimertinib and lowest for brigatinib.

LIMITATIONS

- Drug prices exclude confidential discounts and rebates, which may affect real-world costs.
- Complete treatment adherence and no treatment discontinuation were assumed, which may not reflect real-world clinical practice.
- Factors like trial population differences, treatment settings, and additional healthcare costs (administration, adverse events) were not considered, possibly impacting the generalizability and cost estimates.
- Prior approved indications for these therapies were not taken into consideration.

CONCLUSION

- Variations exist in cost per mPFS month for targeted monotherapies treating a/mNSCLC between the UK and Germany, with cost per mPFS month generally being lower in the UK.
- Line of therapy explains some of the variation as cost per mPFS months for 1L treatments on an average are within 5% difference between the 2 markets, where as for 2L therapies the cost difference is about 25%.
- Future research should explore company size, population size, time to market, etc. as potential explanatory variables.

ABBREVIATIONS

1L: first line; 2L: second line; mNSCLC: metastatic non-small cell lung cancer; mPFS: median progression free survival; mDoT: median duration of treatment; UK: United Kingdom; DE: Germany; RI: result immature; NE: not estimated; NA: not available ALK+ve: anaplastic lymphoma kinase positive; EGFR: epidermal growth factor receptor; HER2: human epidermal growth factor receptor 2; KRAS: Kirsten rat sarcoma virus gene; METex14: mesenchymal-epithelial transition factor gene exon; PD-L1: programmed cell death ligand-1; RET: rearranged during transfection; ROS-1: ROS proto-oncogene 1, receptor tyrosine kinase

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