Diagnosis and treatment of advanced *ALK* rearrangement-positive non-small-cell lung cancer in Portugal: results of a national questionnaire

Drugs – Real World Outcomes

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SUPPLEMENTARY INFORMATION

Table S1 Sociodemographic characterization of the physicians who responded to the questionnaire

Characteristic	North (n=6)	Centre (n=3)	LVT (n=9)	Alentejo (n=1)	Algarve (n=1)	Azores (n=1)	Madeira (n=1)
Age (years)							
<30	0	0	0	0	0	0	0
30-45	2	1	4	0	0	1	1
46-60	2	2	3	0	0	0	0
>60	2	0	2	1	1	0	0
Specialty							
Pulmonology	4	3	7	1	1	0	0
Oncology	2	0	2	0	0	1	1
Practiced the most of the time							
Public institution	4	3	6	1	1	1	1
Private institution	2	0	3	0	0	0	0

LVT Lisbon and Tagus Valley

Table S2 Diagnosis of *ALK*-positive NSCLC in the institutions under study

Diagnosis	North (n=6)	Centre (n=3)	LVT (n=9)	Alentejo (n=1)	Algarve (n=1)	Azores (n=1)	Madeira (n=1)
Anatomopathological study							
At the institution	3	2	7	1	1	1	1
Outside the institution	3	1	2	0	0	0	0
Molecular study							
In the institution, reflexive	2	0	1	1	0	1	1
Outside the institution, reflexive	3	0	2	0	1	0	0
In the institution, upon request	0	0	2	0	0	0	0
Outside the institution, upon request	1	3	4	0	0	0	0
Most frequent detection method							
FISH	0	0	0	0	0	0	0
IHQ	0	0	0	1	0	0	1
NGS	6	3	9	0	1	1	0
Mean wait time for molecular study results (days)							
<14	1	0	2	1	0	0	0
14-21	5	1	7	0	1	1	1
>21	0	2	0	0	0	0	0
Access to detection of *ALK* TKI resistance mutations							
Yes	6	2	7	0	1	1	0
No	0	1	2	1	0	0	1
Access to NGS of liquid biopsies							
Yes	4	3	8	1	1	1	0
No	2	0	1	0	0	0	1

ALK anaplastic lymphoma kinase, *FISH* fluorescence *in situ* hybridization, *IHC* immunohistochemistry, *LVT* Lisbon and Tagus Valley, *NGS* next-generation sequencing

Table S3 First-line therapy that was more frequent in different populations of patients with *ALK*-positive NSCLC in the institutions under study

Therapeutics 1st line	**North** (n=6)	**Centre** (n=3)	**LVT** (n=9)	**Alentejo** (n=1)	**Algarve** (n=1)	**Azores** (n=1)	**Madeira** (n=1)
Most frequent							
Crizotinib	0	0	0	0	0	0	0
Alectinib	6	3	9	1	1	1	1
Ceritinib	0	0	0	0	0	0	0
Brigatinib	0	0	0	0	0	0	0
Patients with brain MX							
Crizotinib	0	0	0	0	0	0	0
Alectinib	6	2	8	0	1	1	1
Ceritinib	0	0	0	0	0	0	0
Brigatinib	0	1	1	1	0	0	0
Metastatic volume: CT instead of TKI							
Yes	0	0	0	0	1	0	0
No	6	3	9	1	0	1	1
Patients with PS ≥ 2							
Crizotinib	0	0	1	0	0	1	1
Alectinib	6	3	8	1	1	0	0
Ceritinib	0	0	0	0	0	0	0
Brigatinib	0	0	0	0	0	0	0
Patients aged ≥80 years							
Crizotinib	0	0	1	0	0	0	1
Alectinib	5	3	8	1	1	1	0
Ceritinib	0	0	0	0	0	0	0
Brigatinib	1	0	0	0	0	0	0

CT chemotherapy, *LVT* Lisbon and Tagus Valley, *MX* metastases, *PS* performance status, *TKI* tyrosine kinase inhibitor

Table S4 Second-line therapies in several populations of patients with *ALK-positive* NSCLC in the institutions under study

Therapeutics 2nd line	**North** (n=6)	**Centre** (n=3)	**LVT** (n=8)	**Alentejo** (n=1)	**Algarve** (n=1)	**Azores** (n=1)	**Madeira** (n=1)
Extra-CNS oligoprogression							
Change drug	0	0	0	0	0	1	0
Local TX and same drug	6	3	8	1	1	0	1
Local TX and change drug	0	0	0	0	0	0	0
Asymptomatic CNS oligoprogression							
Change drug	1	2	0	0	0	0	0
Local TX and same drug	5	1	8	1	1	1	1
Local TX and change drug	0	0	0	0	0	0	0
Symptomatic CNS oligoprogression							
Change drug	1	0	0	0	0	0	0
Local TX and same drug	3	1	7	0	1	1	1
Local TX and change drug	2	2	1	1	0	0	0
Asymptomatic systemic progression							
Always change the drug	0	0	1	0	0	1	1
Maintain drug in some cases	6	3	8	1	1	0	0
Symptomatic systemic progression, 1L crizotinib							
Alectinib	2	1	7	0	0	1	1
Ceritinib	0	0	0	0	0	0	0
Brigatinib	1	0	1	0	1	0	0
N/A	3	2	0	1	0	0	0
Symptomatic systemic progression, 1L alectinib							
Lorlatinib	2	2	3	0	0	1	1
Detection of resistance mutations	4	1	5	1	1	0	0
Symptomatic systemic progression, 1L brigatinib							
Lorlatinib	1	2	2	0	1	1	1
CT	0	0	0	0	0	0	0
Detection of resistance mutations	5	1	6	1	0	0	0

1L 1st line, *CNS* central nervous system, *CT* chemotherapy, *LVT* Lisbon and Tagus Valley, *N/A* not applicable due to the non-use of crizotinib in the 1st line, *TX* treatment

Table S5 Further therapies in patients with *ALK*-positive NSCLC in the institutions under study

Later therapies after progression under lorlatinib	**North** (n=6)	**Centre** (n=3)	**LVT** (n=8)	**Alentejo** (n=1)	**Algarve** (n=1)	**Azores** (n=1)	**Madeira** (n=1)
CT	3	1	1	1	1	1	1
Detection of resistance mutations	3	2	7	0	0	0	0
Rechallenge with another TKI without detection of resistance mutations	0	0	0	0	0	0	0
Detection of resistance mutations							
It was useful	2	1	4	0	0	0	0
It was not useful	4	1	3	1	1	0	0
Do not have access	0	1	1	0	0	0	1
Have access, but do not ask	0	0	0	0	0	1	0
Immunotherapy is an option							
Yes	2	0	3	0	0	1	1
No	4	3	5	1	1	0	0

CT chemotherapy, *LVT* Lisbon and Tagus Valley, *TKI* tyrosine inhibitor kinase~~; s/sem~~

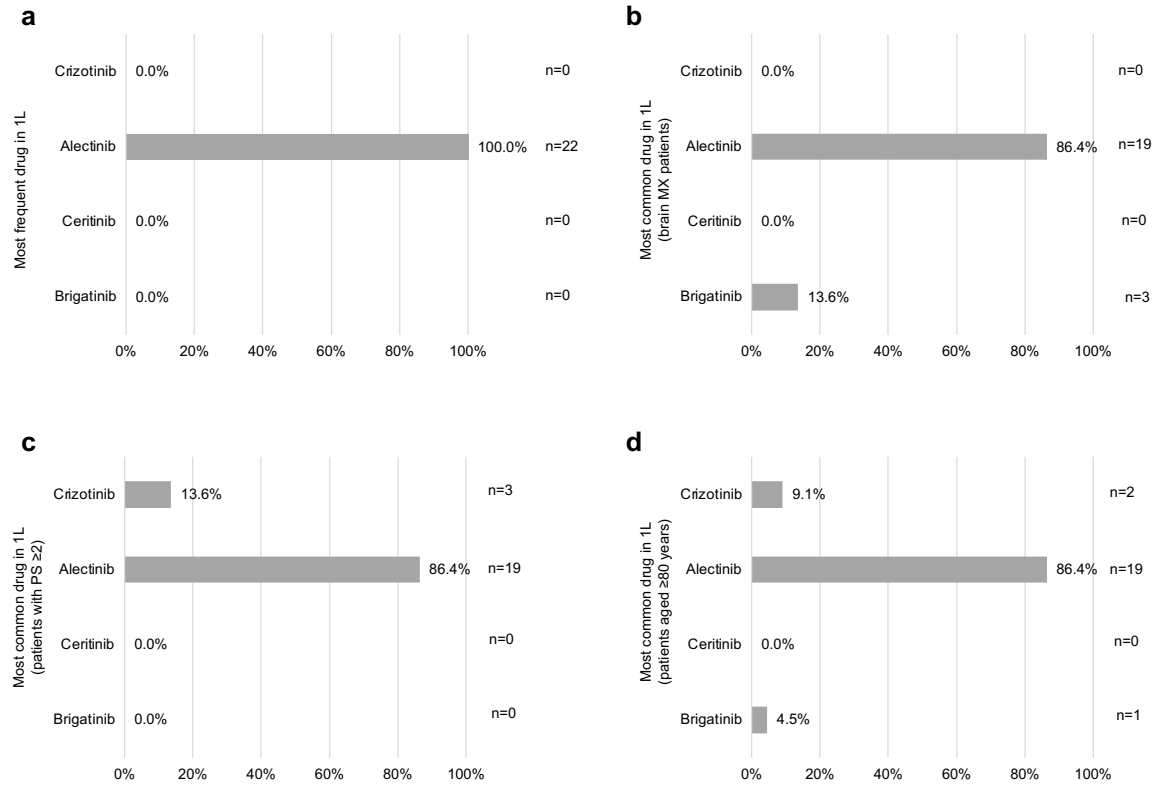
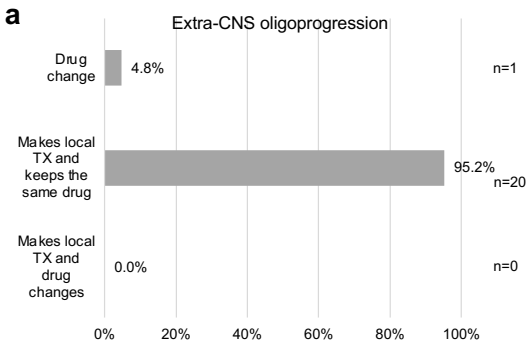
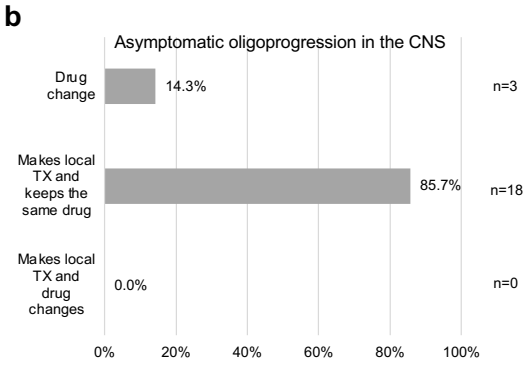
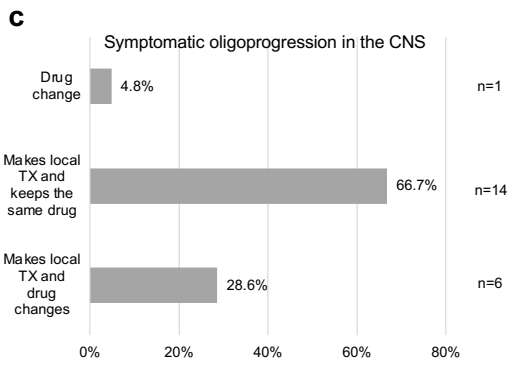
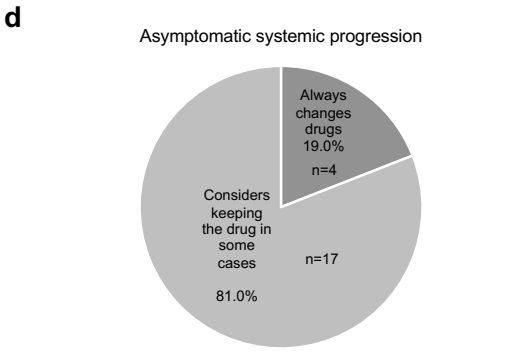


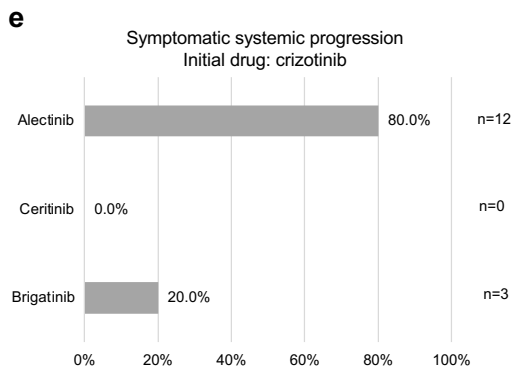
Fig. S1 Most common first-line therapy in different populations of patients with *ALK*-positive NSCLC in the studied institutions (**a**) General population (**b**) Patients with brain metastases (**c**) Patients with PS ≥ 2 (**d**) Patients aged ≥ 80 years. *1L* 1st line, *MX* metastases, *PS* performance status

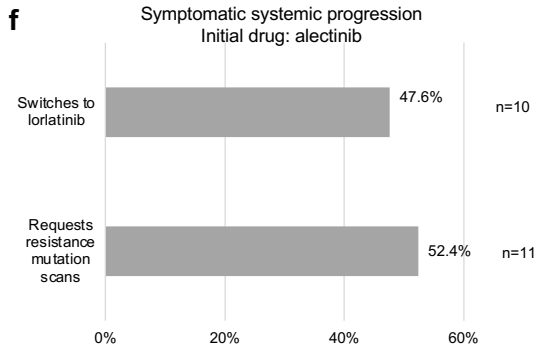

a
Extra-CNS oligoprogression
Drug change
4.8%
n=1
Makes local TX and keeps the same drug
95.2%
n=20
Makes local TX and drug changes
0.0%
n=0
0%
20%
40%
60%
80%
100%


b
Asymptomatic oligoprogression in the CNS
Drug change
14.3%
n=3
Makes local TX and keeps the same drug
85.7%
n=18
Makes local TX and drug changes
0.0%
n=0
0%
20%
40%
60%
80%
100%


c
Symptomatic oligoprogression in the CNS
Drug change
4.8%
n=1
Makes local TX and keeps the same drug
66.7%
n=14
Makes local TX and drug changes
28.6%
n=6
0%
20%
40%
60%
80%


d
Asymptomatic systemic progression
Always changes drugs 19.0%
n=4
Considers keeping the drug in some cases
81.0%
n=17


e
Symptomatic systemic progression
Initial drug: crizotinib
Alectinib
80.0%
n=12
Ceritinib
0.0%
n=0
Brigatinib
20.0%
n=3
0%
20%
40%
60%
80%
100%


f
Symptomatic systemic progression
Initial drug: alectinib
Switches to lorlatinib
47.6%
n=10
Requests resistance mutation scans
52.4%
n=11
0%
20%
40%
60%

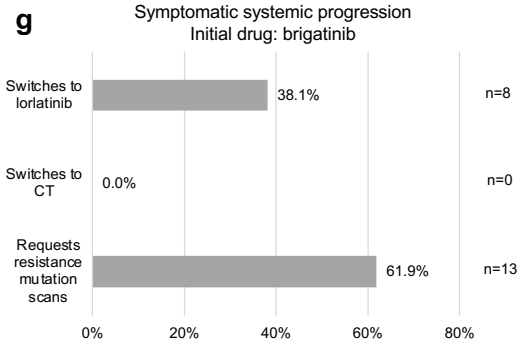

g
Symptomatic systemic progression
Initial drug: brigatinib
Switches to lorlatinib
38.1%
n=8
Switches to CT
0.0%
n=0
Requests resistance mutation scans
61.9%
n=13
0%
20%
40%
60%
80%

Fig. S2 Second-line therapy in different populations of patients with *ALK*-positive NSCLC in the studied institutions (**a**) Patients with extra-CNS oligoprogression (**b**) Patients with asymptomatic oligoprogression in the CNS (**c**) Patients with symptomatic oligoprogression in the CNS (**d**) Patients with asymptomatic systemic progression (**e**) Patients with symptomatic systemic progression; initial drug: crizotinib (**f**) Patients with symptomatic systemic progression; initial drug: alectinib (**g**) Patients with symptomatic systemic progression; initial drug: brigatinib. *CNS* central nervous system, *CT* chemotherapy, *TX* treatment