Mail this to me:

Roche

M-IN-00002479

Role of ALECENSA in 1L ALK+ mNSCLC Patients - ALEX Study

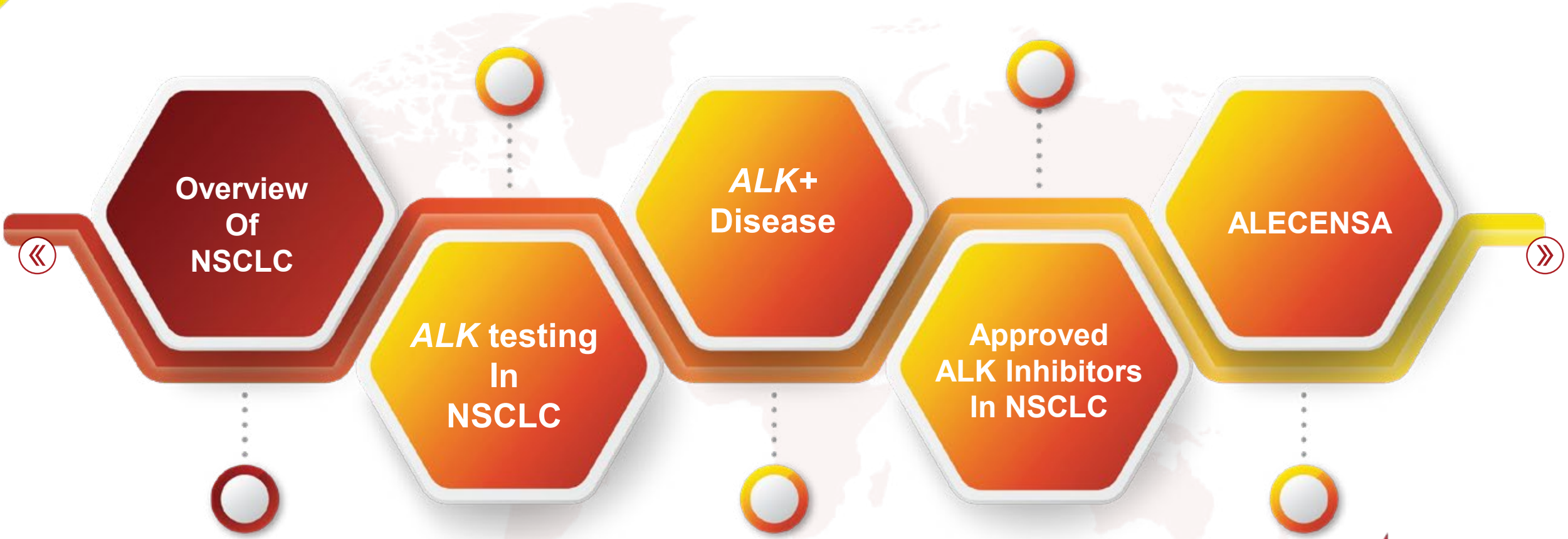
Dr.
Designation:
Hospital:

ALECENSA
alectinib 150 mg capsules

Disclaimer

- The content in this presentation is intended for healthcare professionals in India only.
- The medical information in this presentation is provided as an information resource only and is not to be used or relied on for any diagnostic or treatment purposes.
- Roche India does not promote or support the use of medications manufactured by it in off label indications.
- For specific information regarding various therapeutic agents, including Roche products, please refer to the approved full prescribing information.

Content



Click on the icons above to navigate to the relevant section

Please note: hyperlinks are only active in Slide Show mode

Lung Cancer Is A Significant Global Health Issue

Lung cancer is the second most commonly diagnosed cancer worldwide and the leading cause of cancer-related deaths[1,2]

2.2 million

New Cases Per Year

1.8 million

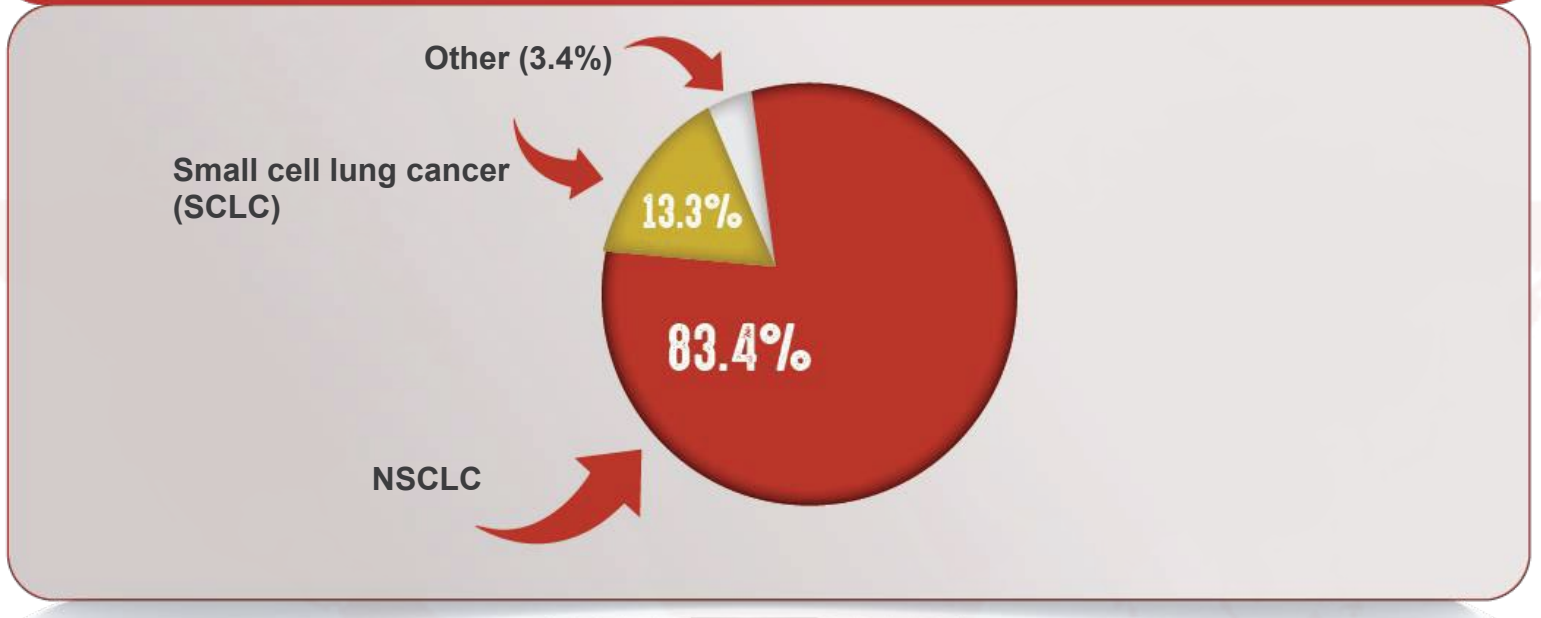
Deaths Per Year

ALECENSA® alectinib 150 mg capsules

1. Sung H., et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries , CA CANCER J CLIN 2021;71:209–249
2. Available at: http://globocan.iarc.fr. Last accessed: May 2021

Lung Cancer Is A Heterogeneous Disease

Adenocarcinoma is the most common form of lung cancer[1,2]



Non-small cell lung cancer (NSCLC)

- **Adenocarcinoma** 43.3% (52%)
- Squamous cell carcinoma 22.6% (27%)
- Non-small cell carcinoma 10.5% (13%)
- Other specified carcinomas 4.9% (6%)
- Large cell carcinoma 2.1% (3%)

ALECENSA® alectinib 150 mg capsules

1. Howlader N, et al. SEER Cancer Statistics Review, 1975–2012, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2012/, based on November 2014 SEER data submission, posted to the SEER web site, April 2015. Accessed 25 Sept 2017. 2. Richer AL, et al. Pharmacogenomics Personalized Med 2015;8:63-79.

Lung Cancer Incidence And Mortality (2020): India[1,2]

~72k

New Cases
Per Year

~66k

Deaths
Per Year

Lung cancer is one of the most common cancer among men[1,2]

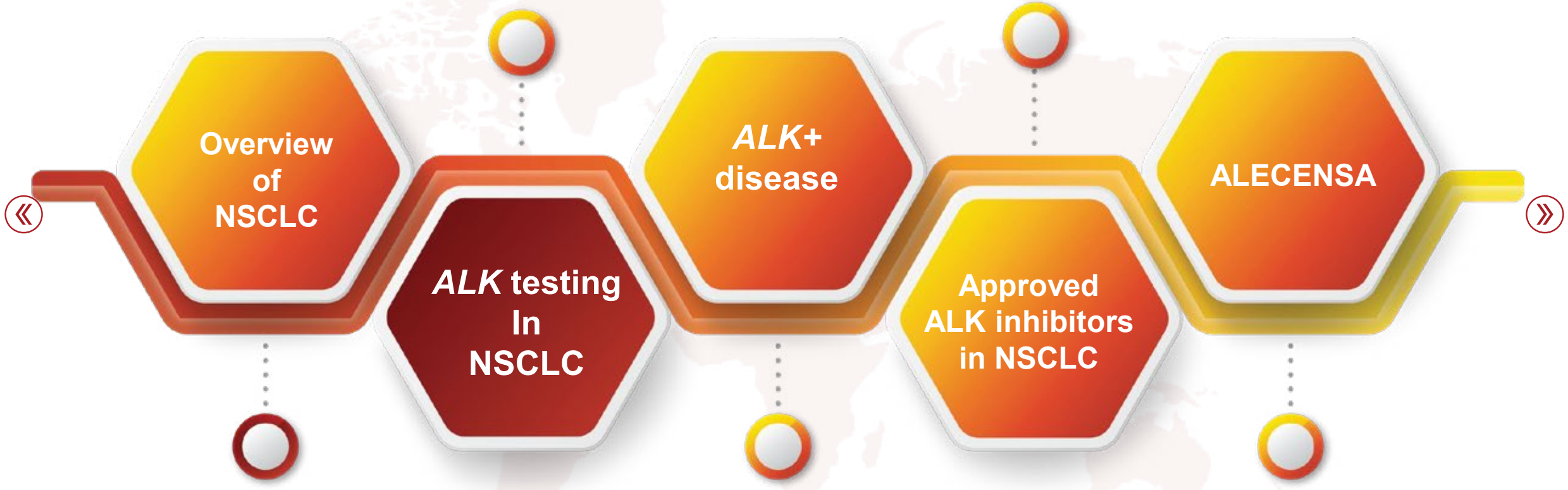
~51k

New Cases
Per Year **(Males)**

ALECENSA® alectinib 150 mg capsules

1. Mathur P., et al. Cancer Statistics, 2020: Report From National Cancer Registry Programme, India JCO Global Oncol 6:1063-10759
2. Available at: http://gco.iarc.fr. Last accessed: May 2021

ALK Testing In NSCLC



Click on the icons above to navigate to the relevant section

Please note: hyperlinks are only active in Slide Show mode

ALECENSA alectinib 150 mg capsules

Molecular Testing Is An Important And Recommended Aspect Of Routine Practice[1-3]

Routine testing in clinical practice for *EGFR* mutations **and** *ALK* rearrangements is recommended in guidelines published by various groups and authoritative organisations for all adeno-carcinoma histology[1-3]

Identifying the molecular profile of a tumour facilitates the clinical decision-making process, and helps ensure that clinicians select the most appropriate treatment option

ALECENSA® alectinib 150 mg capsules

1. IASLC Atlas of ALK Testing 2013
2. Lindeman, et al. J Thorac Oncol 2013;
3. NCCN NSCLC guidelines V 3.2016

ALK Testing: Overview Of Testing Methods

- Fluorescence *in-situ* hybridisation (FISH)
- Immunohistochemistry (IHC)
- Reverse-transcriptase polymerase chain reaction (RT-PCR)
- Next-generation sequencing (NGS)

ALECENSA® alectinib 150 mg capsules

ALK+ NSCLC Disease

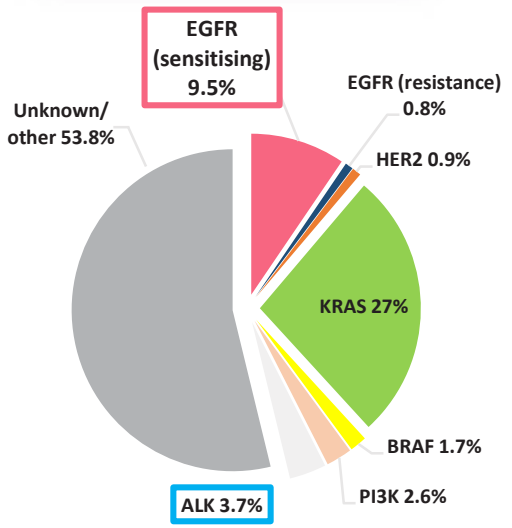
Click on the icons above to navigate to the relevant section

Please note: hyperlinks are only active in Slide Show mode

The Incidence Of ALK+ NSCLC Is Relatively Uniform Across Ethnicities

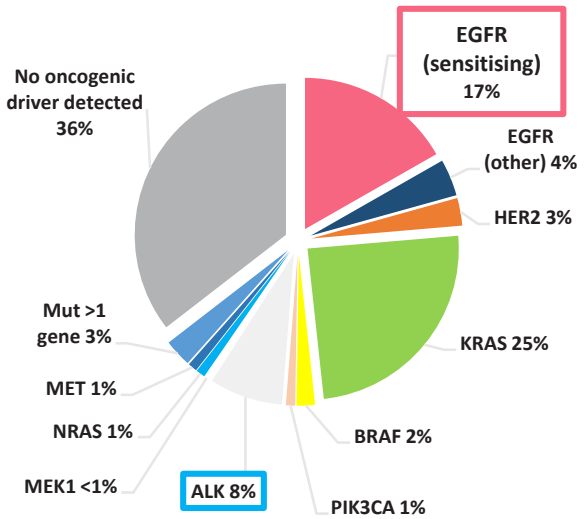
Although the incidence of ***ALK+* mutations** varies by ethnicity (Asian vs Caucasian), the incidence of ***ALK+* NSCLC** is relatively uniform across ethnicities[1]

Europe[2]
All histologies



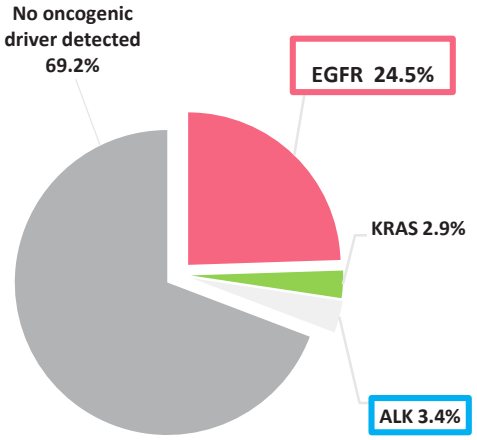
(n=991)

USA[3]
Adenocarcinoma



(n=733)

East Asia[4]
All histologies



(n=208)

Patient populations and size of patient groups shown are not uniform

1. Dearden, et al. Ann Oncol 2013; 2. Barlesi, et al. ASCO 2013
3. Johnson, et al. ASCO 2013; 4. Li, et al. PLoS One 2013

ALECENSA alectinib 150 mg capsules

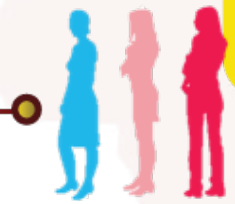
ALK+ Disease Is A Distinct Subset Of NSCLC

ALK+ disease occurs in ~5% of patients with advanced NSCLC[1–5]

More than 75,000 patients per year diagnosed globally[7]

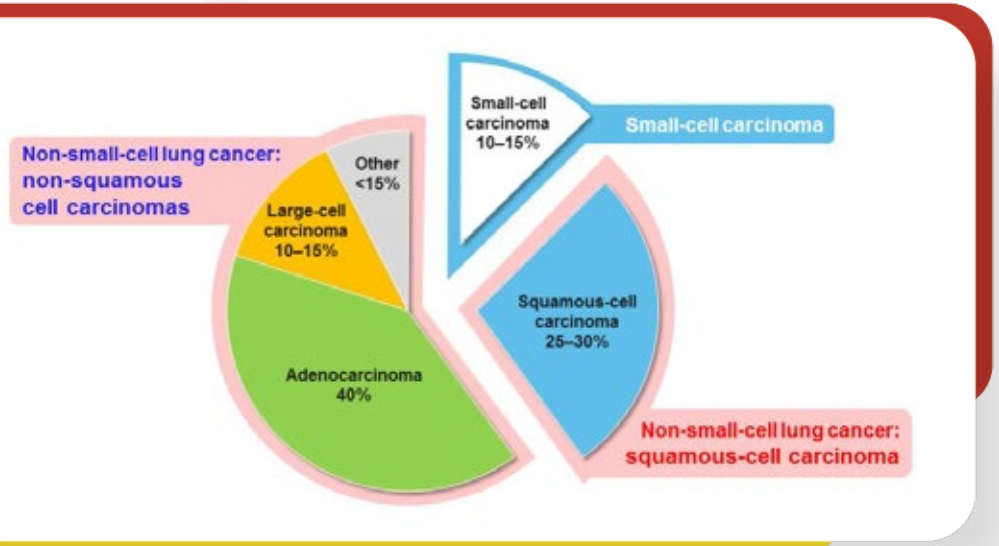
The incidence of *ALK*+ NSCLC is higher in

- Patients with non-squamous histology[2,8]
- Never or former smokers[2,8]
- Younger patients[2,8]
- Females[2]
- Patients who do not have *EGFR* or *KRAS* mutations[2,8]



Clinical characteristics do not always predict the presence of *ALK*+ NSCLC[9,10]

Histological classification of lung cancer[6]



ALK = anaplastic lymphoma kinase
EGFR = epidermal growth factor receptor
NSCLC = non-small cell lung cancer

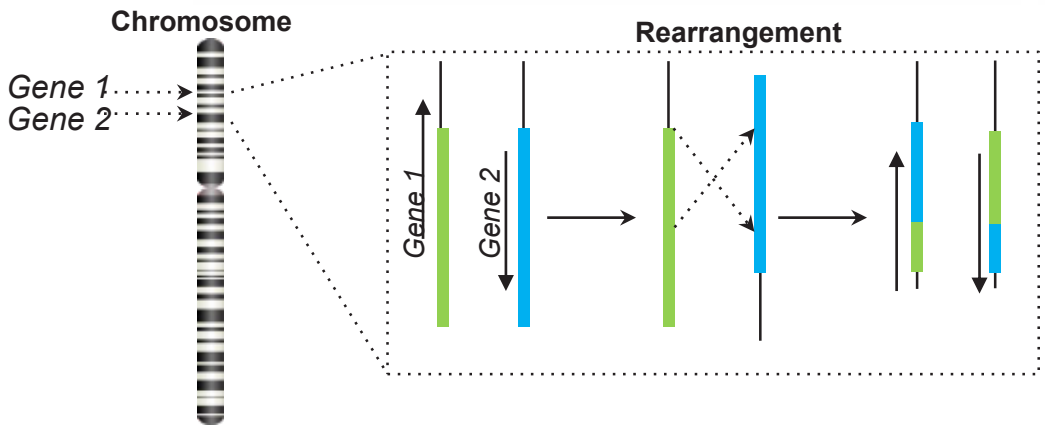
1. Dearden, et al. Ann Oncol 2013; 2. Gridelli, et al. Cancer Treat Rev 2014
3. Hallberg, et al. Nat Rev Cancer 2013; 4. Rikova, et al. Cell 2007
5. Soda, et al. Nature 2007; 6. American Cancer Society 2013
7. Torre, et al. CA Cancer J Clin 2015; 8. Perez, et al. Lung Cancer 2014
9. Lindeman, et al. J Thorac Oncol 2013; 10. Leighl, et al. J Clin Oncol 2014

ALECENSA® alectinib 150 mg capsules

ALK+ NSCLC Is Defined By A Rearrangement Of The ALK Gene

- In *ALK*+ NSCLC, the *ALK* gene undergoes a **rearrangement** within the chromosome[1–3]
- The *ALK* rearrangement results in a structural alteration of the chromosome and in the expression of an ALK-fusion protein[1–3]
- The rearrangement was first discovered in a subset of patients by Soda, et al., in 2007[1]

Chromosomal Rearrangement



1. Soda, et al. Nature 2007;
2. Hallberg, et al. Nat Rev Cancer 2013
3. Rikova, et al. Cell 2007

ALECENSA® alectinib 150 mg capsules

The Incidence Of *ALK*+ NSCLC In India[1,2]

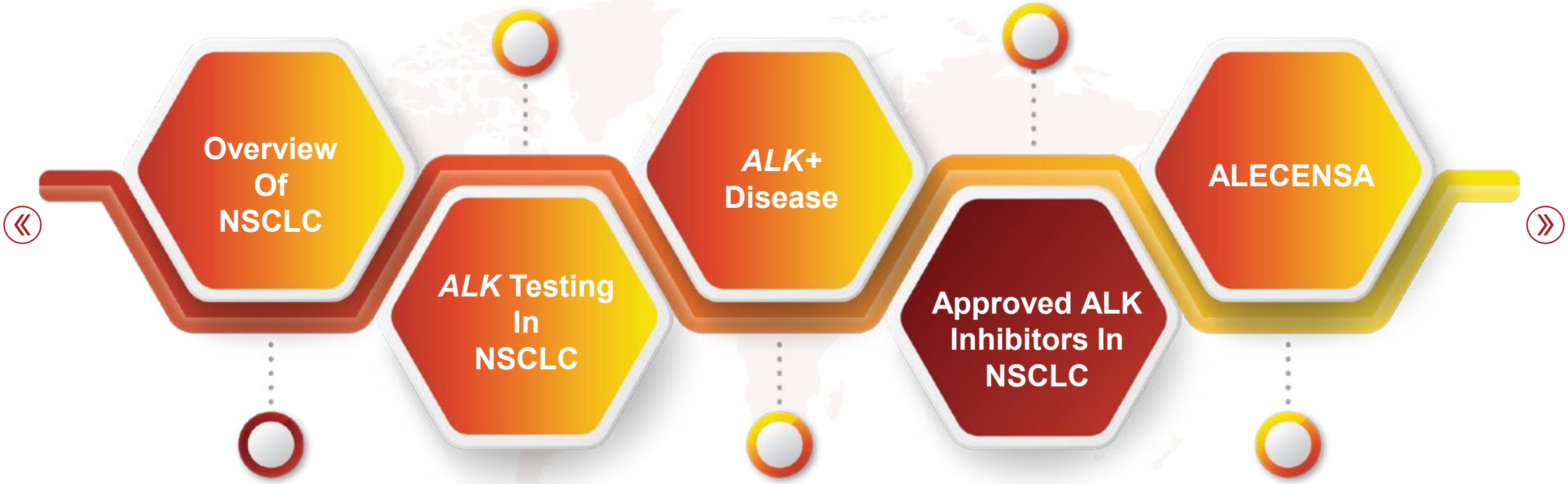
2.7% — 4 to 5% — 13.2%

- The ALK mutation is reported in ~ 7% of lung cancers, found more commonly in young patients with adenocarcinomas with a history of never or light smoking[1]
- However, the incidence has been variable across different regions of India[2]

ALECENSA® alectinib 150 mg capsules

1. Rana V, Ranjan P, Jagani R, Rathi KR, Kumar D, Khera A. A study of therapy targeted EGFR/ALK mutations in Indian patients with lung adenocarcinoma: A clinical and epidemiological study. Med J Armed Forces India. 2018 Apr;74(2):148-153. doi: 10.1016/j.mjafi.2017.09.005. Epub 2017 Nov 28. PMID: 29692481; PMCID: PMC5912110. ; 2. Mehta A* Talwar V EUSTM 2016, yr:2016 vol:3 iss:2 pg:83 -159; 3. Bal A, Singh N. APMIS. 2016 Oct;124(10):832-8

Approved ALK Inhibitors In NSCLC



Click on the icons above to navigate to the relevant section

Please note: hyperlinks are only active in Slide Show mode

Currently Approved First-line Treatments For Advanced ALK+ NSCLC

Crizotinib	Ceritinib	Alectinib	Brigatinib	Lorlatinib
Key trial: PROFILE 1014[1]	**Key trial:** ASCEND-4[2]	**Key trial:** ALEX[3–6]	**Key trial:** ALTA-1L[7,8]	**Key trial:** CROWN[9]
FDA approval in 1L: Aug 2011 EMA approval in 1L: Nov 2015	FDA approval in 1L: May 2017 EMA approval in 1L: Jun 2017	FDA approval in 1L: Nov 2017 EMA approval in 1L: Dec 2017	FDA approval in 1L: May 2020 EMA approval in 1L: Apr 2020	FDA approval in 1L: March 2021 EMA approval in 1L: Not approved
mPFS 10.9 months[1†]	mPFS 16.6 months[2‡]	mPFS ALEX: 34.8 months[5§] ALESIA: 41.6 months[6]	mPFS 29.4 months[8§,¶]	mPFS NE[9‡]
Dose: 250mg BID	Dose: 450 / 750mg* QD	Dose: 600mg† BID	Dose: 180mg‡ QD	Dose: 100mg QD

*450mg QD with food is EMA and FDA-recommended. Ceritinib can be taken at 750mg QD by patients who are unable to take ceritinib with food

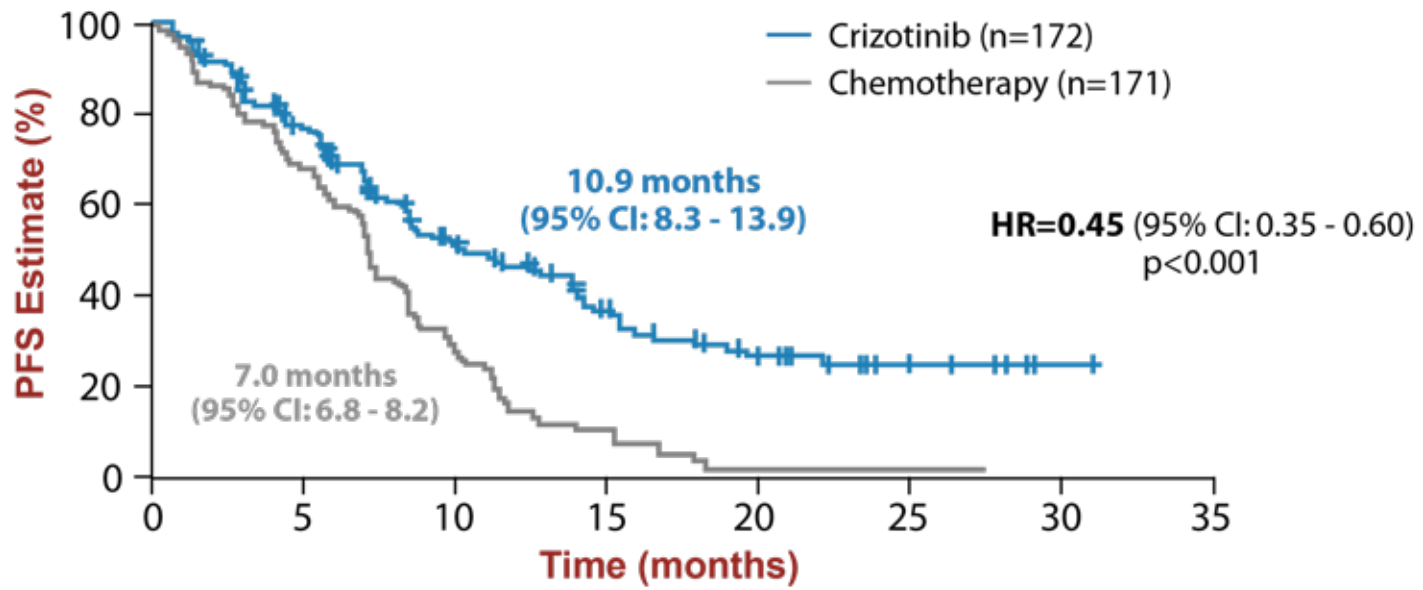
†Median PFS by IRC; ‡Median PFS by BIRC; §Median PFS by INV

¶INV-assessed, however the 1° endpoint of ALTA-1L is PFS by BIRC assessment (**24.0 months**)[7]

1. Solomon, et al. N Engl J Med 2014; 2. Soria, et al. Lancet 2017; 3. Peters, et al. N Engl J Med 2017
4. Camidge, et al. J Thorac Oncol 2019; 5. Mok, et al. Ann Oncol 2020; 6. Zhou C, et al. ESMO Asia 2022 (Abs. LBA11); 7. Camidge, et al. N Eng J Med 2018; 8. Camidge, et al. J Clin Oncol 2020; 9. Shaw, et al. N Engl J Med 2020

ALECENSA alectinib 150 mg capsules

CRIZOTINIB: Crizotinib Demonstrated A Significant PFS Benefit Versus Chemotherapy In PROFILE 1014 Study



Crizotinib was the first ALK TKI to demonstrate a PFS benefit versus chemotherapy

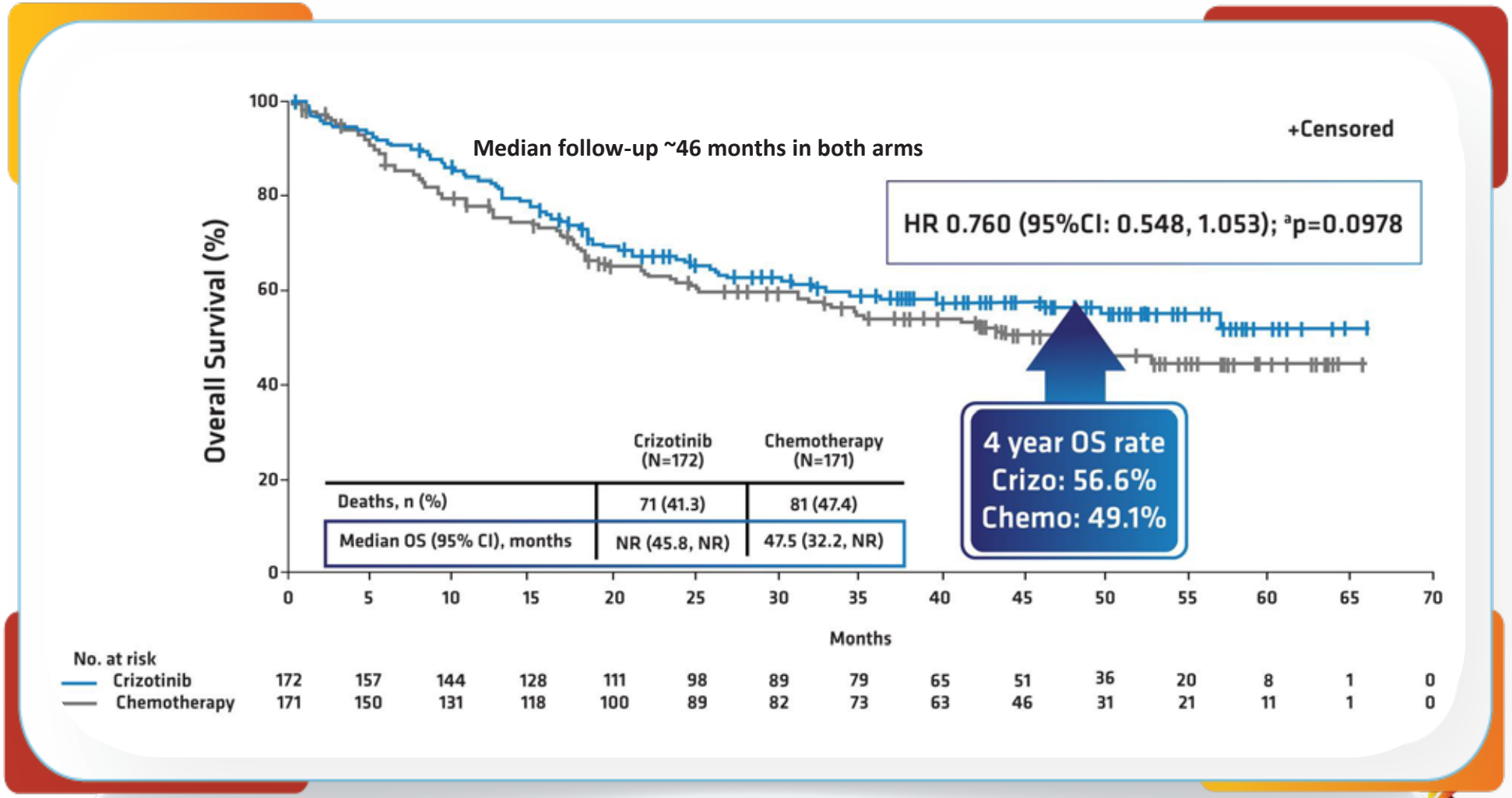
Subsequent studies have investigated the efficacy of other ALK TKIs versus crizotinib
Median PFS with crizotinib in these studies (9.3–12.7 months)[2–4] was comparable to that seen in PROFILE 1014

Data cut-off: 30 November 2013. IRC assessed
ALK = anaplastic lymphoma kinase; CI = confidence interval; HR = hazard ratio
IRC = independent review committee; PFS = progression-free survival; TKI = tyrosine kinase inhibitor

1. Solomon, et al. N Engl J Med 2014; 2. Mok, et al. Ann Oncol 2020
3. Camidge, et al. J Clin Oncol 2020; 4. Horn, et al. WCLC 2020; 5. Shaw, et al. N Engl J Med 2020

ALECENSA alectinib 150 mg capsules

Final Primary OS Analysis (ITT Population)



[a]2-sided p-value from the log-rank test stratified by ECOG PS, race, brain metastases

NCT01154140
Mok, et al. ESMO 2017 (Abstract LBA50)
(updated data from congress presentation)

Crizotinib: In PROFILE 1014, The Most Common Adverse Events Reported With Crizotinib Were Vision Disorders And Gastrointestinal AEs

Event, %[1]	Crizotinib (n=171) Any grade	Crizotinib (n=171) Grade 3/4	Chemotherapy (n=169) Any grade	Chemotherapy (n=169) Grade 3/4
Vision disorders	73	1	9	0
Diarrhoea	66	3	14	1
Nausea	59	2	58	2
Oedema	53	1	12	1
Vomiting	51	2	36	3
Constipation	46	2	31	0
Upper RTI	40	0	12	1
Elevated transaminases	39	14	13	2
Decreased appetite	35	2	34	1
Fatigue	32	3	39	2
Cough	30	0	21	0
Neuropathy	29	1	23	0
Abdominal pain	29	0	12	0
Headache	28	1	15	0
Dysgeusia	26	0	5	0

Event, %[1]	Crizotinib (n=171) Any grade	Crizotinib (n=171) Grade 3/4	Chemotherapy (n=169) Any grade	Chemotherapy (n=169) Grade 3/4
Dizziness	26	0	10	1
Pain in extremity	26	0	8	0
Neutropenia	25	15	30	15
Pryexia	23	0	11	1
Dypsnoea	23	4	15	2
Back pain	21	0	12	0
Bradycardia	19	2	1	0
Chest pain	18	0	14	1
Stomatitis	18	1	21	1
Asthenia	17	1	24	1
Dyspepsia	16	0	3	0
Anaemia	11	1	33	10
Leukopenia	10	4	15	5
Thrombocytopenia	1	0	18	7

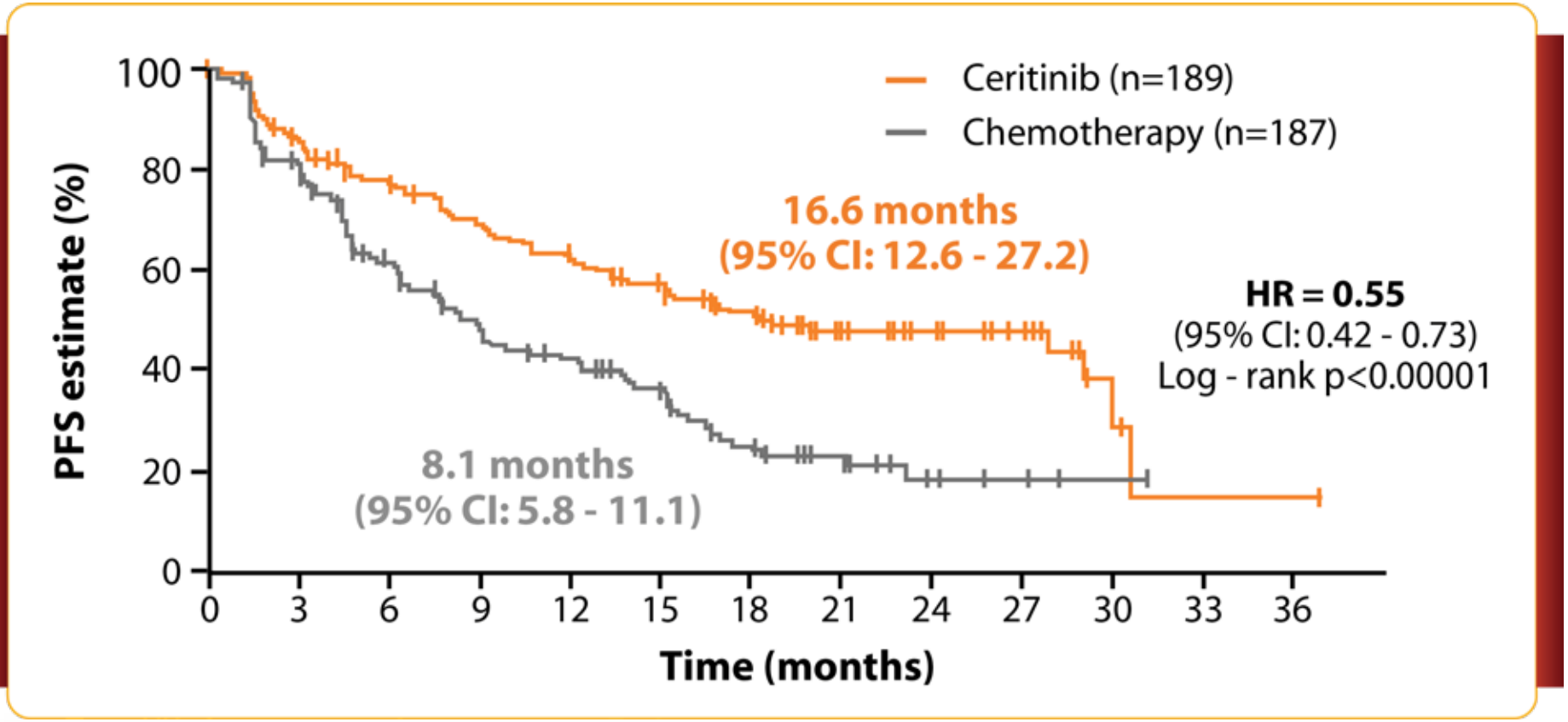
High rates of vision disorders and GI AEs have also been observed with crizotinib in other 1L studies (ALEX and ALTA-1L) where crizotinib was the comparator arm[2,3]

Data cut-off: 30 November 2016
Median duration of treatment: crizotinib 14.7 months, chemotherapy 4.1 months
1L = first-line; AE = adverse event; GI = gastrointestinal; RTI = respiratory tract infection

1. Solomon, et al. J Clin Oncol 2018
2. Mok, et al Ann Oncol 2020
3. Camidge, et al. J Clin Oncol 2020

ALECENSA alectinib 150 mg capsules

Ceritinib, Like Crizotinib In PROFILE 1014, Demonstrated A Significant PFS Benefit Versus Chemotherapy In ASCEND-4



Median PFS was prolonged with ceritinib (16.6 months) versus chemotherapy (8.1 months)[1]
Median PFS with chemotherapy was similar to that seen in PROFILE 1014 (7.0 months)[2]

Data cut-off: 24 June 2016. BIRC assessed
BIRC = blinded independent review committee; CI = confidence interval
HR = hazard ratio; PFS = progression-free survival

1. Soria, et al. Lancet 2017; 2. Solomon, et al. N Engl J Med 2014

High Rates Of Gastrointestinal-related Toxicities Were Associated With Ceritinib In ASCEND-4

Event,%	Ceritinib (n=189) All Grade	Ceritinib (n=189) Grade 3/4	Chemotherapy (n=175) All Grade	Chemotherapy (n=175) Grade 3/4
Diarrhoea	85	5	11	1
Nausea	69	3	55	5
Vomiting	66	5	36	6
ALT increased	60	31	22	3
AST increased	53	17	19	2
GGT increased	37	29	10	2
Decreased appetite	34	1	31	1
Blood alkaline phosphate increased	29	7	5	1
Fatigue	29	4	30	3
Abdominal pain	25	2	7	0
Cough	24	0	16	0
Weight decreased	24	4	15	1

Event,%	Ceritinib (n=189) All Grade	Ceritinib (n=189) Grade 3/4	Chemotherapy (n=175) All Grade	Chemotherapy (n=175) Grade 3/4
Blood creatine increased	22	2	10	0
Abdominal pain upper	21	2	6	0
Non-cardiac chest pain	20	1	10	1
Back pain	19	2	18	2
Constipation	19	0	22	0
Pyrexia	18	0	14	1
Asthenia	18	3	21	3
Headache	16	0	12	1
Dyspnoea	15	2	20	6
Anaemia	15	2	35	7
Neutropenia	5	1	22	11
WBC count decreased	4	0	18	4

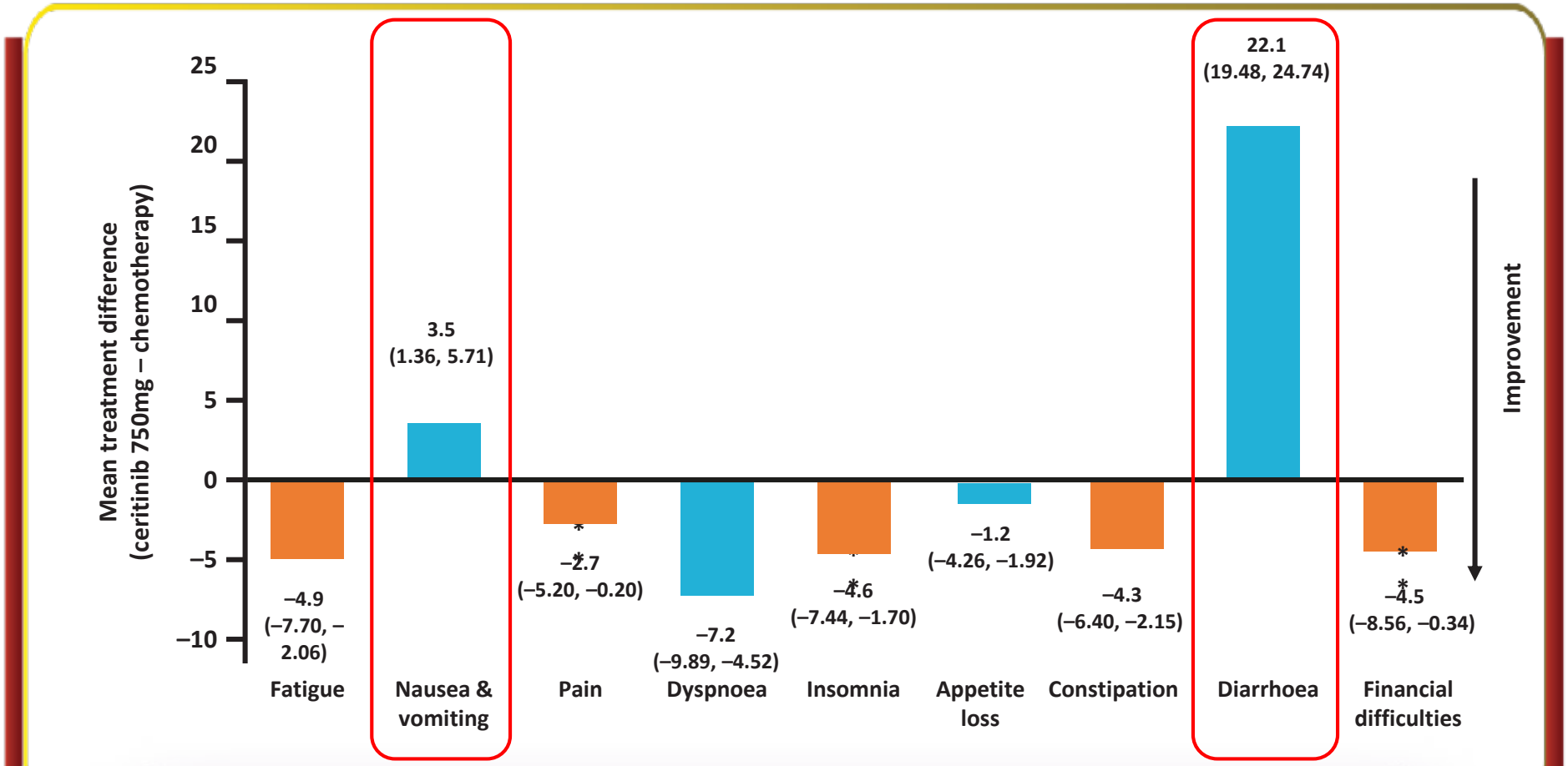
Diarrhoea, Nausea and **Vomiting** were the most frequent AEs occurring with **1L Ceritinib** in ASCEND-4

Data cut-off: 24 June 2016
Median duration of treatment exposure: ceritinib 66.4 weeks, chemotherapy 26.9 weeks
1L = first-line; AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase
GGT = gamma-glutamyltransferase; GI = gastrointestinal; WBC = white blood cell

Soria, et al. Lancet 2017

ALECENSA alectinib 150 mg capsules

ASCEND – IV: PRO Data Showed A Greater Impact On QoL With Ceritinib Versus Chemotherapy



GI toxicity (in particular diarrhoea, nausea, and vomiting) reported as worse for ceritinib than chemotherapy

NCT01828099
De Castro, et al. WCLC 2016 (Abstr PL03.07) (updated data from congress presentation)

NCT01828099
*p<0.001; **p<0.05

ALECENSA alectinib 150 mg capsules

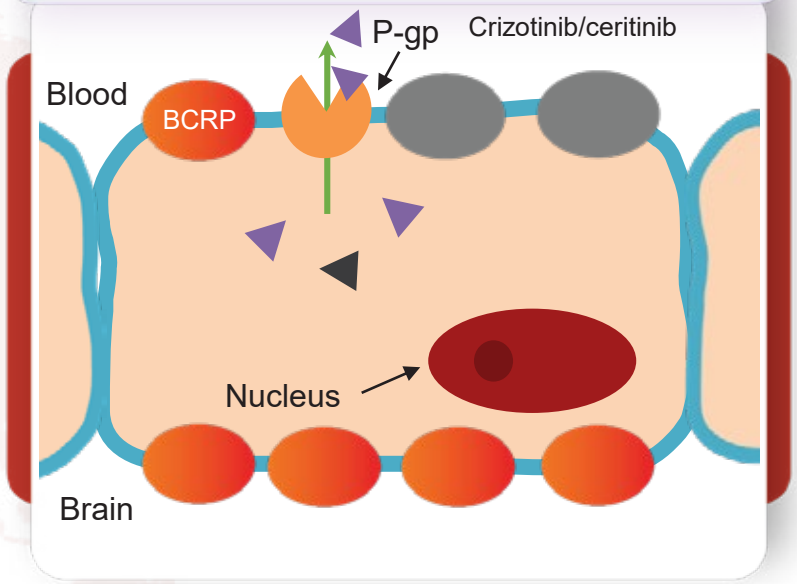
Crizotinib And Ceritinib Are Actively Exported Out Of The Blood-Brain-Barrier

Drugs enter the brain by crossing the blood-brain-barrier[1]

The blood-brain barrier contains drug efflux transporter proteins, such as P-gp and BCRP, which can eject drugs out of the blood-brain-barrier through active efflux before they cross into the CNS[1,2]

Crizotinib is a substrate for P-gp, and ceritinib is a substrate for both P-gp and BCRP[3–5]

Efflux transporter proteins may prevent small molecules crossing the blood-brain-barrier

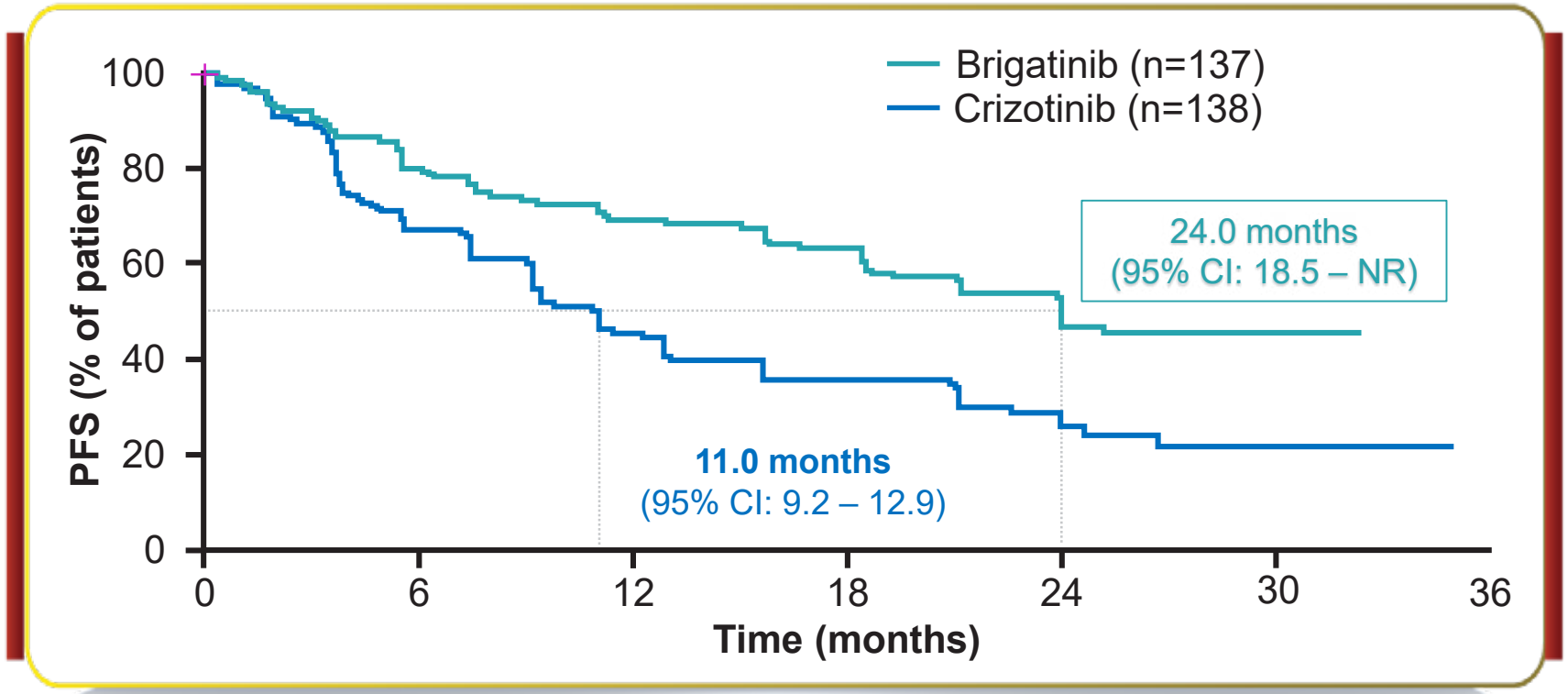


The CNS exposure of crizotinib and ceritinib may therefore be inadequate to control the disease in this location, and the CNS may form a sanctuary site for tumour growth[6,7]

ALECENSA alectinib 150 mg capsules

1. Misra, et al. J Pharm Pharmaceut Sci 2003
2. Thiebaut, et al. Proc Natl Acad Sci 1987; 3. Tang, et al. Int J Cancer 2014
4. Kort, et al. Pharmacol Res 2015; 5. Katayama, et al. EBioMedicine 2016
6. Dagogo-Jack and Shaw. Ann Oncol 2016; 7. Rusthoven and Doebele. J Clin Oncol 2016

Brigatinib: ALTA-1L (Second Interim Analysis): PFS By BIRC In The ITT Population (Primary Endpoint)



HR=0.49
(95% CI: 0.35–0.68)

p<0.0001

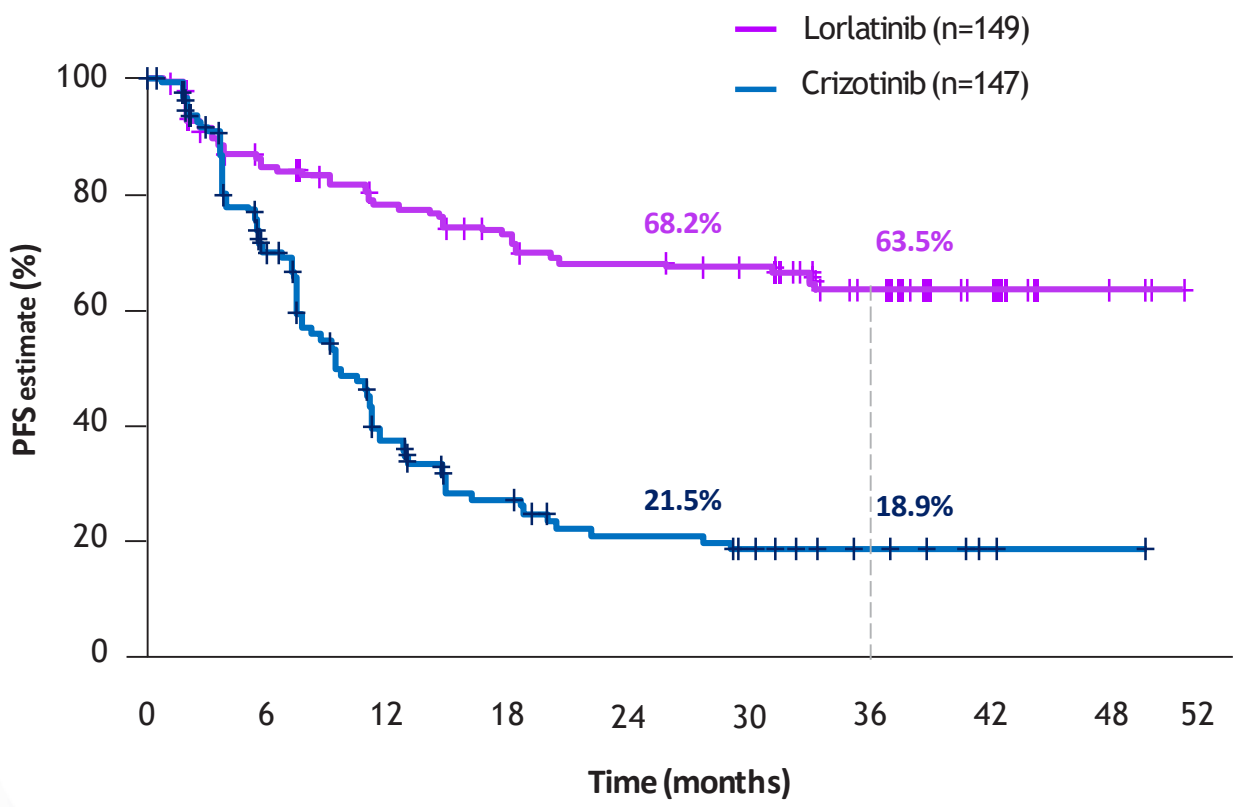
	Brigatinib (n=137)	Crizotinib (n=138)
Events, n (%)	**63** (46)	**87** (63)
2-year PFS, % (95% CI)	**48** (39–57)	**26** (18–35)

Second interim analysis: 28 June 2019
Median duration of follow-up: 24.9 months (brigatinib) and 15.2 months (crizotinib)
BIRC = blinded independent review committee; CI = confidence interval
HR = hazard ratio; ITT = intent-to-treat; NR = not reached; PFS = progression-free survival

Camidge, et al. J Clin Oncol 2020

Lorlatinib: Median PFS (BICR) Was Longer With Lorlatinib Than Crizotinib In Patients With Treatment-naïve Advanced *ALK*+ NSCLC In CROWN Study

PFS by BICR (primary endpoint) in the ITT population[1]



	Lorlatinib (n=149	Crizotinib (n=147)
Median duration of follow-up, months	36.7	29.3
Events	49	92
Median PFS by BICR, months (95% CI)	NR (NR–NR)	9.3 (7.6–11.1)
HR (95% CI)	**0.27** (0.18–0.39)	
Median PFS by INV, months (95% CI)	NR (NR–NR)	9.1 (7.4–10.9)
HR (95% CI)	**0.19** (0.13–0.27)	

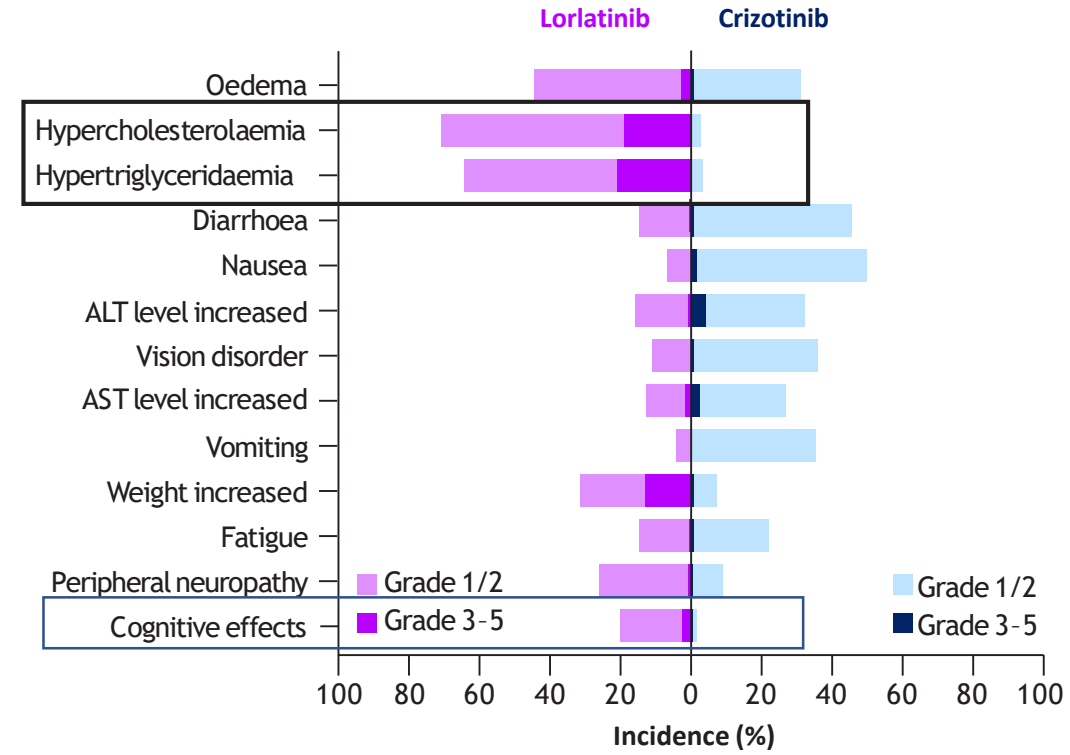
ALECENSA alectinib 150 mg capsules

CI, confidence interval; HR, hazard ratio; ITT, intent to treat; NR, not reached.
[1]Solomon B, et al. AACR 2022 (Abs. CT223 /2); [2]Mok T, et al. Ann Oncol 2020

CROWN: Lorlatinib Has A Unique Safety Profile Compared To Other ALK TKIs, Causing CNS Adverse Events

- **Most common TRAEs with lorlatinib: Hypercholesterolaemia (~72%) and Hypertriglyceridaemia (~65%)**[1]

Any grade TRAEs in ≥20% of patients within either treatment arm[1]



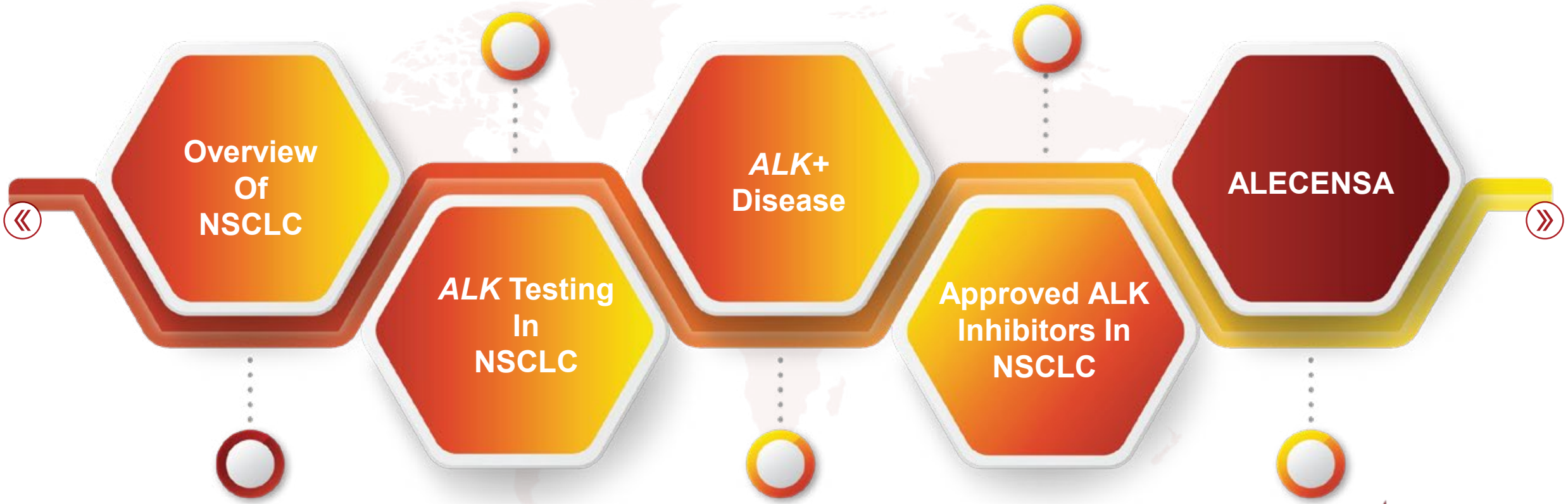
Safety profile similar to previous interim analysis[2] CNS toxicity associated with **lorlatinib**, such as cognitive, mood and speech effects, is a cause for concern

ALECENSA alectinib 150 mg capsules

TKI, tyrosine kinase inhibitor; TRAE, treatment-related adverse event.

[1]Solomon B, et al. AACR 2022 (Abs. CT223/2); [2]Shaw A, et al. N Engl J Med 2020; [3]Peters S, et al N Engl J Med 2017; [4]Mok T, et al. Ann Oncol 2020.

ALECENSA In *ALK*+ NSCLC



Click on the icons above to navigate to the relevant section

Please note: hyperlinks are only active in Slide Show mode

Key Features Of ALECENSA (Alectinib)

Selectivity

Potency

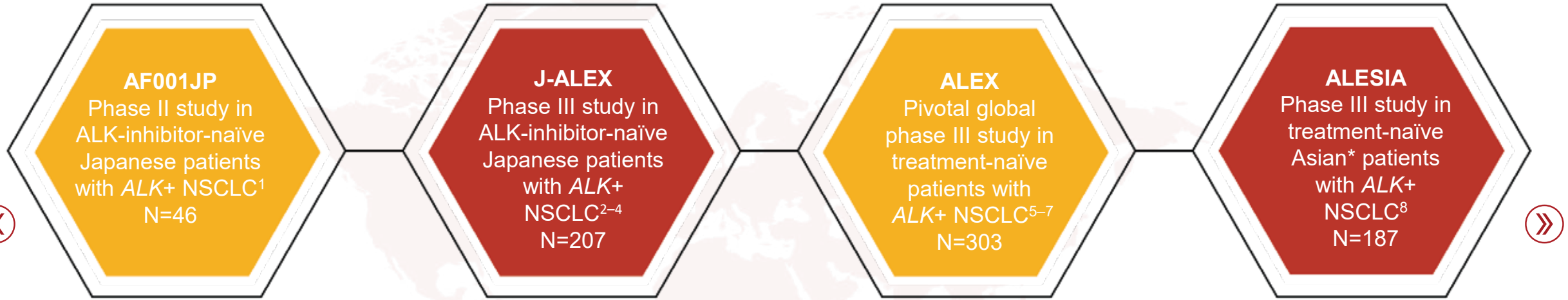
Resistance Mutation

CNS Penetration

Safety

ALECENSA alectinib 150 mg capsules

Evidence Base For Alectinib In The 1L Treatment Of ALK+ NSCLC



Alectinib has the largest body of evidence, with* consistent results in three phase III trials *supporting alectinib as the preferred 1L treatment option for patients with previously untreated, advanced ALK+ NSCLC

*ALESIA enrolled patients from China, South Korea and Thailand

1. Nishio, et al. WCLC 2017; 2. Hida, et al. Lancet 2017; 3. Nishio, et al. Lung Cancer 2018
4. Nakagawa, et al. Lung Cancer 2020; 5. Peters, et al. N Eng J Med 2017
6. Camidge, et al. J Thorac Oncol 2019; 7. Mok, et al. Ann Oncol 2020; 8. Zhou, et al. Lancet Resp Med 2019

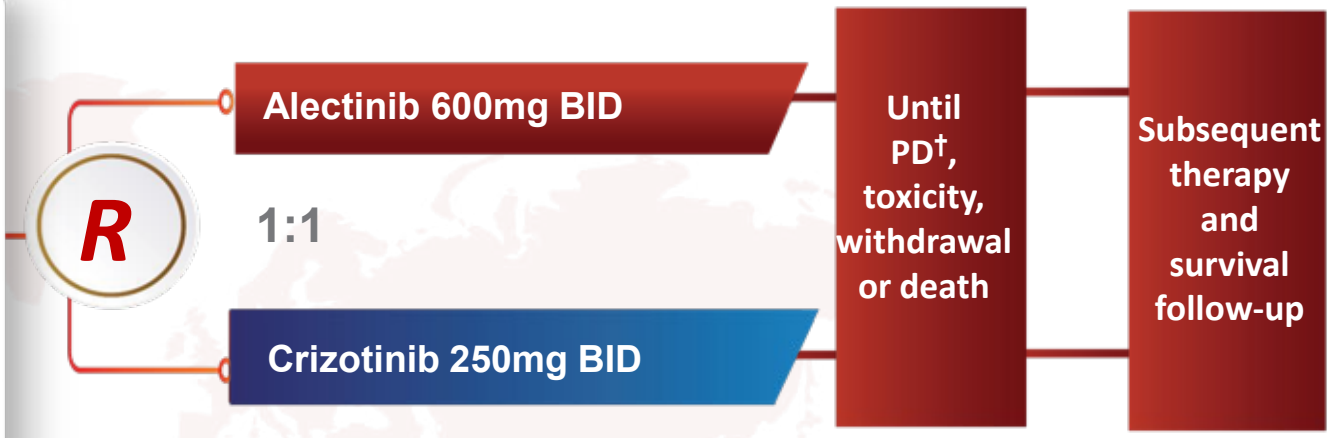
ALECENSA® alectinib 150 mg capsules

ALEX Phase III Study

ALEX: Study Design

- Stage IIIB/IV NSCLC
- *ALK*+ disease according to IHC test*
- Treatment naïve
- ECOG PS 0–2(n=303)

(n=303)



Stratification Factors

- CNS metastases at baseline (presence vs absence)
- Asian vs non-Asian
- ECOG (0–1 vs 2)

Primary Endpoint

- PFS (investigator-assessed)

Secondary Endpoints

- ORR
- DoR
- OS
- PFS (IRC)
- CNS ORR
- Safety
- Time to CNS progression (IRC)

*IHC test is being developed by Ventana as a companion diagnostic to Alectinib . Sufficient tumour tissue is required to test for *ALK*+ disease via IHC and FISH. The first patient was enrolled in August 2014.
†Isolated asymptomatic CNS progression, treatment until systemic or symptomatic CNS PD allowed.
BID = twice daily; DoR = duration of response; ECOG PS = Eastern Cooperative Oncology Group performance status;
FISH = fluorescence in-situ hybridisation; IHC = immunohistochemistry; IRC = independent review committee; ORR = objective response rate; OS = overall survival; PD = progressive disease; PFS = progression-free survival; QoL = quality of life

Camidge, et al. ASCO 2018 (Abstract 9043)

ALECENSA alectinib 150 mg capsules

ALEX: Data Cuts And Analyses To Date

Data cut-off	Analysis	Median follow-up (months)		Key publication/ presentation
9 February 2017	Primary analysis	ALC: 18.6	CRZ: 17.6	Peters, et al. N Eng J Med 2017
1 December 2017	1st exploratory analysis	ALC: 27.8	CRZ: 22.8	Camidge, et al. J Thorac Oncol 2019
30 November 2018	2nd exploratory analysis	ALC: 37.8	CRZ: 23.0	Mok, et al. ESMO 2019 / Mok, et al. Ann Oncol 2020
29 November 2019	3rd exploratory analysis	ALC: 48.2	CRZ: 23.3	Peters, et al. ASCO 2020 / Mok, et al. Ann Oncol 2020

ALEX is the **most comprehensive study of 1L alectinib**, which is being investigated in a global patient population and has published data from a primary analysis and three subsequent exploratory analyses

ALECENSA® alectinib 150 mg capsules

ALEX: Baseline Characteristics

Patient characteristics	Crizotinib (n=151)	Alectinib (n=152)
Median age, years (range)	54 (18–91)	58 (25–88)
Male / female, %	42 / 58	45 / 55
Asian / non-Asian,* %	46 / 54	45 / 55
ECOG PS 0–1 / 2,* %	93 / 7	93 / 7
CNS metastases by IRC* - yes / no, %	38 / 62	42 / 58
Active / past / non smoker, %	3 / 32 / 65	8 / 32 / 61
Stage IIIB / IV, %	4 / 96	3 / 97
Adenocarcinoma / squamous cell carcinoma / other, %	94 / 1 / 5	90 / 3 / 7
CNS metastases by IRC – yes / no, %	38 / 62	42 / 58
Prior brain radiation - yes / no, %	14 / 86	17 / 83
CNS metastases by treatment – n brain surgery / radiosurgery / whole brain radiotherapy / other %	22 5 / 18 / 73 / 5	27 4 / 19 / 63 / 15

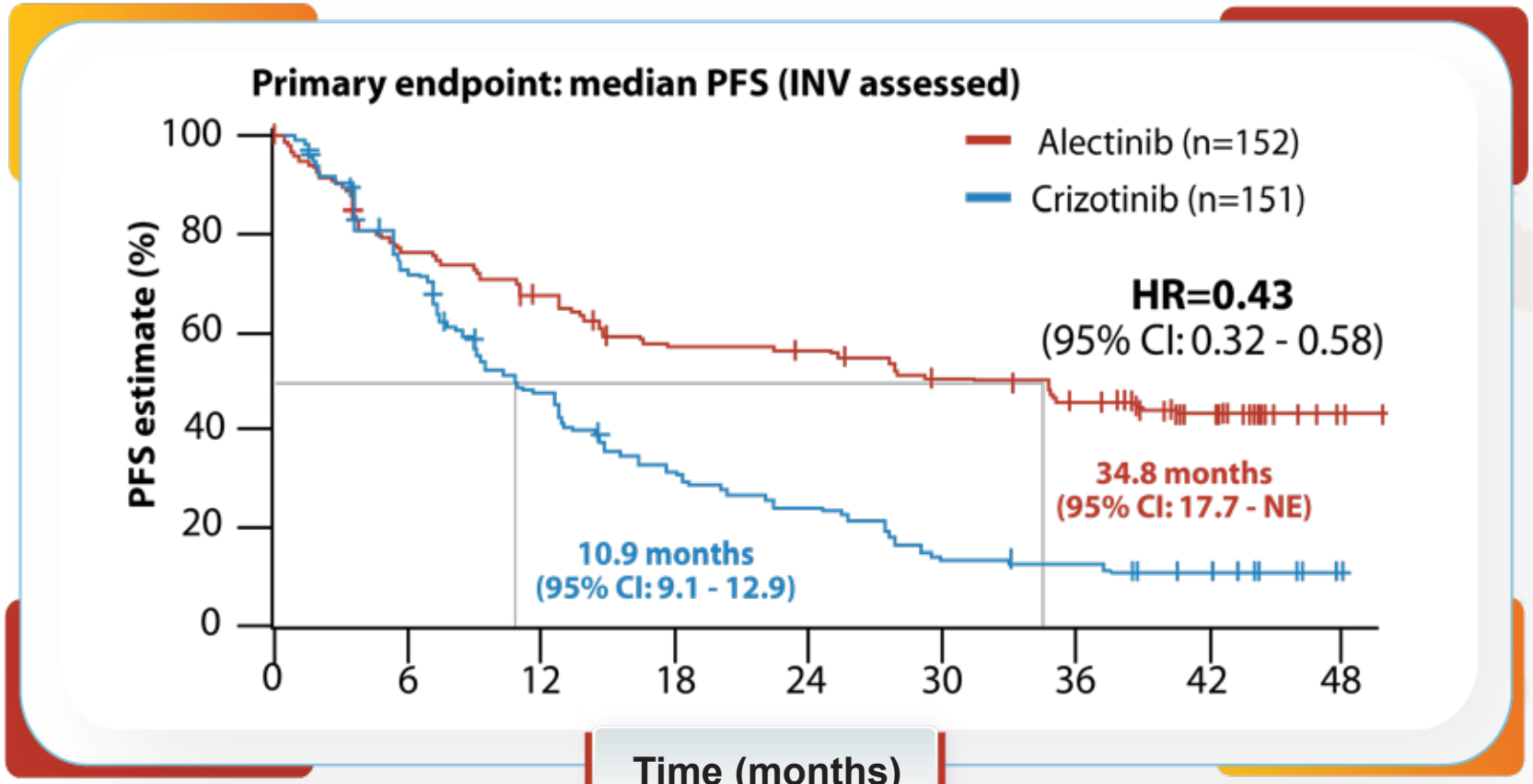
- All patients underwent tumour imaging at baseline.
- ALEX is the first phase III trial to prospectively capture the evolution of CNS disease with routine brain imaging every 8 weeks in all patients while on treatment

NCT02075840

Peters, et al. NEJM 2017

ALECENSA alectinib 150 mg capsules

ALEX: Final, Mature INV-assessed PFS



Proven protection from the disease

Nearly **3 years** **freedom from progression**[1]

(34.8 months [95% CI: 17.7, NE])

The final PFS analysis of ALEX demonstrated that alectinib has the longest mature median PFS of **34.8 months** in the 1L setting, providing a **3x longer efficacy benefit** compared with crizotinib

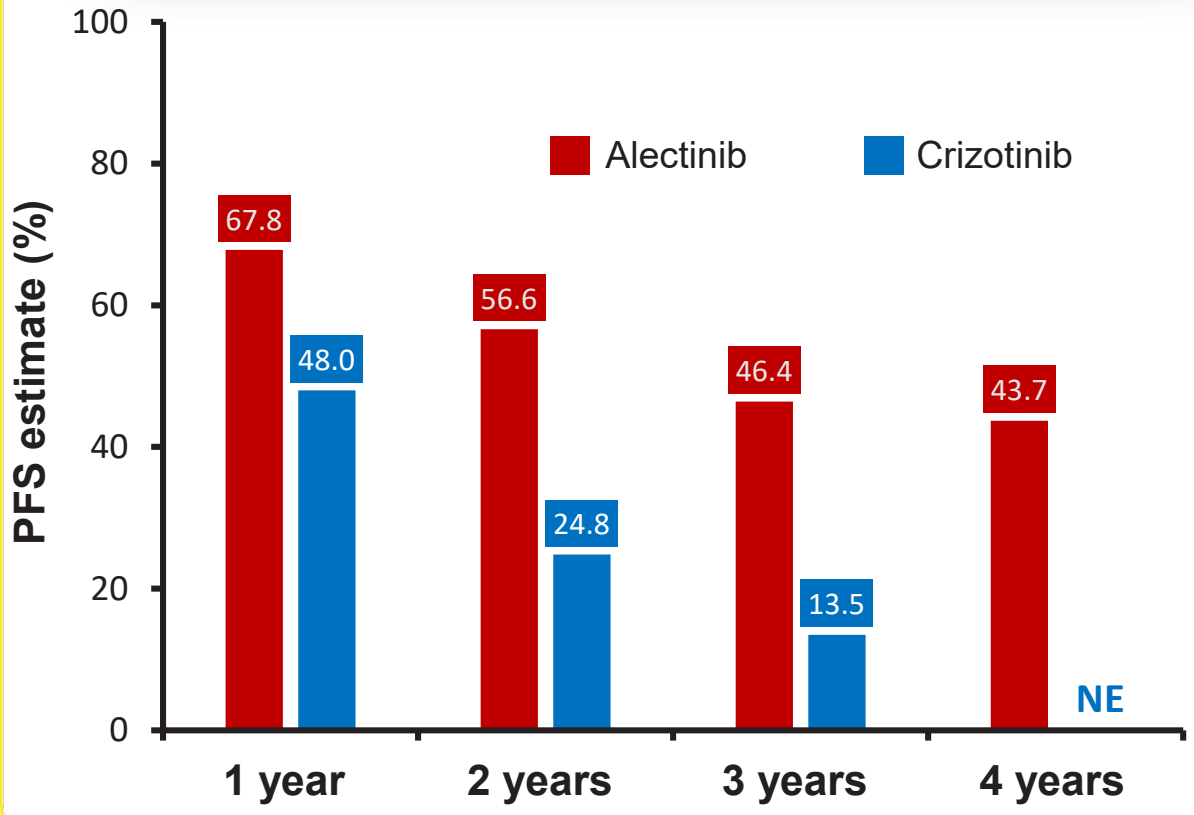
ALECENSA® alectinib 150 mg capsules

Second exploratory analysis (data cut-off: 30 November 2018)

Mok, et al. Ann Oncol 2020

ALEX (Exploratory Analysis 2): Final PFS Event-free Rate (Up To 4-years) In The ITT Population

PFS event-free rate for ITT population, %



In patients treated with alectinib, **43.7%** of patients were event-free at 4 years (4-year event-free rate was not estimable in crizotinib-treated patients)

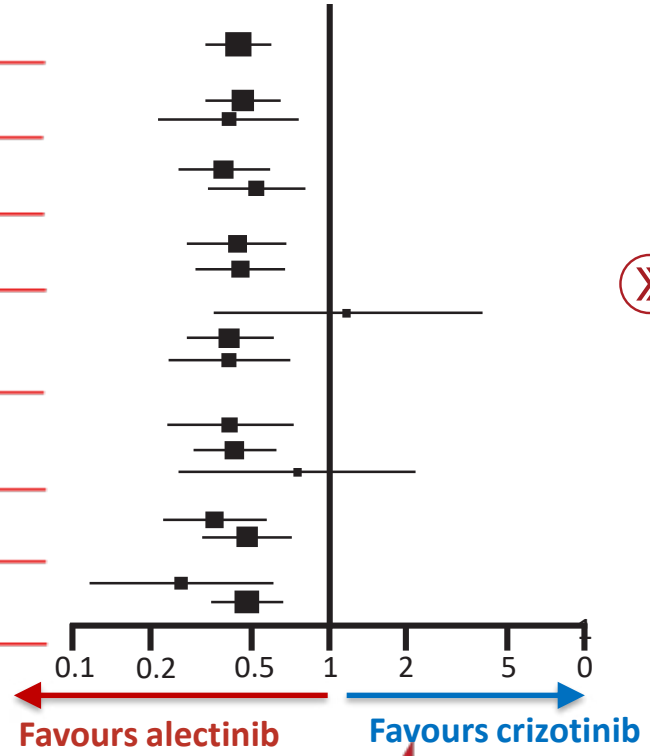
Exploratory analysis 2 (data cut-off: 30 November 2018)
ITT = intent-to-treat; NE = not estimable; PFS = progression-free survival

Mok, et al. Ann Oncol 2020

ALECENSA alectinib 150 mg capsules

ALEX (Exploratory Analysis 1): PFS Subgroup Analysis In The ITT Population

Baseline risk factors	Alectinib (n=152) Total n	Alectinib (n=152) n	Alectinib (n=152) Events	Alectinib (n=152) Median (months)	Crizotinib (n=151) n	Crizotinib (n=151) Events	Crizotinib (n=151) Median (months)	Hazard ratio	95% Wald CI
All patients	303	152	72	34.8	151	116	10.9	0.43	(0.32–0.59)
Age									
<65 years	233	115	56	34.8	118	89	11.1	0.45	(0.32–0.63)
≥65 years	70	37	16	34.8	33	27	9.1	0.40	(0.21–0.75)
Sex									
Female	171	84	37	34.8	87	64	11.1	0.38	(0.25–0.58)
Male	132	68	35	27.7	64	52	10.4	0.51	(0.33–0.79)
Race category									
Asian	138	69	32	34.8	69	51	9.6	0.43	(0.27–0.67)
Non-asian	165	83	40	NE	82	65	11.1	0.44	(0.30–0.66)
Smoking status									
Active smoker	17	12	8	3.9	5	4	5.6	1.16	(0.35–3.90)
Non-smoker	190	92	43	34.8	98	75	10.9	0.40	(0.27–0.59)
Past smoker	96	48	21	34.8	48	37	10.8	0.40	(0.23–0.69)
ECOG performance status									
0	97	43	18	34.9	54	37	12.9	0.40	(0.23–0.71)
1	186	99	48	34.8	87	70	10.9	0.42	(0.29–0.61)
2	20	10	6	3.7	10	9	5.8	0.74	(0.25–2.15)
CNS mets at baseline (IRC)									
Yes	122	64	33	27.7	58	51	7.4	0.35	(0.22–0.56)
No	181	88	39	34.8	93	65	14.7	0.47	(0.32–0.71)
Prior brain radiation									
Yes	47	26	11	34.9	21	18	12.7	0.26	(0.11–0.59)
No	256	126	61	34.8	130	98	10.8	0.47	(0.34–0.65)



Consistent with the primary analysis, the HR for investigator-assessed PFS was below 1.0 for all subgroups by baseline risk factor, with the exception of active smokers (n=12)

The magnitude of PFS treatment effect was consistent across the majority of subgroups, indicating benefit of Alectinib over crizotinib

ALECENSA alectinib 150 mg capsules

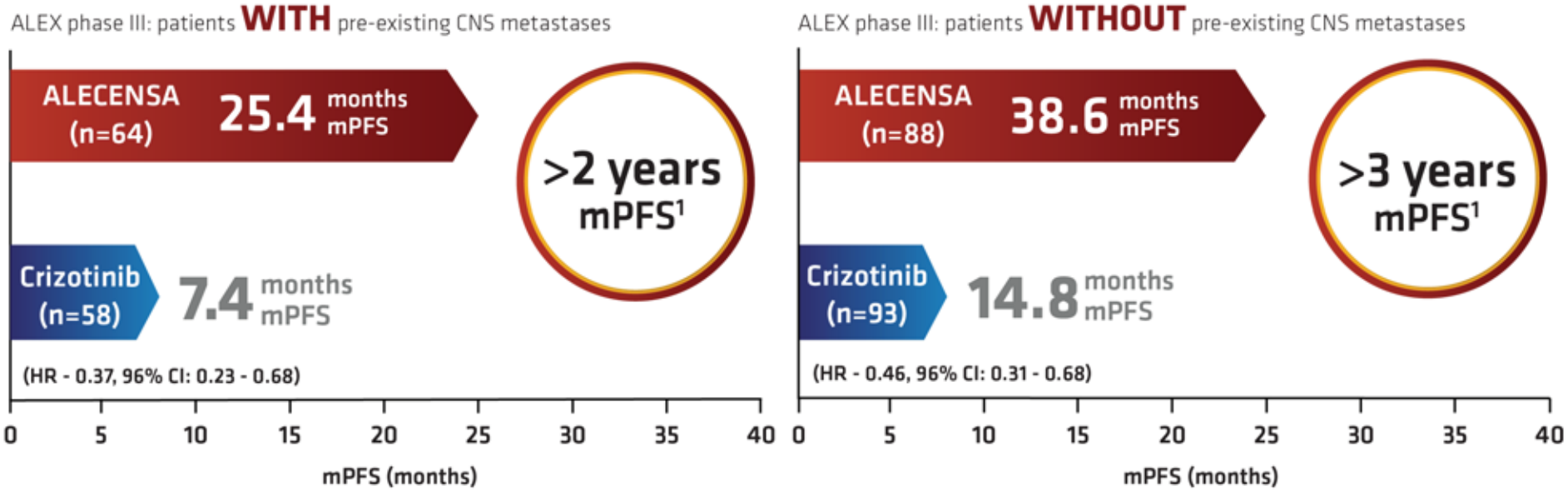
Exploratory analysis 1 (data cut-off: 1 December 2017) Investigator assessed

CI = confidence interval; CNS = central nervous system; ECOG PS = Eastern Cooperative Oncology Group performance status; HR = hazard ratio; IRC = independent review committee; IRC = independent review committee; ITT = intent-to-treat mets = metastases; PFS = progression-free survival

Camidge, et al. J Thorac Oncol 2019

ALEX: *Secondary Endpoint – PFS By Baseline CNS Metastases Status*

Efficacy that lasts for years regardless if baseline CNS metastases[1]



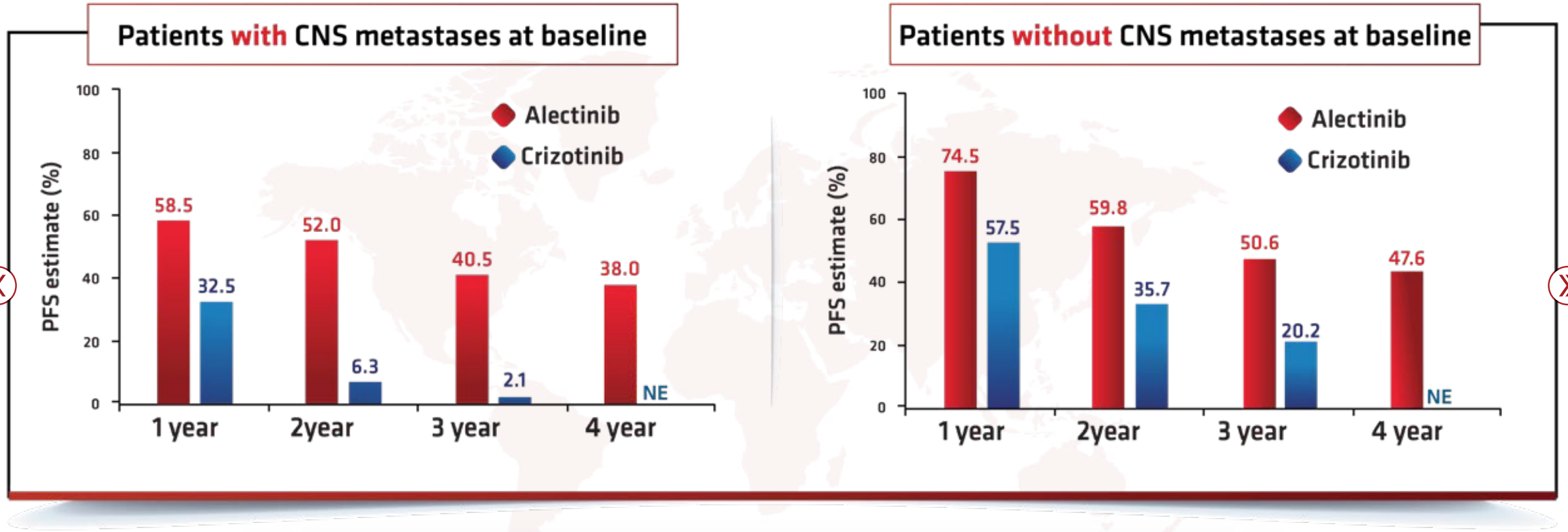
Investigator assessed

Protection that lasts years
irrespective of CNS metastases at baseline

CI: confidence interval; CNS: central nervous system; HR: hazard ratio; mPFS: median progression-free survival.

1. Mok T et al. Ann Oncol. 2020;31(8):1056–64.

ALEX : Final PFS Event-free Rate



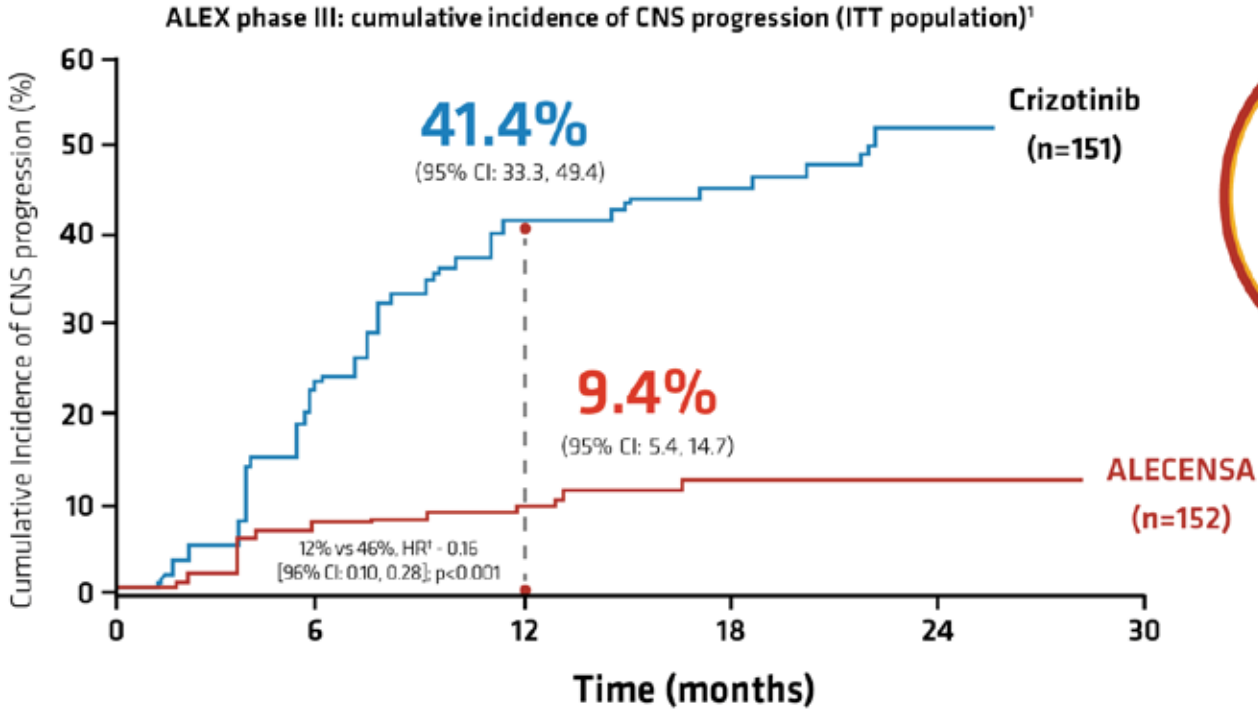
The PFS event-free rate was higher with alectinib than with crizotinib, irrespective of the absence or presence of baseline CNS metastases

ALECENSA® alectinib 150 mg capsules

Exploratory analysis 2 (data cut-off: 30 November 2018)
CNS = central nervous system; NE = not estimable; PFS = progression-free survival
Mok, et al. Ann Oncol 2020

ALEX Phase III: Cumulative Incidence Of CNS Progression (ITT Population)[1]

Alecensa 1L reduces the risk of CNS progression events*†



84%
reduction vs crizotinib[1]

*At 1 year. †Cause specific hazard ratio; adjusted for competing risk of non-CNS progression and death. CI: confidence interval; CNS: central nervous system; HR: hazard ratio; ITT: intention-to-treat.

1. Peters S et al. N Engl J Med. 2017;377(9):829–38.

ALECENSA alectinib 150 mg capsules

ALEX: ORR

ITT population	Crizotinib (n=151)	Alectinib (n=152)
Responders, n (%)	114 (75.5)	126 (82.9)
(95% CI)	(67.8–82.1)	(76.0–88.5)
p-value	0.09	
CR, n (%)	3 (2)	7 (5)
PR, n (%)	111 (74)	119 (78)
SD, n (%)	24 (16)	9 (6)
DoR, months (95% CI)	11.1 (7.5–13.0)	33.1 (31.3–NE)

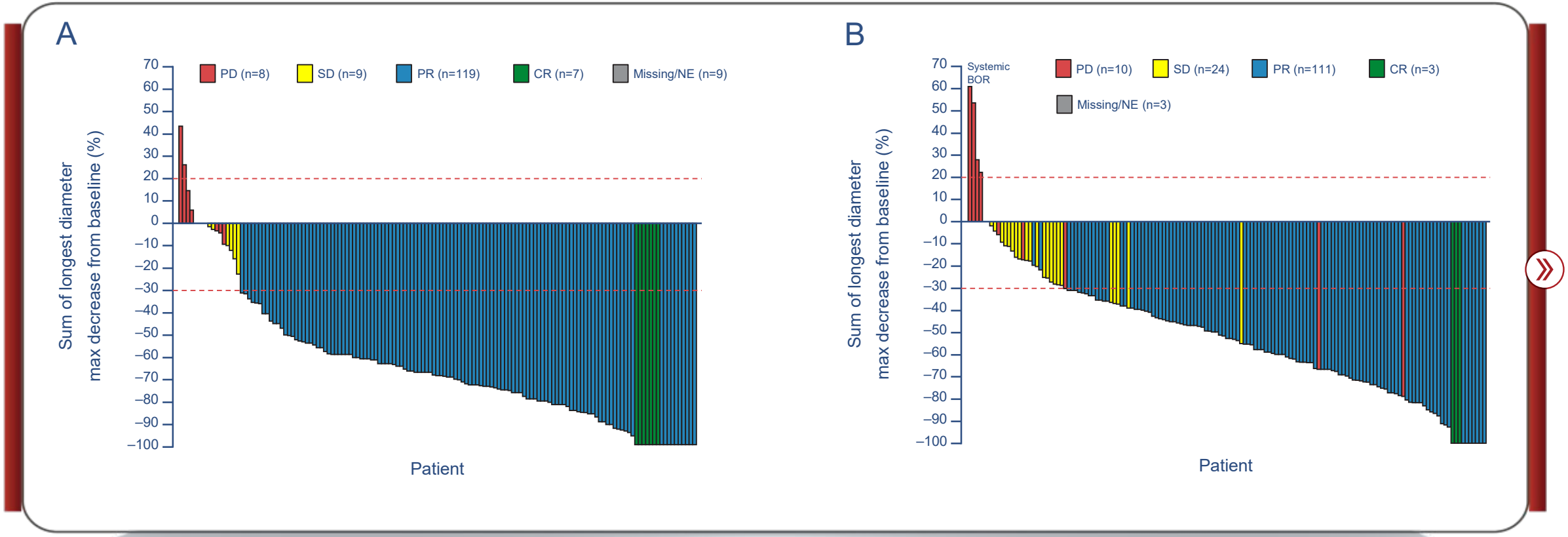
- **Both alectinib and crizotinib achieved a high ORR.**
- **However, the DoR was longer with Alectinib suggesting a prolonged response, which appears to translate into the significant PFS benefit observed with Alectinib versus crizotinib**

Investigator assessed
CR = complete response; PR = partial response; SD = stable disease

Camidge, et al. ASCO 2018 (Abstract 9043)

ALECENSA alectinib 150 mg capsules

ALEX: *Investigator-assessed Systemic Best Overall Responses In The ITT Population (A) Alectinib; (B) Crizotinib*



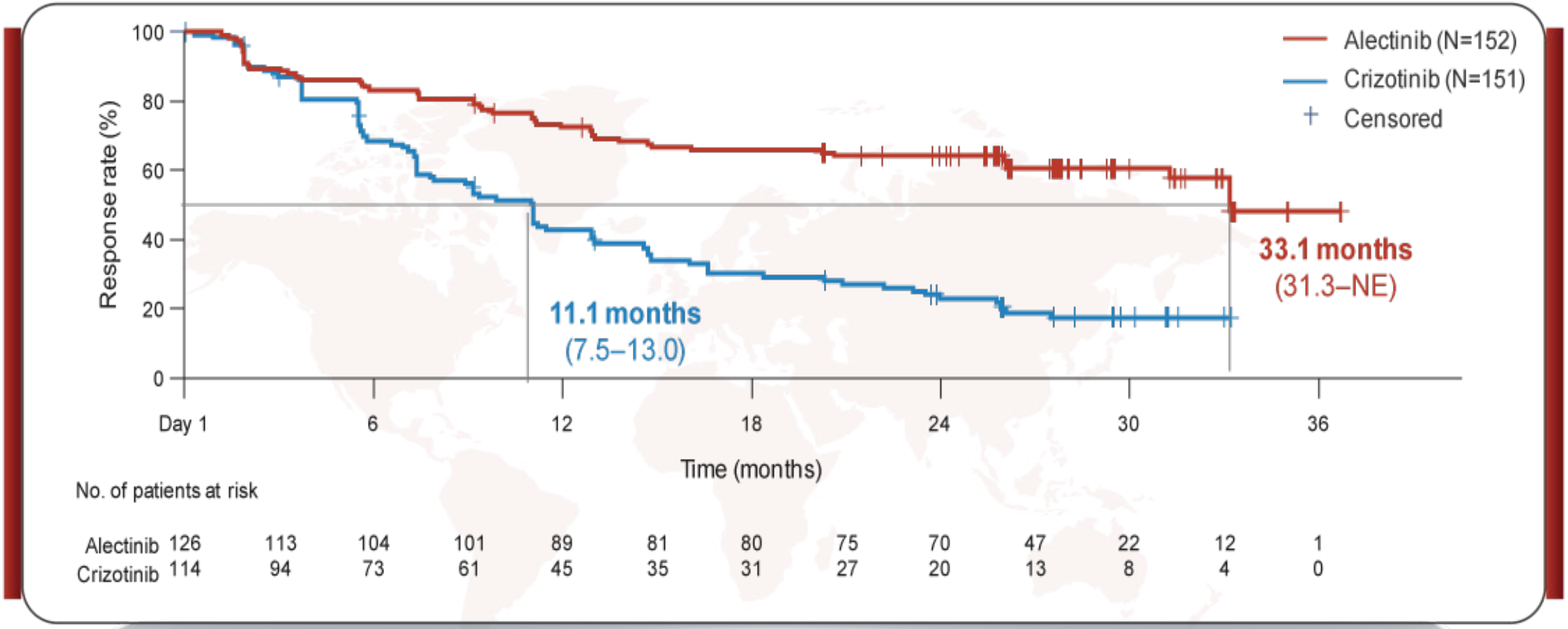
Best overall response of Alectinib is comparable to Crizotinib

BOR, best overall response; SD, standard deviation.

Camidge, et al. ASCO 2018 (Abstract 9043)

ALECENSA alectinib 150 mg capsules

ALEX: Investigator-assessed DoR



DoR was longer with Alectinib than Crizotinib

BOR, best overall response; SD, standard deviation.
Camidge, et al. ASCO 2018 (Abstract 9043)

ALEX: Risk Of CNS Progression

ITT population	Crizotinib (n=151)	Alectinib (n=152)	Cause-specific HR (95% CI)	p value (log-rank)
CNS Progression without prior systemic PD, n (%)	**68** (45)	**18** (12)	0.16 (0.10 to 0.28)	<0.0001*
Systemic progression without prior CNS PD, n (%)	**33** (22)	**36** (24)	0.81 (0.49 to 1.31)	0.38
Death without prior CNS or systemic PD, n (%)	**9** (6)	**11** (7)	0.68 (0.26 to 1.77)	0.43

For each patient, the first event of CNS progression, systemic progression or death was counted. Therefore, patients who had CNS progression first were no longer at risk for systemic progression or death in this analysis.

Treatment with Alectinib significantly reduced the risk of CNS progression in patients without prior systemic

IRC RECIST

Cause-specific stratified HRs and 95% CI were estimated by Cox regression where patients with competing events were censored at the time of these events. P values are from two-sided stratified cause-specific log-rank tests. Strata are race and CNS metastases at baseline

PD = progressive disease

*p value presented by Shaw, et al. ASCO 2017

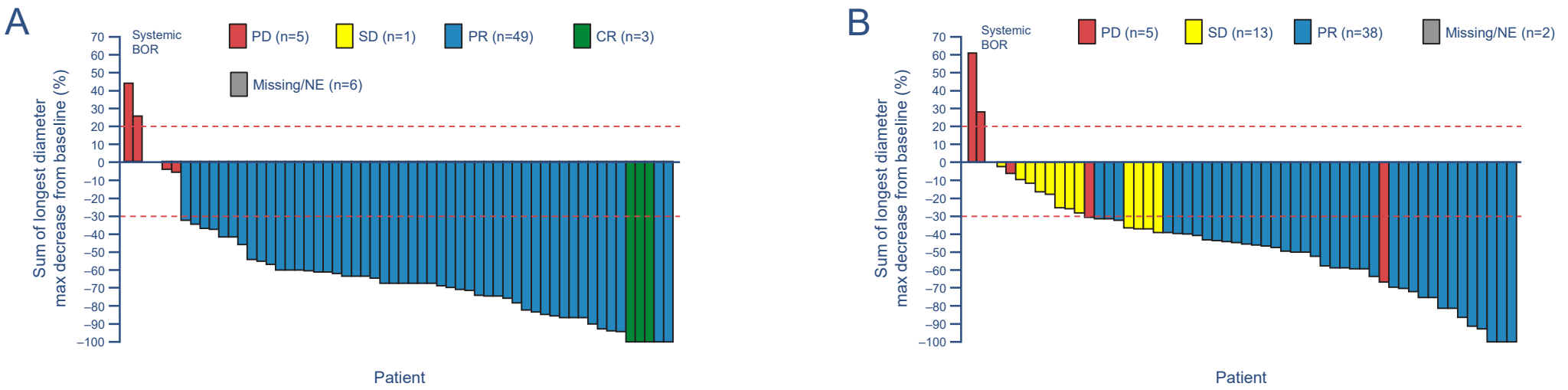
NCT02075840

Peters, et al. NEJM 2017; Shaw et al. ASCO 2017

ALECENSA alectinib 150 mg capsules

ALEX: *Investigator-assessed Best Overall Responses According To Measurable/Non Measurable Baseline CNS Metastasis*

Patients with measurable and/or non-measurable baseline CNS metastases



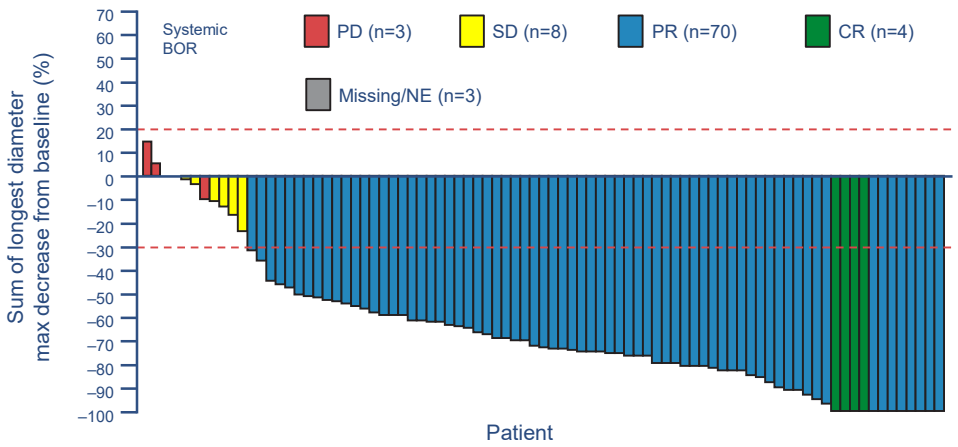
3/64 and **49/64** patients treated with **alectinib** had a CR or PR, respectively (**Figure 4A**); vs compared with **0/58 (CR)** and **38/58 (PR)** for patients treated with **crizotinib** (**Figure 4B**).

ALECENSA alectinib 150 mg capsules

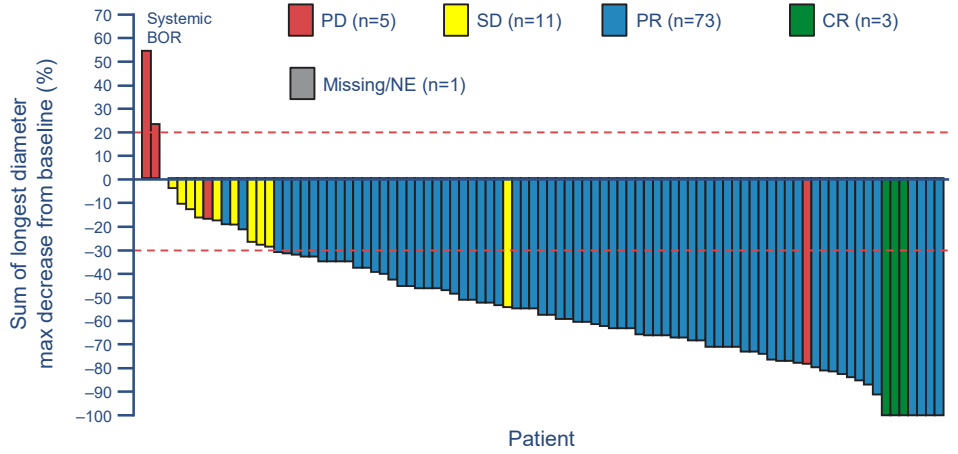
Camidge, et al. ASCO 2018 (Abstract 9043)

ALEX: *Investigator-assessed Best Overall Responses According To Without CNS Mets*

Patients without baseline CNS metastases



D



4/88 and **70/88** patients treated with **alectinib** had a CR or PR, respectively (Figure 4C), compared with **3/93 (CR)** and **73/93 (PR)** for patients treated with **crizotinib** (Figure 4D).

ALECENSA® alectinib 150 mg capsules

Camidge, et al. ASCO 2018 (Abstract 9043)

ALEX: Tumor Reduction In Responders

Responders, n (%)	Alectinib (n=126)	Crizotinib (n=114)
>50% tumor reduction	**114** (90.5)	**73** (64.0)
>75% tumor reduction	**55** (43.7)	**29** (25.4)
Responders with measurable and/or non−measurable CNS lesions at baseline	**Alectinib (n=52)**	**Crizotinib (n=38)**
>50% tumor reduction	**45** (86.5)	**20** (52.6)
>75% tumor reduction	**18** (34.6)	10 (26.3)
Responders without CNS lesions at baseline	**Alectinib (n=74)**	**Crizotinib (n=76)**
>50% tumor reduction	**69** (93.2)	**53** (69.7)
>75% tumor reduction	**37** (50.0)	**19** (25.0)

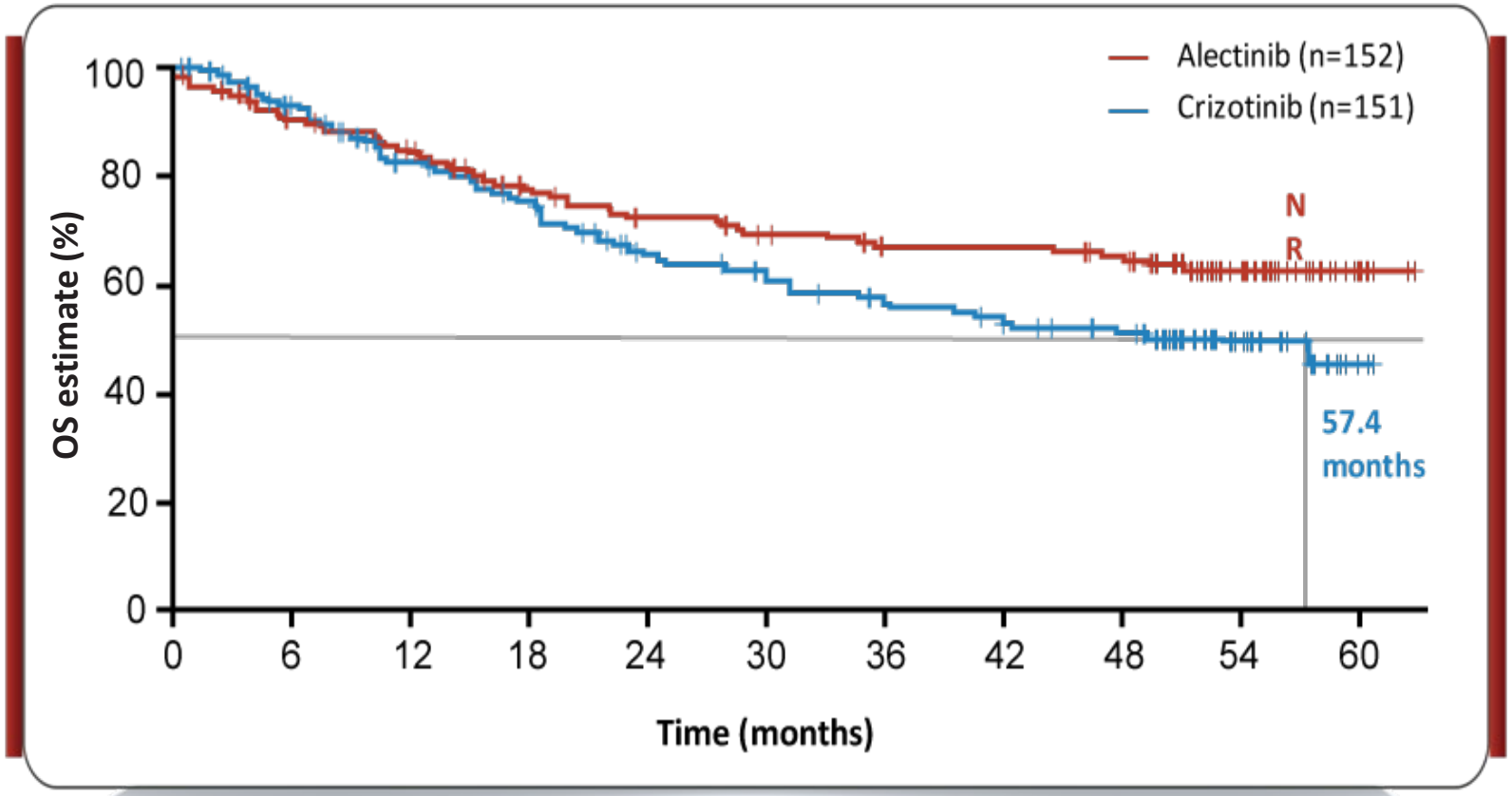
In the ITT population, **43.7% of responders treated with alectinib** demonstrated a >75% tumor reduction compared with **25.4%** of responders treated with **crizotinib**

ALECENSA alectinib 150 mg capsules

Camidge, et al. ASCO 2018 (Abstract 9043)

ALEX: 5-year OS

ALECENSA 1L has a >60% OS rate at 5 years – the highest of any ALK+ therapy[1]



HR=0.67
(95% CI: 0.46–0.98)
p=0.0376*

Superior Survival That Lasts Years

6/10 alive at 5 years (62.5 % VS 45.5% P=0.038)

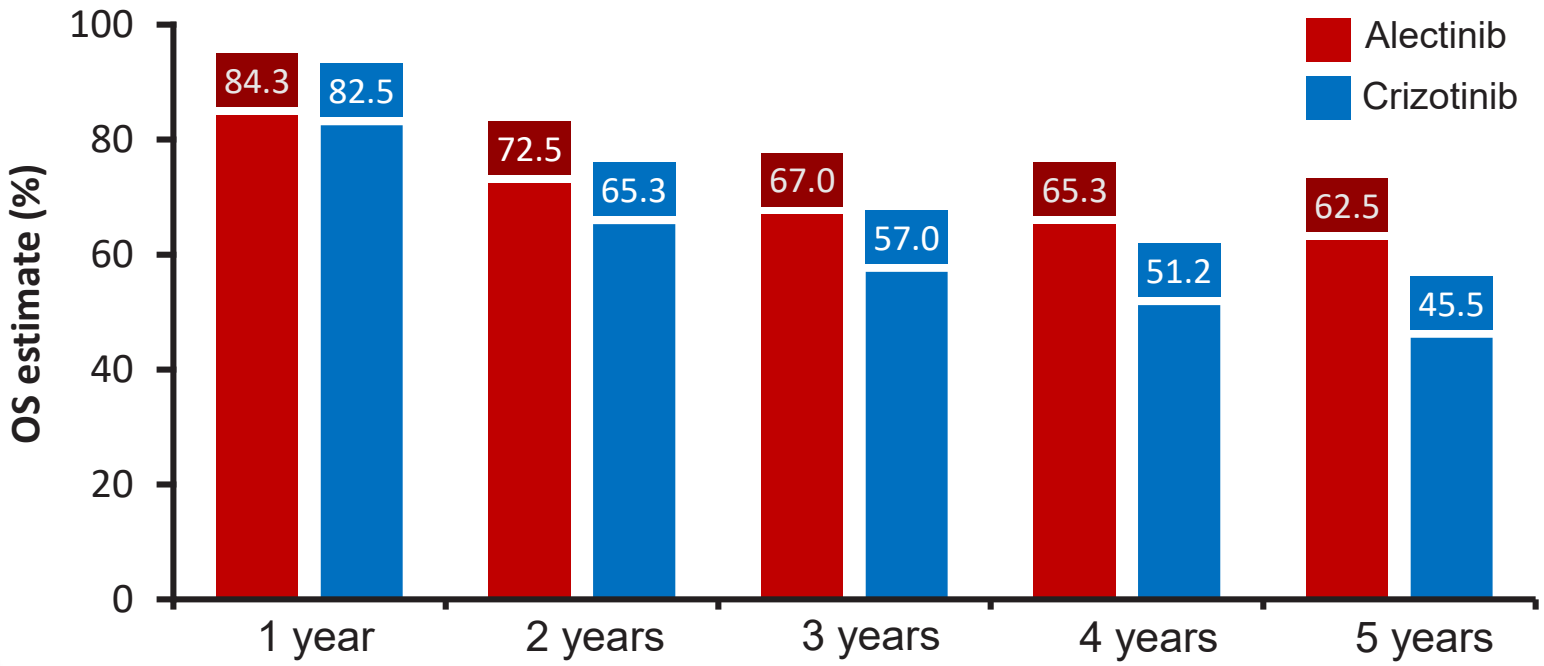
	Alectinib	Crizotinib
Deaths, n (%)	51 (34)	62 (41)

After a median duration of follow up of **48.2 months for alectinib**, **OS data remain immature** (37% of events recorded in the ITT population)

Third exploratory analysis (data cut-off: 29 November 2019)
*Formal statistical testing of OS was not planned; the OS data reported from this exploratory analysis are descriptive only

1. Mok, et al. Ann Oncol 2020

ALEX: 5-year Survival Rates



5-year survival rates:

Alectinib: 62.5%
(95% CI: 54.3–70.8)

Crizotinib: 45.5%
(95% CI: 33.6–57.4)

Patients receiving **alectinib** demonstrated a **clinically meaningful improvement** in 5-year survival rate versus **crizotinib**: **62.5% with alectinib** and **45.5% with crizotinib**

ALECENSA alectinib 150 mg capsules

Third exploratory analysis (data cut-off: 29 November 2019)

Mok, et al. Ann Oncol 2020

ALEX: Safety Profile

Safety population	Alectinib (n=152)	Crizotinib (n=151)
Median treatment duration, months	28.1	10.8
All grade AEs, n (%)	**147** (96.7)	**147** (97.4)
Serious AEs, n (%)	**59** (38.8)	**48** (31.8)
Grade 3–5 AEs, n (%)	**79** (52.0)	**85** (56.3)
Fatal AEs, n (%)	**7** (4.6)	**7** (4.6)
AEs leading to dose reduction, n (%)	**31** (20.4)	**30** (19.9)
AEs leading to dose interruption, n (%)	**40** (26.3)	**40** (26.5)
AEs leading to treatment discontinuation, n (%)	**22** (14.5)	**22** (14.6)

With a **~3x longer treatment duration for alectinib**, the rates of dose reductions, interruptions and discontinuations were similar with alectinib and crizotinib; this demonstrates that **alectinib is well tolerated over long-term use**

ALECENSA alectinib 150 mg capsules

Third exploratory analysis (data cut-off: 29 November 2019)

Mok, et al. Ann Oncol 2020

ALEX: AEs In ≥10% Of Patients In Either Treatment Arm

Any Grade AE, n (%)	Alectinib (n=152)	Crizotinib (n=151)
Nausea	**25** (16)	**75** (50)
Diarrhoea	**24** (16)	**70** (46)
Vomiting	**15** (10)	**62** (41)
ALT increased	**27** (18)	**51** (34)
Constipation	**56** (37)	**51** (34)
Peripheral oedema	**29** (19)	**50** (33)
AST increased	**26** (17)	**44** (29)
Fatigue	**34** (22)	**28** (19)
Dizziness	**15** (10)	**23** (15)
Dysgeusia	**4** (3)	**22** (15)

(Continued) Any Grade AE, n (%)	Alectinib (n=152)	Crizotinib (n=151)
Visual impairment	**3** (2)	**18** (12)
Rash	**21** (14)	**17** (11)
Headache	**15** (10)	**17** (11)
Upper RT infection	**21** (14)	**16** (11)
Arthralgia	**20** (13)	**13** (9)
Anaemia	**40** (26)	**12** (8)
Back pain	**20** (13)	**12** (8)
Insomnia	**18** (12)	**10** (7)
Myalgia	**26** (17)	**3** (2)
Increased blood bilirubin	**33** (22)	**2** (1)

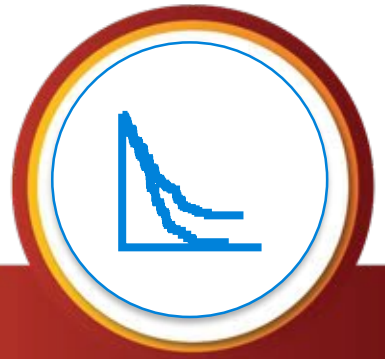
The safety profile of alectinib continues to remain consistent and manageable; no new safety signals were observed at the latest data cut in ALEX

ALECENSA® alectinib 150 mg capsules

Third exploratory analysis (data cut-off: 29 November 2019)

Mok, et al. Ann Oncol 2020

ALECENSA Is The Preferred 1L Treatment Option And Standard Of Care For Patients With *ALK*+ NSCLC,[1,2] Because...



...it has demonstrated a median PFS of
ALEX: 34.8 months[3,4]
ALESIA: 41.6 months[5]
in the 1L setting

…it effectively protects against and treats
CNS metastases[6–9]

...it is the only ALK TKI to have demonstrated a clinically meaningful benefit in OS vs crizotinib
<u>5 year survival rate:</u>
ALEX: 62.5% vs 45.5%[3]
ALESIA: 66.4% vs 56.0%[5]

...and it is well-tolerated, with a well-characterised, manageable safety profile that is maintained with long-term use[3–6]

ALECENSA alectinib 150 mg capsules

1. NCCN NSCLC guidelines. V6 2020; 2. Planchard, et al. Ann Oncol 2019
3. Mok, et al. Ann Oncol 2020; 4. Camidge, et al. J Thorac Oncol 2019; 5. Zhou C, et al. ESMO Asia 2022 (Abs. LBA11); 6. Peters, et al. N Engl J Med 2017; 7. Gadgeel, et al. Ann Oncol 2018; 8. Nishio, et al. Lung Cancer 2018; 9. Zhou, et al. Lancet Resp Med 2019

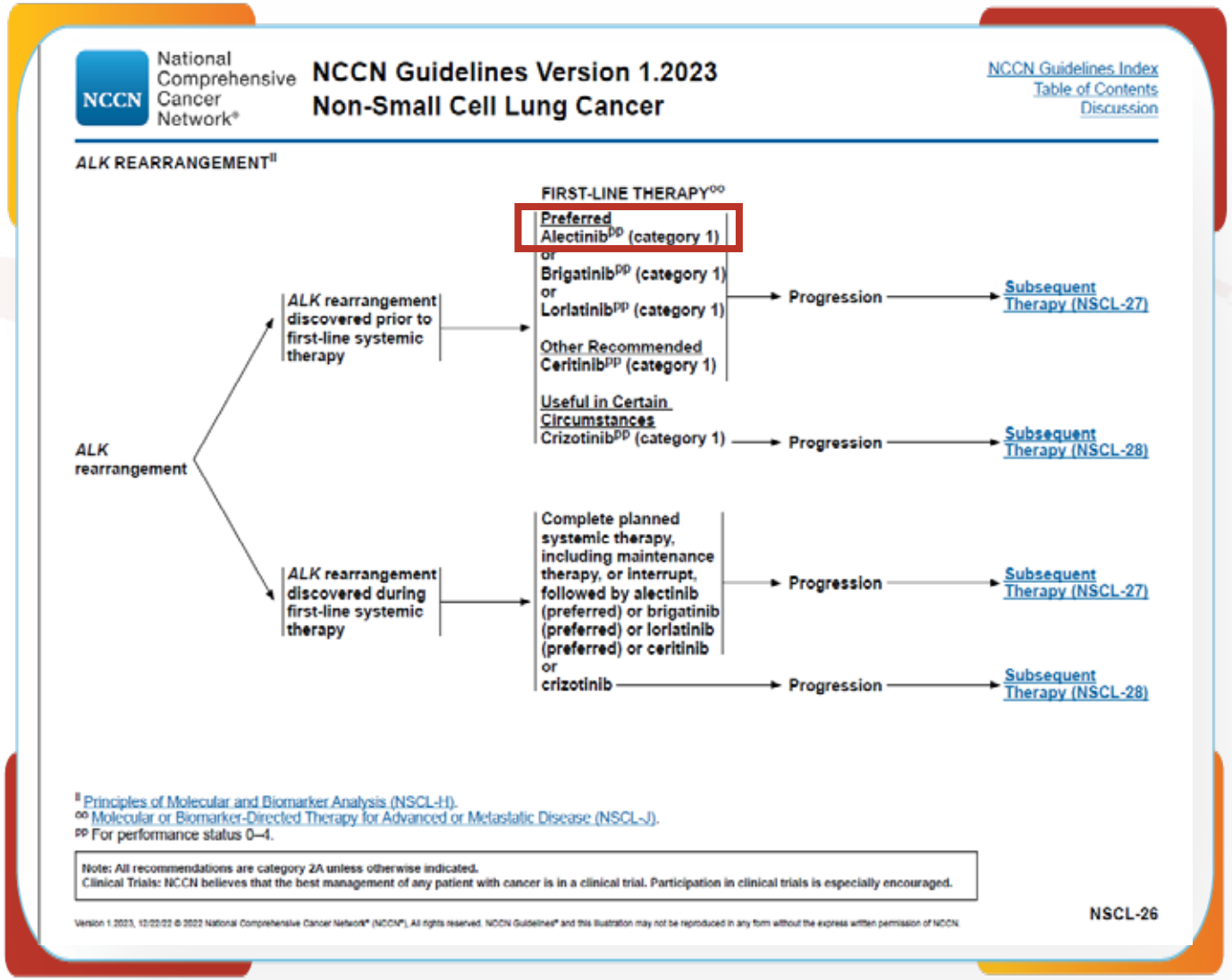
ALEX: Efficacy Conclusions

- ALEX data confirms that alectinib shows superior investigator-assessed PFS versus crizotinib (HR, 0.43), with a median PFS of 34.8 months; Alectinib demonstrated superior efficacy versus crizotinib regardless of baseline CNS metastases
- Longer DoR with Alectinib (vs crizotinib) suggesting that Alectinib provides a 'Prolonged' response, which appears to translate into the significant PFS benefit observed
- Alectinib demonstrated impressive CNS efficacy, both in terms of protecting against the development of CNS metastases and delaying the progression of CNS metastases
- NCCN CAT 1 Preferred - Alectinib as the standard of care for the first-line treatment of patients with advanced ALK+ NSCLC

ALECENSA alectinib 150 mg capsules

Camidge, et al. ASCO 2018 (Abstract 9043); NCCN Feb'2018

Clinical Guidelines For 1L Treatment Of *ALK*+ NSCLC



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

***ALK* REARRANGEMENT**[ll]

FIRST-LINE THERAPY[oo]

***ALK* rearrangement discovered prior to first-line systemic therapy**

Preferred
Alectinib[pp] (category 1)
or
Brigatinib[pp] (category 1)
or
Lorlatinib[pp] (category 1)

Other Recommended
Ceritinib[pp] (category 1)

Useful in Certain Circumstances
Crizotinib[pp] (category 1)

→ Progression → Subsequent Therapy (NSCL-27)

→ Progression → Subsequent Therapy (NSCL-28)

***ALK* rearrangement**

***ALK* rearrangement discovered during first-line systemic therapy**

Complete planned systemic therapy, including maintenance therapy, or interrupt, followed by alectinib (preferred) or brigatinib (preferred) or lorlatinib (preferred) or ceritinib
or
crizotinib

→ Progression → Subsequent Therapy (NSCL-27)

→ Progression → Subsequent Therapy (NSCL-28)

[ll] Principles of Molecular and Biomarker Analysis (NSCL-H).
[oo] Molecular or Biomarker-Directed Therapy for Advanced or Metastatic Disease (NSCL-J).
[pp] For performance status 0–4.

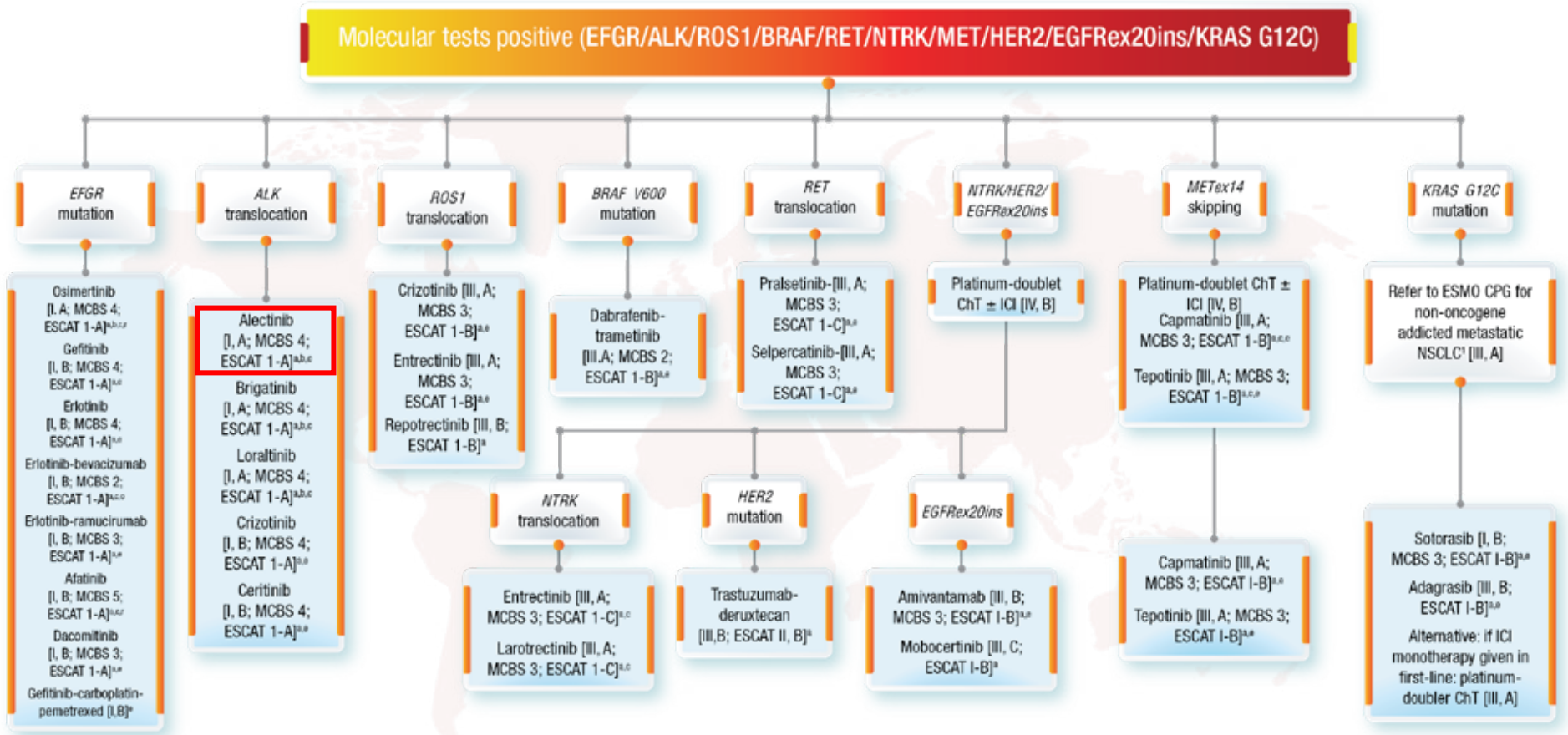
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

NSCL-26

ALECENSA® alectinib 150 mg capsules

1. NCCN NSCLC guidelines. V1. 2023; 2. Planchard, et al. Ann Oncol 2019

ESMO Guidelines



When you diagnose a patient with ALK+ advanced NSCLC, think of the positives ALECENSA® could bring as a first-line treatment.

ALECENSA®...

- Offers the longest overall survival demonstrated in first-line ALK+ advanced NSCLC vs. crizotinib[1]
- Median progression-free survival:
  ALEX: 34.8 months[1]
  ALESIA: 41.6 months[2]
- A well-established long-term safety profile,[1] with >52,000 patients treated worldwide.[2]

Think positive, think ALECENSA® alectinib 150 mg capsules

ALK anaplastic lymphoma kinase; NSCLC, non-small cell lung cancer.

1. Mok, et al. Ann Oncol 2020; 2. Zhou C, et al. ESMO Asia 2022 (Abs. LBA11); 3. Data on File

Doing Now What Patients Need Next

ALECENSA® alectinib 150 mg capsules

Mail this to me:

ALECENSA®
alectinib 150 mg capsules

Disclaimer:

1. ® = Registered Trade Mark F. Hoffmann - La Roche Limited, Basel, Switzerland.
2. For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.
3. Full prescribing information available on request.
4. For scientific information on Roche Medicinal Product please write to india.medinfo@roche.com
5. For all Adverse Events/Special Situation Reports with Roche Medicinal Product please report the same to india.drugsafety@roche.com within one business day/24 hours.

Marketed in India by:
Roche Products (India) Pvt. Ltd.
146-B, 166 A, Unit No. 7, 8, 9, 8th Floor, R City Office, R City Mall
Lal Bahadur Shastri Marg, Ghatkopar, Mumbai - 400 086
Tel: +91(22)50457300
Fax: +91(22)50457301

http://bit.ly/Roche_Alecensa_PI

Please use the QR code/ click on the link for the latest Prescribing Information (PI). For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

Input Code: M-IN-00002479
Valid Upto: This promotional input is not valid after 27/03/2024 or any update