ESMO 2022 Industry Satellite Symposium

Redefining Lung Cancer **Together:** Now and Next

Disclosures

Stephen V Liu: advisory board/consultancy for Amgen, AstraZeneca, Bayer, Beigene, Blueprint, Boehringer-Ingelheim, Bristol-Myers Squibb, Catalyst, Daiichi Sankyo, Eisai, Elevation Oncology, Genentech/Roche, Gilead, Guardant Health, Janssen, Jazz Pharmaceuticals, Lilly, Merck/MSD, Novartis, Regeneron, Sanofi, Takeda, and Turning Point Therapeutics; received research grant (to institution) from Alkermes, Blueprint, Bristol-Myers Squibb, Elevation Oncology, Genentech, Gilead, Merck, Merus, Nuvalent, Pfizer, RAPT and Turning Point Therapeutics

Frédérique Penault-Llorca: consultancy for AbbVie, Amgen, AstraZeneca, Bayer, BMS, Clovis, Daiichi Sankyo, Diaceutics, Eli Lilly, Illumina, Invitae, MSD, Novartis, Pfizer, Roche and Ventana; received research grants: AbbVie, AstraZeneca, Bayer, BMS, Illumina, MSD and Roche

Martin Reck: consulting fees and honoraria for speaker's bureaus: Amgen, AstraZeneca, BMS, Boehringer Ingelheim, Eli Lilly and Company, Merck, MSD, Mirati, Novartis, Pfizer, Roche, and Sanofi; participated on the data safety monitoring or advisory board: Amgen, AstraZeneca, BMS, Boehringer Ingelheim, Eli Lilly and Company, Merck, MSD, Mirati, Novartis, Pfizer, Roche and Sanofi

Stefania Vallone: no relevant affiliations or financial involvement to declare

Paul Van Schil: participated in expert groups and advisory boards for BMS, MSD, AstraZeneca, Roche and Janssen; received speaker's honoraria from BMS, MSD, AstraZeneca, Roche and Janssen; board member and president-elect of IASLC; treasurer of BACTS

Stephen V Liu

Georgetown University
Washington DC, USA

Welcome and introduction

Agenda

Timing	Proposed topic	Speaker
13.00–13.05	**Welcome and introduction**	Stephen V Liu
13.05–13.15	**Patient perspective: Where are we now?**	Stefania Vallone
13.15–13.25	**Biomarkers in lung cancer: Challenges and opportunities**	Frédérique Penault-Llorca
13.25–13.45	**Immunotherapy, targeted therapy and beyond: Navigating options for metastatic disease**	Stephen V Liu Martin Reck
13.45–14.05	**Treatment choice in resectable lung cancer: New insights, new outlooks**	Martin Reck Paul Van Schil
14.05–14.25	**Panel discussion and Q&A**	All
14.25–14.30	**Meeting close**	Stefania Vallone Stephen V Liu

Symposium faculty

Stephen V Liu – Chair

Georgetown University
Washington DC, USA

Stefania Vallone

Women Against Lung Cancer in Europe
Turin, Italy

Frédérique Penault-Llorca

Centre Jean Perrin
Clermont-Ferrand, France

Martin Reck

LungenClinic
Großhansdorf, Germany

Paul Van Schil

University Hospital of Antwerp
Edegem (Antwerp), Belgium

Throughout the symposium, feel free to send your questions by:

Live audience

Scan the QR code on your badge
Select the session name:
“REDEFINING LUNG CANCER TOGETHER: NOW AND NEXT”

Online attendees

Type in the chat box next to the streaming video

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Redefining Lung Cancer **Together:** Now and Next

Stefania Vallone

Women Against Lung Cancer in Europe
Turin, Italy

Patient perspective: Where are we now?

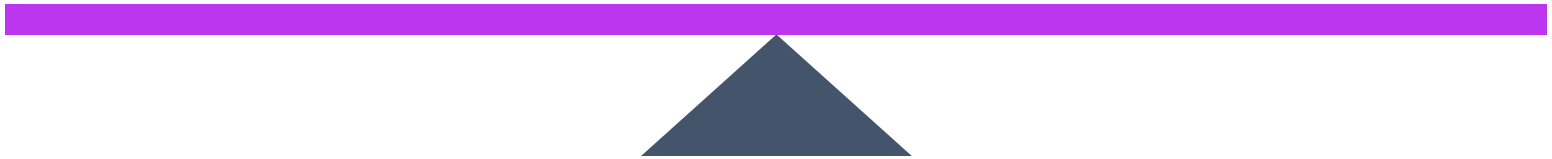
stefania.vallone@womenagainstlungcancer.eu

www.womenagainstlungcancer.org

With innovative treatments, people are outliving their prognosis

Improved survival and availability of later-line treatments provides hope

Delayed or inaccessible testing and treatments create fear



EPROPA: https://www.epropa.eu/en/

New treatments have opened new doors, but challenges can not be ignored

Availability of molecular tests varies among countries

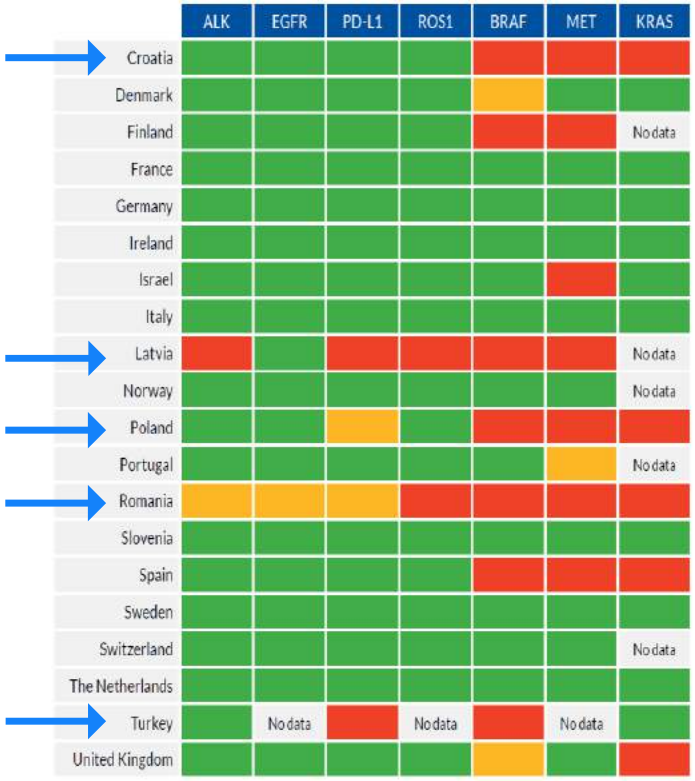


Table 1. Availability of lung cancer molecular tests (November 2019).

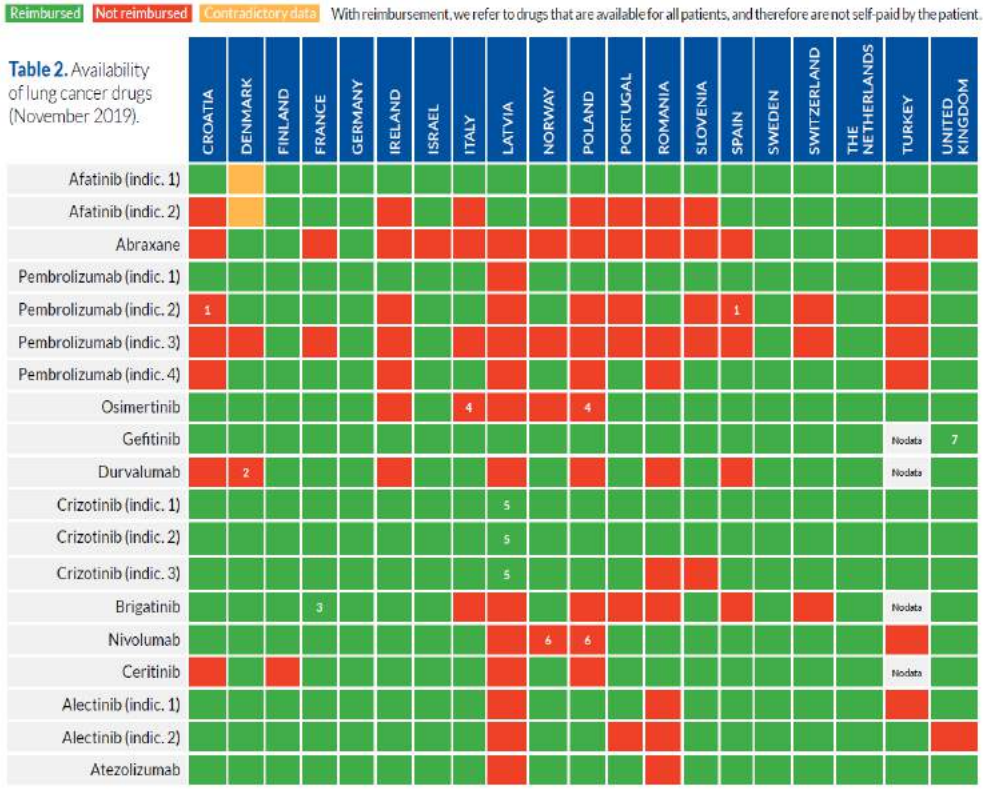
Reimbursed

Not reimbursed

Contradictory data

With reimbursement, we refer to tests that are available for all patients, and therefore are not self-paid by the patient

Access to new treatments remains a challenge



Reimbursed | **Not reimbursed** | **Contradictory data**

Lung Cancer Europe (LUcE) position paper (2020): https://www.lungcancereurope.eu/wp-content/uploads/2021/12/LuCE-POSITION-PAPER-English.pdf

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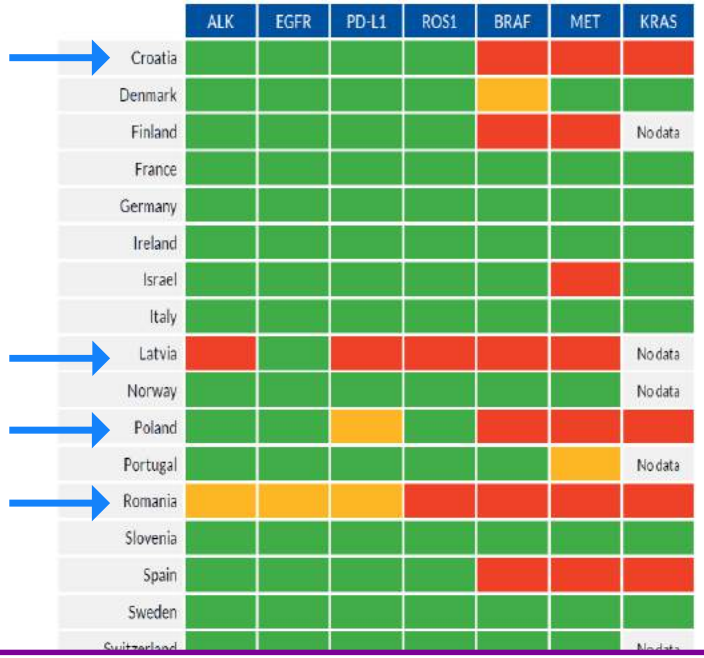

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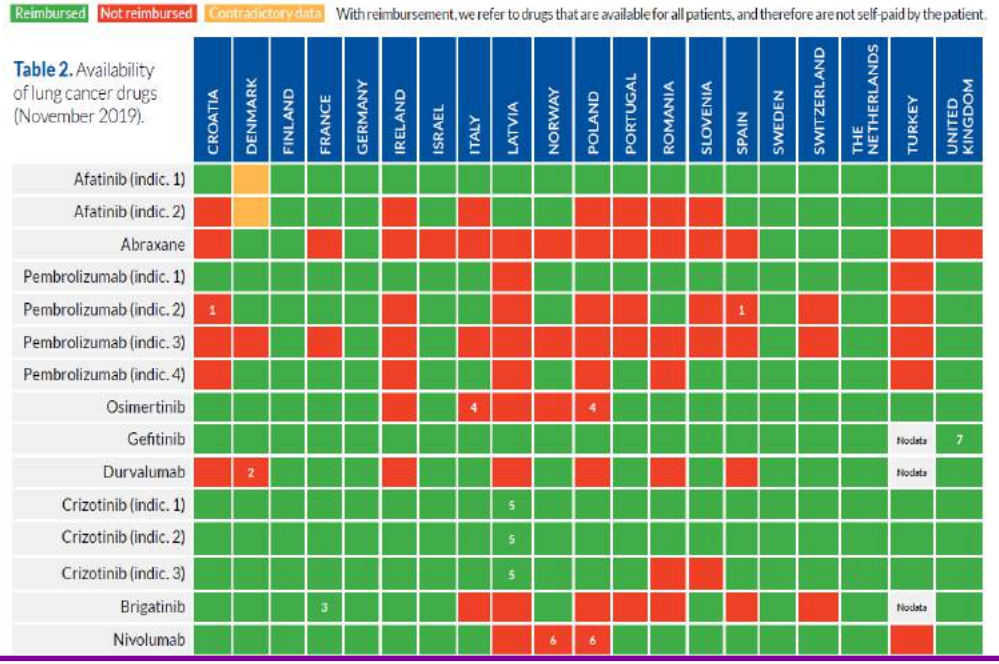
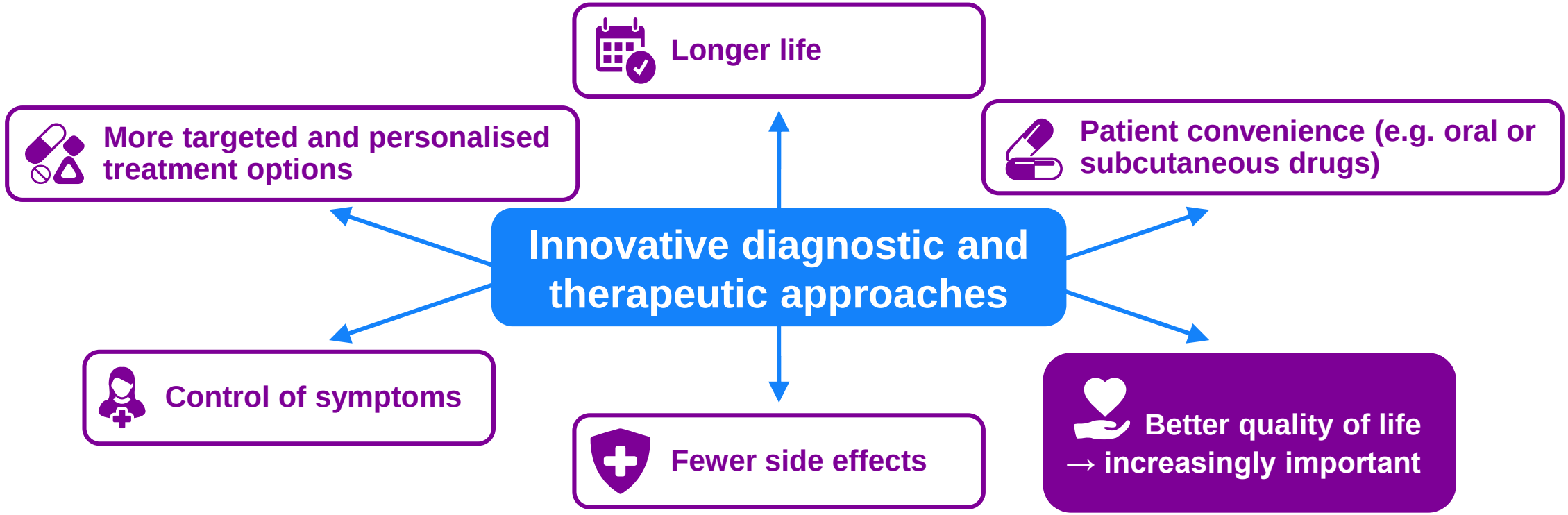


Availability and access to appropriate diagnosis and care vary across Europe

Patient programmes such as **EPROPA** (European Program for ROutine testing of Patients with Advanced lung cancer) aim to **improve access to molecular diagnosis and clinical trials**

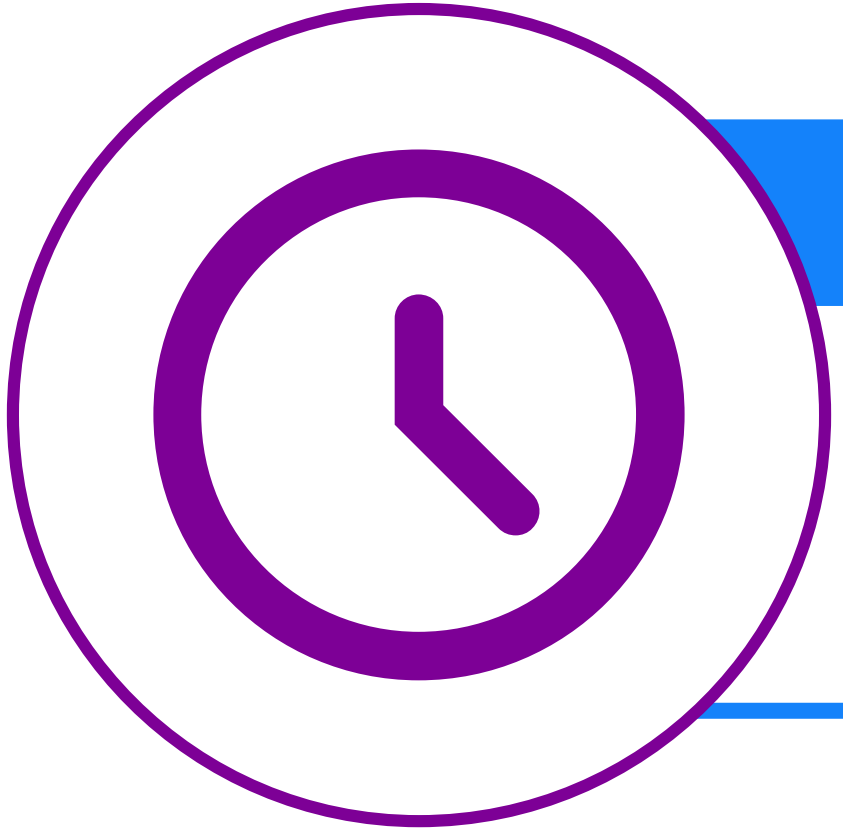
Lung Cancer Europe (LUcE) position paper (2020): https://www.lungcancereurope.eu/wp-content/uploads/2021/12/LuCE-POSITION-PAPER-English.pdf

Value of new approaches for patients with lung cancer



For patients, innovative treatments represent more than medicine…
It's hope until the next breakthrough treatment

Time matters for patients



Early diagnosis is critical

Multidisciplinary Teams (MDTs) can provide care for a **better disease management** and an **improved wellbeing**

MDTs are needed to deliver a ‘person-centred’ level of care

Behind every diagnosis, there are patients, families and caregivers who deserve the most effective, safe and human healthcare

Patient journeys are complex: not only about **health**, but also **psychological**, **emotional** and **social** needs

Multidisciplinary Team (MDT)

- Family doctor
- Oncologist
- Surgeon
- Pulmonologist
- Pathologist
- Radiologist

MDT typically refers to medical staff, that often focus on physical symptoms, but it is important to consider the **benefits of broader support**

MDTs are needed to deliver a ‘person-centred’ level of care

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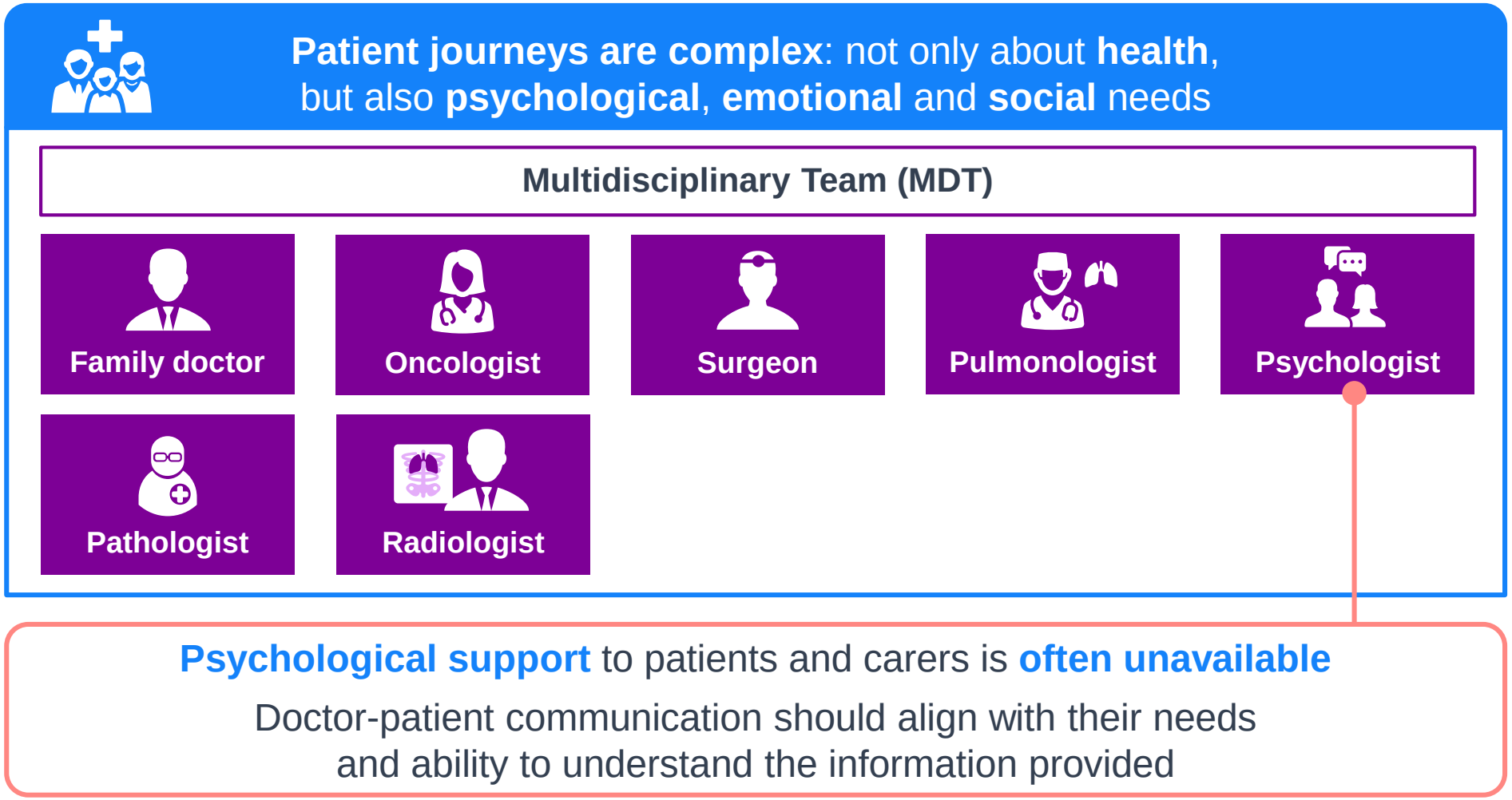

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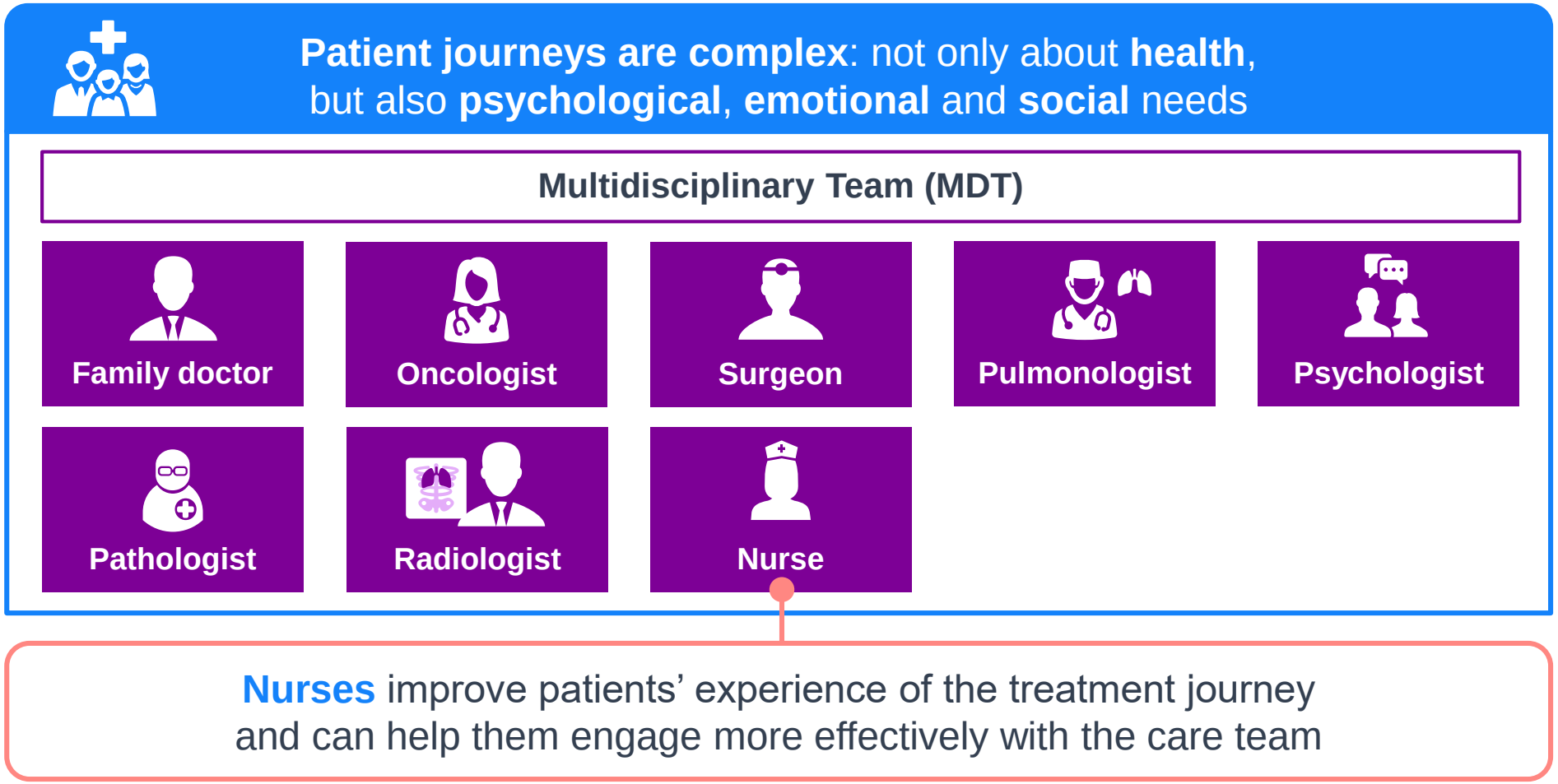

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- Oncologist
- Surgeon
- Pulmonologist
- Psychologist
- Pathologist
- Radiologist
- Nurse
- Social worker

Social workers provide services to improve coping and assess patients’ needs within the institution and/or the community

MDTs are needed to deliver a ‘person-centred’ level of care

Behind every diagnosis, there are patients, families and caregivers who deserve the most effective, safe and human healthcare

Patient journeys are complex: not only about **health**, but also **psychological**, **emotional** and **social** needs

Multidisciplinary Team (MDT)

- Family doctor
- Oncologist
- Surgeon
- Pulmonologist
- Psychologist
- Pathologist
- Radiologist
- Nurse
- Social worker
- Palliative care

Referrals to **palliative care** services are often restricted to ‘end-of-life care’, although they provide numerous benefits

Advances in care have improved the opportunity for patients to advocate for themselves and for other people

2009

2022

Membership

23 countries represented

22 Full members

Belgium, Croatia, France, Denmark, Germany, Greece, Hungary, Israel, Italy, Netherlands, Norway, Poland, Portugal, Spain, Sweden and UK

14 Associate & Individual members

Finland, France, Greece, Italy, Ireland, Latvia, Norway, Poland, Romania, Slovenia, Spain, Switzerland, Sweden and Ukraine

ALK POSITIVE Improving Patient Outcomes Worldwide

BRAF Bombers

The ROS1ders

KRAS KICKERS KRASKICKERS.ORG

MET CRUSADERS

EGFR esisters

Exon20 Group EGFR/HER2 EXON 20 MUTATION GROUP

- **Support patients and caregivers**
- **Increase awareness and education**
- **Improve access to effective diagnosis and treatment**

Accelerate and fund research

Conclusions

Patients are being involved more in their treatment decisions, but **there is still more to do**

All stakeholders have to work together to address the major challenges faced by lung cancer patients

'Alone we can do so little, together we can do so much'

Behind the numbers, there are people...

WALCE – Be MUTual days – Rome 15–16 November 2021

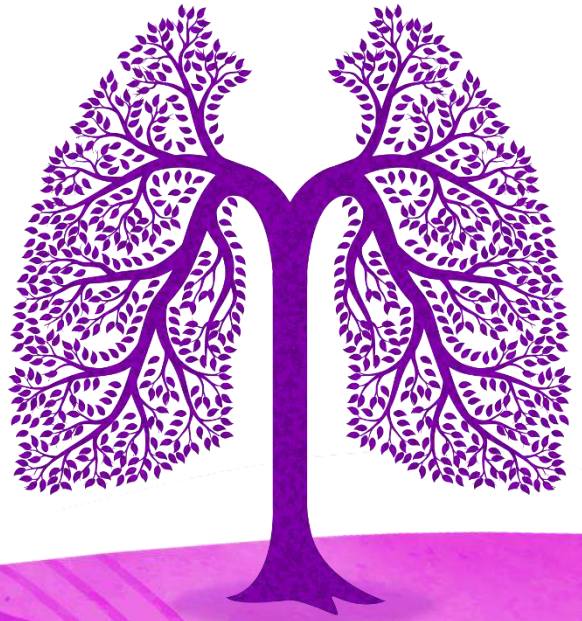
ESMO 2022 Industry Satellite Symposium

Redefining Lung Cancer **Together:** Now and Next

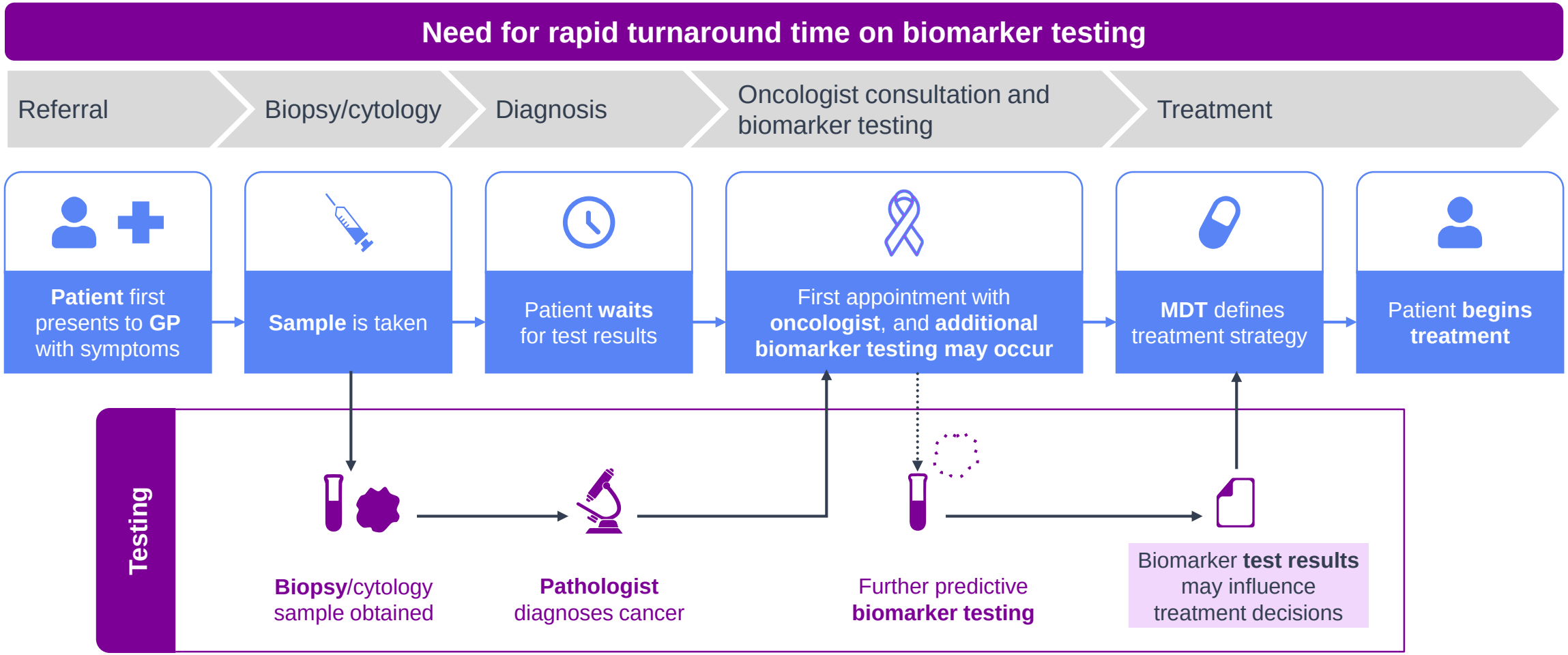
Frédérique Penault-Llorca

Centre Jean Perrin
Clermont-Ferrand, France

Biomarkers in lung cancer: Challenges and opportunities



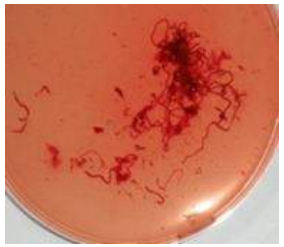
Biomarker testing is a critical part of the patient pathway

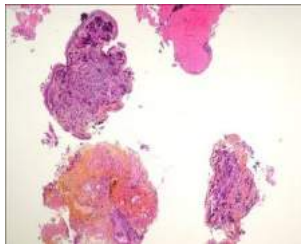


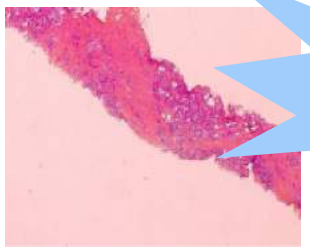
Popat, et al. Oncologist 2021; Courtesy of Professor Frédérique Penault-Llorca

Lung cancer is often diagnosed on small tissue samples or cytology specimens

Tissue management is an interdisciplinary challenge







Tissue is the issue!

The number of **diagnostic and predictive biomarkers is increasing**, while minimally invasive tissue sampling techniques are producing **increasingly limited material**

A **multidisciplinary strategy** is beneficial to ensure:

- Sample size is **maximised** and processing is **optimised**
- A **well-informed testing strategy** that prioritises biomarkers to reduce unnecessary subtyping and tissue usage
- **Early planning** for biomarker testing, to decrease turnaround time and provide optimal treatment
- **Clear reporting** and interpretation of pathology results based on **international standards**

Images courtesy of Professor Frédérique Penault-Llorca

NGS enables simultaneous analysis of a wide range of biomarkers and genetic alterations

Benefits of NGS[1]

- Identifies **clinically meaningful genomic alterations**, opening additional treatment opportunities for patients
- **Simultaneous testing** of multiple genes and alterations will save time and tissue compared with single-marker sequential testing
- Detects genetic alterations with **high sensitivity and high specificity**
- **Solid/liquid** tumour biopsy

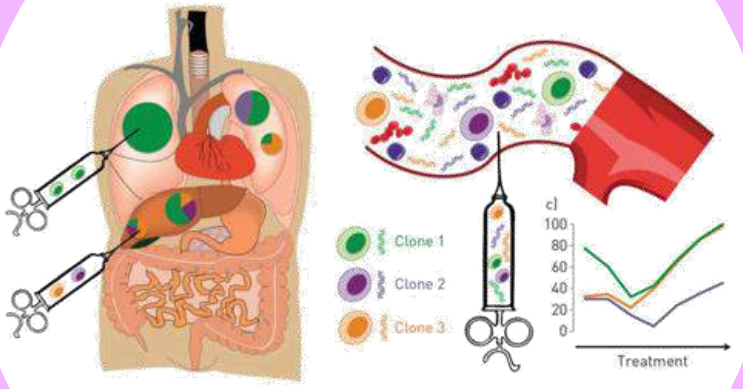
NGS panels are not all the same[1,2]

- **Different sample requirements** (tissue or blood, DNA and/or RNA)
- Different number of **genes**, type of **alterations** and **mutational signatures** detectable (CGP vs small panels)
- Ability to detect **novel** alterations **or only known** alterations

1. Goodwin, et al. Nat Rev Genet 2016; 2. Bormann-Chung, et al. J Mol Diagn 2022

Advantages and limitations of **blood-based NGS** compared with tissue biopsy testing

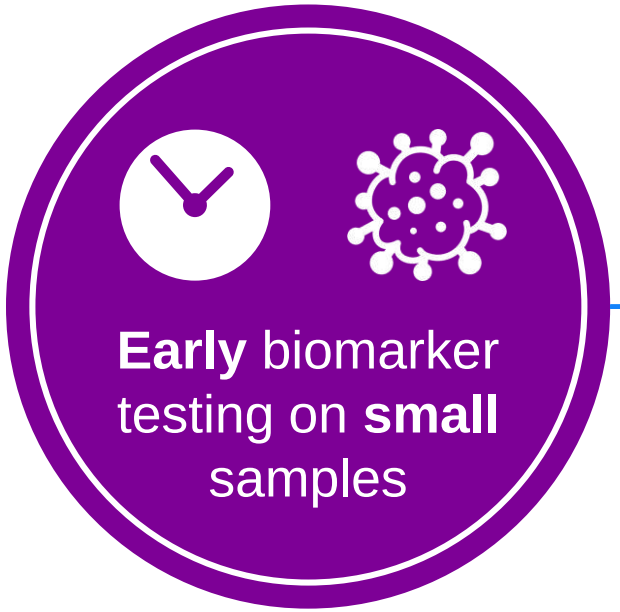
- **Less invasive** than biopsy procedures[1]
- Clinical utility in **patients who are unfit for biopsy** or **with insufficient tissue** sample[1]
- **Less tissue is required** for biomarker testing[2,3]
- Potential tool for **early diagnosis, monitoring** of treatment response and **resistance**[4]



- Risk of missed biomarker due to **lower sensitivity** than tissue-based testing
- **Cannot** be used for **initial** histologic **diagnosis** or **PD-L1** testing

1. Diaz Jr, et al. J Clin Oncol 2014; 2. Penault-Llorca, et al. Virchows Arch 2022; 3. Bonanno, et al. Br J Cancer 2022; 4. Martins, et al. Genes (Basel) 2021

New treatment options for **resectable NSCLC** require a mindset change with biomarker testing



- Biomarker testing in resectable NSCLC should follow the **same approach as for metastatic disease**
- Allows **earlier discussion** of adjuvant treatment options with patients
- **Efficient sample management** is important for fast turnaround time for biomarker results, so as **not to delay surgery**
- Current required biomarkers are ***EGFR, ALK*** and **PD-L1**, to identify patients **most likely to benefit** from approved drugs in this setting

Testing rates in NSCLC have improved, but remain lower than they should be

Three retrospective studies assessed **testing rates for *ALK*, *EGFR*, *ROS1*, PD-L1, and *BRAF*** in the US and Germany (each with >3,000 patients with advanced NSCLC)[1–3]

NGS testing occurred in **36–44% of patients**[1–3]

Most patients were tested for at least one biomarker prior to 1L, but **the proportion of patients who were tested for all biomarkers varied greatly between studies**[1–3]

Generally, testing rates **vary between biomarkers and between countries**[1–4]

Testing rates can still be improved

1. Robert, et al. ASCO 2021; 2. Waterhouse, et al. Clin Lung Cancer 2021; 3. Griesinger, et al. Lung Cancer 2021; 4. Dalurzo, et al. OncoTargets Ther 2021

As more treatments become available, early and efficient testing is essential in lung cancer

Oncogenic drivers in lung cancer

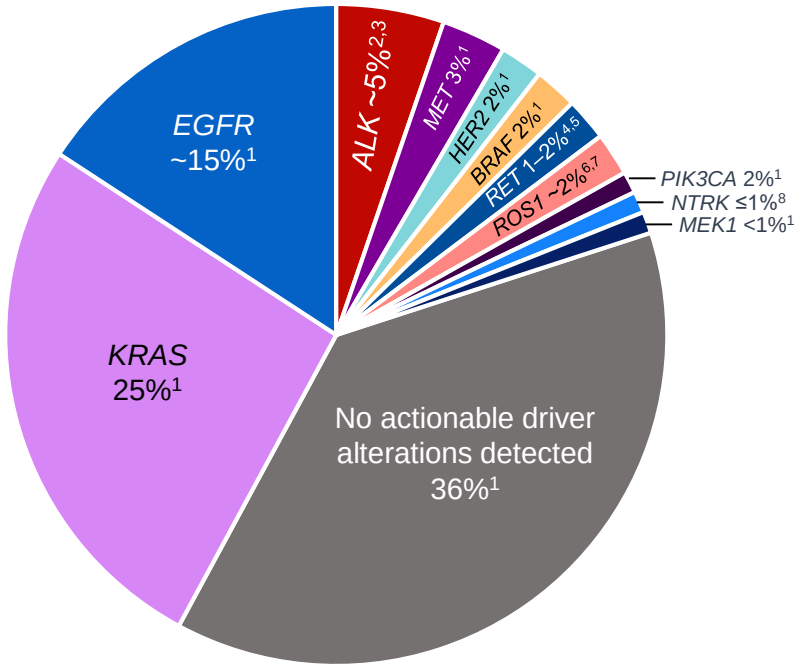


Figure adapted from Pakkala & Ramalingam. JCI Insight 2018

Early, **efficient**, and **comprehensive** biomarker testing can identify key oncogenic drivers for patients with advanced NSCLC

1. Pakkala & Ramalingam. JCI Insight 2018; 2. Barlesi, et al. Lancet 2016; 3. Tian, et al. Lung Cancer 2017; 4. Qiu, et al. Sci Rep 2020; 5. Gainor & Shaw. Oncologist 2013;
6. Bergethon, et al. J Clin Oncol 2012; 7. Dugay, et al. Oncotarget 2017; 8. Farago, et al. JCO Precis Oncol 2018

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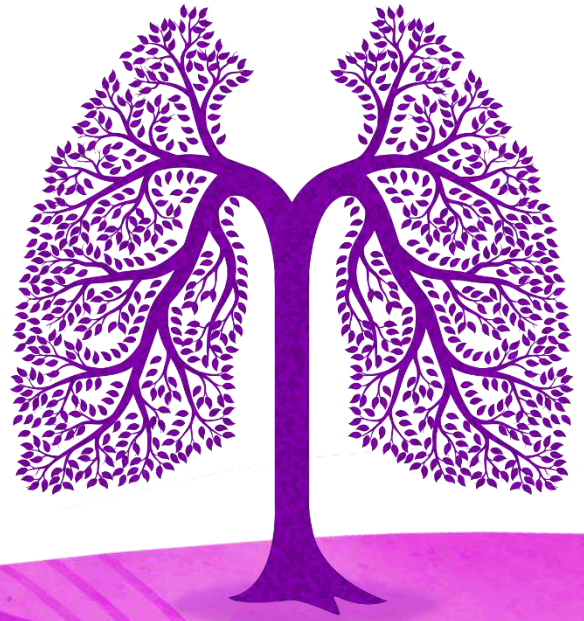
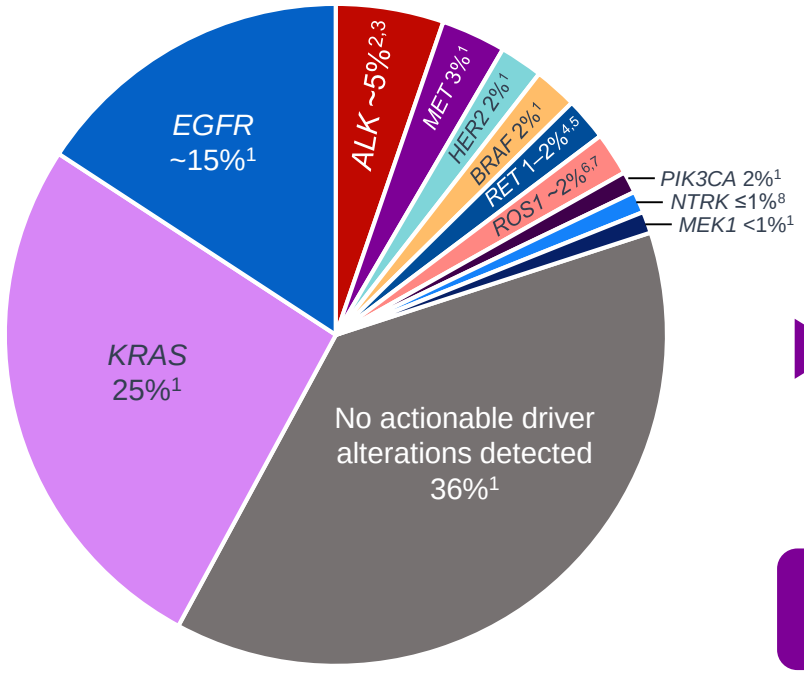
Immunotherapy, targeted therapy and beyond: Navigating options for metastatic disease



The development of multiple targeted therapies has revolutionised the treatment landscape in advanced NSCLC

Oncogenic drivers in lung cancer



Targeting actionable driver alterations

Figure adapted from Pakkala & Ramalingam. JCI Insight 2018

Approved drugs for each biomarker

ALK
- Alectinib
- Brigatinib
- Ceritinib
- Crizotinib
- Lorlatinib
- Ensartinib (China)

EGFR
- Erlotinib
- Afatinib
- Dacomitinib
- Gefitinib
- Osimertinib
- Erlotinib + bevacizumab
- Erlotinib + ramucirumab

NTRK
- Entrectinib▼
- Larotrectinib

ROS1
- Entrectinib▼
- Crizotinib

BRAF V600E
- Dabrafenib + trametinib

RET
- Pralsetinib▼
- Selpercatinib

KRAS G12C
- Sotorasib

MET
- Capmatinib
- Tepotinib

HER2
- Trastuzumab deruxtecan

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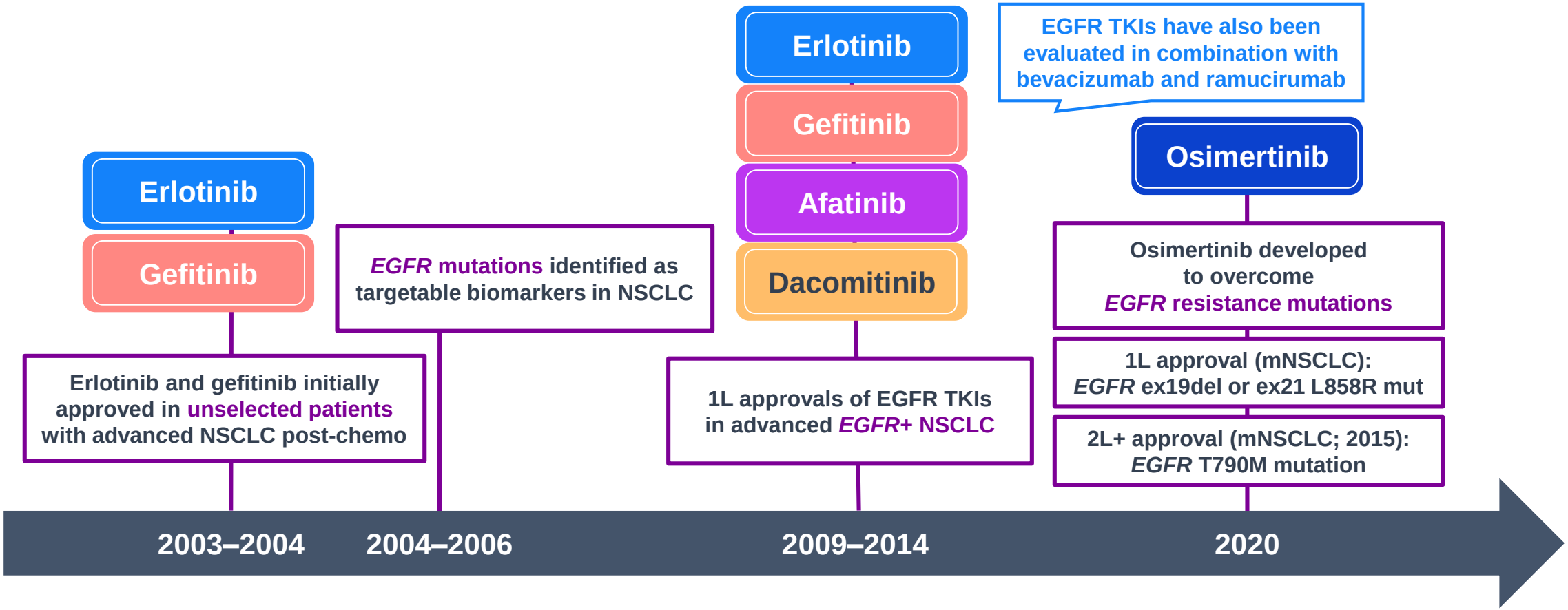
Please report suspected adverse reactions to the National Health Authority in your country and/or Roche Safety contact in your country (www.roche.com and select your country)

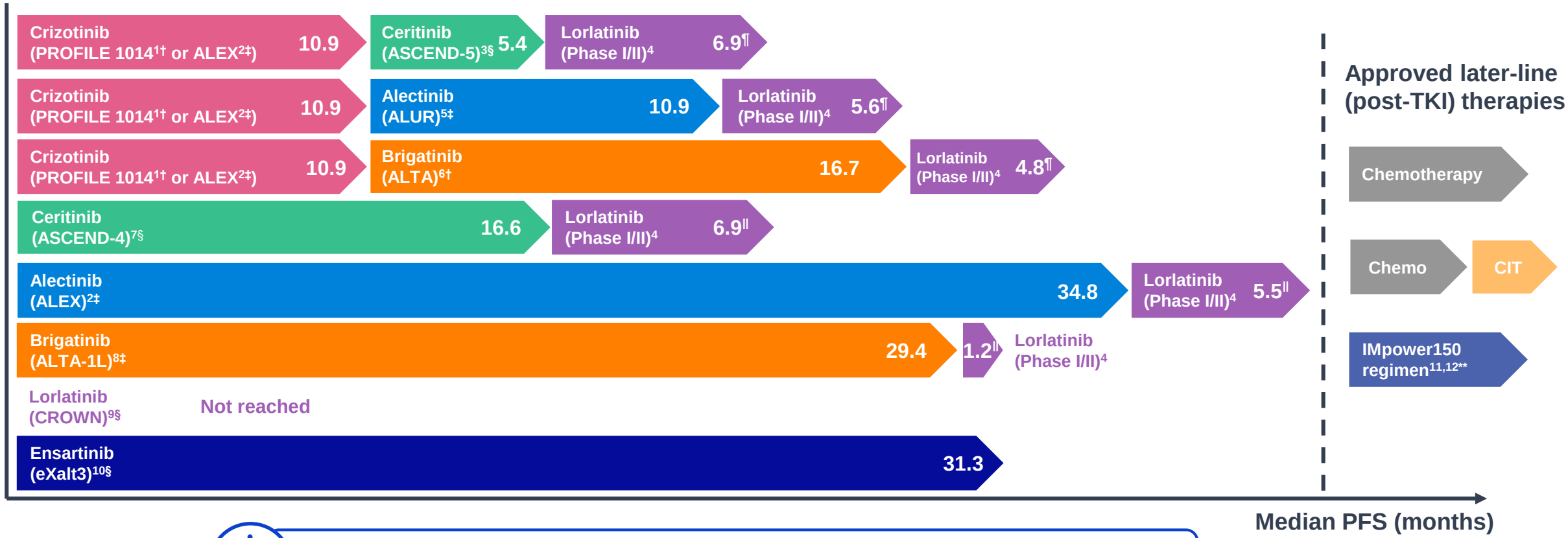
1. Pakkala & Ramalingam. JCI Insight 2018; 2. Barlesi, et al. Lancet 2016; 3. Tian, et al. Lung Cancer 2017; 4. Qiu, et al. Sci Rep 2020; 5. Gainor & Shaw. Oncologist 2013; 6. Bergethon, et al. J Clin Oncol 2012; 7. Dugay, et al. Oncotarget 2017; 8. Farago, et al. JCO Precis Oncol 2018

EGFR was the first actionable marker discovered in advanced/metastatic NSCLC



Russo, et al. Oncotarget 2015

There are now treatment sequence options for patients with advanced *ALK*+ NSCLC



Treatment decisions are based on a balance between efficacy and safety of the drug to ensure the best outcomes for patients

Adapted and updated from Ferrara et al, 2018 for illustration purposes only;[13] note that cross-trial comparisons should be interpreted with caution due to differences in study design, size, patient population and data maturity

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Median PFS for ALK TKIs that are currently approved in the 1L or ≥2L setting are shown; †Median PFS by IRC; ‡Median PFS by INV; §Median PFS by BIRC; ¶Data are from the EXP4 + EXP5 group (patients with two or three prior ALK TKIs ± CT [ceritinib (n=34), alectinib (n=49) and brigatinib (n=7) as the last prior ALK TKI before lorlatinib]); ‖Data are from the EXP3B group (patients with one prior ALK TKI ± CT [ceritinib (n=13), alectinib (n=13) or brigatinib (n=1) as the last prior ALK TKI before lorlatinib]); **EMA-approved only (the IMpower150 regimen is not FDA-approved for use in pretreated, advanced *ALK*+ NSCLC).

1. Solomon, et al. N Eng J Med 2014; 2. Mok, et al. Ann Oncol 2020; 3. Shaw, et al. Lancet Oncol 2017; 4. Felip, et al. Ann Oncol 2021; 5. Wolf, et al. ESMO Open 2022; 6. Huber, et al. J Thorac Oncol 2020; 7. Soria, et al. Lancet 2017; 8. Camidge, et al. J Clin Oncol 2020; 9. Solomon, et al. AACR 2022; 10. Wu, et al. WCLC 2020; 11. Socinski, et al. ASCO 2018; 12. TECENTRIQ SmPC (EMA: https://www.ema.europa.eu/en/documents/product-information/tecentriq-epar-product-information_en.pdf); 13. Ferrara, et al. J Thorac Oncol 2018

The development of multiple targeted therapies has revolutionised the treatment landscape in advanced NSCLC

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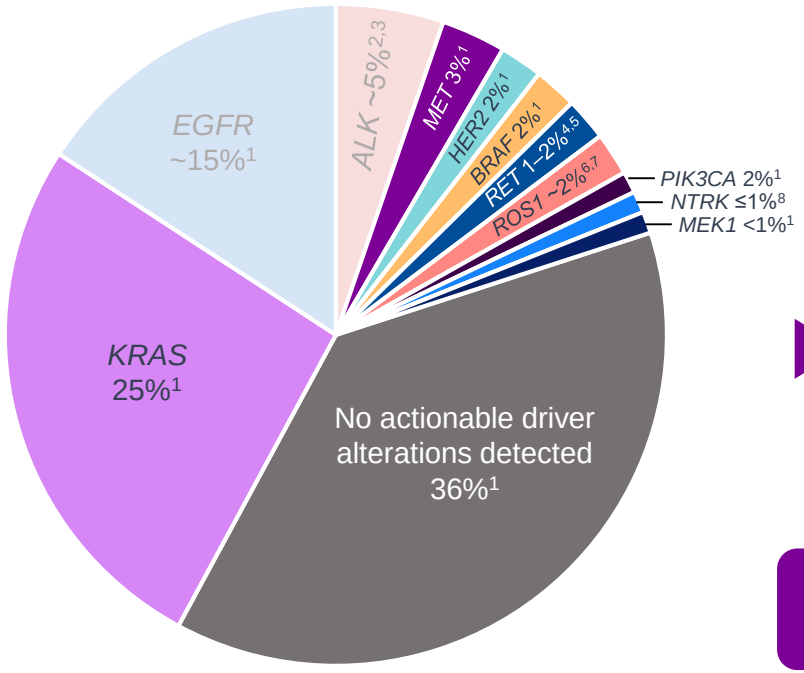

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Crizotinib and entrectinib▼ are approved 1L ROS1 inhibitors for the treatment of patients with advanced *ROS1* fusion-positive NSCLC

	Crizotinib[1,2] (N=53)
Median survival follow-up, months	62.6
ORR, % (95% CI)	**72*** (58, 83)
Median DoR, months (95% CI)	**24.7** (15.2, 45.3)
Median PFS, months (95% CI)	**19.3** (15.2, 39.1)
Median OS, months (95% CI)	**51.4** (29.3, NR)

There is limited evidence on the CNS efficacy of crizotinib[3–5]

Crizotinib†

Key trial:
PROFILE 1001[1,2]

Note that cross-trial comparisons should be interpreted with caution due to the differences in study design, size, patient population and data maturity

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Please report suspected adverse reactions to the National Health Authority in your country and/or Roche Safety contact in your country (www.roche.com and select your country). *Primary endpoint was investigator-assessed ORR; †Crizotinib is approved by the US FDA (https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/202570s030lbl.pdf) and EU EMA (https://www.ema.europa.eu/en/documents/product-information/xalkori-epar-product-information_en.pdf) for this indication. NR, not reached

1. Shaw, et al. Ann Oncol 2019; 2. https://clinicaltrials.gov/ct2/show/NCT00585195; 3. Shaw, et al. Ann Oncol 2019; 4. Costa, et al. J Clin Oncol 2011; 5. Dagogo-Jack & Shaw. Ann Oncol 2016

Crizotinib and entrectinib▼ are approved 1L ROS1 inhibitors for the treatment of patients with advanced *ROS1* fusion-positive NSCLC

	Entrectinib[1] (N=172)
Median survival follow-up, months	37.8
ORR, % (95% CI)	**67.4**† (59.9, 74.4)
Median DoR, months (95% CI)	**20.4**† (14.8, 34.8)
Median PFS, months (95% CI)	**16.8** (12.2, 22.4)
Median OS, months (95% CI)	**44.1** (40.1, NE)
CNS ORR, % (95% CI)	*n=51* **49.0** (34.8, 63.4)

Entrectinib*

Key trials:
STARTRK-NG,[2] **ALKA-372-001, STARTRK-1 and STARTRK-2**[1,3]

An ongoing, randomised, phase III head-to-head trial aims to directly compare the efficacy and safety of entrectinib and crizotinib in patients with advanced/ metastatic *ROS1* fusion-positive NSCLC[4]

Repotrectinib[5] **and lorlatinib**[6] **are other investigational ROS1 inhibitors in development and not approved for 1L treatment of patients with advanced *ROS1* fusion-positive NSCLC**

Note that cross-trial comparisons should be interpreted with caution due to the differences in study design, size, patient population and data maturity

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Please report suspected adverse reactions to the National Health Authority in your country and/or Roche Safety contact in your country (www.roche.com and select your country). *Entrectinib is approved by the US FDA (https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212725s000lbl.pdf) and the EU EMA (https://www.ema.europa.eu/en/documents/product-information/rozlytrek-epar-product-information_en.pdf) for this indication; †Primary endpoints were ORR and DoR. NE, not estimable

1. Fan, et al. WCLC 2022 (Abs 879); 2. Desai, et al. Neuro Oncol 2022; 3. Entrectinib trials: NCT02097810, NCT02568267, EudraCT 2012-000148-8;
4. Dingemans, et al. J Clin Oncol 2022; 5. Yun, et al. Clin Cancer Res 2020; 6. Shaw, et al. Lancet Oncol 2019

Selpercatinib and pralsetinib▼ are RET inhibitors for the treatment of patients with advanced *RET* fusion-positive NSCLC

	Selpercatinib[1]	
	Prior platinum treatment (n=247)	**Treatment naïve (n=69)**
Median survival follow-up, months	24.7	21.9
ORR, %* (95% CI)	**61.1** (54.7, 67.2)	**84.1** (73.3, 91.8)
Median DoR, months (95% CI)	**28.6**† (20.4, NE)	**20.2**† (13.0, NE)
Median PFS, months (95% CI)	**24.9**† (19.3, NE)	**22.0**† (13.8, NE)
CNS ORR, % (95% CI)	*n=26* **84.6** (65.1, 95.6)	

Selpercatinib

Key trials:
LIBRETTO-001[1]
LIBRETTO-431[2]

Selpercatinib is approved for the **1L treatment** of patients with advanced RET fusion-positive NSCLC in the **US and EU**[3,4]

Note that cross-trial comparisons should be interpreted with caution due to the differences in study design, size, patient population and data maturity
The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Please report suspected adverse reactions to the National Health Authority in your country and/or Roche Safety contact in your country (www.roche.com and select your country). *Primary endpoint; IRC-assessed; †Data are immature
NE, not estimable
1. Drilon, et al. ELCC 2022 (Abs 27P); 2. https://clinicaltrials.gov/ct2/show/NCT04194944
3. RETSEVMO Prescribing Information (FDA: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213246s000lbl.pdf)
4. European Commission: RETSEVMO Product Information (https://ec.europa.eu/health/documents/community-register/html/h1527.htm)

Selpercatinib and pralsetinib▼ are RET inhibitors for the treatment of patients with advanced *RET* fusion-positive NSCLC

	Pralsetinib[1]	
	Prior platinum treatment (n=126)	**Treatment naïve (n=68)**
ORR, %*† (95% CI)	**62** (53, 70)	**79** (68, 88)
Median DoR, months† (95% CI)	**22.3** (15.1, NR)	**NR** (9.0, NR)
Median follow-up, months	16.7	7.4
Median PFS, months† (95% CI)	*n=136* **16.5** (10.5, 24.1)	*n=75* **13.0**§ (9.1, NR)
Median follow-up, months	18.4	9.2
Intracranial ORR, % (95% CI)	*n=10* **70** (35, 93)	

Pralsetinib

Key trials:
ARROW[1]
AcceleRET-LUNG[2]

Pralsetinib is approved for the **1L treatment** of patients with advanced RET fusion-positive NSCLC in the **US and EU**[3,4]

See updated ARROW data in the **poster** session on Monday, 12.00 CEST

Note that cross-trial comparisons should be interpreted with caution due to the differences in study design, size, patient population and data maturity
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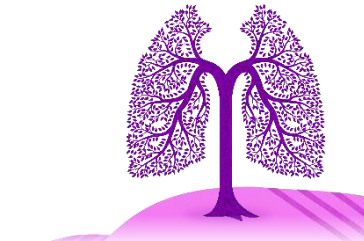
▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Please report suspected adverse reactions to the National Health Authority in your country and/or Roche Safety contact in your country (www.roche.com and select your country). *Co-primary endpoint; BICR-assessed; †The measurable disease population is the primary population for analysis for ORR and DOR and the efficacy population is the primary population for analysis for PFS; §Data are immature. NR, not reached

1. Griesinger, et al. Ann Oncol 2022; 2. https://clinicaltrials.gov/ct2/show/NCT04222972
3. GAVRETO Prescribing Information (FDA: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213721s000lbl.pdf)
4. GAVRETO SmPC (EMA: https://www.ema.europa.eu/en/documents/product-information/gavreto-epar-product-information_en.pdf)

KRAS inhibitors are emerging treatments for patients with advanced NSCLC harbouring a *KRAS* G12C mutation



Sotorasib[1–6]

Sotorasib is **approved** in the US and EU
for patients with **previously treated**
KRAS G12C mutation-positive advanced NSCLC[1,2]

Phase II multicentre, open-label trial (monotherapy)[3,4]
ORR: 37% (n=46/126)
21% of patients had ≥1 grade 3–5 TRAE

Phase Ib multicentre, open-label trials (CIT combo)[5–6]
ORR: 29% (n=17/58)
Grade 3–4 TRAE were mostly liver enzyme elevations

Updated sotorasib data will be presented at the **Presidential Symposium III** on Monday, 16.30 CEST

Note that cross-trial comparisons should be interpreted with caution due to the differences in study design, size, patient population and data maturity
The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
1. LUMAKRAS Prescribing Information (FDA: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214665s000lbl.pdf); 2. LUMAKRAS SmPC (EMA: https://www.ema.europa.eu/en/documents/product-information/lumykras-epar-product-information_en.pdf); 3. Skoulidis, et al. N Engl J Med 2021; 4. https://clinicaltrials.gov/ct2/show/NCT03600883; 5. Li, et al. WCLC 2022 (Abs OA03.06);
6. https://clinicaltrials.gov/ct2/show/NCT04185883

KRAS inhibitors are emerging treatments for patients with advanced NSCLC harbouring a *KRAS* G12C mutation

Sotorasib[1–6]

Sotorasib is **approved** in the US and EU for patients with **previously treated** *KRAS* G12C mutation-positive advanced NSCLC[1,2]

Phase II multicentre, open-label trial (monotherapy)[3,4]
ORR: 37% (n=46/126)
21% of patients had ≥1 grade 3–5 TRAE

Phase Ib multicentre, open-label trials (CIT combo)[5–6]
ORR: 29% (n=17/58)
Grade 3–4 TRAE were mostly liver enzyme elevations

Adagrasib[7]

Adagrasib and **GDC-6036** are investigational KRAS inhibitors in development and **not approved** for treatment of patients with advanced NSCLC harbouring a *KRAS* G12C mutation

GDC-6036[8,9]

Phase I dose-escalation trial (monotherapy)[8,9]
Unconfirmed ORR: 53% (n=30/57)
17% of patients had ≥1 grade 3–5 TRAE

Note that cross-trial comparisons should be interpreted with caution due to the differences in study design, size, patient population and data maturity
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1. LUMAKRAS Prescribing Information (FDA: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214665s000lbl.pdf); 2. LUMAKRAS SmPC (EMA: https://www.ema.europa.eu/en/documents/product-information/lumykras-epar-product-information_en.pdf); 3. Skoulidis, et al. N Engl J Med 2021; 4. https://clinicaltrials.gov/ct2/show/NCT03600883; 5. Li, et al. WCLC 2022 (Abs OA03.06); 6. https://clinicaltrials.gov/ct2/show/NCT04185883; 7. Jänne, et al. N Engl J Med 2022; 8. Sacher, et al. WCLC 2022 (OA03.04); 9. https://clinicaltrials.gov/ct2/show/NCT04449874

KRAS inhibitors are also being studied in combination with other agents

Combinations may depend on trial design and setting

Examples of KRAS inhibitor + SHP2 inhibitor studies

CodeBreak 101 *(multi-arm trial)*: **≥2L sotorasib + RMC-4630**[1,2]

- Preliminary data (n=6) in patients with KRAS G12C inhibitor-naïve NSCLC showed promising disease control rates (100%)
- 22% of patients treated with the combination had a grade ≥3 TRAE

NCT04449874 *(multi-arm trial)*: **GDC-6036 + GDC-1971**[3]

- Ongoing phase I/Ib dose-escalation and dose-expansion trial

Examples of KRAS inhibitor + other agents studies

NCT04449874 *(multi-arm trial)*: **GDC-6036 + atezolizumab, cetuximab, bevacizumab, erlotinib, or inavolisib**[3]

- Ongoing phase I/Ib dose-escalation and dose-expansion trial

NCT05375994: VS-6766 (RAF/MEK clamp) + adagrasib[4,5]

- Ongoing phase I/II, multicentre non-randomised open-label trial

No combination treatments are currently licenced for KRAS inhibitors
Note that cross-trial comparisons should be interpreted with caution due to the differences in study design, size, patient population and data maturity
The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
1. https://clinicaltrials.gov/ct2/show/NCT04185883; 2. Falchook, et al. WCLC 2022 (Abs OA03.03); 3. https://clinicaltrials.gov/ct2/show/NCT04449874
4. https://clinicaltrials.gov/ct2/show/NCT05375994; 5. Minchom, et al ASCO 2022 (Abs 9018)
Information from clinicaltrials.gov correct as of 10 September 2022

We now understand and manage NSCLC as a disease of both genomic and immunological complexity

Lung driver mutations

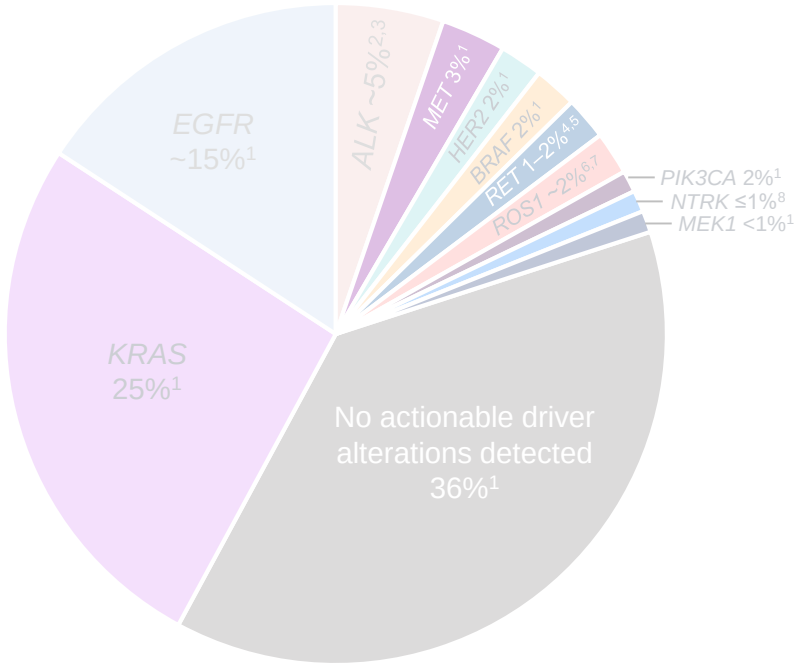
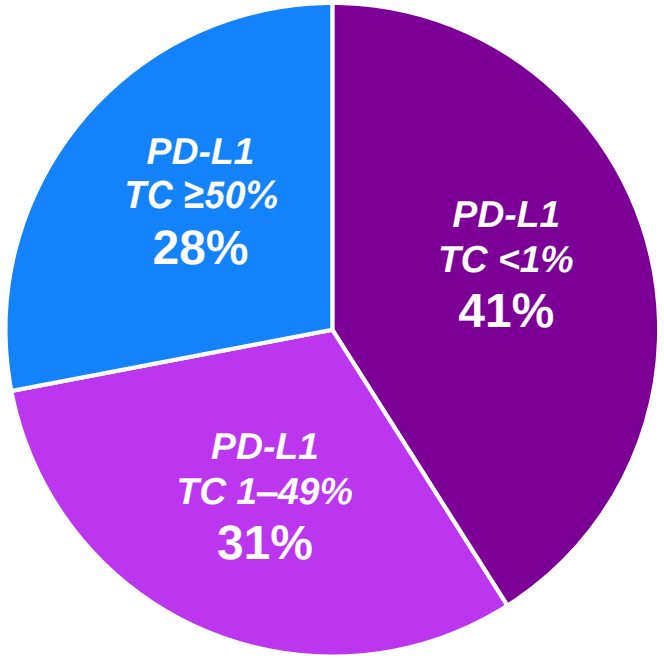


Figure adapted from Pakkala & Ramalingam. JCI Insight 2018

PD-L1 expression[8–14] (Expression on TCs*)



The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU

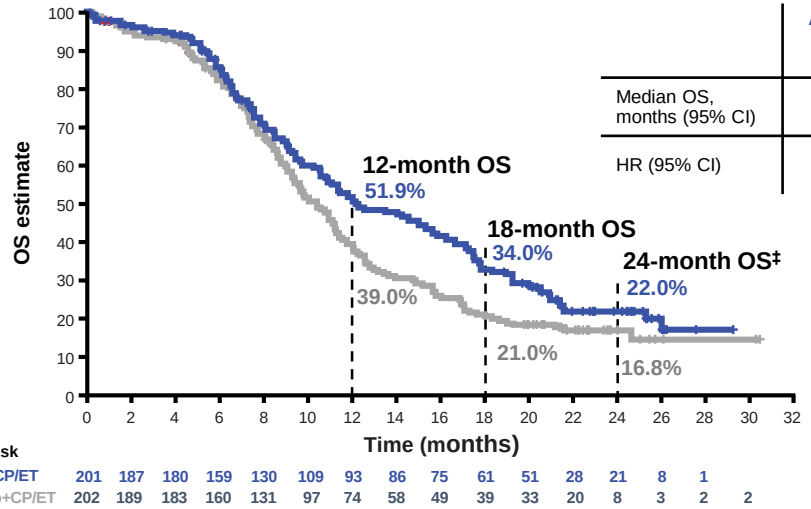
*PD-L1 high is TC/TPS ≥50%, PD-L1 low is TC/TPS 1–49%, PD-L1 negative is TC/TPS <1%

1. Pakkala & Ramalingam. JCI Insight 2018; 2. Barlesi, et al. Lancet 2016; 3. Tian, et al. Lung Cancer 2017; 4. Qiu, et al. Sci Rep 2020; 5. Gainor & Shaw. Oncologist 2013; 6. Bergethon, et al. J Clin Oncol 2012; 7. Dugay, et al. Oncotarget 2017; 8. Wakelee, et al. ASCO 2021; 9. Carbone, et al. WCLC 2021; 10. Forde, et al. AACR 2021 (Abs CT003); 11. Kowanetz, et al. AACR 2018; 12. Gandhi, et al. N Engl J Med 2018; 13. Paz-Ares, et al. N Engl J Med 2018; 14. Paz-Ares, et al. Lancet 2021

SCLC is an aggressive disease that remains difficult to treat

- Most patients present with extensive-stage (ES) disease, poor overall prognosis, a high incidence of brain metastases and comorbidities[1,2]
- **IMpower133** first established **CIT + chemotherapy as a standard of care in international guidelines[3] for patients with 1L ES-SCLC**, after more than 20 years without meaningful improvements in OS[4]

IMpower133 overall survival[5,6]



	Atezolizumab + CP/ET (N=201)	Placebo + CP/ET (N=202)
Median OS, months (95% CI)	12.3 (10.8, 15.8)	10.3 (9.3, 11.3)
HR (95% CI)	0.76 (0.60, 0.95) *p*=0.0154*	

- The **CASPIAN** trial later showed a median OS of 13.0 months for durvalumab + chemotherapy vs 10.3 months for the chemotherapy arm (HR=0.73; *p*=0.0047)[7]

*Provided for descriptive purposes only. ‡With a median follow-up of 22.9 months, 24-month landmark estimates are still unstable

1. Carter, et al. RadioGraphics 2014; 2. Sabari, et al. Nat Rev Clin Oncol 2017; 3. Dingemans, et al. Ann Oncol 2021; 4. Horn et al. New Engl J Med 2018; 5. Reck, et al. ESMO 2019 (Abs 1736O); 6. Liu, et al. ESMO 2020 (Abs 1781MO); 7. Paz Ares, et al. Lancet 2019

Challenges with SCLC

Unlike NSCLC, there are currently **no actionable biomarkers** for 1L treatment of SCLC

PD-L1 expression is low on SCLC tumour cells[1]

The phase III IMpower133 and CASPIAN studies **showed no correlation between outcomes and PD-L1 expression**[2,3]

SCLC subtypes do not have a known clinical utility – further understanding is required to meet the **high unmet need** for new treatment options in SCLC[4,5]

Development of new treatment options remains challenging in SCLC

Anti-PD(L)1 + Anti-TIGIT + chemo

SKYSCRAPER-02:
1L atezolizumab + tiragolumab[6,7]

- Co-primary endpoints: PFS not met, OS unlikely to reach statistical significance
- **Control arm of atezolizumab + chemotherapy performed as expected** (mOS = 13.6 months), replicating the clinically meaningful results of **IMpower133**[8]
- Study **included patients with treated or untreated asymptomatic brain metastases**
- No new safety signals identified

KEYVIBE-008:
1L pembrolizumab + vibostolimab + chemo[9]

- Ongoing trial, currently enrolling (target enrolment N=450)

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU

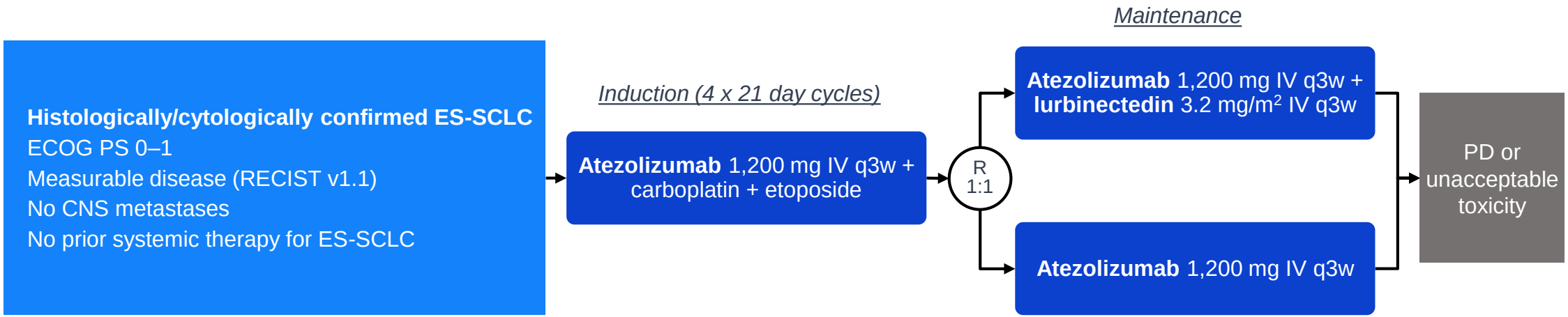
1. Antonia, et al. Lancet Oncol 2016; 2. Horn, et al. AACR 2020 (Abs CT220); 3. Paz-Ares, et al. ESMO 2019 (Abs LBA89); 4. Sabari, et al. Nat Rev Clin Oncol 2017; 5. Gay, et al Cancer Cell 2021; 6. https://www.clinicaltrials.gov/ct2/show/NCT04256421; 7. Rudin, et al. ASCO 2022; 8. Horn, et al. N Engl J Med 2018; 9. https://www.clinicaltrials.gov/ct2/show/NCT05224141
Information from clinicaltrials.gov correct as of 10 September 2022

Other anti-PD-L1 combinations are being investigated in 1L ES-SCLC

Anti-PD-L1 + transcription inhibitor

IMforte: 1L atezolizumab + lurbinectedin as maintenance treatment[1]

- Lurbinectedin has already shown encouraging activity in combination with atezolizumab in the phase I/II 2SMALL trial[2]



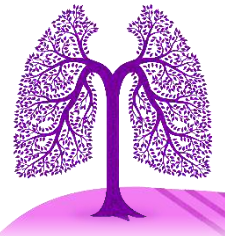
Primary endpoints: PFS and OS

- **Ongoing trial, currently enrolling**

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU

ES-SCLC, extensive-stage small-cell lung cancer; 1. https://clinicaltrials.gov/ct2/show/NCT05091567; 2. Ponce Aix, et al. SITC 2021 (Abs 464)
Information from clinicaltrials.gov correct as of 10 September 2022

In NSCLC, many 1L cancer immunotherapy (CIT) regimens are approved



CIT monotherapy

- Atezolizumab
- Cemiplimab
- Pembrolizumab*

PD-L1 high NSCLC

CIT + chemotherapy

- Atezolizumab + carboplatin + nab-paclitaxel (NSQ)
- Pembrolizumab + pemetrexed + platinum chemotherapy (NSQ)
- Pembrolizumab + carboplatin + paclitaxel (SQ)

CIT + chemotherapy + anti-VEGF

- Atezolizumab + bevacizumab + carboplatin + paclitaxel

NSQ only

CIT + CIT

- Nivolumab + ipilimumab

FDA only, PD-L1 positive NSCLC

CIT + CIT + chemotherapy

- Nivolumab + ipilimumab + chemotherapy

CIT regimens are well established in NSCLC, but not all patients respond to treatment

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
*Approved in PD-L1 positive NSCLC in some regions
NSQ, non-squamous; SQ, squamous

What evidence can we follow when making decisions between treatment paradigms?

Evidence suggests actionable driver mutations should be targeted before CIT therapy is given

Limited evidence for efficacy of CIT monotherapy in *EGFR*+ NSCLC[1,2]

Emerging evidence of toxicity if CIT monotherapy is given before TKI therapy in *EGFR*+ NSCLC

- No efficacy and concerning AE profile in a phase II feasibility study of CIT in TKI-naïve, PD-L1+ and *EGFR*+ NSCLC[3]
- Severe immune-related AEs were observed when osimertinib was given after CIT in a retrospective study of 126 patients at MSKCC[4]

MSKCC, Memorial Sloan Kettering Cancer Center

1. Lee, et al. JAMA Oncol 2018; 2. Garon, et al. J Clin Oncol 2019; 3. Lisberg, et al. J Thorac Oncol 2018; 4. Schoenfeld, et al. Ann Oncol 2019

There are patients in the clinic who are not well represented in phase III trials

Patients **ineligible for platinum-doublet chemotherapy**

IPSOS phase III trial[1]

Stage IIIB–IV NSCLC — **N=453**

No prior systemic treatment for advanced disease

Patients deemed ineligible for platinum-doublet chemotherapy due to ECOG PS 2/3 or elderly with comorbidities/contraindications

No *EGFR*/*ALK*, any PD-L1 status

No active or untreated CNS metastases

R 2:1

Atezolizumab 1,200 mg IV q3w → **PD or loss of clinical benefit**

Vinorelbine (po or IV) **or gemcitabine** (IV) dosing per local SmPC → **PD**

Crossover not permitted

IPSOS met its primary endpoint of OS
Data will be presented on Monday, 16.30 CEST at the **Presidential Symposium III**

Patients with **untreated brain metastases**

ATEZO-BRAIN phase II trial[2,3]

Treatment-naïve, stage IV non-squamous NSCLC — **N=40**

Untreated brain metastases

No *EGFR*/*ALK*, any PD-L1 status

Measurable systemic and brain lesions, no neurologic symptom

Induction

Atezolizumab 1,200 mg + pemetrexed + carboplatin
IV q3w for 4–6 cycles

Maintenance

Pemetrexed + atezolizumab 1,200 mg

PD, unacceptable toxicity or max 2 years

- CIT + chemo was well tolerated and might delay the need for WBRT in some patients with untreated brain metastases[3]

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
OS, overall survival; WBRT, whole-brain radiotherapy. 1. https://clinicaltrials.gov/ct2/show/NCT03191786; 2. https://clinicaltrials.gov/ct2/show/NCT03526900; 3. Nadal et al. ASCO 2022 (Abs 9010)
Information from clinicaltrials.gov correct as of 10 September 2022

What are we doing to improve patient outcomes?

New CIT combinations to enhance the anti-tumour activity of anti-PD(L)1 agents

Anti-PD(L)1 + Anti-TIGIT

- First phase II data with this MoA: encouraging efficacy of **atezolizumab + tiragolumab** in **CITYSCAPE**[1]
- The phase III **SKYSCRAPER-01** trial (locally advanced/recurrent NSCLC with high PD-L1 expression, N=560) is ongoing[2]

- The atezolizumab + tiragolumab combination with or without chemotherapy is also currently being investigated across different lung cancer settings[2–5]

SKYSCRAPER-06 (phase II/III)
Previously untreated advanced non-squamous NSCLC in combination with chemotherapy (N=500)

SKYSCRAPER-03 (phase III)
Unresectable stage III NSCLC with no PD after concurrent platinum-based chemoradiation (N=800)

SKYSCRAPER-05 (phase II)
Resectable stage II, IIIA and select IIIB (T3N2) NSCLC (N=82)

- Other anti-PD(L)1 + anti-TIGIT trials are ongoing in 1L NSCLC, including:
  - **KEYVIBE-003**: Phase III trial of **pembrolizumab + vibostolimab**[6]
  - **ARC-10**: Phase III trial of **zimberelimab ± domvanalimab**[7]

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU.
1. Cho, et al. Lancet Oncology 2022; 2. https://clinicaltrials.gov/ct2/show/NCT04294810; 3. https://clinicaltrials.gov/ct2/show/NCT04619797; 4. https://clinicaltrials.gov/ct2/show/NCT04513925; 5. https://clinicaltrials.gov/ct2/show/NCT04832854; 6. https://clinicaltrials.gov/ct2/show/NCT04738487; 7. https://www.clinicaltrials.gov/ct2/show/NCT04736173
Information from clinicaltrials.gov correct as of 10 September 2022

What are we doing to reduce treatment burden?

Subcutaneous formulation to shorten administration time and treatment burden

Phase III IMscin001 trial (atezolizumab SC)[1,2]

Shorter administration time

Less invasive than IV

- **IMscin001 met its primary PK endpoints**
- **Consistent safety profile** compared with IV atezolizumab in patients with CIT-naïve, locally advanced or metastatic NSCLC

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
PK, pharmacokinetics
1. https://www.roche.com/media/releases/med-cor-2022-08-02; 2. https://clinicaltrials.gov/ct2/show/NCT03735121
Information from clinicaltrials.gov correct as of 10 September 2022

ESMO 2022 Industry Satellite Symposium

Redefining Lung Cancer **Together:** Now and Next

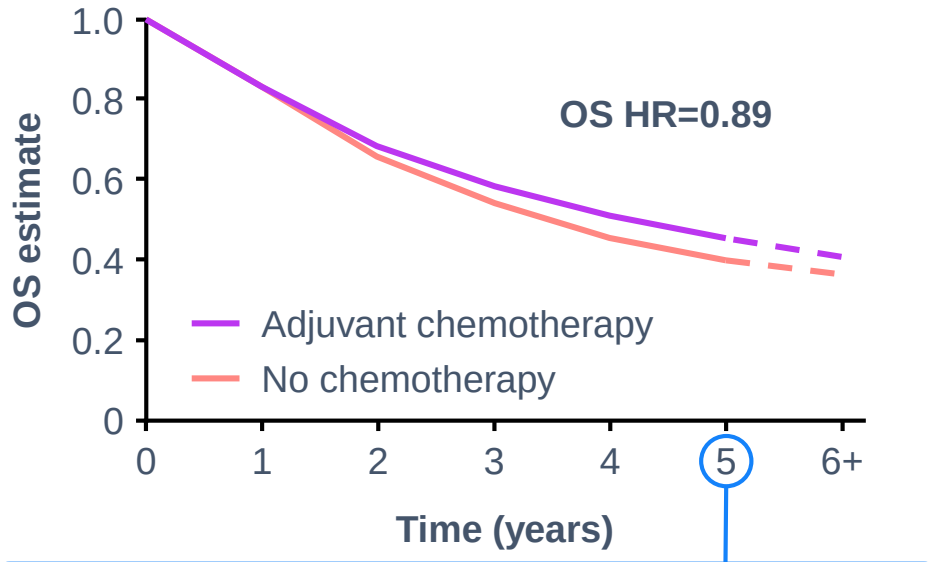
Martin Reck

LungenClinic
Großhansdorf, Germany

Treatment choice in resectable lung cancer: New insights, new outlooks

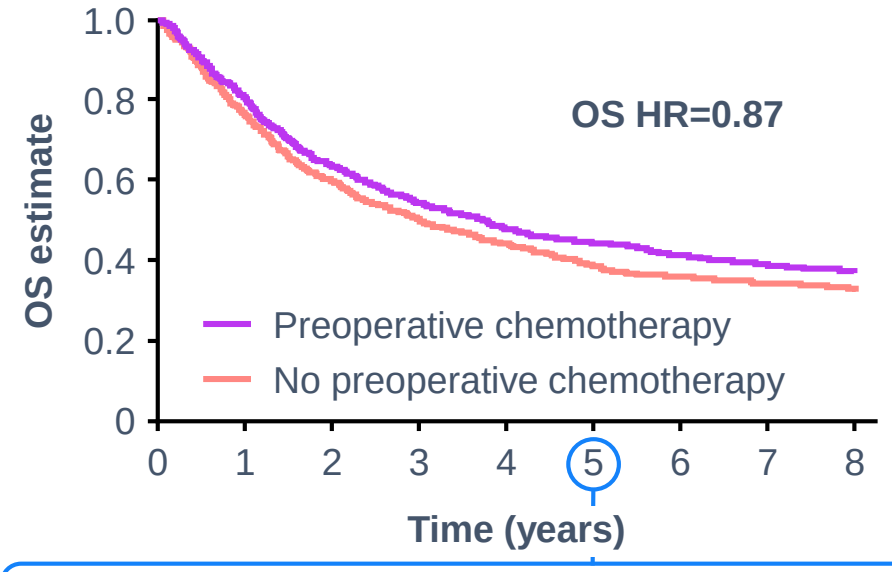
In the early-stage NSCLC setting, adjuvant and neoadjuvant chemotherapy have resulted in a modest benefit

Adjuvant chemotherapy vs no chemotherapy (LACE meta-analysis)[1]



~5% improvement in 5-year OS across all patients

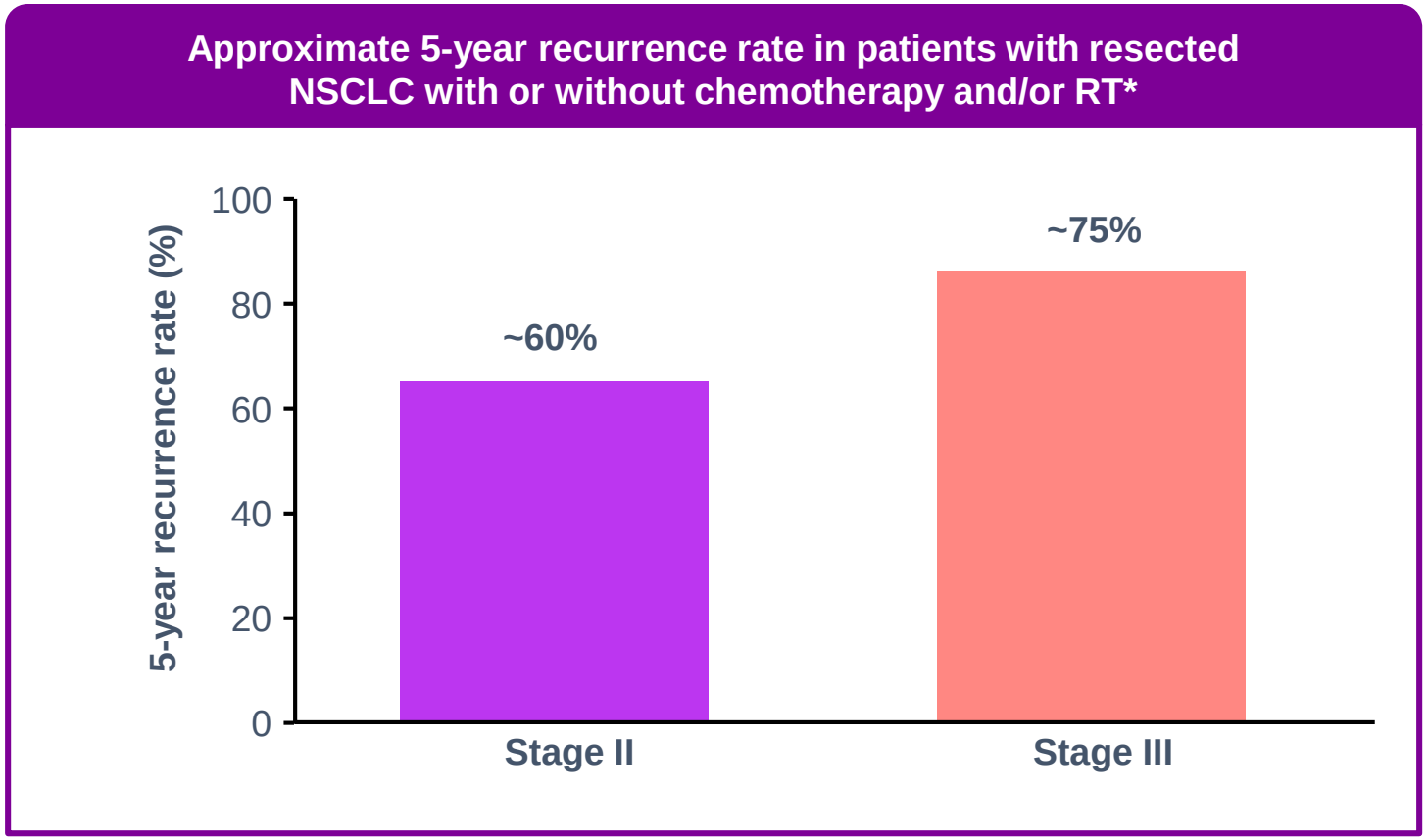
Neoadjuvant chemotherapy vs no chemotherapy (NSCLC meta-analysis collaborative group)[2]



~5% improvement in 5-year OS across all patients

1. Pignon, et al. *Lung adjuvant cisplatin evaluation: A pooled analysis by the LACE Collaborative Group*. J Clin Oncol 2008;26(21):3552–3559. https://ascopubs.org/doi/pdf/10.1200/JCO.2007.13.9030;
2. NSCLC Meta-analysis Collaborative Group. Lancet 2014. Reproduced with permission from Elsevier under CC-BY license

We need new options because the risk of recurrence with stage II–III NSCLC remains high, despite availability of adjuvant chemotherapy



*Adapted from Figure 3, number of events for disease-free survival, in Pignon, et al. J Clin Oncol 2008
Pignon, et al. J Clin Oncol 2008

ADAURA: Improved DFS with adjuvant osimertinib vs placebo in patients with *EGFR*+, stage IB–III NSCLC

- **Completely resected, *EGFR*+, stage IB–IIIA NSCLC (AJCC 7th ed.)**
- Optional adjuvant chemotherapy

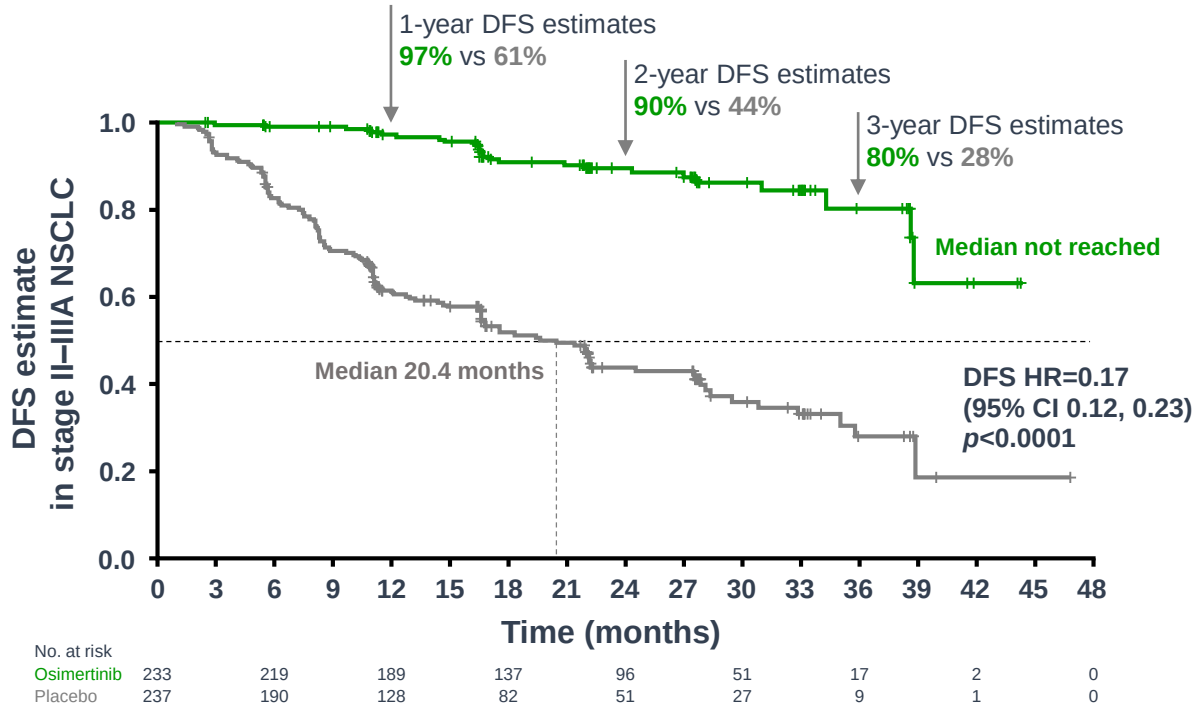
R 1:1

N=682

Osimertinib (80mg qd for 3 years)

Placebo (qd for 3 years)

Primary endpoint: DFS in stage II–IIIA



Ongoing phase III trials in EGFR+, resectable disease

NeoADAURA (NCT04351555)

Neoadjuvant osimertinib ± chemotherapy vs chemotherapy *EGFR*+, stage II–IIIB (N2)* NSCLC

ADAURA2 (NCT05120349)

Adjuvant osimertinib vs placebo *EGFR*+, stage IA2–IA3* NSCLC

The safety profile was consistent with the known safety profile of osimertinib

Ongoing study information correct based on clinicaltrials.gov as of 10 September 2022; *Per AJCC 8th edition

Herbst, et al. ASCO 2020 (Abs LBA5); Wu et al. N Engl J Med 2020
Information from clinicaltrials.gov correct as of 10 September 2022

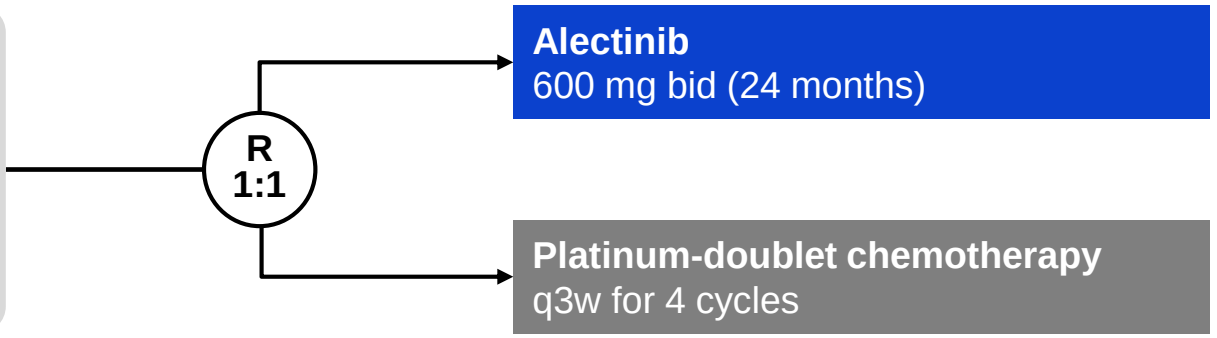
Ongoing phase III studies are investigating targeted therapies for other driver mutations in patients with resectable NSCLC

ALINA (adjuvant alectinib in resectable *ALK*+ NSCLC) – *first study to read out (2023; enrolment closed)*

Completely resected stage IB (≥4cm)–IIIA*
***ALK*+ NSCLC** (UICC/AJCC 7th edition)
ECOG PS 0–1

N=257

Stratification factors:
Disease stage (IB vs II vs III); race (Asian vs non-Asian)



Primary endpoint:
Investigator-assessed DFS

Secondary endpoints:
OS, safety, drug plasma concentration

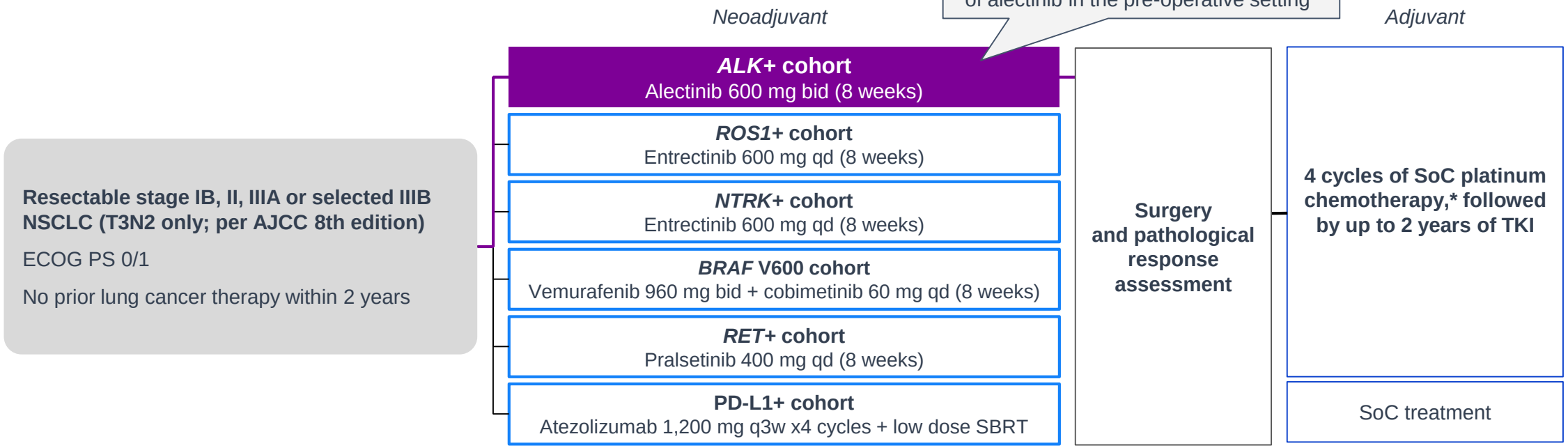
Ongoing phase III trials with later readout	
LIBRETTO-432 (NCT04819100)	Estimated primary readout: 2028
Adjuvant selpercatinib vs placebo *RET*+, stage IB–IIIA NSCLC	

*Per AJCC 7th edition
https://www.clinicaltrials.gov/ct2/show/NCT03456076
Information from clinicaltrials.gov correct as of 10 September 2022

Until phase III readouts, preliminary phase II data are available for driver mutations in patients with resectable NSCLC

NAUTIKA1 (neoadjuvant + adjuvant setting)[1]

Preliminary data (n=5) show that **neoadjuvant alectinib** was well tolerated, demonstrating the feasibility of alectinib in the pre-operative setting[2]



Primary endpoint:
- Investigator-assessed MPR rate

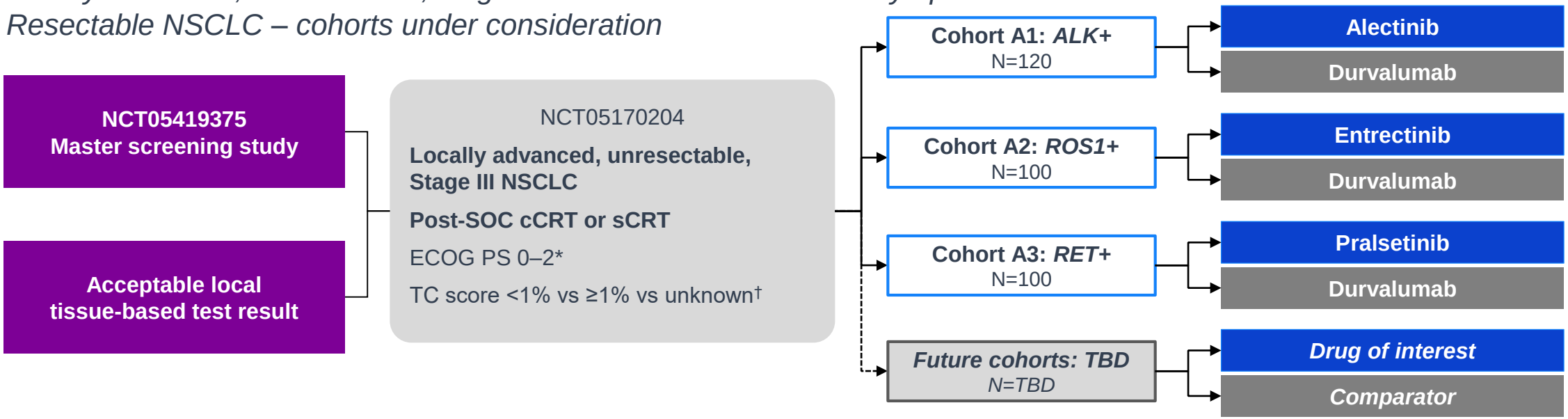
Key secondary endpoints:
Investigator-assessed radiographic response, pathologic CR, DFS, EFS, OS, safety

*Unless contraindicated or patient refusal. Molecular testing by local testing in CLIA certified laboratory or LCMC4 LEADER neoadjuvant screening trial
CR, complete response; MPR, major pathologic response; SBRT, stereotactic body radiotherapy
1. https://www.clinicaltrials.gov/ct2/show/NCT04302025; 2. Lee, et al. WCLC 2022 (Abs EP02.04-005)
Information from clinicaltrials.gov correct as of 10 September 2022

Platform studies evaluate multiple treatment regimens in multiple biomarker-defined patient populations

NCT05419375 & NCT05170204[1,2]

Locally advanced, unresectable, stage III NSCLC – cohorts currently open
Resectable NSCLC – cohorts under consideration

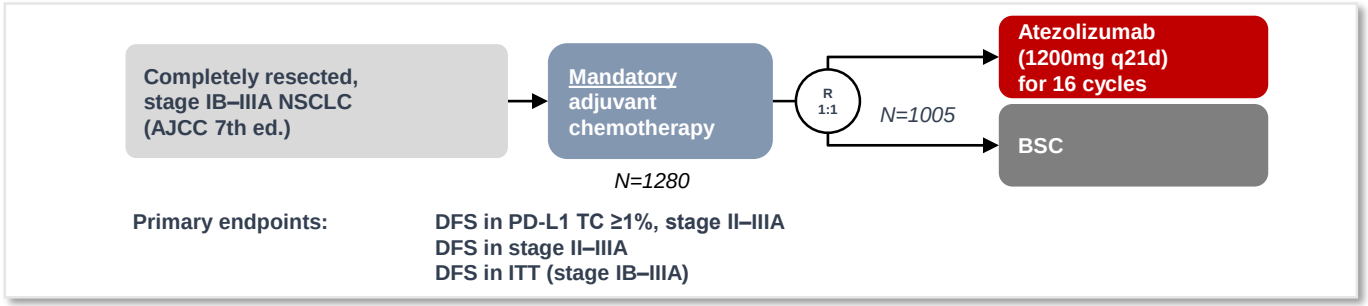


Primary endpoint:
- PFS per BICR

Key secondary endpoints:
Distant metastasis-free survival, Time to CNS progression, ORR, DoR, OS, Safety

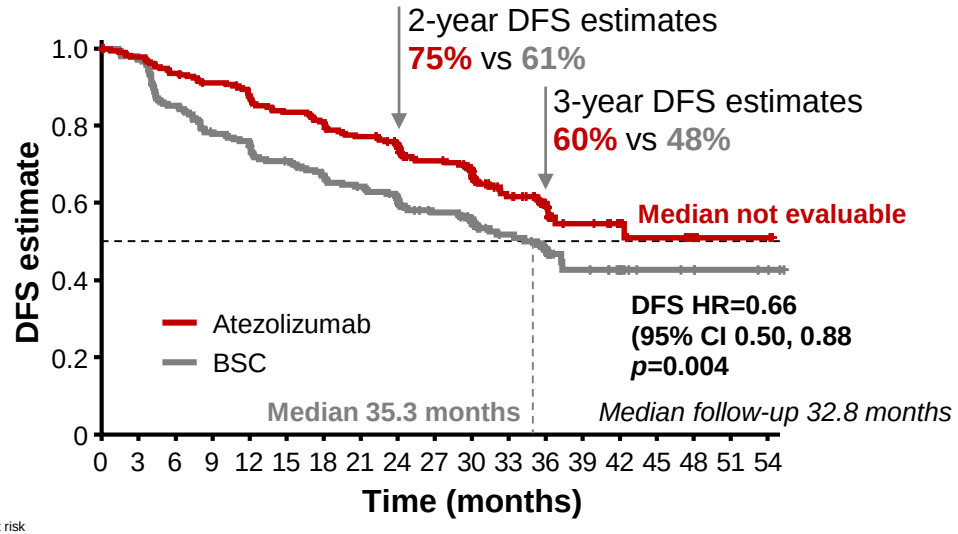
*For future cohorts, the ECOG PS inclusion criteria may differ; †Irrespective of assay (Local SP263 or 22c3 or Central SP263)
c/sCRT, concurrent/sequential chemoradiotherapy
1. https://clinicaltrials.gov/ct2/show/NCT05419375; 2. https://clinicaltrials.gov/ct2/show/NCT05170204
Information from clinicaltrials.gov correct as of 10 September 2022

IMpower010: Improved DFS was seen with atezolizumab in the PD-L1 TC ≥1%, stage II–IIIA population



DFS in PD-L1 TC ≥1%, stage II–IIIA NSCLC (co-primary endpoint)[1,2]

ASCO 2021 (DFS IA, data cut-off: 21 January 2021)

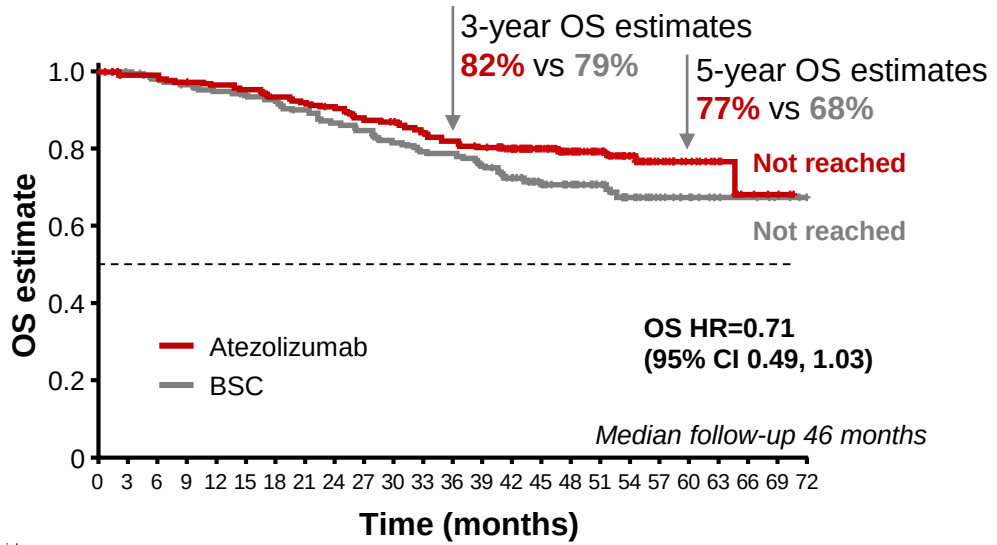


No. at risk

Atezolizumab	248	235	225	217	206	198	190	181	159	134	111	76	54	31	22	12	8	3	3
BSC	228	212	186	169	160	151	142	135	117	97	80	59	38	21	14	7	6	4	3

OS in PD-L1 TC ≥1%, stage II–IIIA NSCLC[3]*

WCLC 2022 (first OS IA, data cut-off: 18 April 2022)



No. at risk

Atezolizumab	248	241	241	237	234	231	225	222	218	210	208	200	195	190	172	140	1	16	83	56	37	23	12	5	3	NE
BSC	228	220	214	210	205	201	198	192	185	180	172	167	166	158	140	1	10	95	72	49	27	15	8	7	4	NE

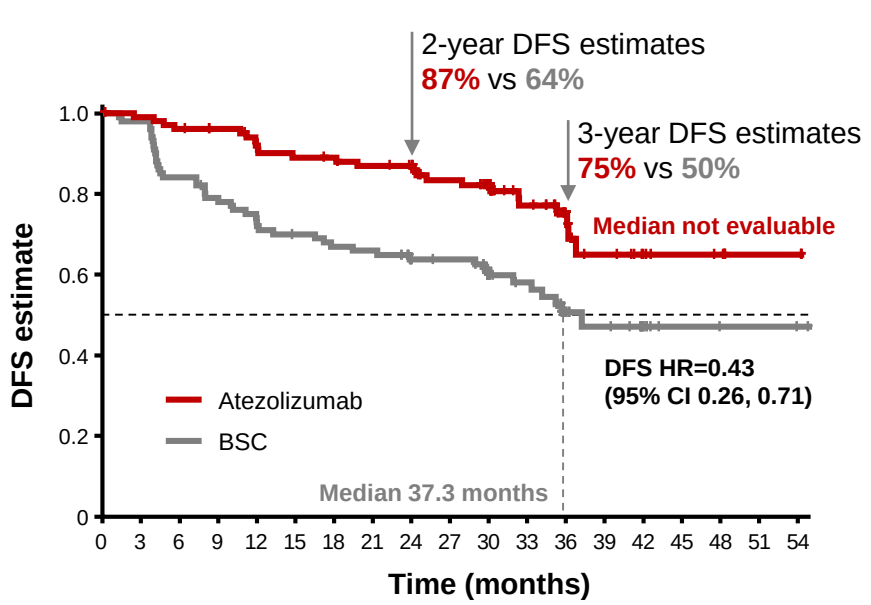
In the EU, TECENTRIQ (atezolizumab) is only indicated as monotherapy as adjuvant treatment following complete resection and platinum-based chemotherapy for adult patients with NSCLC with a high risk of recurrence whose tumours have PD-L1 expression on ≥50% of tumour cells and who do not have *EGFR* mutant or *ALK*-positive NSCLC
Unstratified HR. *At this first pre-specified OS IA, the OS data are still immature

1. Wakelee, et al. ASCO 2021 (Abs 8500); 2. Felip, et al. Lancet 2021; 3. Felip, et al. WCLC 2022 (Abs PL03.09)

IMpower010: The largest DFS benefit with atezolizumab was seen in the PD-L1 TC ≥50%, stage II–IIIA population

DFS in PD-L1 TC ≥50%, stage II–IIIA NSCLC[1]*

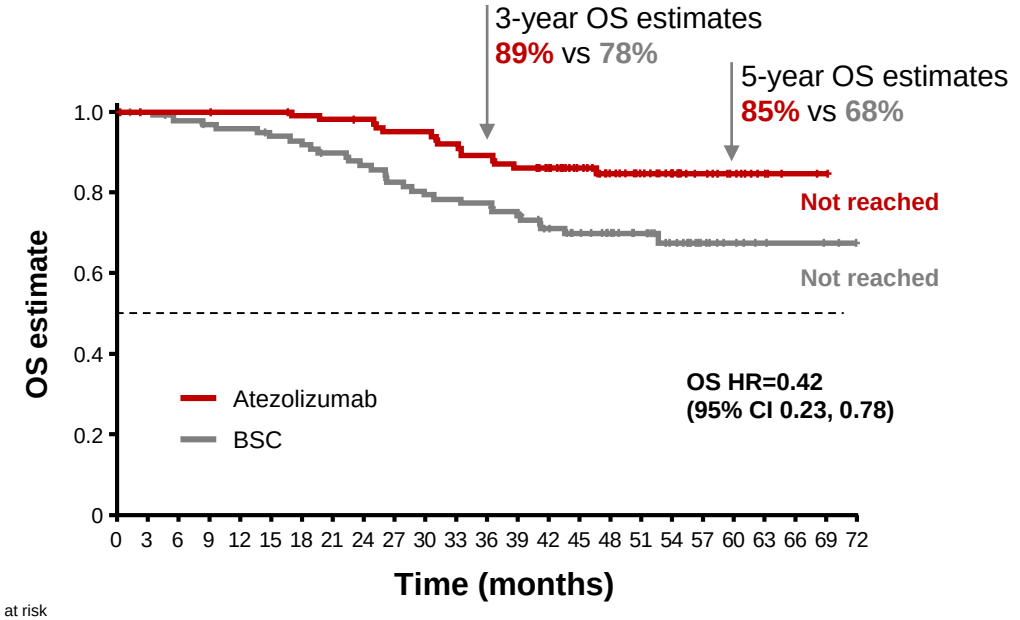
ELCC 2022 (DFS IA, data cut-off: 21 January 2021)



No. at risk										
Atezolizumab	106	98	89	87	78	56	26	9	4	1
BSC	103	84	72	65	57	42	17	9	3	2

OS in PD-L1 TC ≥50%, stage II–IIIA NSCLC[2]*‡

WCLC 2022 (first OS IA, data cut-off: 18 April 2022)



No. at risk																								
Atezolizumab	106	104	104	104	103	103	101	100	99	96	96	93	90	87	83	69	58	41	32	20	13	6	2	1	NE
BSC	103	101	98	96	95	92	90	87	84	80	77	76	75	71	64	52	45	35	24	14	8	4	3	2	NE

Unstratified HR

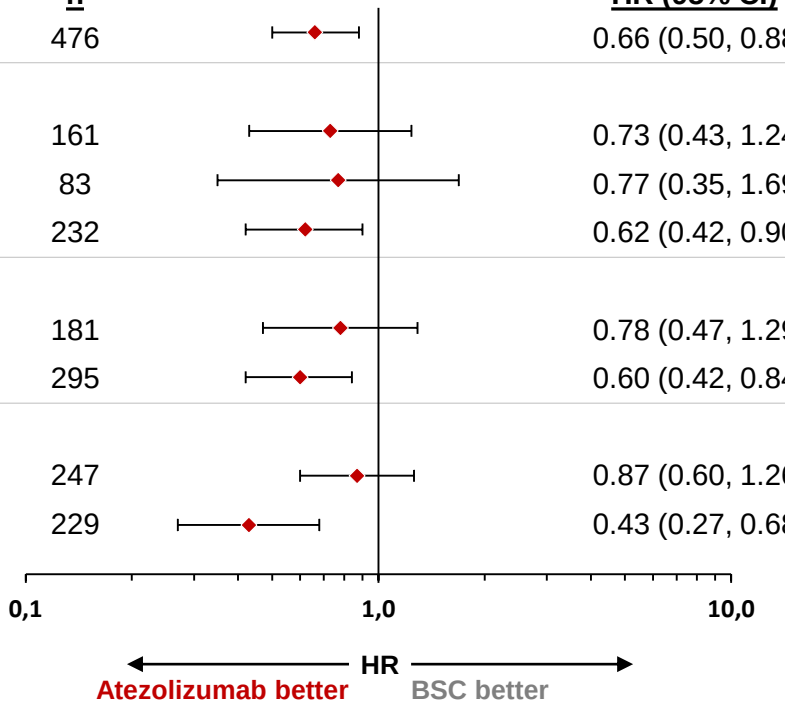
*Excluding patients with *EGFR*+/*ALK*+ NSCLC; ‡At this first pre-specified OS IA, the OS data are still immature

1. Felip, et al. ELCC 2022 (Abs 80O); 2. Felip, et al. WCLC 2022 (Abs PL03.09)

IMpower010: A DFS benefit was maintained across most key clinical subgroups

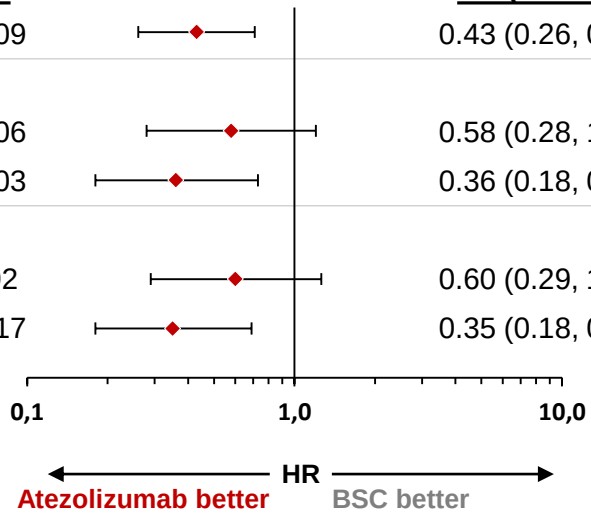
DFS subgroups in PD-L1 TC ≥1%, stage II–IIIA NSCLC[1,2]

Subgroup	n	HR (95% CI)‡
All patients	476	0.66 (0.50, 0.88)
Stage		
IIA	161	0.73 (0.43, 1.24)
IIB	83	0.77 (0.35, 1.69)
IIIA	232	0.62 (0.42, 0.90)
Histology		
Squamous	181	0.78 (0.47, 1.29)
Non-squamous	295	0.60 (0.42, 0.84)
PD-L1 expression status		
TC 1–49%§	247	0.87 (0.60, 1.26)
TC ≥50%	229	0.43 (0.27, 0.68)



DFS subgroups in PD-L1 TC ≥50%, stage II–IIIA NSCLC[3]*

Subgroup	n	HR (95% CI)¶
All patients	209	0.43 (0.26, 0.71)
Stage		
II	106	0.58 (0.28, 1.20)
IIIA	103	0.36 (0.18, 0.73)
Histology		
Squamous	92	0.60 (0.29, 1.26)
Non-squamous	117	0.35 (0.18, 0.69)

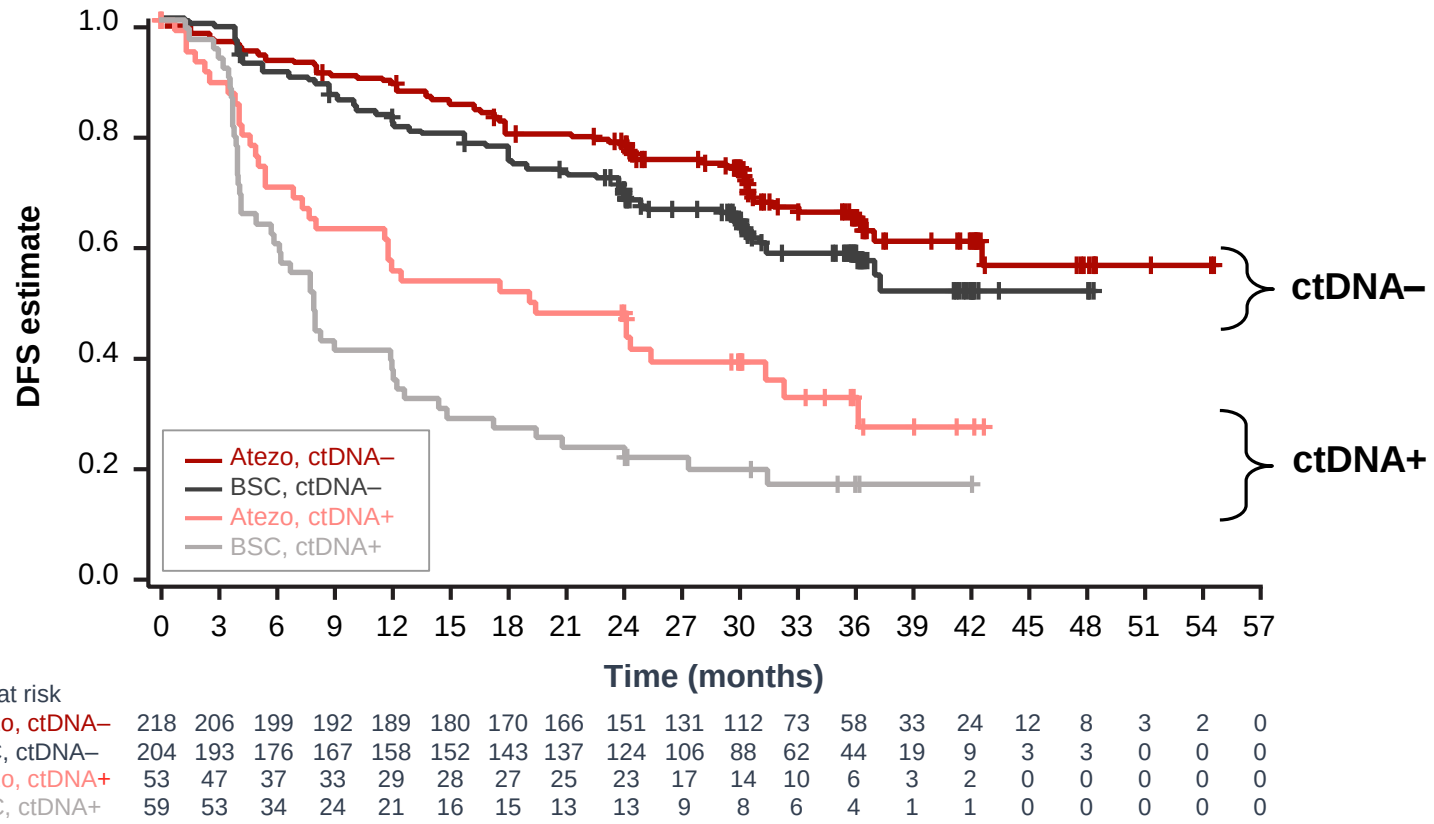


Grade 3–4 AEs occurred in 22% of the atezolizumab arm and 12% of the best supportive care arm[1]

Clinical cut-off: 21 January 2021
*Excluding patients with *EGFR*+/*ALK*+ NSCLC; ‡Stratified HRs for all patients, unstratified HRs for all other subgroups; §DFS analysis in the PD-L1 TC 1–49% subgroup was exploratory; ¶Unstratified HRs
1. Wakelee, et al. ASCO 2021 (Abs 8500); 2. Felip, et al. Lancet 2021; 3. Felip, et al. ELCC 2022 (Abs 80O)

IMpower010: ctDNA positivity was strongly prognostic

DFS in stage II–IIIA by **ctDNA status**



No. at risk

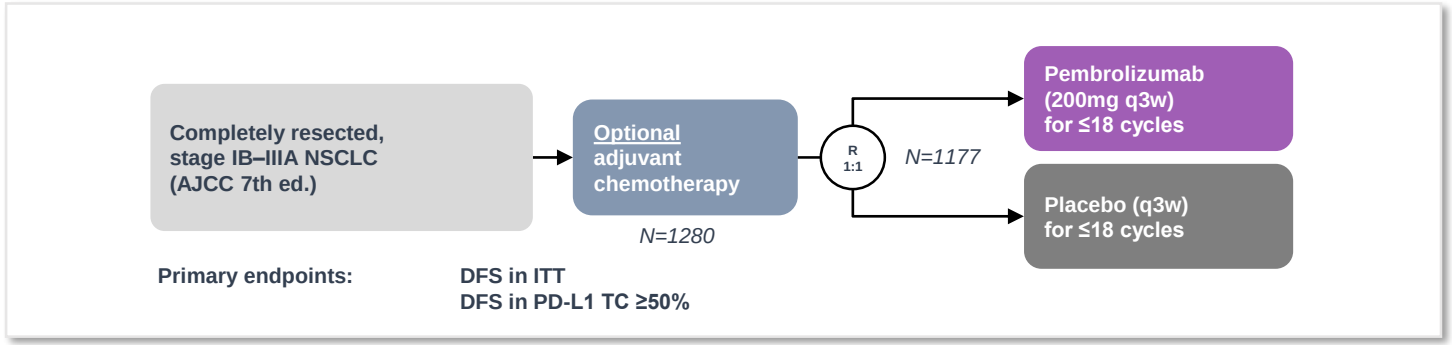
Atezo, ctDNA–	218	206	199	192	189	180	170	166	151	131	112	73	58	33	24	12	8	3	2	0
BSC, ctDNA–	204	193	176	167	158	152	143	137	124	106	88	62	44	19	9	3	3	0	0	0
Atezo, ctDNA+	53	47	37	33	29	28	27	25	23	17	14	10	6	3	2	0	0	0	0	0
BSC, ctDNA+	59	53	34	24	21	16	15	13	13	9	8	6	4	1	1	0	0	0	0	0

ctDNA–	**Atezo (n=218)**	**BSC (n=204)**
mDFS, months	NR	NR
HR (95% CI)	**0.72** (0.52, 1)	

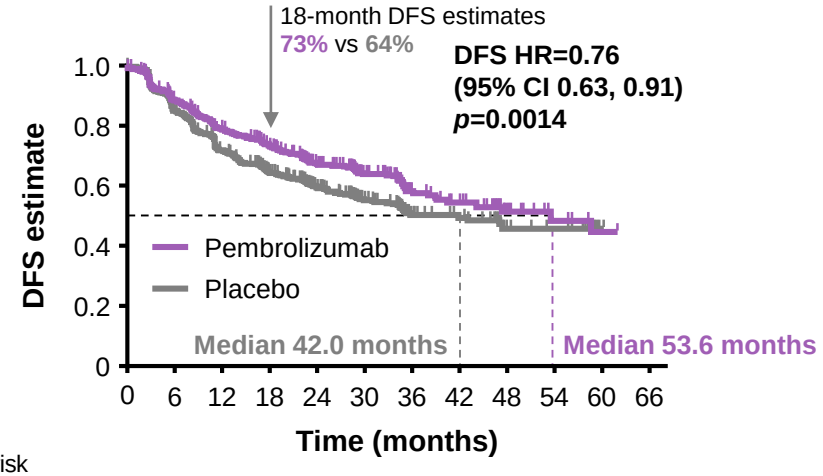
ctDNA+	**Atezo (n=53)**	**BSC (n=59)**
mDFS, months	19.1	7.9
HR (95% CI)	**0.61** (0.39, 0.94)	

Clinical cut-off: 21 January 2021
NR, not reached
Zhou, et al. ESMO IO 2021 (Abs 2O)

KEYNOTE-091: One dual primary endpoint of a DFS benefit in the overall population was met



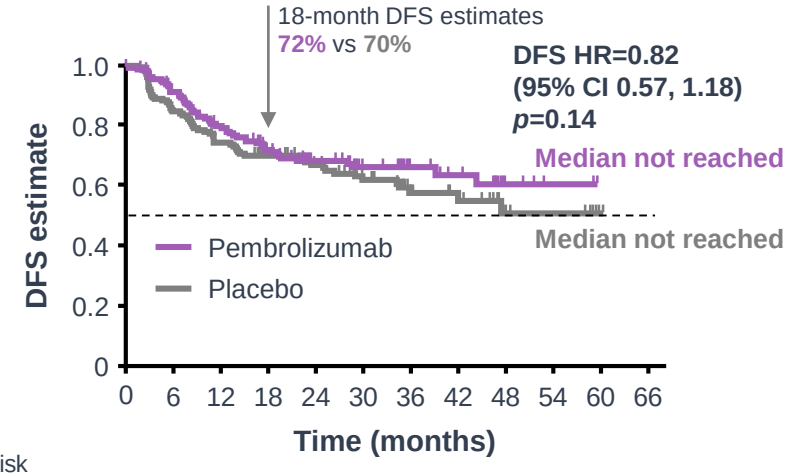
DFS in overall population (all stage IB–IIIA NSCLC) (dual primary endpoint)



No. at risk

Pembrolizumab	590	493	434	358	264	185	82	70	28	16	1	0
Placebo	587	493	409	326	241	160	72	57	22	18	1	0

DFS in PD-L1 TC (PD-L1 ≥50%, stage IB–IIIA NSCLC)* (dual primary endpoint)



No. at risk

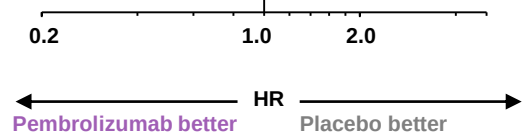
Pembrolizumab	168	145	126	99	69	50	26	22	7	4	0	0
Placebo	165	140	121	100	75	54	28	22	8	6	1	0

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
Data cut-off: 20 September, 2021; response assessed per RECIST v1.1 by investigator review; *At the interim analysis, this dual primary endpoint did not meet statistical significance
Paz-Ares, et al. ESMO Plenary 2022 (Abs VP3-2022)

KEYNOTE-091: A DFS benefit was seen in most clinical subgroups within the overall population

DFS subgroups in PD-L1 unselected, stage IB–IIIA, completely resected NSCLC

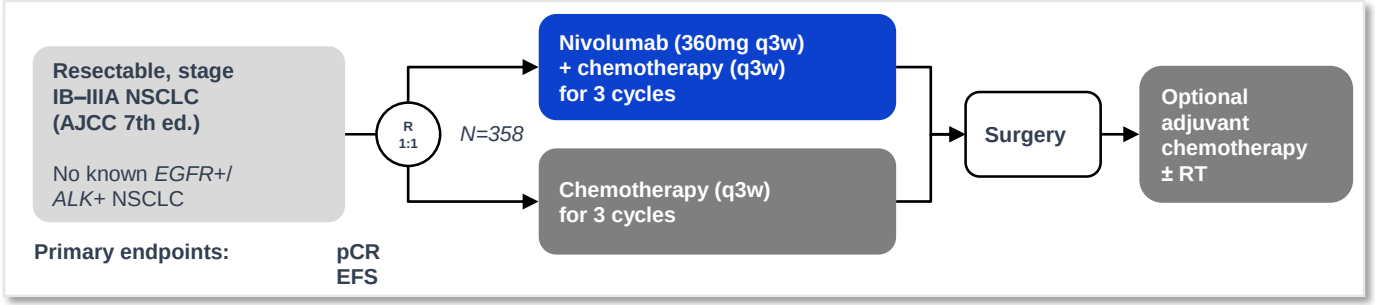
Subgroup	n	HR (95% CI)
Overall	1177	0.76 (0.63, 0.91)
Received adjuvant chemotherapy		
No	167	1.25 (0.76, 2.05)
Yes	1010	0.73 (0.60, 0.89)
Pathologic stage		
IB	169	0.76 (0.43, 1.37)
II	667	0.70 (0.55, 0.91)
IIIA	339	0.92 (0.69, 1.24)
Histology		
Non-squamous	761	0.67 (0.54, 0.83)
Squamous	416	1.04 (0.75, 1.45)
PD-L1 TPS		
<1%	465	0.78 (0.58, 1.03)
1–49%	379	0.67 (0.48, 0.92)
≥50%	333	0.82 (0.57, 1.18)



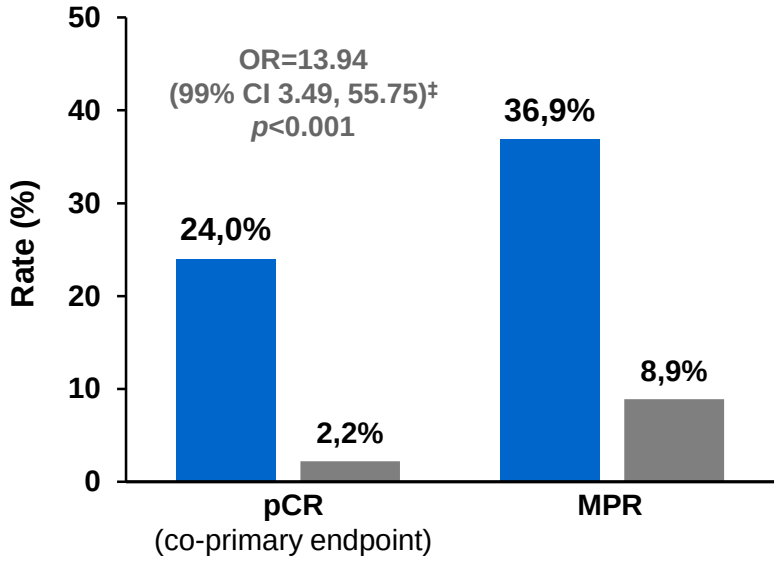
Grade ≥3 AEs occurred in 34% of patients in the pembrolizumab arm vs 26% in the placebo arm

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
Data cut-off: 20 September 2021; response assessed per RECIST v1.1 by investigator review
Paz-Ares, et al. ESMO Plenary 2022 (Abs VP3-2022)

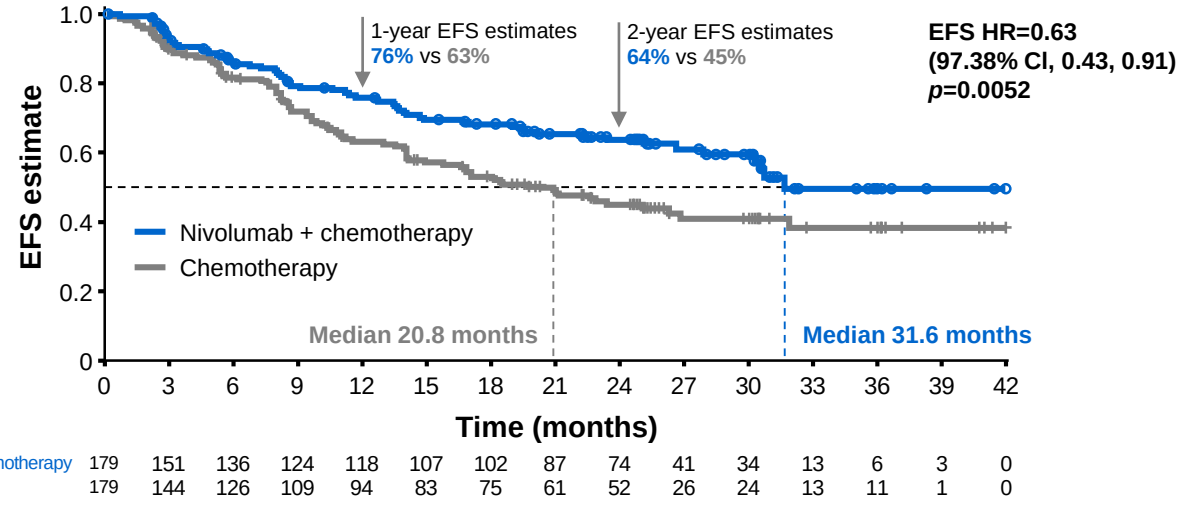
CheckMate 816: Neoadjuvant nivolumab + chemotherapy improved pathological response and EFS compared with chemotherapy alone



Pathological response in ITT population[1,2]*



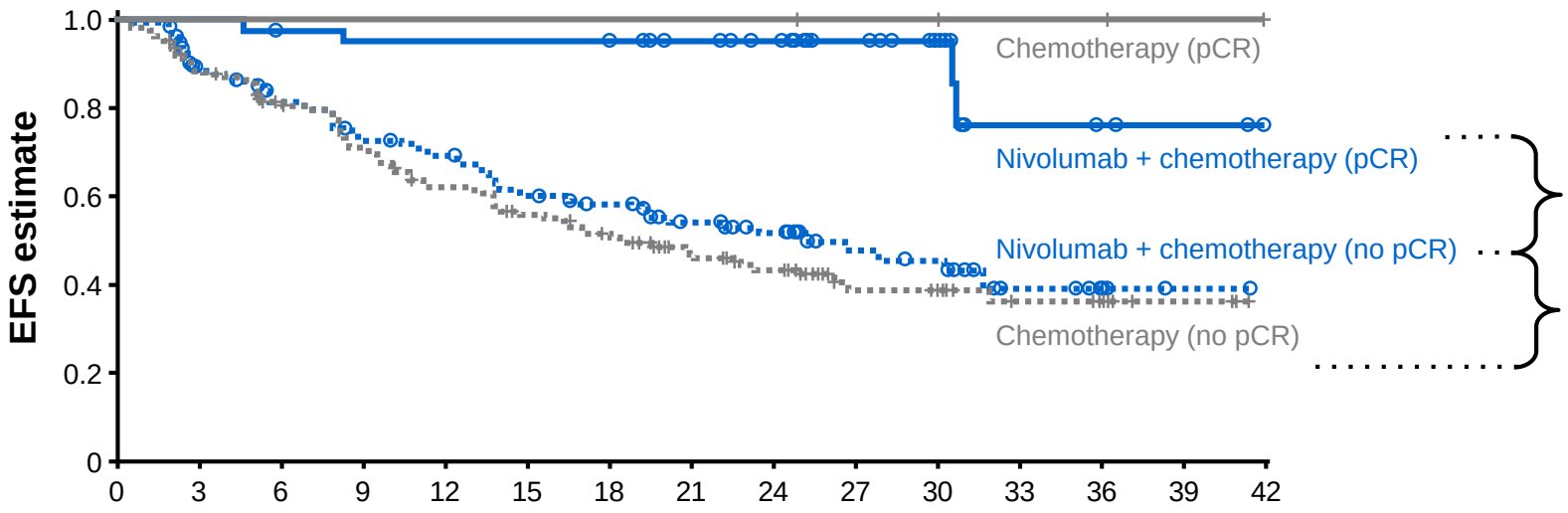
EFS in ITT population[2,3]* (co-primary endpoint)



No. at risk														
Nivolumab + chemotherapy	179	151	136	124	118	107	102	87	74	41	34	13	6	3	0
Chemotherapy	179	144	126	109	94	83	75	61	52	26	24	13	11	1	0

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
Minimum follow-up: 21 months; median follow-up, 29.5 months; pCR, MPR and EFS are per BICR
*Per BIPR; ≥5 stations, including ≥3 mediastinal, were recommended for assessment of pCR and MPR; pCR: 0% residual viable tumour cells in both primary tumour (lung) and sampled lymph nodes; MPR: ≤10% residual viable tumour cells in both the primary tumour (lung) and sampled lymph nodes; ITT principle: patients who did not undergo surgery counted as non-responders for primary analysis; ‡Calculated by stratified Cochran–Mantel–Haenszel method. MPR, major pathologic response
1. Forde, et al. AACR 2021 (Abs CT003); 2. Forde, et al. N Engl J Med 2022; 3. Girard, et al. AACR 2022 (Abs CT012)

CheckMate 816: EFS was improved in patients who achieved a pCR compared with those who did not



No. at risk															
Nivo + chemo pCR	43	43	41	40	40	40	40	35	32	19	14	6	3	2	0
Chemo pCR	4	4	4	4	4	4	4	4	4	3	2	2	2	1	0
Nivo + chemo no pCR	136	108	95	84	78	67	62	52	42	22	20	7	3	1	0
Chemo no pCR	175	140	122	105	90	79	71	57	48	23	22	11	9	3	0

EFS for patients achieving pCR vs not achieving pCR
(nivolumab + chemotherapy)*

EFS HR: 0.13
(95% CI: 0.05, 0.37)

EFS in patients not achieving a pCR
(nivolumab + chemotherapy vs chemotherapy)

EFS HR: 0.84
(95% CI: 0.61, 1.17)

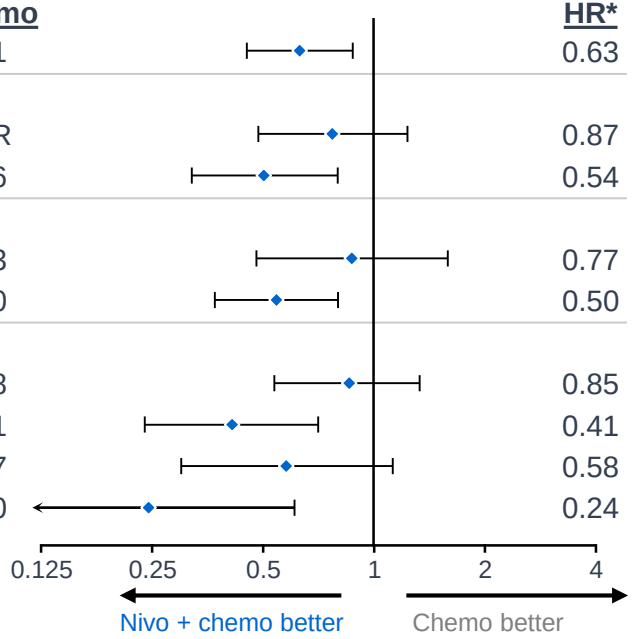
Grade 3–4 treatment-related AEs: 34% with nivolumab + chemotherapy vs 37% with chemotherapy alone

The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
Minimum follow-up: 21 months; median follow-up, 29.5 months
*HR was not computed for the chemotherapy arm due to only 4 patients having a pCR
Girard, et al. AACR 2022 (Abs CT012)

CheckMate 816: An EFS benefit was shown across most clinically relevant subgroups

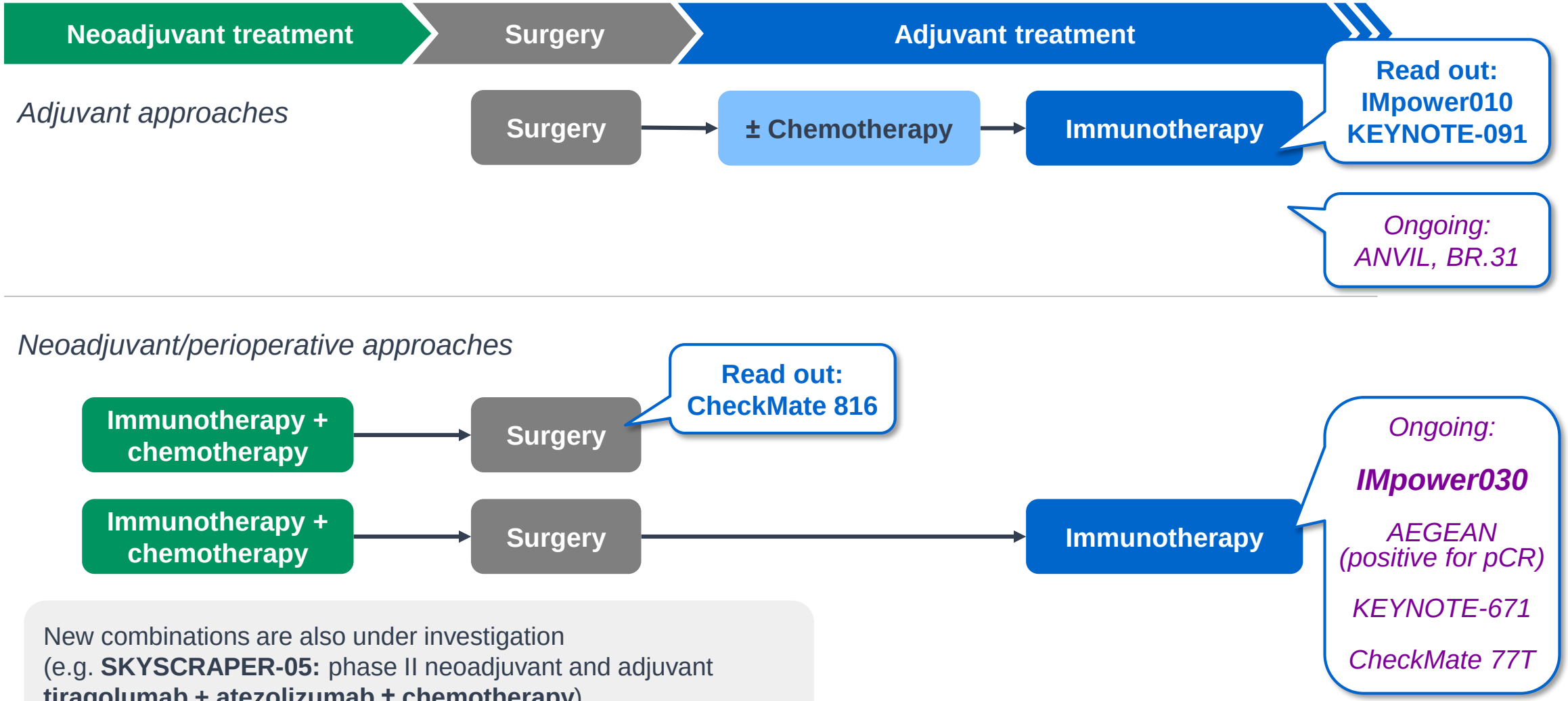
EFS subgroups in PD-L1 unselected, stage IB–IIIA NSCLC

Subgroup	n	Median EFS, months: Nivo + chemo	Median EFS, months: chemo	HR*
Overall	358	32	21	0.63
Stage				
IB–II	127	NR	NR	0.87
IIIA	228	32	16	0.54
Histology				
Squamous	182	31	23	0.77
Non-squamous	176	NR	20	0.50
PD-L1 expression				
PD-L1 TC <1%	155	25	18	0.85
PD-L1 TC ≥1%	178	NR	21	0.41
PD-L1 TC 1–49%	98	NR	27	0.58
PD-L1 TC ≥50%	80	NR	20	0.24



The content of this symposium may include scientific information about experimental or investigational compounds, indications and services that are not yet approved in the EU
EFS per BICR; *Unstratified. NR, not reached
Girard, et al. AACR 2022 (Abs CT012); Forde, et al. N Engl J Med 2022

CIT trials in patients with resectable NSCLC are changing the treatment landscape



New combinations are also under investigation
(e.g. **SKYSCRAPER-05:** phase II neoadjuvant and adjuvant **tiragolumab + atezolizumab ± chemotherapy**)

Paul Van Schil

University Hospital of Antwerp
Edegem (Antwerp), Belgium

The surgeon’s perspective on the treatment landscape in early-stage NSCLC

MDT considerations before surgery: resectability and operability

Technical resectability

Can all visible disease be adequately removed?

Opportunity for an R0 resection: tumour position, size, invasion

Functional operability

Can the patient endure the procedure?

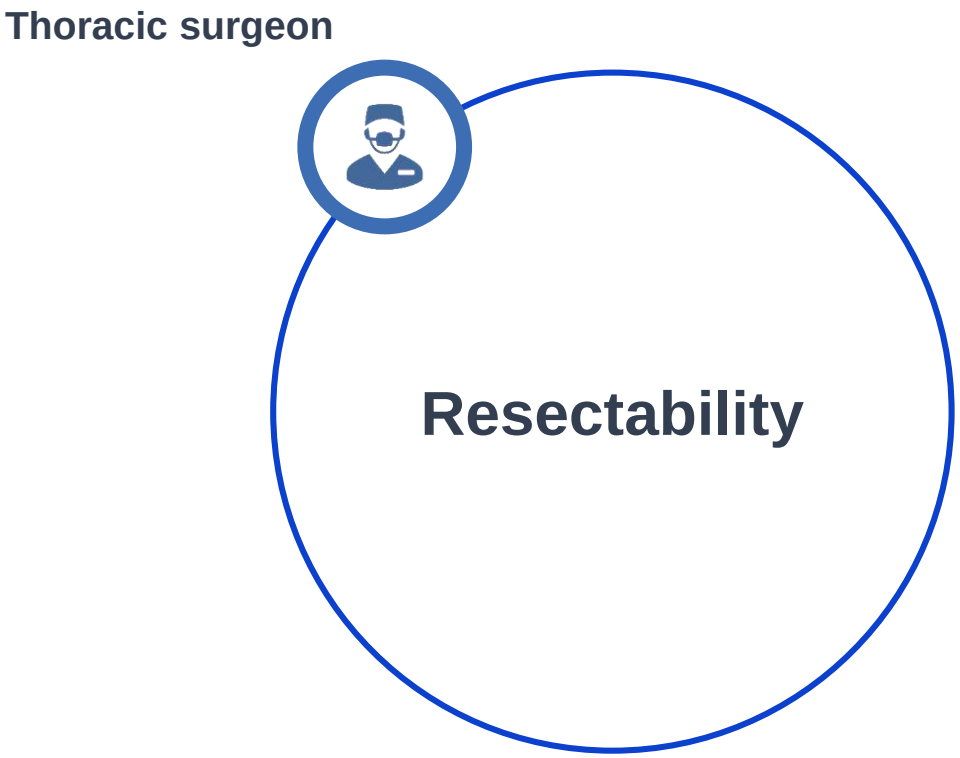
Cardiac and pulmonary assessments

Will the procedure be potentially curative?

Lymph node involvement, metastases, histological subtype

Shamji & Beauchamp. Review Thorac Surg Clin 2021

MDT considerations before surgery: resectability and operability



NSCLC stages indicated for surgery

Definite	
Stage	
IA	
IB	
IIA	
IIB	
IIIA	**T3N1**
	T4N0–1*

Investigational	
Stage	
IIIA	**N2**
	T4N0–1*
IIIB	**T4N2**
	N3

Exceptional	
Stage IV	**(oligometastases)**
M1a	Contralateral nodule
M1b	Single distant metastasis – single organ (adrenal, brain, bone)

*Certain subgroups

Complete resection is the surgical goal

R0 – *Complete resection, no residual tumour*

R1 – *Microscopic residual tumour*

R2 – *Macroscopic residual tumour*

R(un) – *Uncertain resection, inadequate lymph node dissection*

Rami-Porta, et al. Lung Cancer 2005

Complete resection is the surgical goal

R0 – *Complete resection*

- Free resection margins proved microscopically
- Systematic or lobe-specific systematic nodal dissection:
  - ≥6 nodal stations (3 mediastinal, including station 7)
  - No extracapsular extension in nodes removed separately or at the margin of the lung specimen
  - Highest mediastinal lymph node must be negative

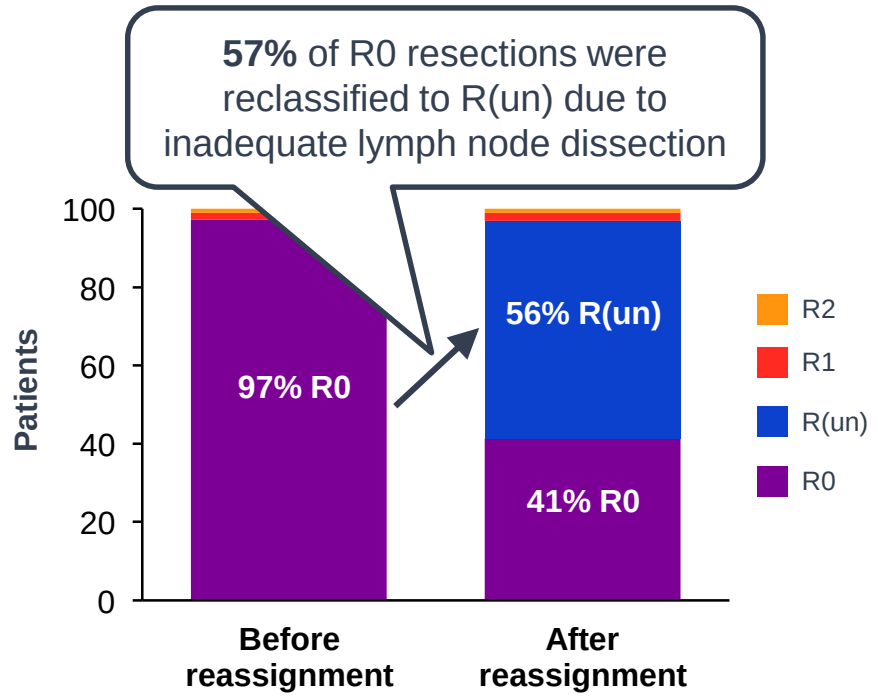
Rami-Porta, et al. Lung Cancer 2005

R(un) is an important new category of resection outcome

R(un) – *uncertain resection*

- Resection margins are free of disease microscopically but less rigorous lymph node dissection has been performed
- Highest mediastinal node removed is positive
- Bronchial margin shows carcinoma *in situ*
- Pleural lavage cytology is positive

Re-analysis of 14,712 patients from the IASLC database[1]

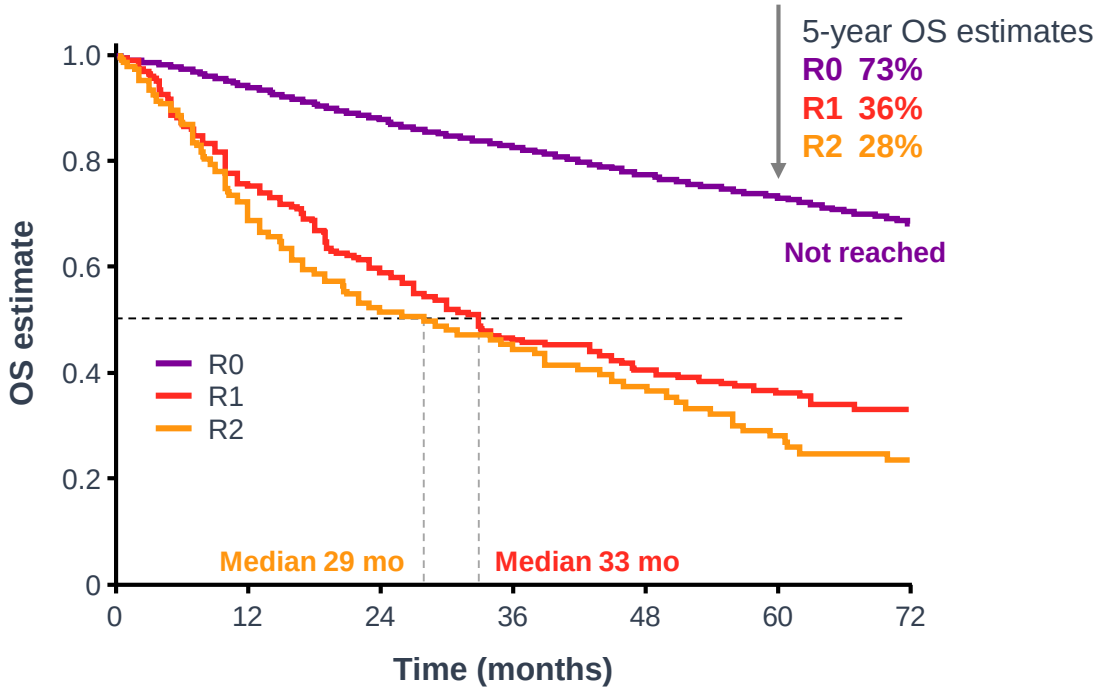


Prognostic significance of the R factor is being analysed in randomised trials[2,3]

1. Edwards, et al. J Thorac Oncol 2020; 2. Thomas, et al. ASCO 2022; 3. O'Brien, et al. ASCO 2022

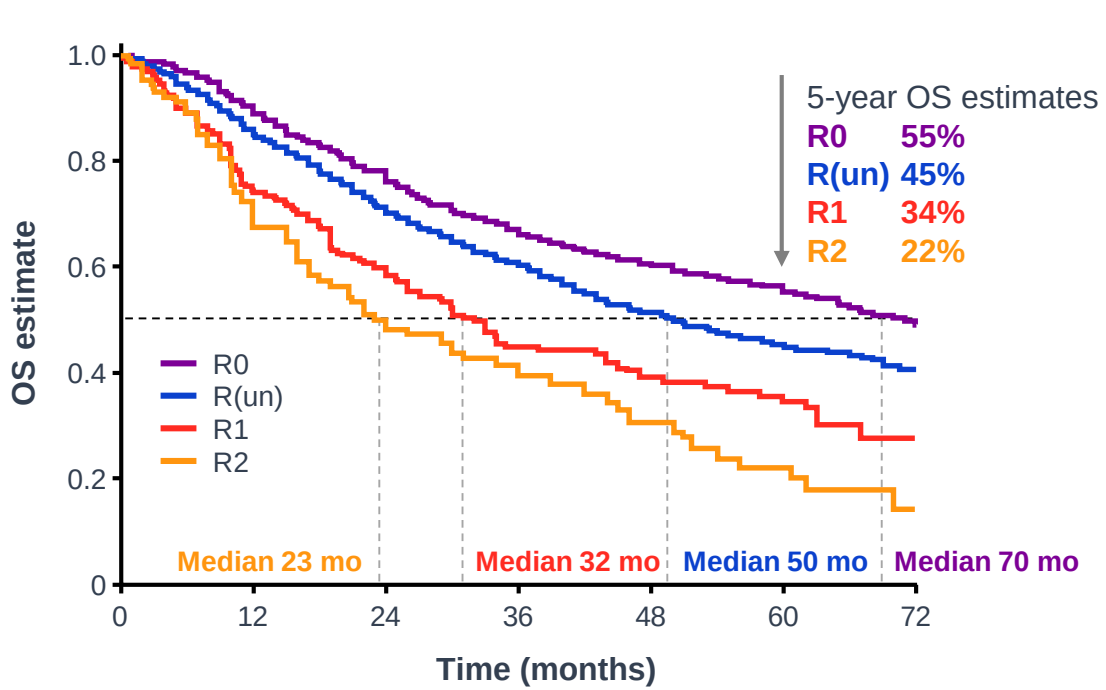
R descriptors have an important impact on prognosis

Survival per conventional R status



R0	14293	12787	11354	10124	8828	6591
R1	263	181	134	97	78	58
R2	156	94	64	46	37	27

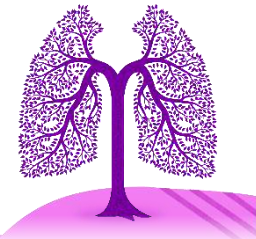
Re-classification: Survival per R status in pN+ cases



R0	1398	1185	988	818	699	562
R(un)	1794	1410	1066	823	637	495
R1	200	136	99	64	45	33
R2	102	57	37	23	18	12

mo, months

Conclusion



- Every (potentially resectable) lung cancer case to be discussed in an **MDT**
  - Include a **thoracic surgeon**
- MDT must consider both **technical resectability** and **functional operability**
- **Pre-operative evaluation** is important to define resectability (definite vs investigational vs exceptional)
- **Aim** of every surgical intervention for lung cancer = **complete R0 resection**
- **Systematic nodal dissection** is recommended
- **Avoid uncertain resection**, R(un), due to a poorer prognosis

ESMO 2022 Industry Satellite Symposium

Redefining Lung Cancer **Together:** Now and Next

Panel Discussion Q&A

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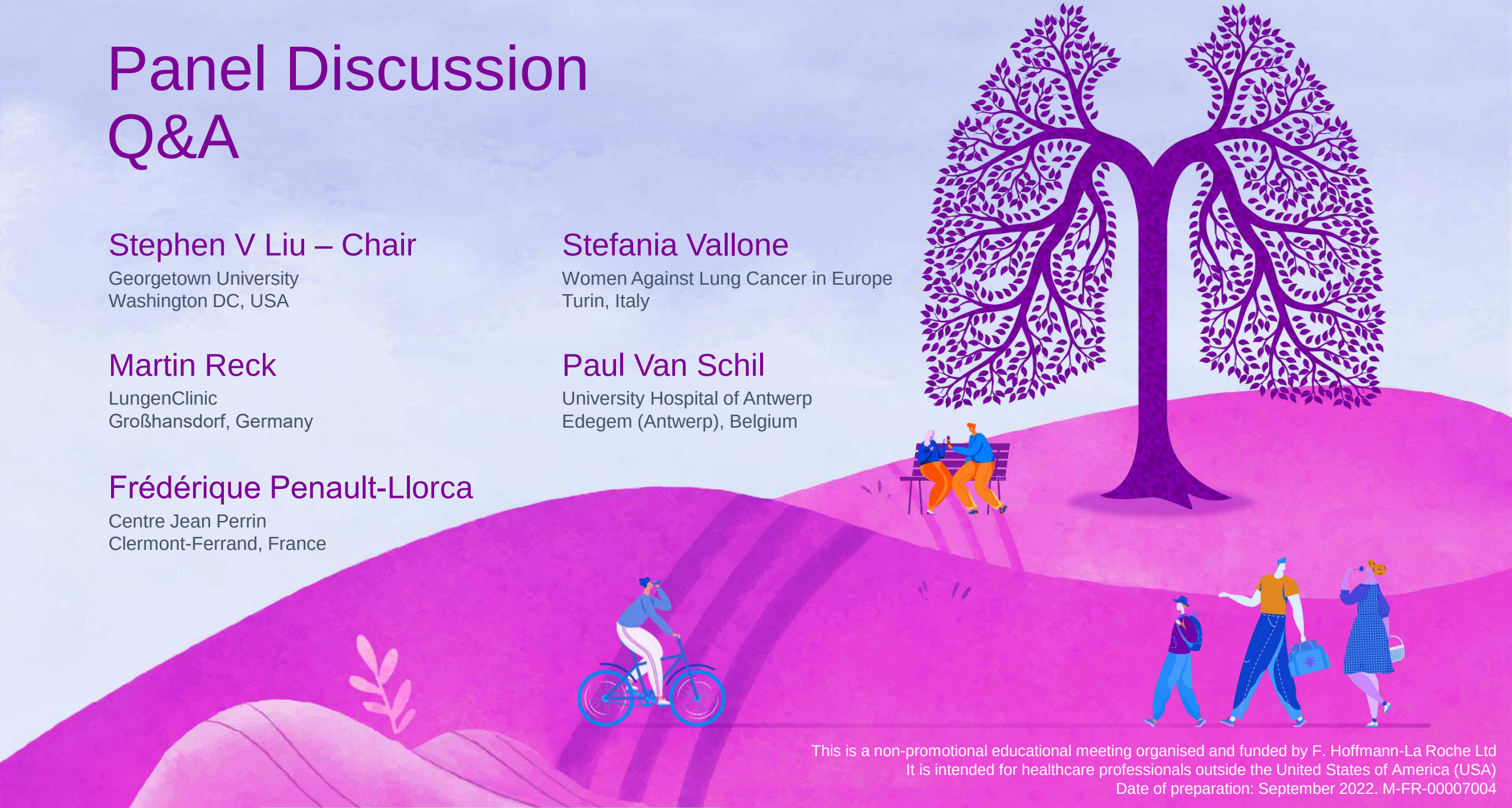

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Closing remarks

Stephen V Liu

Georgetown University
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Women Against Lung Cancer in Europe
Turin, Italy

Thank you for attending!

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