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THE HEART OF MEDICAL EDUCATION

LUNG CONNECT

ROS1+ NSCLC: FROM IDENTIFICATION TO NEXT-GENERATION THERAPY

Dr Maurice Pérol, MD
Léon Bérard Cancer Center, Lyon, France

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EDUCATIONAL OBJECTIVES

1. **Increase awareness of *ROS1* rearrangements in NSCLC** and the clinical importance of identifying this rare but actionable genomic alteration

2. **Improve understanding of optimal biomarker testing strategies**, emphasising the need for comprehensive molecular profiling to ensure patients with *ROS1*-positive disease are accurately identified

3. **Update healthcare professionals on the evolving treatment landscape for *ROS1*-positive NSCLC**, including the role of next-generation targeted therapies and their potential implications for clinical practice

NSCLC, non-small cell lung cancer

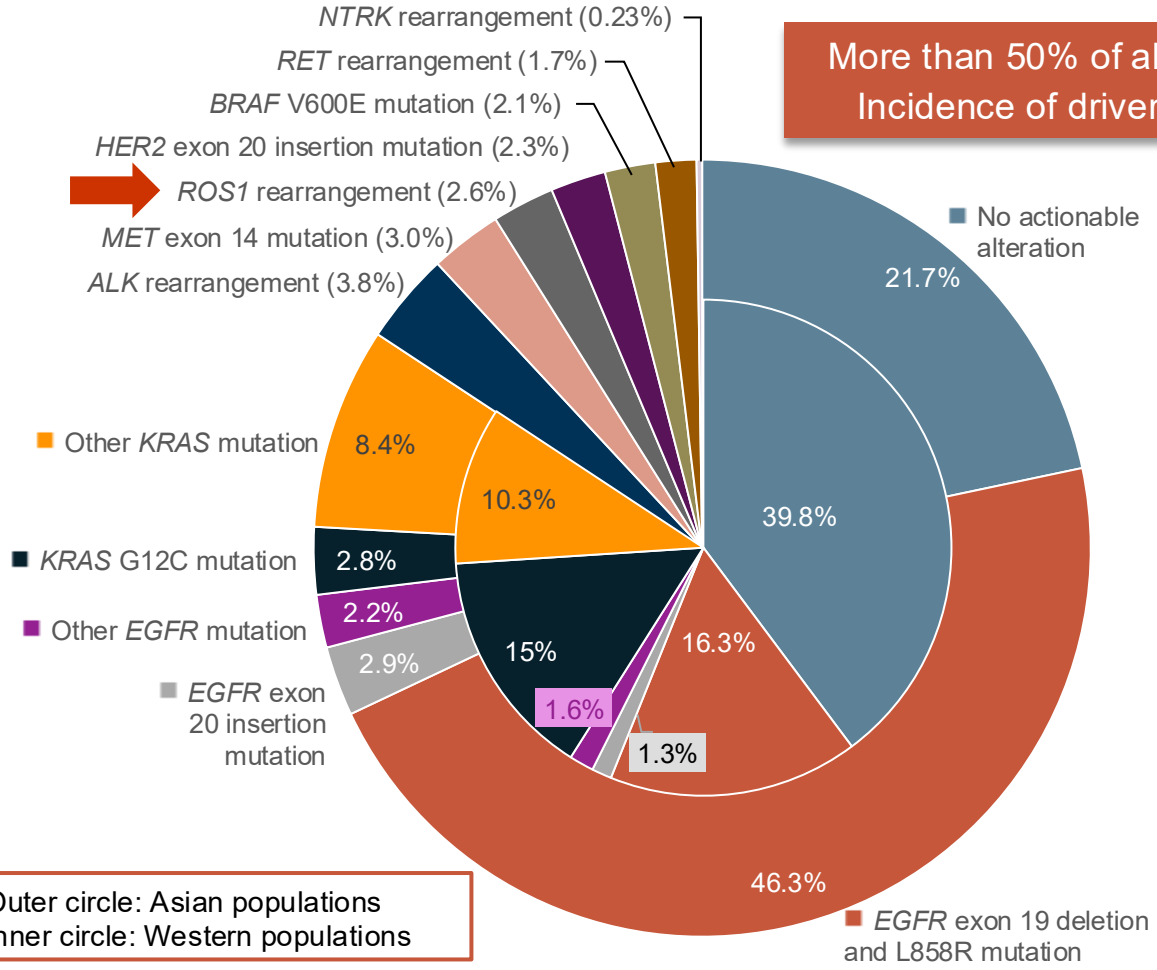
CLINICAL TAKEAWAYS

- **Identify every *ROS1* fusion**—although rare, patients with *ROS1*-positive NSCLC derive significant benefit from targeted TKIs compared to chemotherapy or immunotherapy
- **Use upfront comprehensive NGS (ideally RNA based)** to detect *ROS1* rearrangements and avoid missed opportunities for targeted therapy
- **Next-generation ROS1 TKIs** overcome key resistance mutations and provide improved intracranial activity
- **Early molecular profiling** enables timely access to the most effective targeted therapies and improves patient outcomes

NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

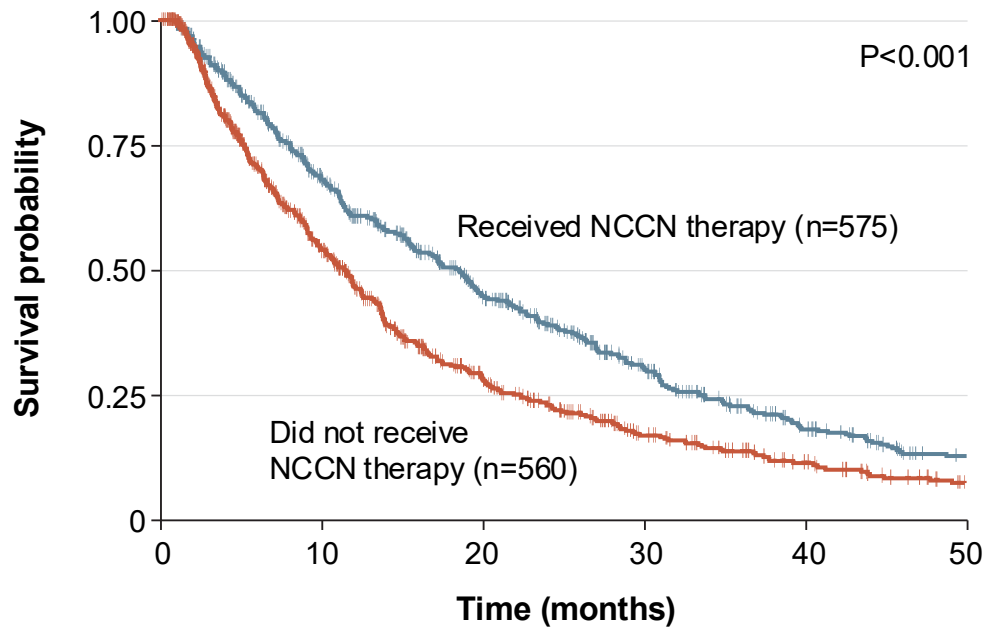
IDENTIFICATION OF ACTIONABLE GENOMIC ALTERATIONS IMPROVES NSCLC PATIENT OUTCOME

More than 50% of all lung adenocarcinomas harbour driver oncogenes
Incidence of driver mutations is variable among ethnic populations[1]



Outer circle: Asian populations
Inner circle: Western populations

Patients with targetable mutations[2,a]



No. at risk						
Received NCCN therapy	2	168	142	91	59	32
Did not receive NCCN therapy	55	196	93	54	28	13

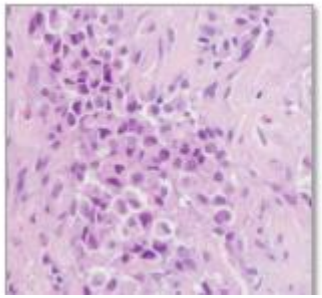
[a] As outlined in NCCN guidelines

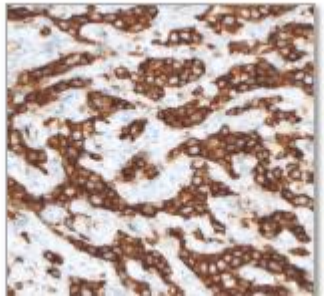
NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer

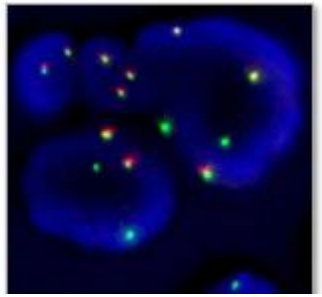
1. Tan AC and Tan DSW. J Clin Oncol. 2022;40:611-25; 2. Singal G, et al. JAMA. 2019;321(14):1391-9

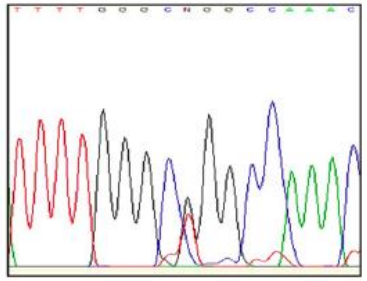
PHENOTYPIC AND GENOTYPIC CHARACTERISATION OF NSCLC

Histology Cytology	IHC	FISH	Sequencing/NGS DNA - RNA	ctDNA
Sq *vs* NSq *vs* NOS TTF1 p40	**PD-L1** **ALK** **ROS1**/MET/ NTRK/HER2	***ALK*/*ROS1*/** *NTRK*/*MET*/ *HER2*	Depending on technique: • Mutations • Rearrangements • Tumour mutational burden	• Baseline • Monitoring • Residual disease • Resistance



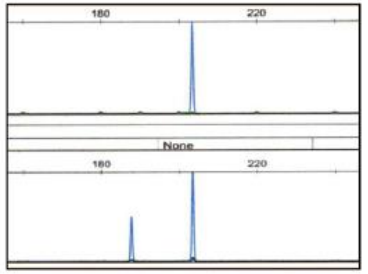






Sanger sequencing

Lower sensitivity
Selected genes



PCR-based methods
e.g. Cobas®, Idylla™

Selected genes

Targeted next generation sequencing (NGS)

Many genes (broad testing)

Example turnaround time[a]:					
1-2 d	1-2 d	3-5 d	~7 d	7-21 d	7-10 d

[a] Turnaround times vary and depend on each institution workflow

ctDNA, circulating tumour DNA; d, days; FISH, florescence in-situ hybridisation; IHC, immunohistochemistry; NGS, next-generation sequencing; NOS, not otherwise specified; NSCLC, non-small cell lung cancer; NSq, non-squamous; PCR, polymerase chain reaction; Sq, squamous; TTF1, thyroid transcription factor-1

Penault-Llorca F, Socinski MA. Oncologist. 2025;30(3):oyae357; Agrawal M, et al. J Med Sci Health 2023; 9(1):37-42; Repetto M, et al. Cancer Treatment Reviews 2024; 127: 102733; Malla M, et al. J Clin Oncol 2022; 40: 2846-2857

CLINICAL AND HISTOLOGICAL PRESENTATION

- Younger patients (median age **45–50 years**)
- Female predominance
- Never- or light-smoker
- Predominantly adenocarcinoma (especially acinar and solid)
- TTF-1 positive in >90%
- Frequently presents with CNS involvement
- Frequent VTE events[2]

Clinical characteristics should never replace molecular testing

CNS, central nervous system; TTF-1, Thyroid transcription factor 1; VTE, venous thromboembolism

1. Wespiser M, et al. Front Oncol. 2026;16:1739598; 2. Ng TL, et al. J Thorac Oncol. 2019;14(4):596-605

NGS: WHO SHOULD BE TESTED AND WHEN?

Key biomarkers[1]

- *EGFR* mutations
- *ALK* rearrangements
- *ROS1* rearrangements
- *BRAF* V600E mutations
- *KRAS*^{G12C} mutations
- *MET* exon 14 skipping mutations
- *RET* rearrangements/fusions
- *HER2* mutations
- *NTRK1/2/3* gene fusions
- PD-L1 protein expression[2]

Testing Scope and Clinical Context[2,3]

- **Histology**
  - All non-squamous and NOS carcinomas
  - Squamous carcinoma for non- or light-smokers
- **Stage**
  - Stage IV disease
  - Stage III disease: *EGFR*m, *ALK*
  - Early stage: *EGFR*m, *ALK*
  - Trend for complete genomic profile at every stage
- **Techniques**
  - Broad multiplex panel-based NGS is preferred over single-gene testing to conserve tissue and efficiently identify targets
- **Sample type**
  - Small tissue biopsies or plasma cell-free DNA (liquid biopsy) assays when tissue is limited

EGFRm, EGFR mutation; NGS, next-generation sequencing; NOS, not otherwise specified

1. Mosele MF, et al. Ann Oncol. 2024;35:588-606; 2. Hendriks LE, et al. Ann Oncol. 2023;34(4):339-57; 3. Penault-Llorca F, Socinski MA. Oncologist. 2025;30(3):oyae357

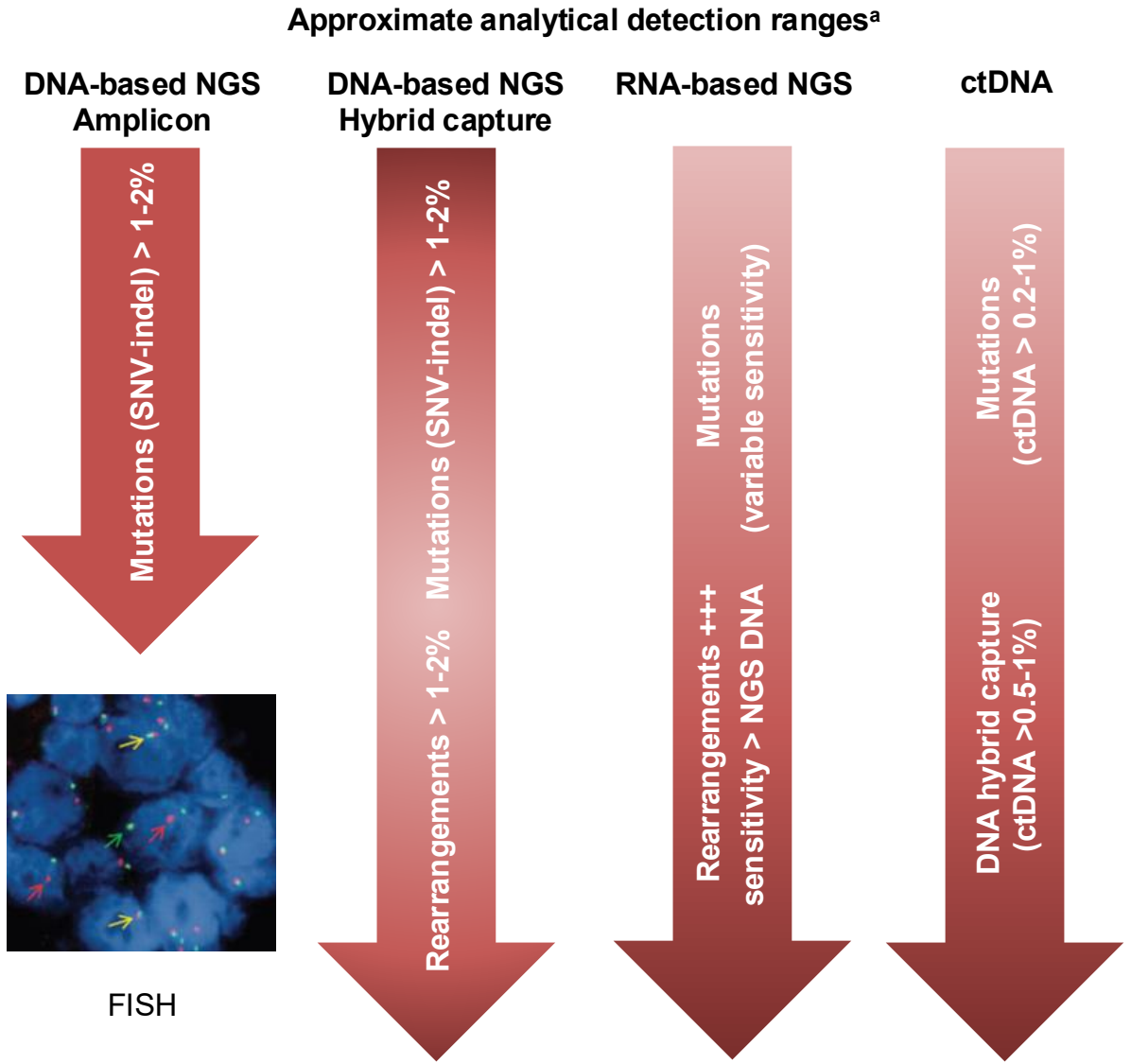
GENOTYPIC CHARACTERISATION OF NSCLC

Mutations

- *EGFR* Exon 18-21
- *KRAS* Exon 2-3
- *BRAF* Exon 15
- *MET* Exon 14 and adjacent introns
  Amplification
- *ERBB2* Exon 20
  Amplification

Fusions

- *ALK* Fusion
- *ROS1* Fusion
- *RET* Fusion
- *NRG1* Fusion
- *NTRK*$_{1/2/3}$ Fusion



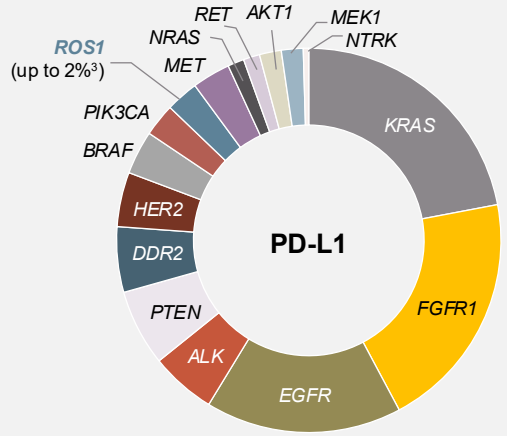
[a]Approximate analytical detection ranges depend on each assay. Values quoted are given for indicative purposes only and provided by Pérol M

ctDNA, circulating tumour DNA; Indel, insertions/deletions; FISH, fluorescence in situ hybridisation; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; SNV, single nucleotide variation

Tan AC and Tan DSW. J Clin Oncol. 2022;40:611-25; Penault-Llorca F, Socinski MA. Oncologist. 2025;30(3):oyae357, Pérol M, personal communication

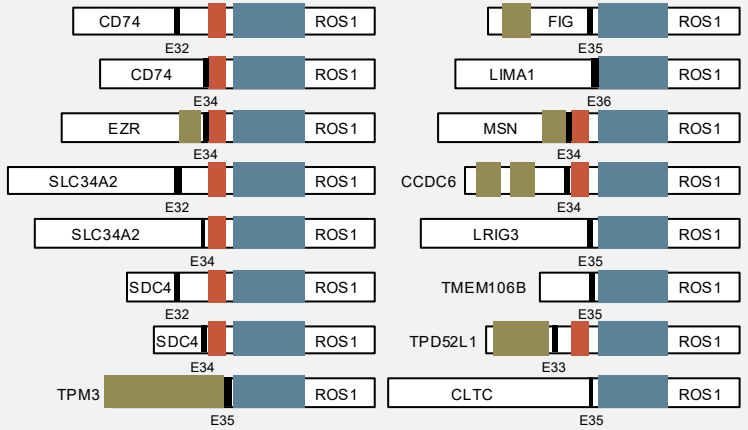
ROS1 FUSIONS: MOLECULAR AND CLINICAL PROFILE

Genetic alterations in NSCLC[1,2]

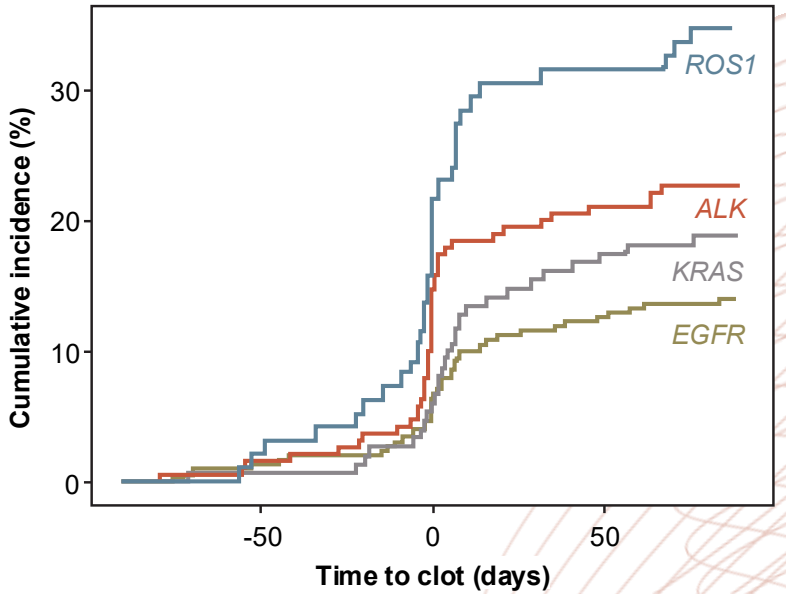


***ROS1* fusions are enriched in females, patients with adenocarcinoma, or patients who have never smoked[3]**

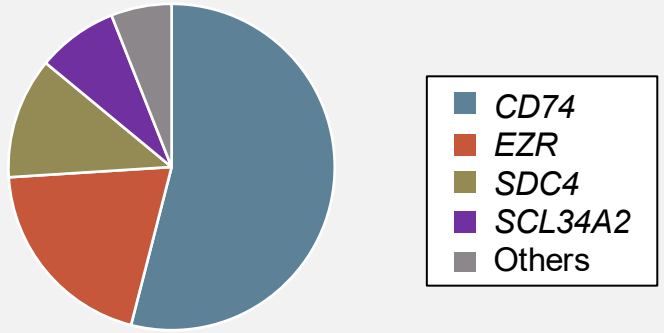
Numerous ROS1 fusion partners have been characterised[4,5]



Thromboembolic events within ±90 days of advanced lung cancer diagnosis[8]



ROS1 rearrangements in NSCLC[6]

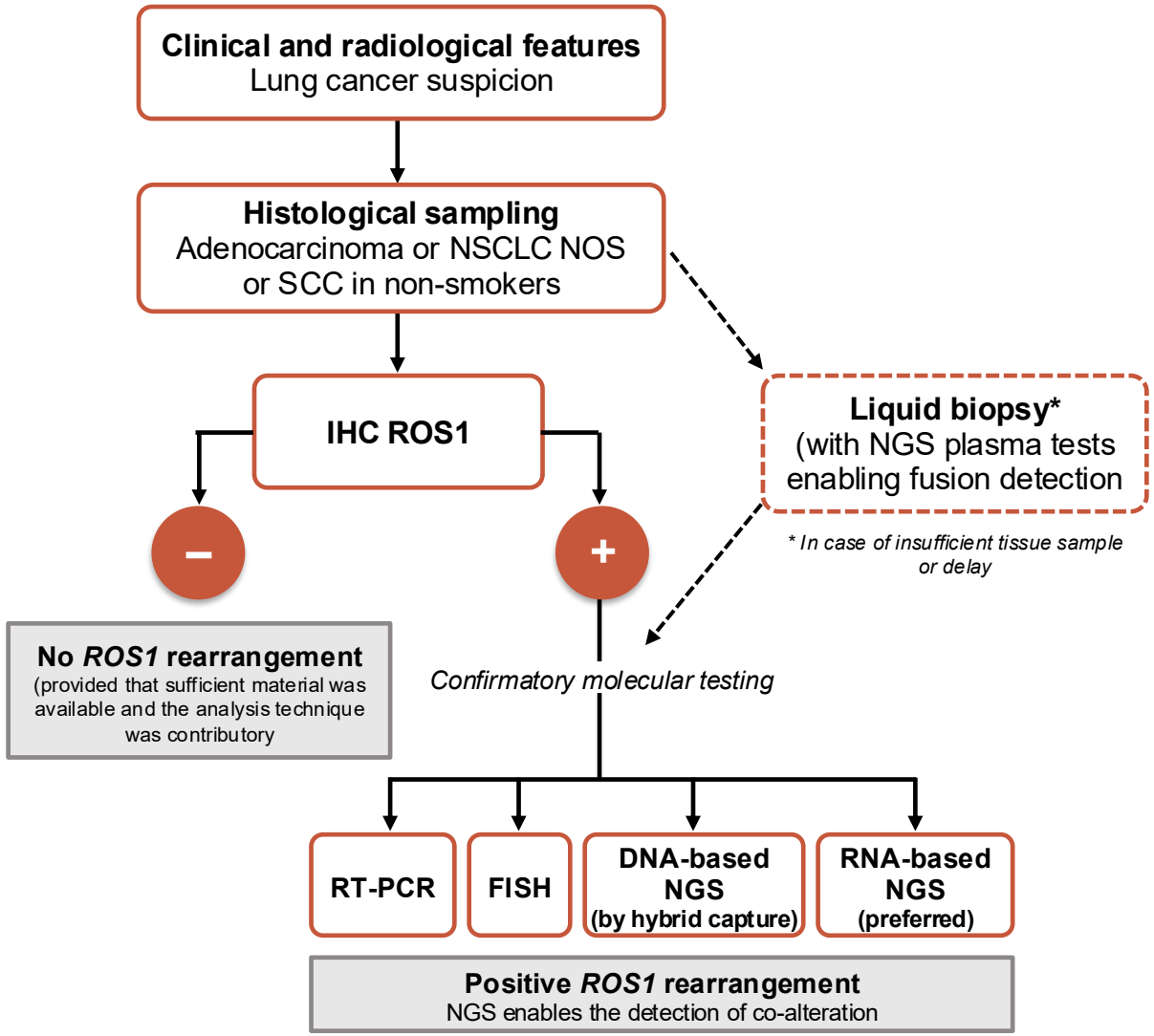


- High incidence of brain metastases[7]
- High incidence of venous thrombo-embolic events[8]

E32-36, exon 32-36; NSCLC, non-small cell lung cancer

1. Drilon A, ESMO 2024; Bristol Myers Squibb Industry Satellite Symposium (ESMO 2024); 2. Kris MG, et al. JAMA. 2014;311:1998-2006; 3. Zhu Q et al. Transl Lung Cancer Res 2015; 4 (3): 300-309; 4. Takeuchi K, et al. Nat Med. 2012;18(3):378-81; 5. Lin JJ and Shaw AT. J Thorac Oncol. 2017;12(11):1611-25; 6. Wespiser M, et al. Front Oncol. 2026;16:1739598; 7. Patil T, et al. J Thorac Oncol. 2018;13(11):1717-26; 8. Ng TL, et al. J Thorac Oncol. 2019;14(4):596-605

HOW TO IDENTIFY *ROS1* REARRANGEMENT IN NSCLC?



FISH, fluorescence in situ hybridisation; IHC, immunohistochemistry; NGS, next-generation sequencing; NOS, not otherwise specified; NSCLC, non-small cell lung cancer; RT-PCR, reverse transcriptase-polymerase chain reaction; SCC, squamous cell carcinoma

Wespiser M, et al. Front Oncol. 2026;16:1739598

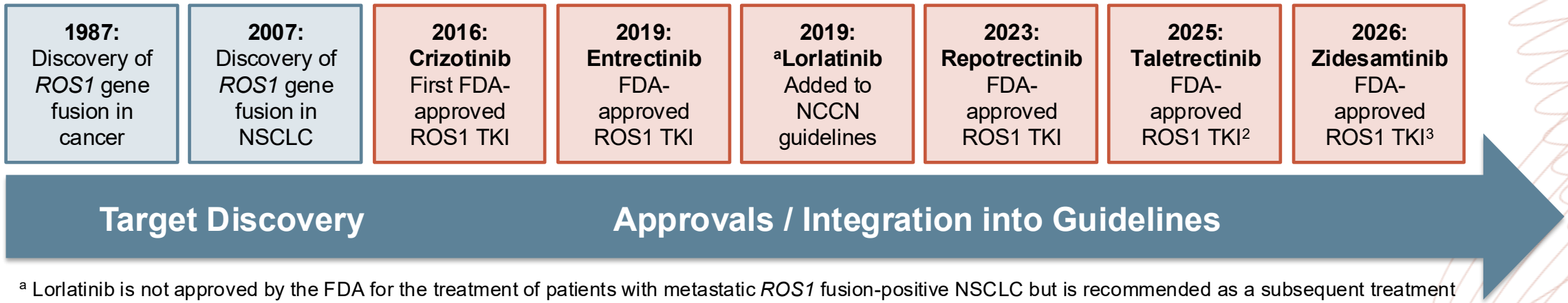
WHY IS RNA-BASED NGS THE PREFERRED METHOD FOR DETECTING *ROS1* FUSIONS?

DNA-based NGS	RNA-based NGS
Detects genomic rearrangements (hybrid capture)	Detects the expressed fusion transcript
Large introns and variable breakpoints may make some fusions difficult to detect	Fusion partners are identified directly, regardless of breakpoint location
May miss some clinically relevant fusions depending on panel design	High sensitivity for fusions, especially known and novel *ROS1* fusions
Useful for comprehensive genomic profiling	**Preferred method for *ROS1* fusion detection**

NGS, next-generation sequencing

Mosele MF, et al. Ann Oncol. 2024;35:588-606 (including Supplementary appendix); Penault-Llorca F, Socinski MA. Oncologist. 2025;30(3):oyae357

ROS1 FUSION IN NSCLC HISTORY[1]



[a] Lorlatinib is not approved by the FDA for the treatment of patients with metastatic *ROS1* fusion-positive NSCLC but is recommended as a subsequent treatment option by the NCCN guidelines and included in the ESMO guidelines

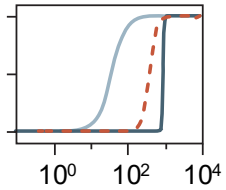
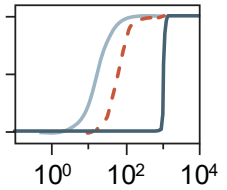
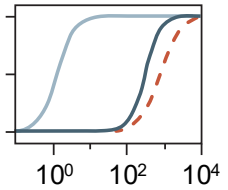
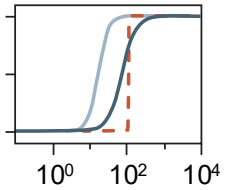
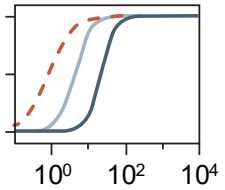
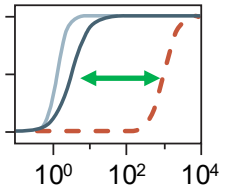
Adapted from Boulanger et al. 2024[1]

ESMO, European Society for Medical Oncology; FDA, Food & Drug Administration; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase; U.S., United States

1. Boulanger MC, et al. Oncologist. 2024;29(11):943-56; 2. U.S. Food and Drug Administration. FDA approves taletrectinib for ROS1-positive non-small cell lung cancer. June 11, 2025. Available here (accessed August 23, 2026); 3. U.S. Food and Drug Administration. FDA approves zidesamtinib for ROS1-positive non-small cell lung cancer. 2026 Jul 22, 2026. Available here (accessed August 23, 2026)

A NEW GENERATION OF ROS1-TARGETING TKIs

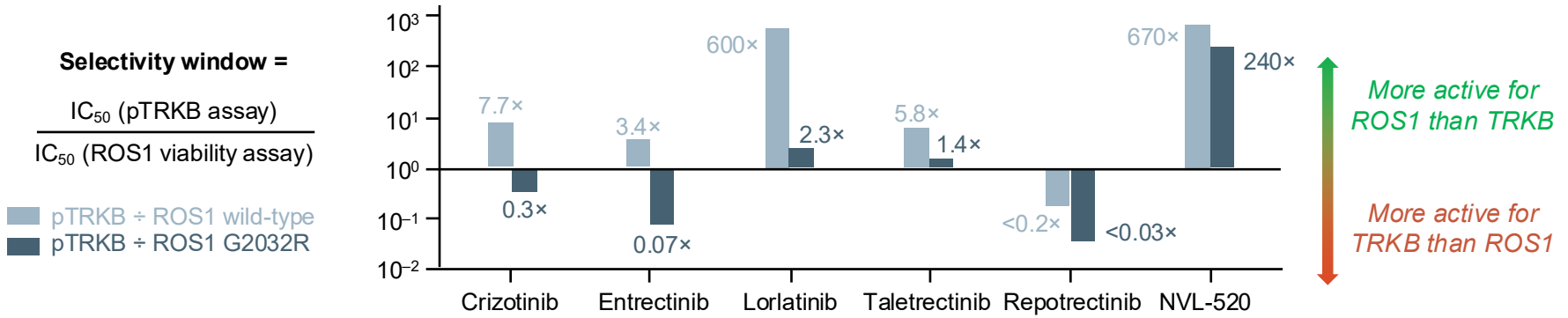
Activity of ROS1 TKIs against ROS1 wild-type, ROS1 G2032R, and TRKB

	Crizotinib	Entrectinib	Lorlatinib	Taletrectnib	Repotrectinib	NVL-520
Inhibition of CD74–ROS1 cell viability or pTRKB (100%, 50%, 0%)						
Concentration (nmol//L)	10^0 10^2 10^4	10^0 10^2 10^4	10^0 10^2 10^4	10^0 10^2 10^4	10^0 10^2 10^4	10^0 10^2 10^4
Ba/F3 CD74–ROS1 wild-type IC_{50} (viability assay)	40 nmol/L ×/÷ 1.4 (n=3)	19 nmol/L ×/÷ 1.8 (n=3)	1.4 nmol/L ×/÷ 1.9 (n=17)	21 nmol/L ×/÷ 1.1 (n=2)	5.5 nmol/L ×/÷ 1.7 (n=17)	1.3 nmol/L ×/÷ 1.3 (n=3)
Ba/F3 CD74–ROS1 G2032R IC_{50} (viability assay)	950 nmol/L ×/÷ 1.0 (n=3)	880 nmol/L ×/÷ 2.1 (n=2)	330 nmol/L ×/÷ 1.4 (n=28)	84 nmol/L ×/÷ 1.8 (n=3)	26 nmol/L ×/÷ 1.4 (n=59)	3.6 nmol/L ×/÷ 2.0 (n=11)
Ba/F3 TRKB IC_{50} (pTRKB assay)	310 nmol/L ×/÷ 1.2 (n=4)	62 nmol/L ×/÷ 1.5 (n=5)	730 nmol/L ×/÷ 1.5 (n=10)	120 nmol/L ×/÷ 1.0 (n=3)	<0.8 nmol/L (n=4)	850 nmol/L ×/÷ 1.1 (n=4)

Selectivity for ROS1 (wild-type or G2032R) over TRKB

Selectivity window =

$$\frac{IC_{50}\text{ (pTRKB assay)}}{IC_{50}\text{ (ROS1 viability assay)}}$$



IC50, half maximal inhibitory concentration; TKI, tyrosine kinase inhibitor

Drilon A, et al. Cancer Discov. 2023;13(3):598-615

ROS1 TKIs IN TKI-NAIVE *ROS1* FUSION+ NSCLC[1]

	Crizotinib[2] PROFILE 1001	Entrectinib[3] ALKA 372-001 STARTRK-1 STARTRK-2 Phase 1/2	Ceritinib[4] Korean Phase 2	Brigatinib[5] Barossa Phase 2	Lorlatinib[6] Phase 1/2	Foritinib[7] Phase 2b Cohort 1	Reprotrectinib[8] TRIDENT-1 Phase 1/2	Taletrectinib[9,10] TRUST I + II Pooled phase 2			Zidesamtinib[11] ARROS-1 Phase 1/2
								All TKI naïve	Prior CT	No prior CT	
Patients, n	53	198	30	28	21	56	71	157	30	127	94
ORR, %	**72.0**	**67.2**	**67.0**	**71.4**	**62.0**	**88.0**	**79.0**	**89.8**	**90.0**	**89.8**	**94.0**
Median PFS, months	**19.3**	**15.8**	**19.3**	**12.0**	**21.0**	**22.1**	**31.1**	**46.1**	**49.6**	**46.1**	**NR** PFS ≥12 mo:90%
CNS activity IC- ORR	NR	27/53 pts (50.9%) Measurable and non-measurable	2/8 pts (25%) Measurable and non-measurable	0/3 pts Measurable	7/11 pts (64%) Measurable and non-measurable	19/21 pts (90%) Measurable and non-measurable	8/9 pts (89%) Measurable	13/17 pts (76.5%) Measurable	NR	NR	10/10 pts (100%) Measurable

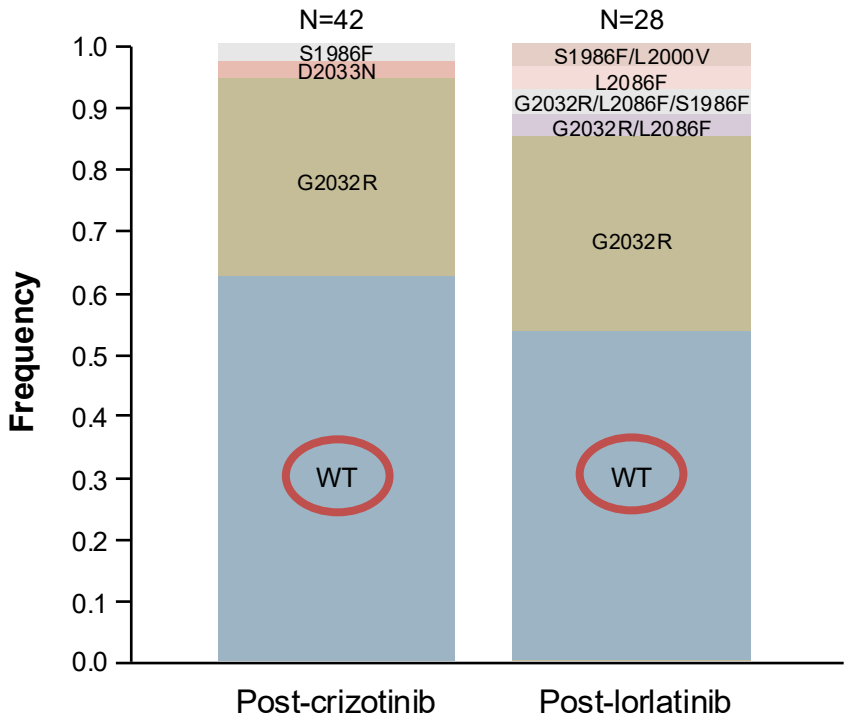
There are no head-to-head studies therefore, this is non-comparative data presented for informational/descriptive purposes. Comparisons between trials should not be made due to differences in study design and patient populations

CNS, central nervous system; CT, chemotherapy; IC-ORR, intracranial-ORR; NR, not reported; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; TKI, tyrosine kinase inhibitor

1. Wespiser M, et al. Front Oncol. 2026;16:1739598; 2. Shaw A, et al. Ann Oncol. 2019;30:1121-6; 3. Krebs M, et al. Abstract # 1290P, ESMO 2024 (poster presentation); 4. Lim SM, et al. J Clin Oncol. 2017;35:2613-8; 5. Niho S, et al. ESMO Open. 2024;9(8):103642; 6. Shaw A, et al. Lancet Oncol. 2019;20:1691-701; 7. Yang JJ, et al. Lancet Respir Med. 2024;12:671-80; 8. Cho BC, et al. Abstract #MA02.03, WCLC 2025 (oral presentation); 9. Bazhenova L, et al. Abstract # CT300, AACR 2026 (oral presentation); 10. Hayashi H, et al. Abstract #P3.277, WCLC 2026 (poster presentation); 11. Drilon AE, et al. Abstract #PL03.06, WCLC 2026 (oral presentation)

SPECTRUM OF RESISTANCE TO ROS1 FUSION INHIBITORS

Frequency of mutations in resistant biopsies[1]



Potency heatmap of ROS1 TKI against resistant clones[2]

	Name	Cell line	Fusion	Mutation	Crizotinib	Entrectinib	Lorlatinib	Taletrectinib	Repotrectinib	NVL-520
Wild-type ROS1 fusion	HCC78	Human cancer cell line	SLC34A2–ROS1	–	45	5.3	0.9	15	7.7	<0.7
	MGH193-1	Patient-derived cell line	EZR–ROS1	–	18	8.7	0.4	5	2.1	1
	Ba/F3	Engineered mouse pro–B cell line	CD74–ROS1	–	40	19	1.2	21	4.6	1.3
			EZR–ROS1	–	5.9	12	0.5	11	2.9	0.3
			GOPC(L)–ROS1	–	33	11	0.3	7.6	3.5	0.2
			GOPC(S)–ROS1	–	110	36	0.3	9.9	2.7	0.2
			CEP85L–ROS1	–	30	13	0.4	6.2	2.1	0.2
	Average potency across 7 wild-type ROS1 fusion cell lines				30	13	0.5	9.7	3.3	0.4
ROS1 fusion with G2032R mutation	MGH9018-1	Patient-derived cell line	CD74–ROS1	G2032R	1,100	610	500	190	32	5.1
	Ba/F3	Engineered mouse pro–B cell line	CD74–ROS1	G2032R	950	880	320	84	25	3.6
			EZR–ROS1	G2032R	630	830	42	19	8.8	0.7
			GOPC(L)–ROS1	G2032R	1,600	1,200	91	27	11	1.1
			GOPC(S)–ROS1	G2032R	1,200	>3,000	>100	>100	>100	6.6
			SLC34A2–ROS1	G2032R	440	220	14	9.4	3.8	0.2
	Average potency across 6 ROS1 G2032R fusion cell lines				920	850	98	44	18	1.6
ROS1 fusion with other resistance mutations	Ba/F3	Engineered mouse pro–B cell line	CD74–ROS1	S1986F	39	26	<0.3	NA	0.84	<0.6
			CD74–ROS1	F2004C	35	60	0.3	13	3.2	0.02
			EZR–ROS1	F2004C	28	66	0.5	13	3.5	0.01
			CD74–ROS1	F2004V	35	38	0.5	8.5	2.5	0.01
			EZR-ROS1	F2004V	11	51	0.6	10	3.6	0.2
			CD74–ROS1	L2026M	110	41	0.8	NA	3.3	1.5
			CD74–ROS1	D2033N	77	79	0.4	NA	2.5	1
			EZR–ROS1	G2101A	25	8.4	0.4	9.3	1.8	0.4

Cell viability IC_{50} (nmol/L)

10^{-1} 10^{0} 10^{1} 10^{2} 10^{3}

IC50, half maximal inhibitory concentration; TKI, tyrosine kinase inhibitor; WT, wild-type

1. Lin JJ, et al. Clin Cancer Res. 2021;27(10):2899-2909; 2. Drilon A et al., Cancer Discov. 2023;13(3):598-615

ROS1 TKIs IN CRIZOTINIB PRE-TREATED *ROS1* FUSION+ NSCLC[1]

	Lorlatinib[2] Phase 1/2	Lorlatinib[3] ALBATROS Phase 2	Repotrectinib[4] TRIDENT-1 Phase 1/2 (No prior CT)	Talectrectinib[5-7] TRUST I + II Phase 2			Zidesamtinib[8] ARROS-1 Phase 1/2	
				1 prior TKI (C or E)	Prior CT	No prior CT	Any prior TKIs	1 prior TKI (C or E)
Patients, n	40	50	56	113	42	71	117	55
ORR, %	**35**	**34**	**41**	**55.8**	**59.5**	**53.5**	**44**	**51**
Median PFS, months	**8.5**	**7.4**	**8.6**	**9.7**	**11.7**	**9.6**	48% at 12 mo	68% at 12 mo
CNS activity IC-ORR	12/24 pts (50%) Measurable + non-measurable	12/13 pts (92.3%) Measurable	5/13 pts (38%) Measurable	21/32 pts (65.6%) Measurable	NR	NR	27/56 pts (48%) Measurable	11/13 pts (85%) Measurable
G2032R ORR	0/6 (0%)	NR	10/17 (59%)	8/13 (61.5%)	NR	NR	14/26 (54%)	5/6 (83%)

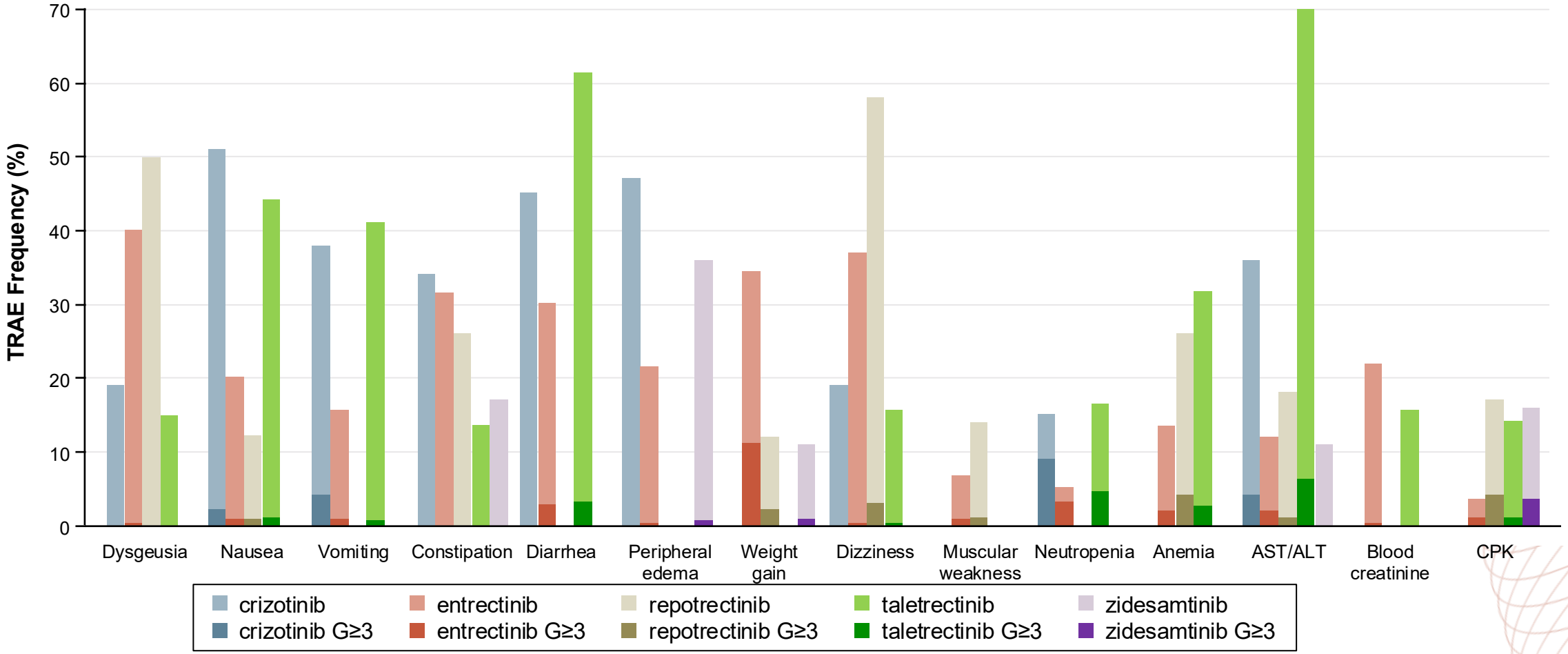
There are no head-to-head studies therefore, this is non-comparative data presented for informational/descriptive purposes. Comparisons between trials should not be made due to differences in study design and patient populations

C, crizotinib; CNS, central nervous system; CT, chemotherapy; E, entrectinib; mo, months; NR, not reported; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; pts, patients; TKI, tyrosine kinase inhibitor

1. Wespiser M, et al. Front Oncol 2026;16:1739598; 2. Shaw A, Lancet Oncol 2019;20(12):1691-1701; 3. Duruisseaux M, Abstract #1987MO, ESMO 2025 (oral presentation); 4. Cho BC, et al. Abstract #MA02.03, WCLC 2025 (oral presentation); 5. Pérol M, et al. J Clin Oncol. 2025;43:1920-9;
6. Liu G, Abstract #CT244, AACR 2026 (poster presentation); 7. Hayashi H, et al. Abstract #P3.277, WCLC 2026 (poster presentation); 8. Drilon AE, et al. Abstract #PL02.15, WCLC 2025 (oral presentation) [J Thorac Oncol. 2025;20:S3. doi: 10.1016/j.jtho.2025.09.018]

TOLERANCE PROFILE OF ROS1 TKIs: TRAEs

SELECT TRAE (OCCURRING IN ≥ 10% PATIENTS



Non-comparative data, for informational/descriptive purposes. Comparisons between trials should not be made due to differences in study design and patient populations

ALT, alanine aminotransferase; AST, aspartate transferase; CPK, creatine phosphokinase; G, grade; TKI, tyrosine kinase inhibitor; TRAEs, treatment-related adverse events

Wespiser M, et al. Front Oncol. 2026;16:1739598

NEXT-GENERATION ROS1 TKIs ARE BEING EVALUATED IN THE FRONTLINE SETTING[1]

- **As with ALK+ NSCLC, the choice of first-line ROS1 TKI is an important treatment decision,** with implications for the duration of disease control, CNS control and subsequent treatment options
- **The tolerability and safety profile of the selected TKI is also important**, particularly given that patients may require prolonged treatment

ROS1+ **advanced NSCLC** → **New generation ROS1 TKI[2]**

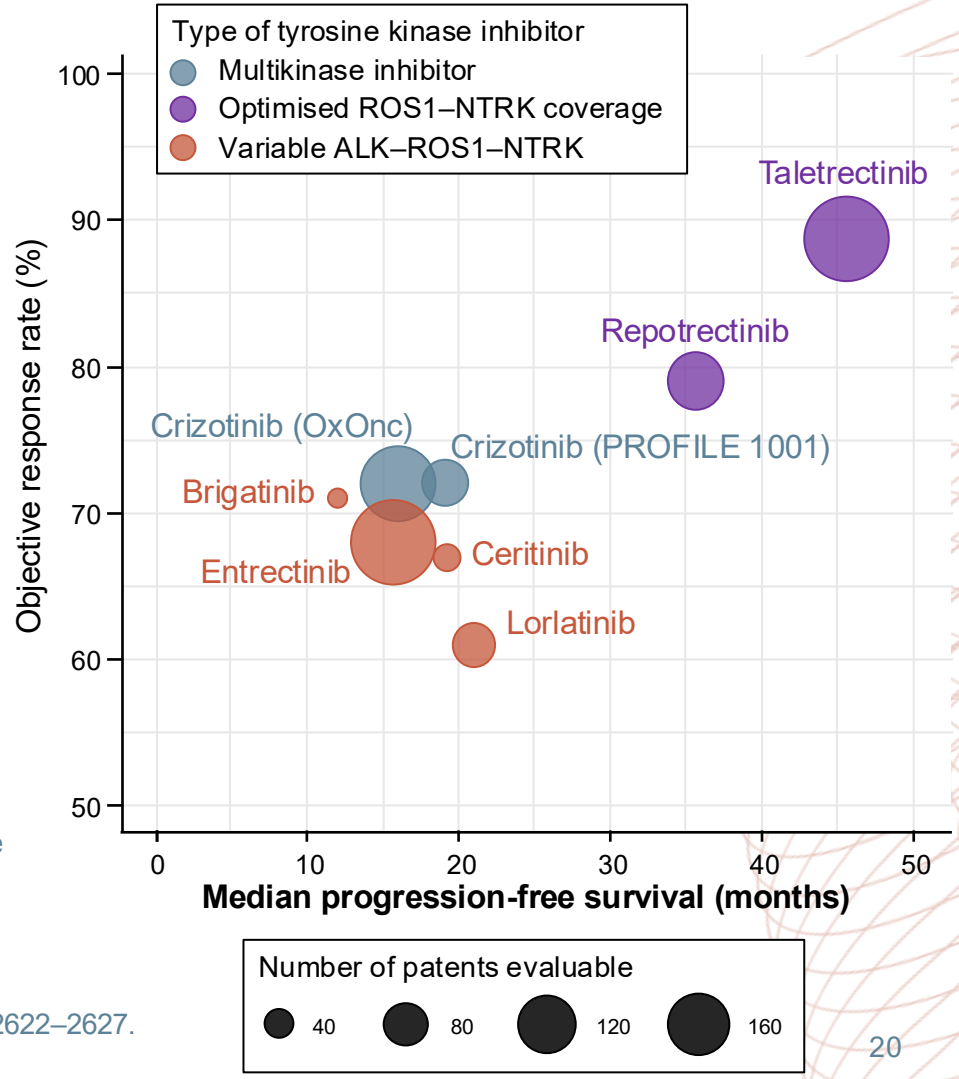
Systemic efficacy, CNS penetration, TRKB inhibition, tolerance profile

- **Ongoing phase 3 trials in ROS1-TKI-naïve advanced/metastatic NSCLC[3]:**
  - **NCT04603807:** entrectinib vs. crizotinib in treatment-naïve ROS1-positive advanced/metastatic NSCLC
  - **NCT06140836 (TRIDENT-3):** repotrectinib vs. crizotinib in ROS1-TKI-naïve advanced/metastatic NSCLC; up to one prior line of systemic therapy permitted
  - **NCT06564324 (TRUST-III):** taletrectinib vs. crizotinib in ROS1-TKI-naïve advanced/metastatic NSCLC; prior chemotherapy for locally advanced/metastatic disease permitted

Adjuvant setting:

  - **NCT07154706 (TRUST-IV):** taletrectinib vs. placebo in patients with resected early-stage ROS1-positive NSCLC

ORR (y-axis) and mPFS (x-axis) across TKI–naive patients treated with ROS1 TKIs



CNS, central nervous system; NSCLC, non-small cell lung cancer; (m)PFS, (median) progression-free survival; pts, patients; TKI, tyrosine kinase inhibitor

1. Desilets A, et al. Cancer. 2025:31 Suppl 1(Suppl 1):e35784; 2. Waliany S and Lin J. J Clin Oncol. 2024; 42(22): 2622–2627. doi:10.1200/JCO.24.01062. Author 3. Available at ClinicalTrials.gov

SUMMARY

- **The Critical Role of Systematic Testing**
  - **Broad Identification:** *ROS1* rearrangements (~2% of NSCLC) occur across all clinical profiles; testing should not be limited by age or smoking history
  - **Diagnostic Gold Standard:** While IHC is a valuable rapid screen, **NGS (preferably RNA-based)** is essential for definitive identification and characterisation of fusion partners
  - **Tissue Stewardship:** Prioritising broad molecular profiling ensures these rare but highly actionable drivers are not missed in the first-line setting
- **Evolution of the Treatment Landscape**
  - **1st-Generation TKIs:** Established the targeted approach but are limited by the eventual development of resistance mutations (e.g. G2032R) and poor CNS (brain) penetration
  - **Next-Generation TKIs:** Represent the new standard of care, specifically engineered to overcome 1st-generation resistance and provide improved intracranial activity to manage/prevent brain metastases

CNS, central nervous system; IHC, immunohistochemistry; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitors

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