European Network of Cancer Registries
Scientific Meeting 2018

THE USE OF BIOMARKERS IN TREATMENT PATTERNS AND SURVIVAL OUTCOMES OF METASTATIC NON-SQUAMOUS NON-SMALL CELL LUNG CANCER

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Summary

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2. Objective
3. Methods
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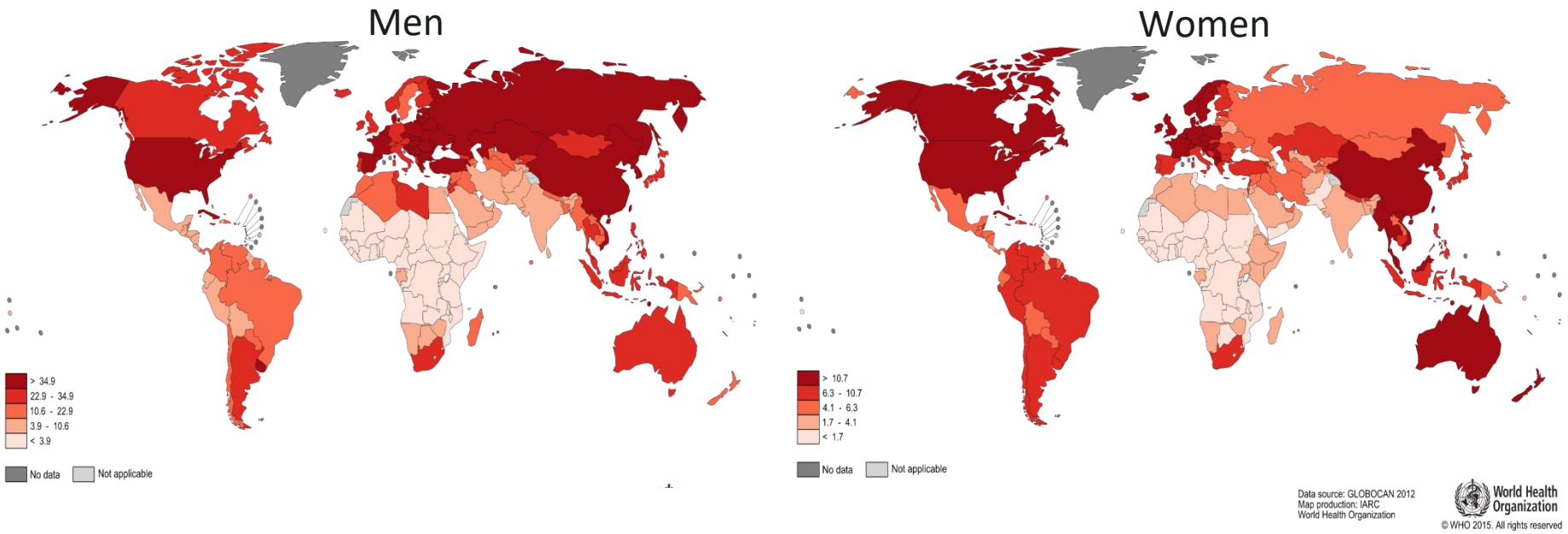
6. Conclusion

Introduction

Lung Cancer is a major health problem and the leading cause of cancer death in the world[1].

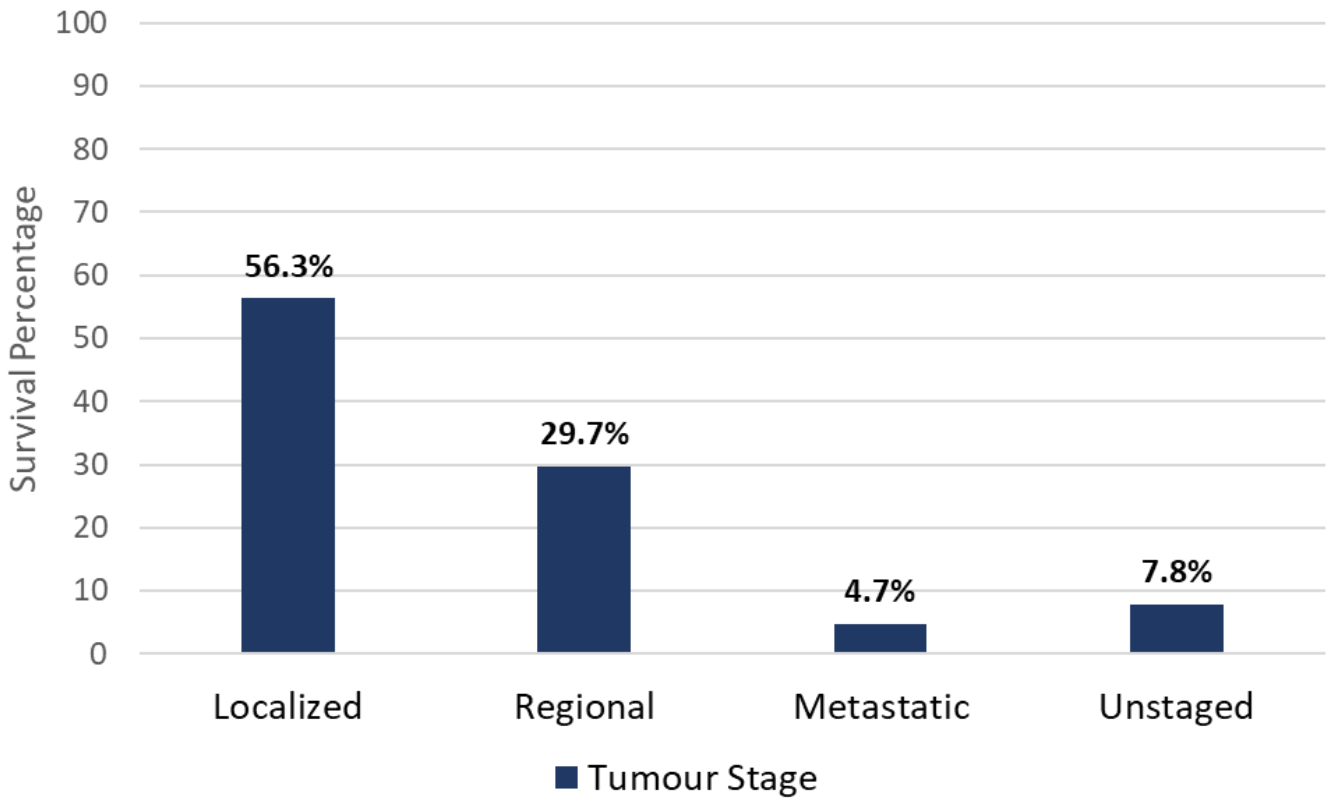
Estimated Lung Cancer mortality worldwide per 100,000 in 2012



[1] International Agency for Research on Cancer. GLOBOCAN 2012: Estimated Cancer Incidence. Mortality and Prevalence Worldwide in 2012.

Introduction

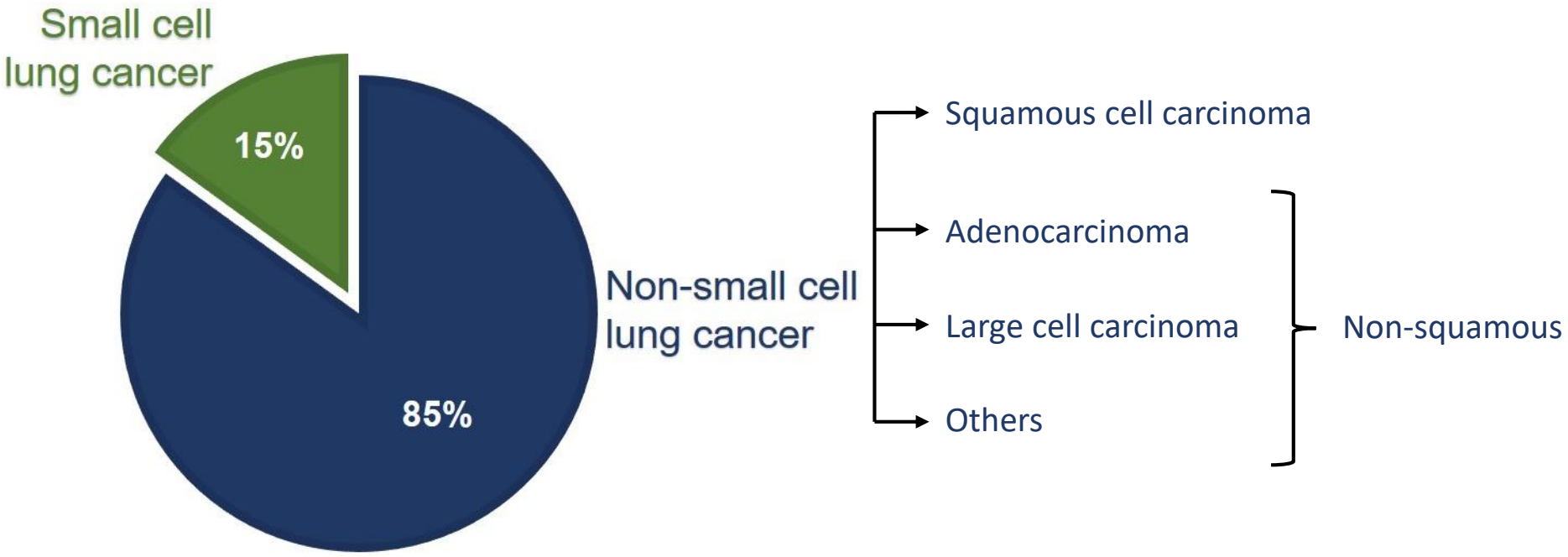
5-year survival in stage IV lung cancer – 4.7%[2].



[2] National Cancer Institute. SEER Cancer Statistics Review: 2008-2014.

Introduction

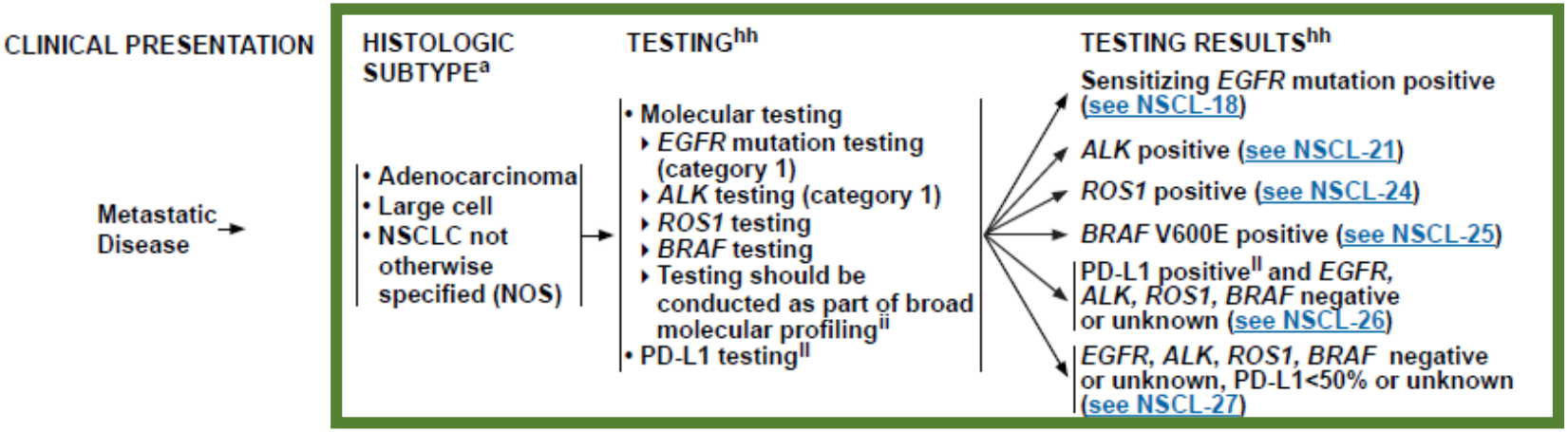
Non-small cell lung cancer (NSCLC) – 85% of all lung cancer cases[3].



[3] Zappa C. Mousa SA. Non-small cell lung cancer: current treatment and future advances. Translational Lung Cancer Research. 2016;5(3):288-300.

Introduction

Treatment algorithm of metastatic disease has been changing in recent years – targeted therapies and immunotherapy.



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Introduction

In patients with EGFR and ALK mutations, targeted therapies should be considered as front-line therapy.

Sensitizing *EGFR* Mutation
- First-line therapy
  - Afatinib
  - Erlotinib
  - Gefitinib
  - Osimertinib
- Subsequent therapy
  - Osimertinib

***ALK* Rearrangement**
- First-line therapy
  - Alectinib
  - Ceritinib
  - Crizotinib
- Subsequent therapy
  - Alectinib
  - Brigatinib
  - Ceritinib

***ROS1* Rearrangement**
- First-line therapy
  - Ceritinib
  - Crizotinib

***BRAF* V600E Mutation**
- First-line therapy
  - Dabrafenib/trametinib
- Subsequent therapy
  - Dabrafenib/trametinib

PD-L1 Expression
- First-line therapy
  - Pembrolizumab
- Subsequent therapy
  - Atezolizumab
  - Nivolumab
  - Pembrolizumab

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Aim of the study

To investigate treatment patterns and survival outcomes in patients with stage IV non-squamous NSCLC harboring EGFR mutations, ALK rearrangements and both EGFR and ALK wild-type (wt)

Methods

Study Design:
Historical population based cohort study.

Inclusion Criteria:

Patients **≥ 18** years old.

Diagnosed with **stage IV non-squamous NSCLC** in **2013-2014**.

Resident in **ROR-Sul** influence area at the time of diagnosis.

Received **systemic treatment**.

Follow-up
Cut-off date May 22nd 2018

Results

684 patients that met the inclusion criteria were included

Characteristic at diagnosis		Distribution (n=684)
Age, years ; median (min-max)		**64** (28-89)
Sex, n (%)	Male	**442** (64.62)
	Female	**242** (35.38)
Histological subtype, n (%)	Adenocarcinoma	**673** (98.39)
	Others	**11** (1.61)
Follow-up time, months; median		**11.77**
Follow-up completeness (%)		**99.27**

Results

Biomarker Patterns

EGFR mutation	Distribution (n=684)
Tested, n (%)	443 (64.77)
Positive (% of tested)	122 (27.54)
Negative (% of tested)	321 (72.46)
Not Evaluated, n (%)	238 (34.80)
Unknown, n (%)	3 (0.44)

Prevalence of EGFR+: 27.54%

Results

Biomarker Patterns

ALK rearrangement	Distribution (n=684)
Tested, n (%)	254 (37.13)
Positive (% of tested)	16 (6.30)
Negative (% of tested)	238 (93.70)
Not Evaluated, n (%)	421 (61.55)
Unknown, n (%)	9 (1.32)

Prevalence of ALK+: 6.30%

Results

Biomarker Patterns

EGFR and ALK	Distribution (n=684)
Tested, n (%)	246 (35.97)
Wild-type (% of tested)	201 (81.71)

Prevalence of WT: 81.71%

Results

Treatment Patterns

122 EGFR + patients

↓

115 received EGFR TKI's

↓

1st Line Therapy:
EGFR TKI's: 66

2nd Line Therapy:
EGFR TKI's: 46

3rd Line Therapy:
EGRR TKI's: 3

16 ALK + patients

↓

7 received ALK TKI's

↓

1st Line Therapy:
ALK TKI's: 0

2nd Line Therapy:
ALK TKI's: 7

Results

Treatment Patterns

201 wt patients

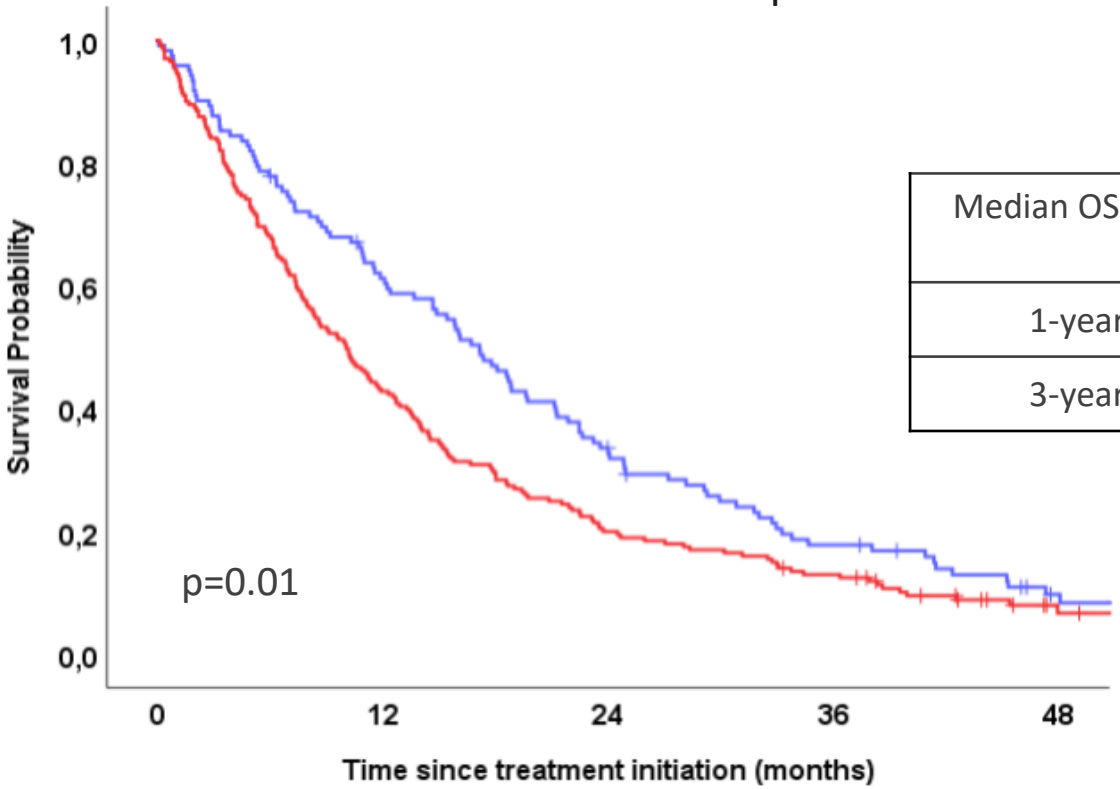
1st Line Therapy:
Platinum Doublet: 183
Monotherapy: 17
EGFR TKI's: 1

2nd Line Therapy:
Monotherapy: 64
EGFR TKI's: 21
Others: 17

Results

Survival Outcomes

Patients harboring a mutation and treated with targeted therapies vs wt-treated

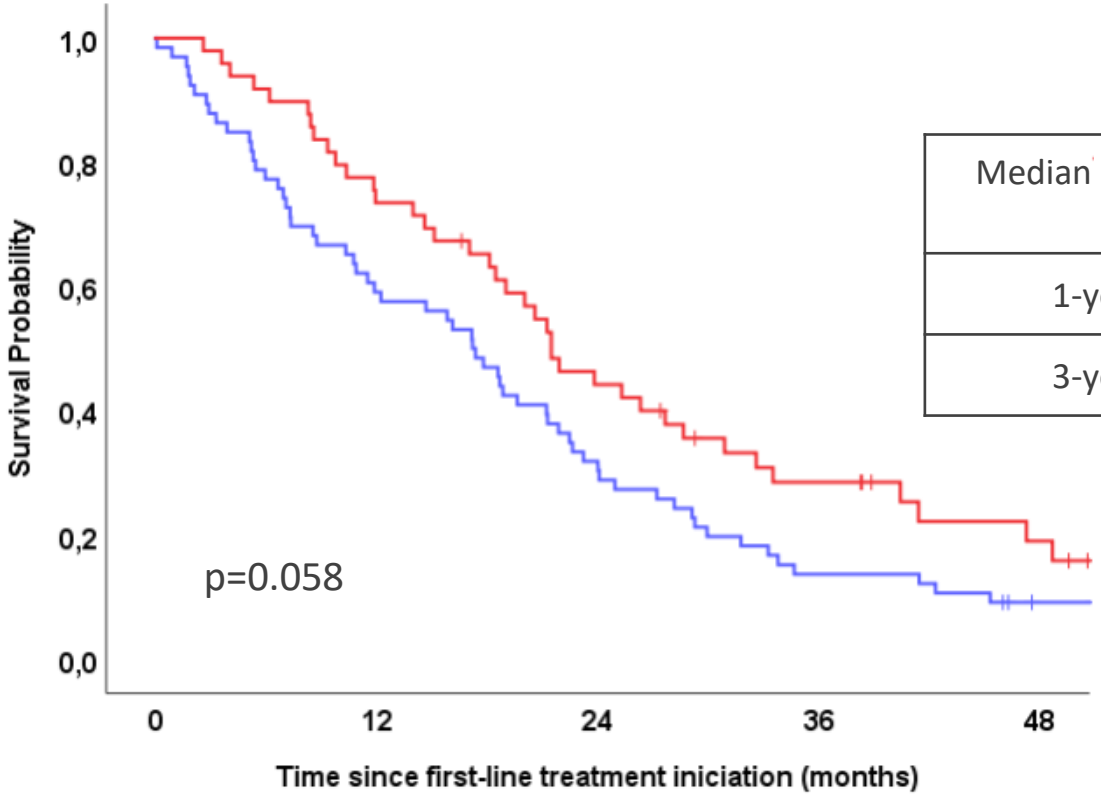


	EGFR/ALK+ n=122	Wild-type n=201
Median OS, months (95% CI)	17.16 (14.04-20.29)	10.06 (8.12-12.00)
1-year rate (%)	61	43
3-year rate (%)	18	13

Results

Survival Outcomes

1st Line Therapy EGFR+: EGFR TKI's vs Chemotherapy



	EGFR TKI's n=66	Chemo n=56
Median OS, months (95% CI)	17.20 (13.20-21.19)	21.47 (17.24-25.69)
1-year rate (%)	59	73
3-year rate (%)	14	29

Discussion

Rate of Testing and Prevalence: Europe[4,5] vs ROR-Sul

	EGFR		ALK	
	Europe	ROR-Sul	Europe	ROR-Sul
Rate of testing (%)	60-78	**64.77**	25-36	**37.13**
Prevalence (%)	15	**27.54**	3-5	**6.30**

[4] de Castro J. Tagliaferri P. de Lima VCC. et al. Systemic therapy treatment patterns in patients with advanced non-small cell lung cancer (NSCLC): PIvOTAL study. Eur J Cancer Care. 2017 Nov; 26(6) [5] Midha A. Dearden S. Mccormack R. EGFR mutation incidence in non-small-cell lung cancer of adenocarcinoma histology: A systematic review and global map by ethnicity (mutMapII). American Journal of Cancer Research. 2015 Aug; 5(9): 2892–2911

Discussion

66 out of 122 EGFR+ patients underwent EGFR TKI's as 1st line therapy.

Possible explanations: determination of biomarker tests being performed after the beginning of 1L treatment OR physicians choosing to begin treatment before the results are available.

Patients harboring an ALK mutation **only received ALK TKI's as 2nd line therapy**.

Explanation: Upfront comparisons with chemotherapy were not available at the time, which is why ALK TKI's were not approved in Portugal as 1L therapies.

Discussion

Survival analysis according to biomarker testing results showed that there is strong evidence that harboring at least a mutation and receive specific therapy is associated with an improved OS compared with wild-type patients.

OS of EGFR+ patients treated with TKIs as 1st line therapy and those treated with chemotherapy **was not statistically significant**.

Possible explanation: OS of 1L treatment with chemotherapy may be overestimated. Confounding (switching), sample size.

Conclusion

- The role of cancer registries.

- The importance of molecular testing:
  - Improved survival outcomes.
  - Spared patients from toxic chemotherapy approaches.

- However, poor prognosis still remains an issue in metastatic NSCLC patients.


QUESTIONS

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