Treatment Pathways, Drug Utilization and Healthcare Resource Consumption in Patients with Metastatic Anaplastic Lymphoma Kinase-Positive Non-Small Cell Lung Cancer: a Real-World Analysis with Administrative Databases in Italy

Appendix 1. List of drugs specific for the treatment of mNSCLC with the related ATC codes.

Drugs specific for mNSCLC	**ATC**
Immunotherapy	
Pemetrexed	L01BA04
Durvalumab (until 2021)	L01XC28
Atezolizumab (until 2019)	L01XC32
EGFR tyrosine kinase inhibitors	
Osimertinib	L01EB04
Gefitinib	L01EB01
Erlotinib	L01EB02
Afatinib	L01EB03
ALK inhibitors	
Crizotinib	L01ED01
Alectinib	L01ED03
Ceritinib	L01ED02
Brigatinib	L01ED04
Lorlatinib	L01ED05
Other protein kinase inhibitors	
Entrectinib	L01EX14
Capmatinib	L01EX17
Tepotinib	L01EX21
Pralsetinib	L01EX23
Nintedanib	L01EX09
Other antineoplastic agents	
Sotorasib	L01XX73

Appendix 2. List of anticancer drugs not specific for the treatment of mNSCLC with the related ATC codes.

Drugs non-specific for mNSCLC	**ATC**
Chemotherapy	
Docetaxel	L01CD02
Immunotherapy	
Bevacizumab	L01FG01
Pembrolizumab	L01FF02
(nab)Paclitaxel	L01CD01 (only minsan 039399011, 039399023)
Nivolumab	L01FF01
Ipilimumab	L01FX04
Cemiplimab	L01FF06
Other inhibitors	
Selpercatinib	L01EX22
Dabrafenib	L01EC02
Trametinib	L01EE01
Larotrectinib	L01EX12

Appendix 3. List of drugs specific for the treatment of SCLC with the related ATC codes.

Drugs specific for SCLC	**ATC**
Topotecan	L01CE01
Etoposide	L01CB01
Doxorubicin	L01DB01
Durvalumab (from 2022)	L01XC28
Atezolizumab (from 2020)	L01XC32

Appendix 4. Cox regression model assessing the relative risk of switch from index-treatment based on therapy, sex, age, comorbidity index (CCI), and the presence of previous brain metastases. The reference group for treatment is brigatinib.

Treatment (Ref.: Brigatinib)	**HR**	**95% CI**		**p**
Alectinib	0.926	0.394	2.18	0.861
Crizotinib	1.466	0.574	3.746	0.424
CT + ALKi	1.459	0.507	4.197	0.484
Sex (Ref.: Female)				
Male	1.159	0.772	1.74	0.478
Age classes (Ref.: 18-49 years)				
50-64 years	1.454	0.811	2.608	0.209
65-79 years	1.517	0.823	2.797	0.182
≥80 years	1.034	0.363	2.943	0.95
CCI (Ref.: 0)				
1	1.379	0.903	2.107	0.137
≥2	1.399	0.675	2.9	0.366
Previous brain metastases	1.211	0.599	2.447	0.594

Abbreviations: ALKi, Anaplastic Lymphoma Kinase inhibitors; CI, confidence interval; CCI, Charlson Comorbidity Index; CT, chemotherapy; HR, hazard ratio.

Appendix 5. Cox regression model assessing the relative risk of death based on treatment type, gender, age, comorbidity index (CCI), and the presence of previous brain metastases. The reference group for treatment is brigatinib. Significant p values are highlighted in bold.

	HR	95% CI		p
Treatment (Ref.: Brigatinib)				
Alectinib	1.570	0.564	4.372	0.388
Crizotinib	2.165	0.733	6.396	0.162
CT + ALKi	0.931	0.228	3.797	0.921
Sex (Ref.: Female)				
Male	1.240	0.840	1.833	0.279
Age classes (Ref.: 18-49 years)				
50-64 years	1.409	0.759	2.617	0.278
65-79 years	1.651	0.880	3.098	0.119
≥80 years	3.673	1.693	7.969	**0.001**
CCI (Ref.: 0)				
1	1.148	0.762	1.729	0.510
≥2	1.219	0.628	2.366	0.559
Previous brain metastases	1.745	0.936	3.255	0.080

Abbreviations: ALKi, Anaplastic Lymphoma Kinase inhibitors; CI, confidence interval; CCI, Charlson Comorbidity Index; CT, chemotherapy; HR, hazard ratio.

Appendix 6. GLM model for predictors of healthcare costs. Significant p values are highlighted in bold.

	HR	95% CI		p
Treatment (Ref.: Brigatinib)				
Alectinib	17,446 €	14,611 €	20,281 €	**<0.001**
Crizotinib	14,534 €	10,509 €	18,558 €	**<0.001**
CT + ALKi	13,859 €	8,660 €	19,058 €	**<0.001**
Gender (Ref.: Female)				
Male	877 €	-1,485 €	3,238 €	0.467
Age classes (Ref.: 18-49 years)				
50-64 years	-544 €	-3,731 €	2,644 €	0.738
65-79 years	-2,080 €	-5,210 €	1,050 €	0.193
≥80 years	-1,825 €	-7,979 €	4,328 €	0.561
CCI (Ref.: 0)				
1	-3,238 €	-5,687 €	-790 €	**0.010**
≥2	-2,979 €	-8,091 €	2,134 €	0.253
Previous brain metastases	-504 €	-4,971 €	3,963 €	0.825

Abbreviations: ALKi, Anaplastic Lymphoma Kinase inhibitors; CI, confidence interval; CCI, Charlson Comorbidity Index; CT, chemotherapy; HR, hazard ratio.