Sessione II

NSCLC avanzato oncogene addicted

Il trattamento della malattia con alterazioni di BRAF, ROS1 & RET

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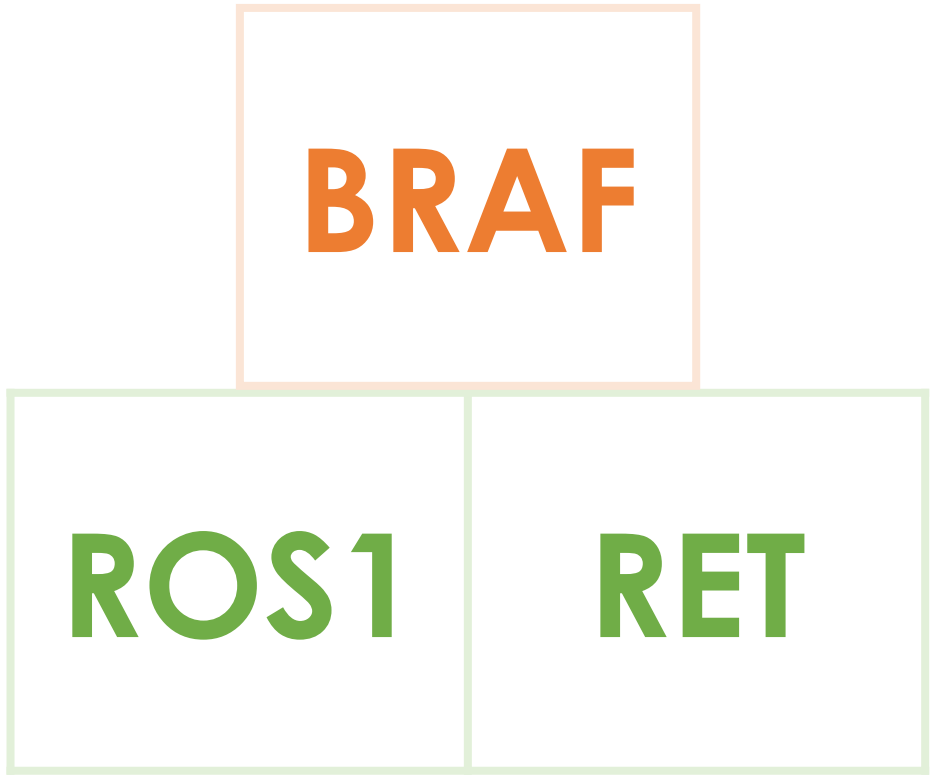
Potenziali conflitti d'interesse da dichiarare

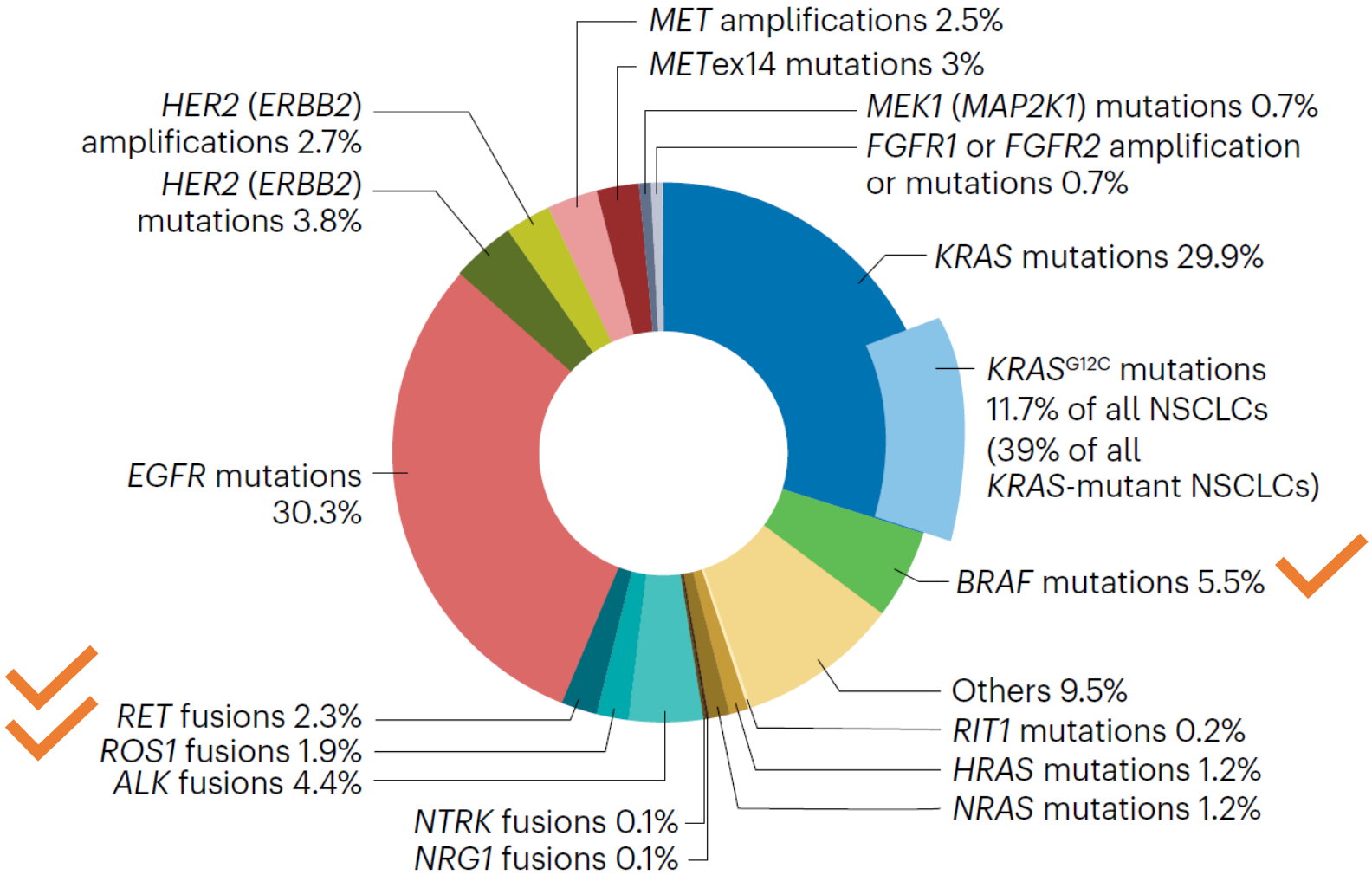
Tipo di affiliazione o supporto finanziario	*Sponsor*
Advisory Board, Speaker's Bureau, Research Funding, Consultant	AstraZeneca
Advisory Board, Speaker's Bureau, Consultant	MSD
Speaker's Bureau, Consultant	Eli Lilly
Speaker's Bureau, Consultant, Research Funding, Consultant	BMS
Advisory Board, Speaker's Bureau, Consultant	Roche
Advisory Board, Speaker's Bureau, Consultant	AMGEN
Advisory Board, Speaker's Bureau, Consultant	Novartis
Advisory Board, Speaker's Bureau, Consultant	Sanofi
Advisory Board, Speaker's Bureau, Consultant	Takeda

Agenda

- Therapy
- Strategy
- Biology & heterogeneity



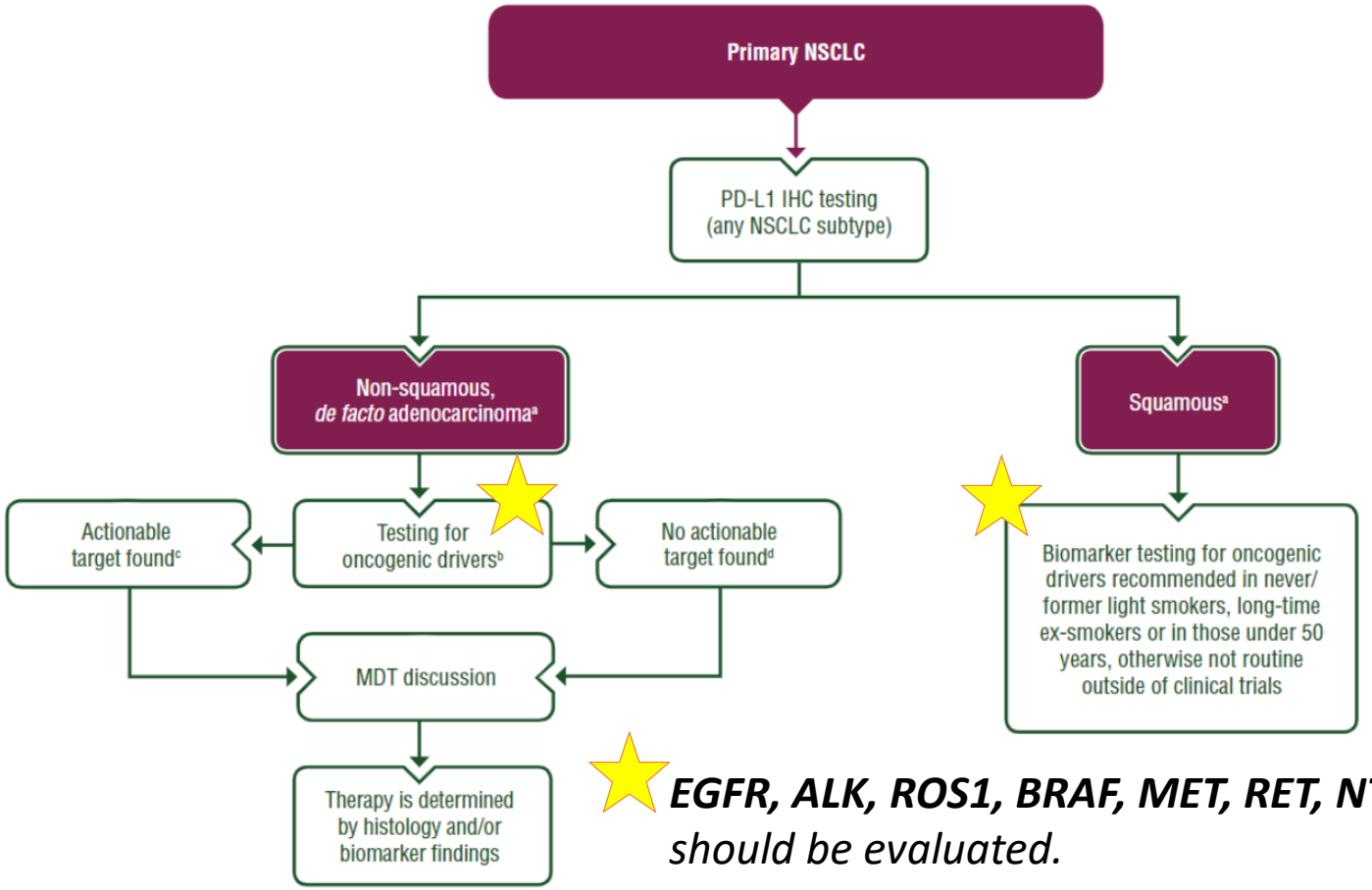
Small slices also make NSCLC the paradigm for personalized medicine



- ✓ **ROS1 fusions**
- ✓ **BRAF V600 mutations**
- ✓ **RET fusions**
- ✓ **NTRK fusions**
- ✓ **METex14 mutations**
- ✓ **HER2 mutations**
- ✓ NRG1 fusions
- ✓ MET amplifications

Otano I et al, Nature Reviews Clinical Oncology 2023

Predictive Biomarkers in advanced NSCLC



- **Reflex testing** preferred (TAT is shorter)
- **Targeted NGS** designed to cover panels of genes is the recommended option
- Priority for **careful handling and preservation of tissue** throughout the process

EGFR, ALK, ROS1, BRAF, MET, RET, NTRK, EGFRex20ins, HER2, KRAS (G12C) *should be evaluated.*

Currently, ***MET, RET, EGFRex20ins, KRAS G12C are for second-line treatment decisions***
(HER2 not yet druggable in clinical practice)

Oncogene-addicted metastatic NSCLC ESMO Clinical Practice Guideline 2023

Agenda

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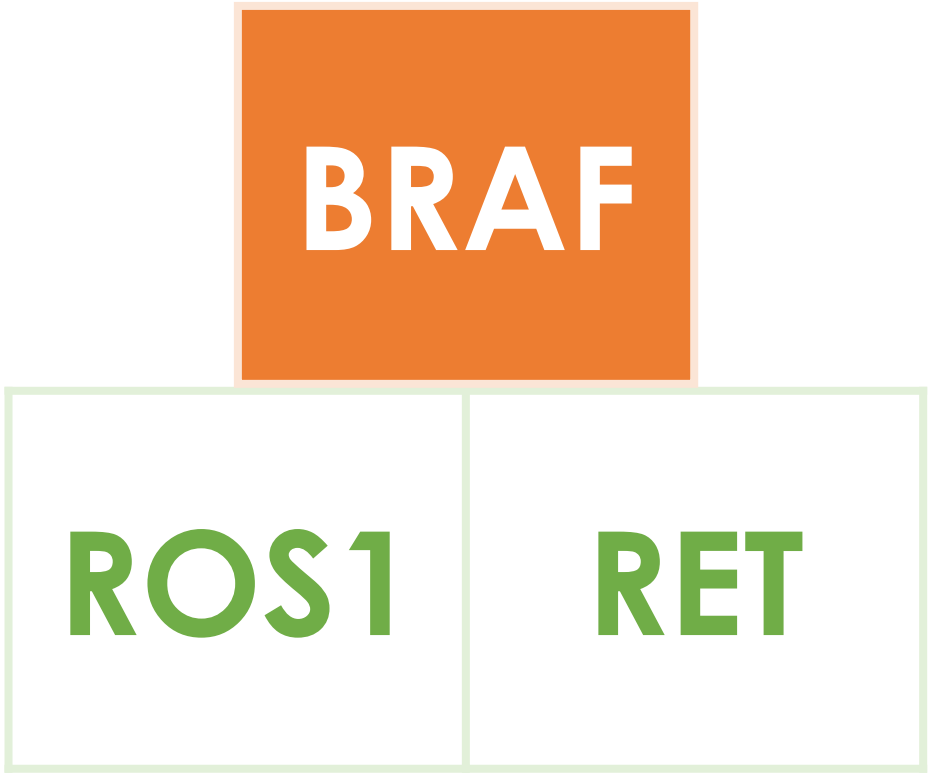
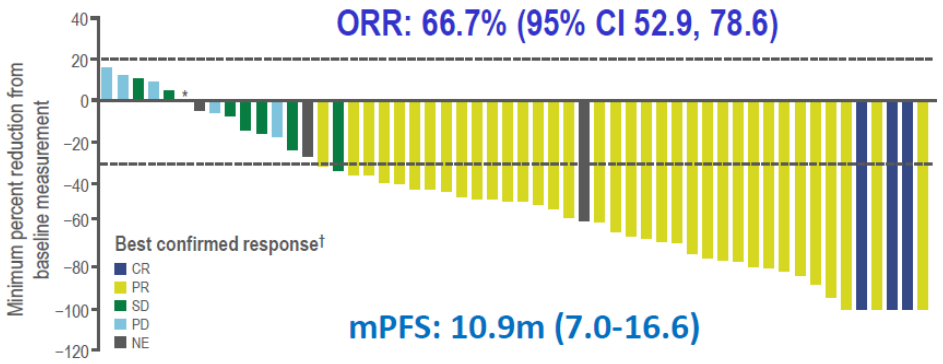
- Strategy
- Biology & heterogeneity

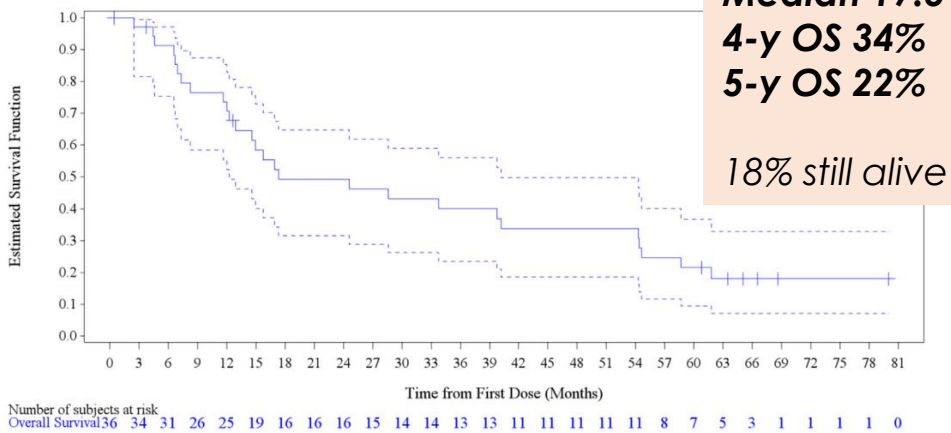


Standard of care

Dabrafenib-trametinib in 1st line [*BRAF p.V600*]

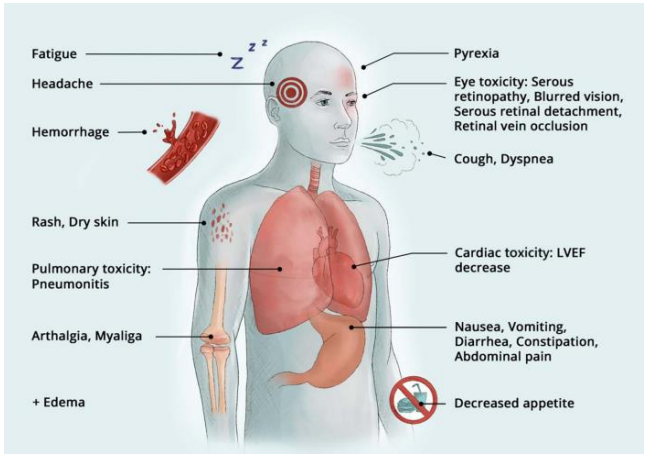
BRAF





OS in treatment-naïve:
Median 17.3 ms
4-y OS 34%
5-y OS 22%

18% still alive



All grades	D	D + T
Fever	35%	↑46%
Nausea	27%	↑40%
Vomiting	20%	↑35%
Diarrhea	16%	↑34%
Skin carcinoma	17%	8%
Hyperkeratosis	29%	-
SAEs	42%	↑56%
Reduction	18%	↑35%
Discont.	6%	↑12%

- Continue if mild and treat to ameliorate symptoms
- It goes away/get better when you stop the drug (!)
- Fever→ acetaminophen, naproxen, steroids
- Monitor with echocardio and ophthalmologic reviews!!

Planchard D, Lancet Oncol 2017
Planchard D, J Thorac Oncol 2022
Gouda MA & Subbiah V, ASCO Ed Book 2023

Trying to improve risk-benefit R

Encorafenib – binimetinib in 1st line [*BRAF p.V600E*]

BRAF

Key eligibility criteria

- Metastatic BRAF V600E–mutant NSCLC
- ECOG performance status 0 or 1
- No *EGFR* mutation, *ALK* fusion, or *ROS1* rearrangement
- No more than 1 prior line of treatment in the advanced setting
- No prior treatment with BRAF or MEK inhibitor
- No symptomatic brain metastases

***BRAF* mutation testing**

- Determined locally by PCR- or NGS-based assay; sent to central laboratory[a]
- Pleural fluid, fresh and archived tissue, and fine needle aspiration were acceptable

Patients enrolled

Treatment naïve n=59

Previously treated n=39

Encorafenib: 450 mg QD

Binimetinib: 45 mg BID

28-day cycles

Treat until progression or unacceptable toxicity

Primary endpoint
- ORR[b] by IRR

Secondary endpoints
- ORR by investigator
- DOR, DCR, PFS, and TTR (all by IRR and investigator)
- OS
- Safety

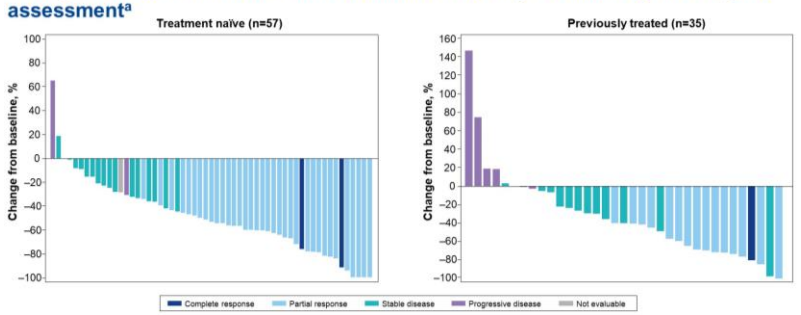
Exploratory endpoints
- Biomarker and pharmacokinetic analyses

Antitumor activity endpoints by IRR

	Treatment naïve (n=59)	Previously treated (n=39)
Objective response rate (95% CI), %[a]	75 (62, 85)	46 (30, 63)
Complete response	9 (15)	4 (10)
Partial response	35 (59)	14 (36)
Stable disease	10 (17)	13 (33)
Progressive disease	2 (3)	3 (8)
Disease control rate at 24 weeks (95% CI), %	64 (51, 76)	41 (26, 58)
Duration of response, median (95% CI), months	NE (23.1, NE)	16.7 (7.4, NE)

All grades	D + T	E + B
Fever	46%	↓ 22%
Nausea	40%	50%
Vomiting	35%	29%
Diarrhea	34%	43%
Fatigue	28%	32%
Oedema	23%	↓11%
SAEs	56%	↓41%
Reduction	35%	↓24%
Discont.	12%	15%

Change from baseline in the sum of diameters of target lesions by investigator assessment[a]



Pyrexia (treatment-related) was the cause of dose interruption of encorafenib plus binimetinib in one patient but did not result in dose reduction or permanent treatment discontinuation

Ahn MJ et al, ASCO 2023

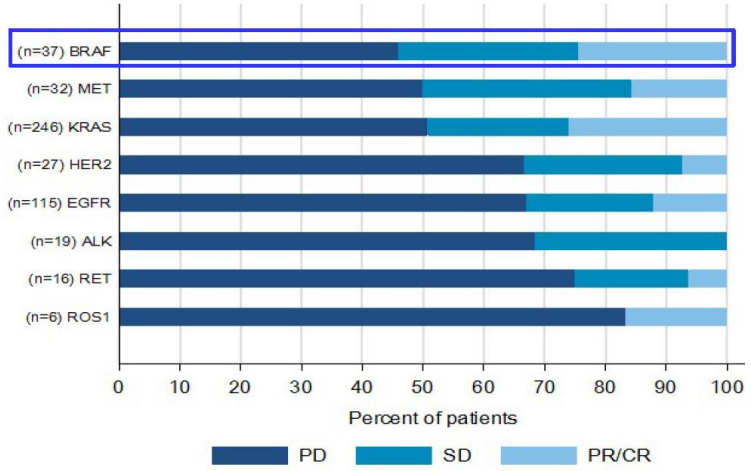
How to manage disease PD?

Role of IO & mechanisms of resistance

BRAF

IO

Driver	PD	SD	CR/PR
BRAF	46%	30%	24%
MET	50%	34%	16%
KRAS	51%	23%	26%
HER2	67%	26%	7%
EGFR	67%	21%	12%
ALK	68%	32%	0
RET	75%	19%	6%
ROS1	83%	0	17%
TOTAL	57%	24%	19%

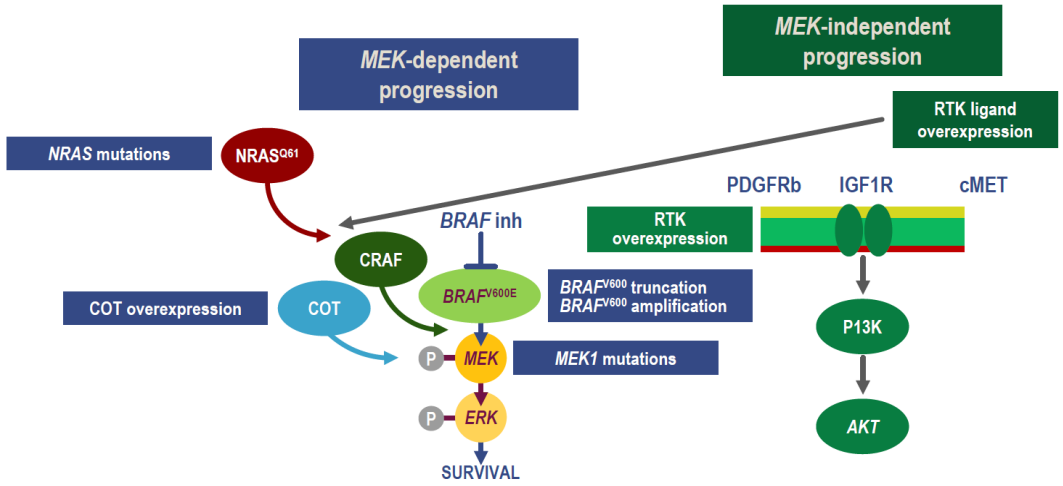


Mazieres J et al, Ann Oncol 2019

Outcome by 1° line regimen	rwTOT
PD-(L)1 mono [N = 26]	7.6 ms
PD-(L)1 + ChT [N = 13]	17.5 ms
Pembro + platinum + pem [N = 12]	20.7

BRAF V600E: rwTOT and rwTTNT similar for PD-(L)1 mono but markedly longer for PD-(L)1+ChT *VS* other cohorts, including the driver-negative cohort

Garassino MC et al, JTO 2023



Reactivation of ERK signaling either upstream or downstream of BRAF kinase (= melanoma) through:
- BRAF splice variants (16%)
- BRAF gene amplification (13%)
- NRAS/KRAS (20%) or MEK1/2 mutations (7%)

BRAF-independent reactivation of ERK signaling

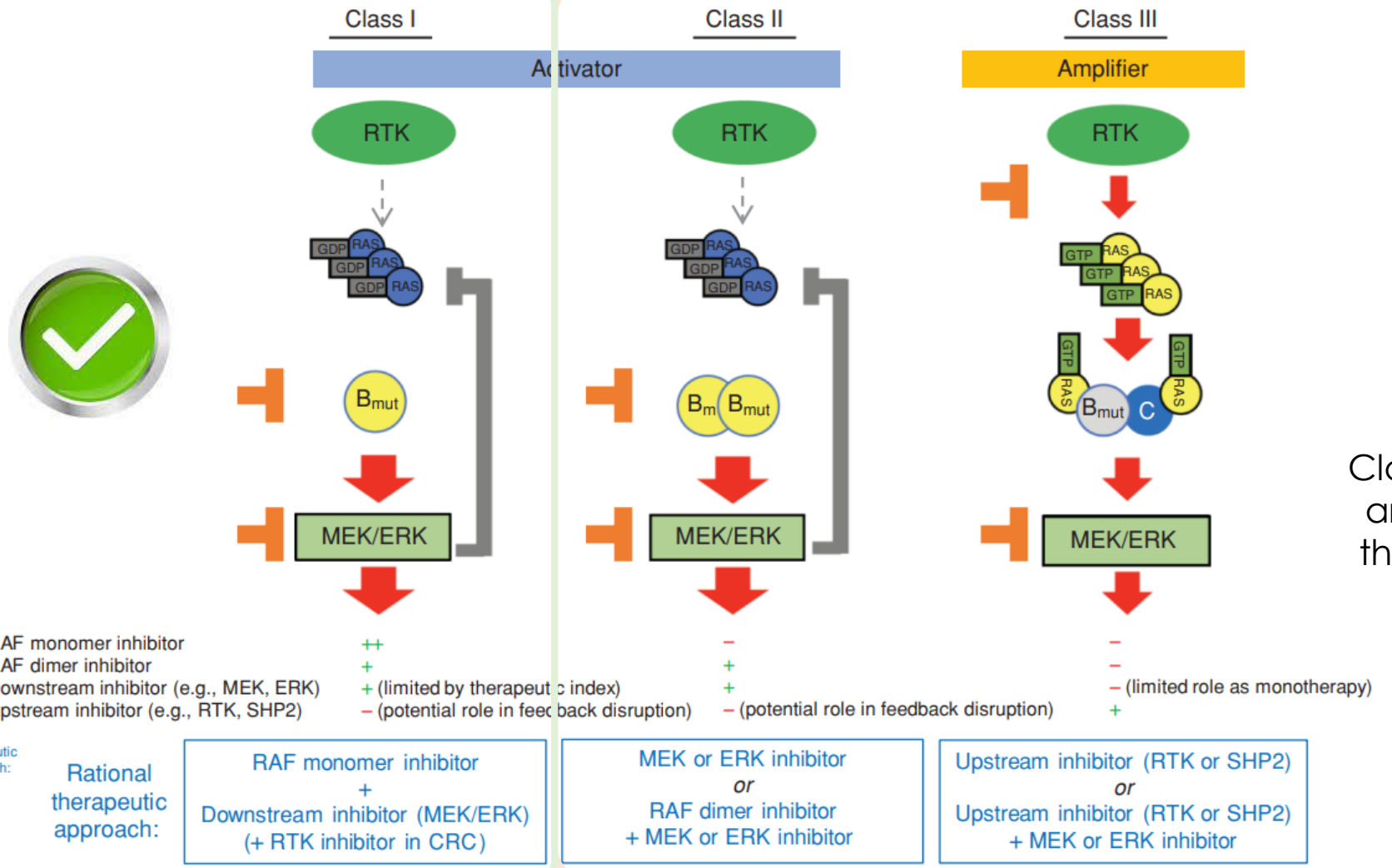
R ?

Facchinetti F et al, JTO 2023
Abdayem P & Planchard D, Clinical Advances in Hematology & Oncology 2022

What about the rest of *BRAF* world?

Non-V600 mutations

BRAF

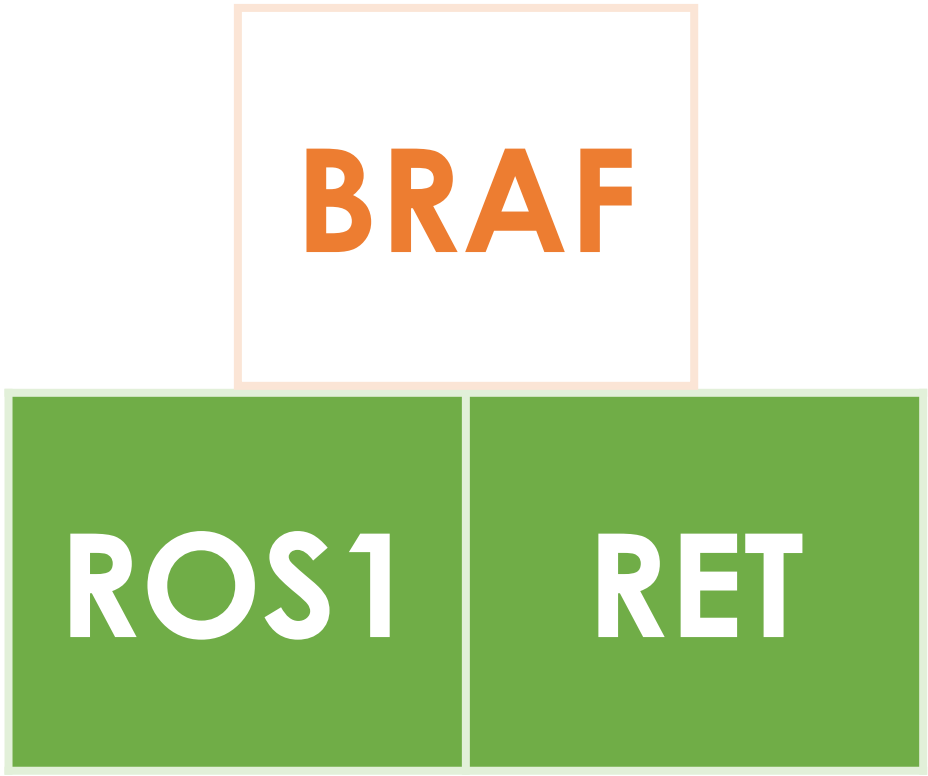


Class-specific therapies are needed to target these different subsets

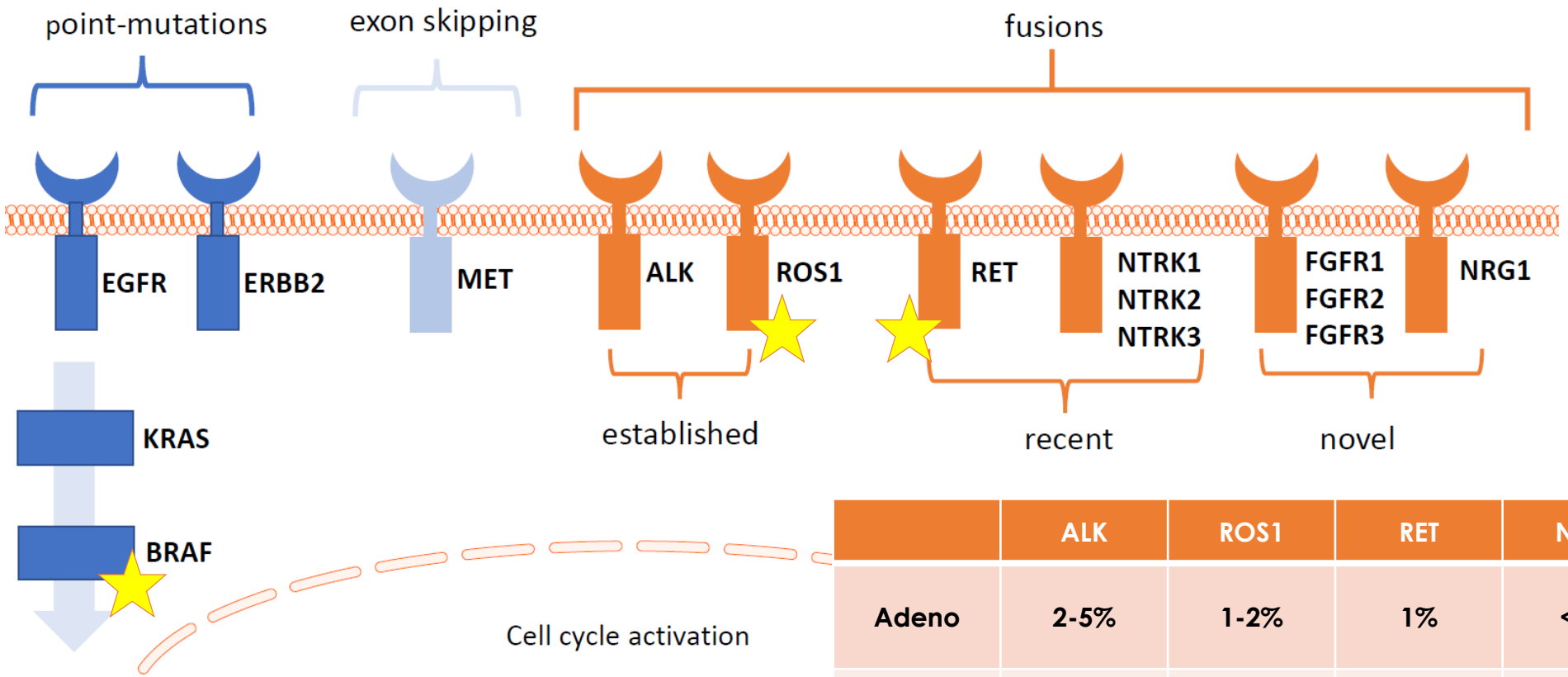
Yaeger R et al, Cancer Discovery 2019

Agenda

- Therapy
- Strategy
- Biology & heterogeneity



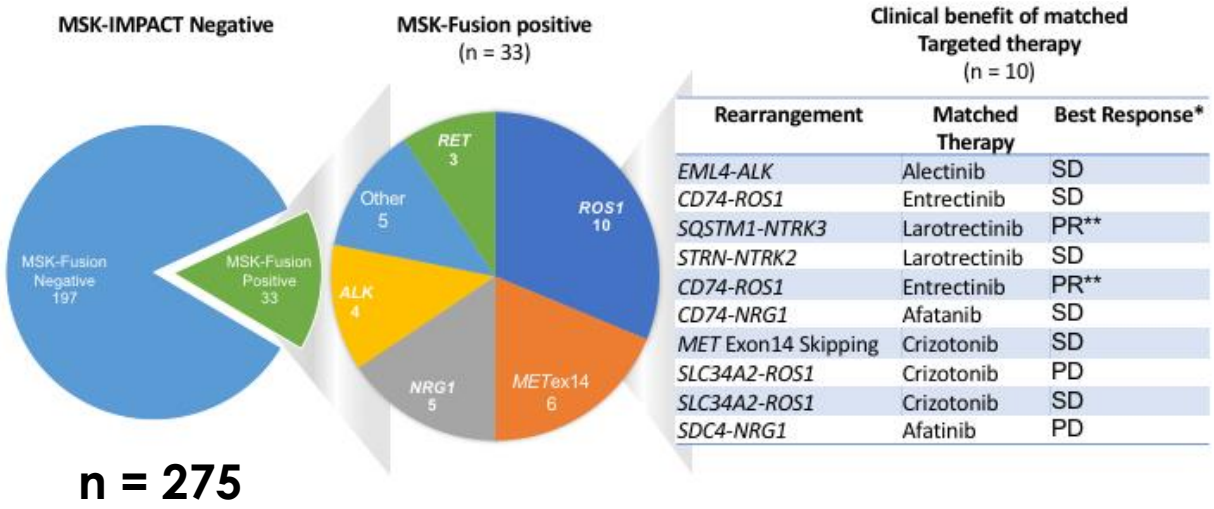
Which type of alterations?



	ALK	ROS1	RET	NTRK	FGFR	NRG1
Adeno	**2-5%**	**1-2%**	**1%**	**<1%**	**<1%**	**<1%** Mucinous k 5-6%
Sq	**<1%**	Case reports	Case reports	Case reports	**1-4%**	Case reports

Modified from Radonic T, ELCC 2023

Targeted RNA is better suited for fusion identification



n = 275

Clinical benefit of matched Targeted therapy (n = 10)

Rearrangement	Matched Therapy	Best Response*
EML4-ALK	Alectinib	SD
CD74-ROS1	Entrectinib	SD
SQSTM1-NTRK3	Larotrectinib	PR**
STRN-NTRK2	Larotrectinib	SD
CD74-ROS1	Entrectinib	PR**
CD74-NRG1	Afatanib	SD
MET Exon14 Skipping	Crizotonib	SD
SLC34A2-ROS1	Crizotonib	PD
SLC34A2-ROS1	Crizotonib	SD
SDC4-NRG1	Afatinib	PD

Pros	Cons
All fusions of interest at once!	RNA is unstable
Fusion partner agnostic	**Higher rate of QC fail**
Inframe fusions	More tissue necessary
Expressed / upregulated (low tumor % input), threshold 50 copies	**Higher costs**
Specific and sensitive (if passes QC)	

Failure rate can be up to 20%!
Material at higher risk for failure
- cytology
- decalified biopsies
- biopsies overweekend in formalin

RNA-based >> DNA-based for fusions and splice site mutations

Hybride DNA and RNA panels
(**one step sequencing**)

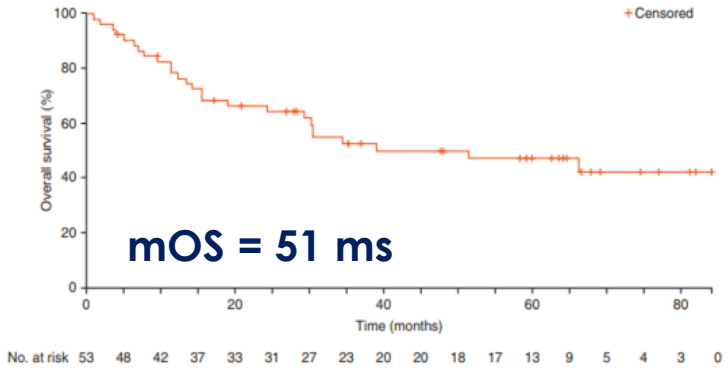
Benayed R et al, Clin Cancer Res 2019
Modified from Radonic T, ELCC 2023

Standard of care

Crizotinib & Entrectinib in 1st line

ROS1

PROFILE 1001: **crizotinib**

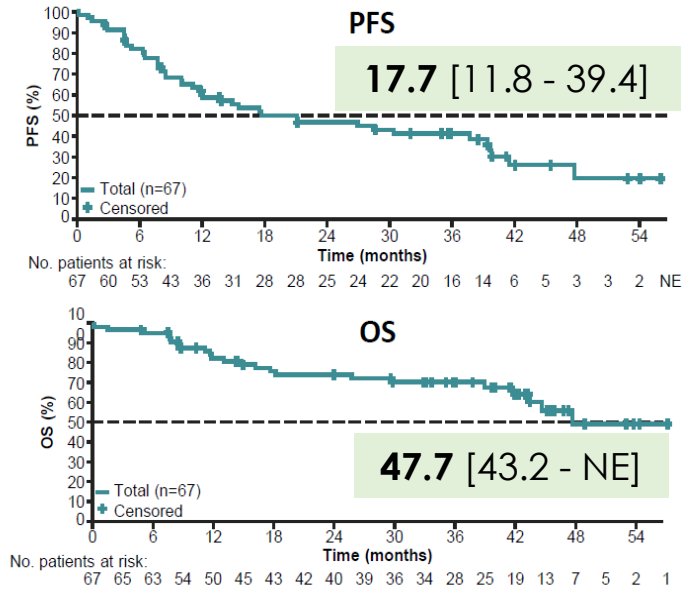


End points	*ROS1*-rearranged NSCLC (*N* = 53)
ORR, % (95% CI)[a]	72 (58–83)
CR, *n* (%)	6 (11)
PR, *n* (%)	32 (60)
SD (≥6 weeks), *n* (%)	10 (19)
PD, *n* (%)	3 (6)
Not evaluated[b]	2 (4)
Median time to first tumor response, weeks (range)[c]	7.9 (4.3–103.6)
Median duration of response, months (95% CI)[d,e]	24.7 (15.2–45.3)
Median PFS, months (95% CI)[d,f]	19.3 (15.2–39.1)

- On-target resistance mutations (*G2032R*)
- CNS progression

Integrated analysis of 3 phase I and II trials: **entrectinib**

	First-line population† (n=67)
ORR, n (%) [95% CI]	**46 (68.7)** [56.2–79.4]
CR	10 (14.9)
PR	36 (53.7)
SD	7 (10.4)
PD	5 (7.5)
Non CR / PD	6 (9.0)
Missing / unevaluable	3 (4.5)
Median DoR, months [95% CI]	**35.6** [13.9–38.8]
icORR	**61%**



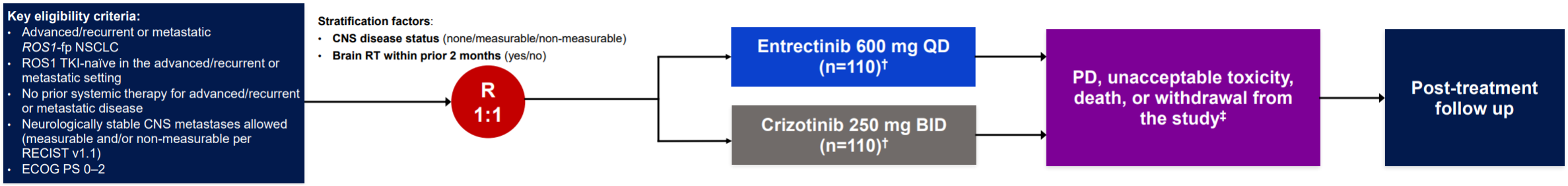
Grade ≥ 3 AEs 43% mainly dysgeusia, weight increase, constipation and diarrhea – **discontinuation 7%**

Shaw AT et al, Ann Oncol 2019
Drilon A et al, JTO Clinical and Research Reports 2022
Fan Y et al, WCLC 2022

Standard of care

Crizotinib VS Entrectinib in 1st line

ROS1



Primary endpoint

- **PFS per BICR** (RECIST v1.1) **in the CNS population**

Secondary efficacy endpoints

- **ORR, DoR** and **PFS** in the ITT population: BICR and investigator assessed (RECIST v1.1)
- **OS** in the CNS and ITT populations
- **CNS-PFS** in the ITT population: BICR assessed (RECIST v1.1)
- **CNS-ORR** and **CNS-DoR** in the CNS population: BICR assessed (RECIST v1.1)

Safety-related endpoints

- **Incidence, type, and severity of AEs** (including serious AEs and AEs leading to dose modifications/interruptions)
- **Study drug withdrawal or death**
- **Change from baseline in treatment-related symptoms** (EORTC QLQ-C30)
- **Frequency of patients' response** of the degree they are troubled by treatment symptoms (EORTC IL46)

PROs endpoints

- **Impact on functioning** (EORTC QLQ-C30) and **lung cancer-specific symptoms** (EORTC QLQ-LC13)

Dingemans AM et al, ASCO 2022

Should we escalate 1st line with new gen TKIs?

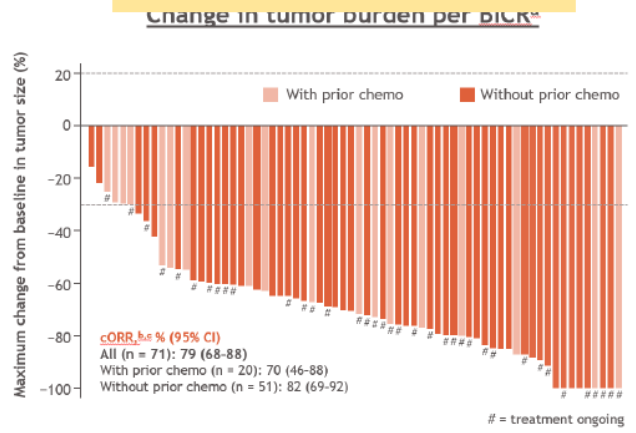
Repotrectinib [TRIDENT-1]

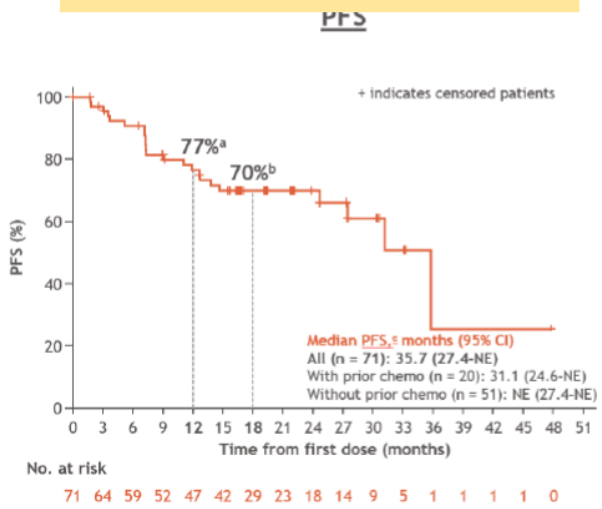
ROS1

Overall RR: 79%
Tx-naïve RR: 82%

Overall mPFS: 35.7mo
Tx-naïve mPFS: NR

Dose reduction: 35%
Dose interruption: 35%
Dose discontinuation: 3%

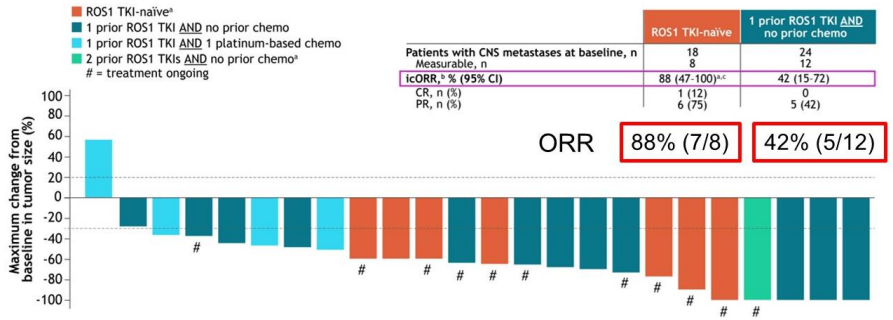




	All patients treated at the RP2D[a] (n = 426)		All patients with *ROS1*+ NSCLC treated at the RP2D (n = 320)	
AEs, n (%)	TEAEs	TRAEs	TEAEs	TRAEs
All patients with AEs	422 (99)	409 (96)	318 (99)	306 (96)
Leading to dose reduction	163 (38)	149 (35)	112 (35)	100 (31)
Leading to drug interruption	213 (50)	150 (35)	158 (49)	107 (33)
Leading to treatment discontinuation	31 (7)	14 (3)	23 (7)	11 (3)
Serious AEs	147 (34)	38 (9)	106 (33)	24 (8)
Grade ≥ 3 AEs	216 (51)	122 (29)	156 (49)	86 (27)
Fatal AEs	19 (4)	0	13 (4)	0

[a] The most common TEAE was dizziness, which was reported in 62% of patients (n = 264); grade ≥ 3 treatment-emergent dizziness was reported in 3% of patients (n = 11); no patients discontinued repotrectinib due to treatment-emergent dizziness[b]

	ROS1 naïve (n=71)		ROS1 pretreated (n=56)	
	with CNS (n=18)	without CNS (n=53)	with CNS (n=24)	without CNS (n=32)
ORR	89%	75%	33%	41%
PFS	87% (PFS at 12m)	77% (PFS at12m)	57% (PFS at 6m)	75% (PFS at 6m)

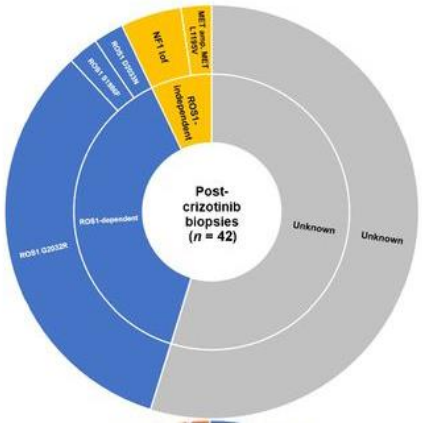


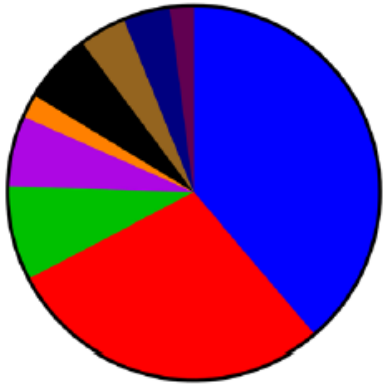
Preventive effect of repotrectinib for BM (only 1.8% of TKI-naïve pts developed a new brain mets)

Cho BC et al, WCLC 2023
Lin JI et al, ASCO 2023

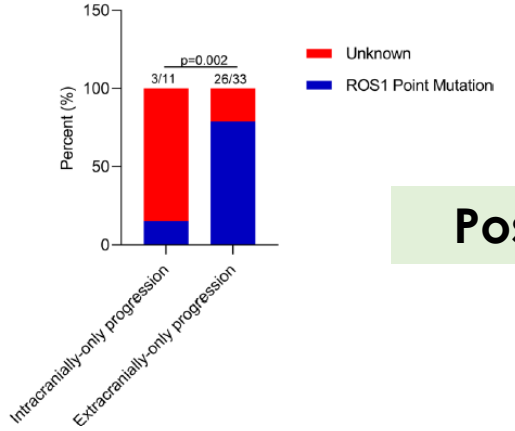
How to manage disease PD?

ROS1





Unknown, 19/49, 38.7%
G2032R, 14/49, 28.6%
G2032K, 4/49, 8.3%
L2026M, 3/49, 6.1%
L1174F, 1/49, 2.0%
L2086F, 3/49, 6.1%
S1986Y, 2/49, 4.1%
S1986F, 2/49, 4.1%
L2155S, 1/49, 2.0%



Post-crizotinib

IC_{50} (nmol/L)	Crizotinib	Entrectinib	Lorlatinib	Repotrectinib	Cabozantinib	Ceritinib	Brigatinib	Taletrectinib	Alectinib
Parental	840.5	1,801.0	>3,000	1,218.0	>3,000	1,117.0	>3,000	>3,000	1,207.0
Nonmutant	5.4	2.7	0.7	2.0	2.8	16.4	9.4	2.6	995.4
G2032R	609.6	436.3	196.6	23.1	17.5	346.4	472.7	53.3	1,091.0
L2000V	37.1	25.9	2.5	10.1	7.6	124.9	78.9	29.8	985.0
L2086F	536.8	440.0	>3,000	587.9	3.6	226.9	159.3	1,265.0	672.5
S1986F/L2000V	159.4	36.1	2.4	7.2	5.1	86.9	62.5	20.3	1,080.0
S1986F/L2086F	469.7	344.2	>3,000	241.2	1.3	154.8	48.5	662.6	919.9
G2032R/L2086F	498.6	335.4	>3,000	248.9	5.0	573.9	450.9	744.2	1,254.0
S1986F/G2032R	594.4	718.5	990.6	65.1	70.1	614.7	717.0	105.4	1,137.0
S1986F/G2032R/L2086F	562.8	1,111.0	2,131.0	1,178.0	9.4	1,116.0	1,341.0	2,432.0	1,150.0

IC_{50} ≤ 50 nmol/L
50 nmol/L < IC_{50} <200 nmol/L
IC_{50} ≥ 200 nmol/L

Lin JL et al, Clin Cancer Res. 202
Zhang Y et al, NPJ 20221

How to manage disease PD?

Clinical data

ROS1

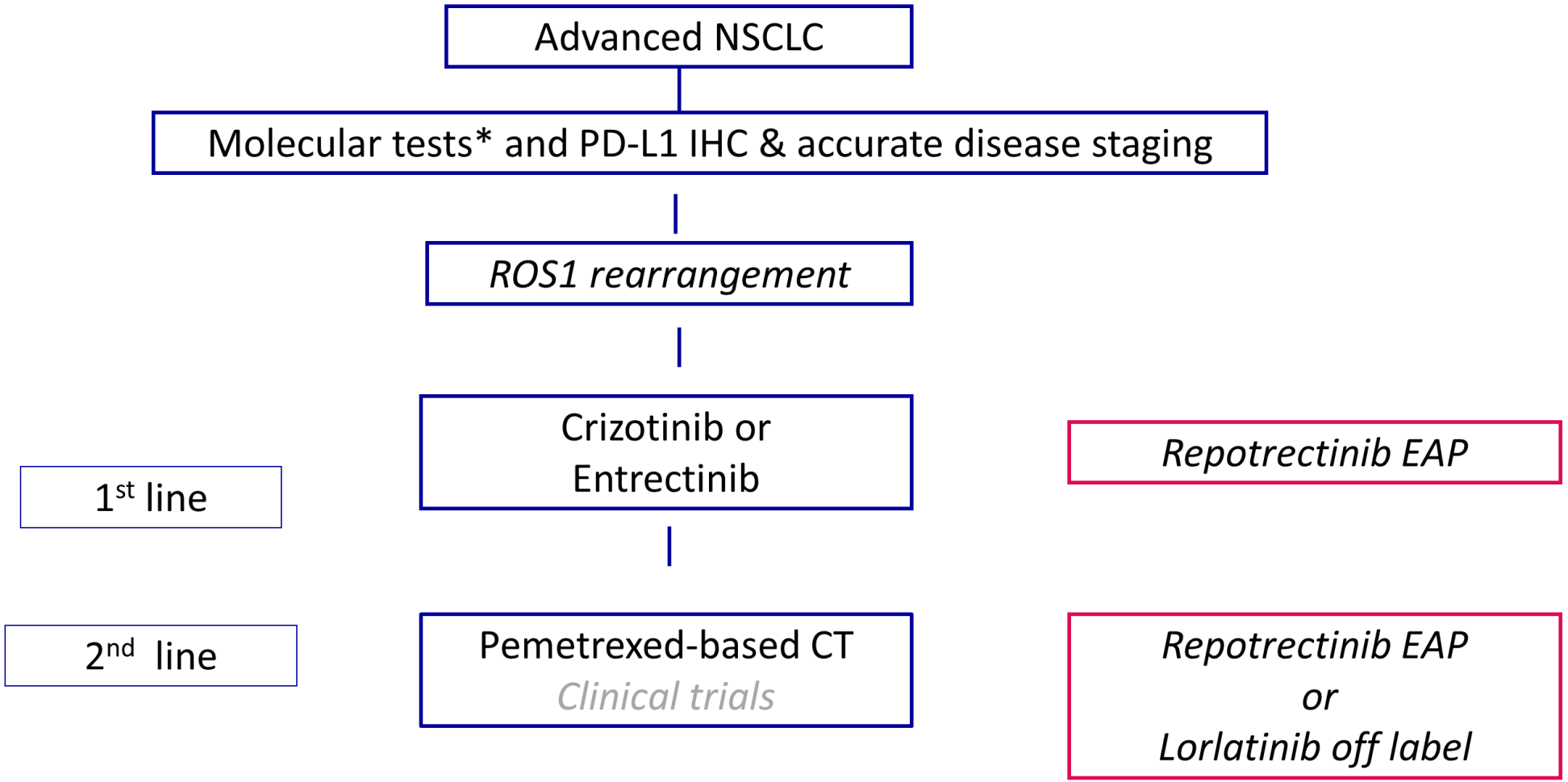
	Lorlatinib (Phase 1/2)	Repotrectinib (TRIDENT-1 Phase 1/2)	Taletrectinib (TRUST China Phase 2)	NVL-520 (ARROS-1 Phase 1)
Patients	N=40	N=56	N=38	N=21
ORR	**35%** **(prior crizotinib)**	**38%** **(only 1 prior ROS1 TKI and no prior chemo)*** *FDA breakthrough therapy designation	**50%** **(prior crizotinib)*** *FDA breakthrough therapy designation	**48%** • **53% (9/17) with ≥2 prior ROS1 TKI, ≥1 chemo** • **50% (9/18) with prior lorlatinib or repotrectinib**
Median PFS	**8.5 months**	**9.0 months**	**9.8 months**	**Not reported**
CNS activity	12/24 (50%) with measurable or nonmeasurable CNS disease	5/13 (38%) with measurable CNS metastases	11/12 (92%) with measurable CNS metastases (TKI-naïve & crizotinib-pretreated)	CNS responses reported
Clinical ROS1 G2032R activity	Response in 0/6 **(0%)** patients with a baseline ROS1 G2032R in plasma	Responses in 10/17 (**59%**) patients with a baseline ROS1 G2032R	Responses in 4/5 (**80%**) patients with a baseline ROS1 G2032R	Responses in 7/9 (**78%**) patients with a baseline ROS1 G2032R
Most common TRAEs or TEAEs (all grades)	Hypercholesterolemia, hypertriglyceridemia, edema, peripheral neuropathy, cognitive/mood effects, weight increased	Dizziness, dysgeusia, constipation, paresthesia, dyspnea, anemia, fatigue, nausea, muscular weakness, ataxia	Diarrhea, nausea, vomiting, ALT increase, AST increase, anemia, neutrophil count decrease	No DLTs or treatment-related SAEs or dizziness reported
Reference	Shaw AT et al., Lancet Oncol 2019	Cho BC et al., WCLC 2023	Li W et al., ELCC 2023	Drilon A et al., EORTC-NCI-AACR 2022

Lin JL, WCLC 2023

How to manage disease PD?

Realistic algorithm of ROS1+ NSCLC in Italy – 2023

ROS1



* NGS recommended;

Courtesy of L. Landi

Standard of care

A not-target 1st line

RET

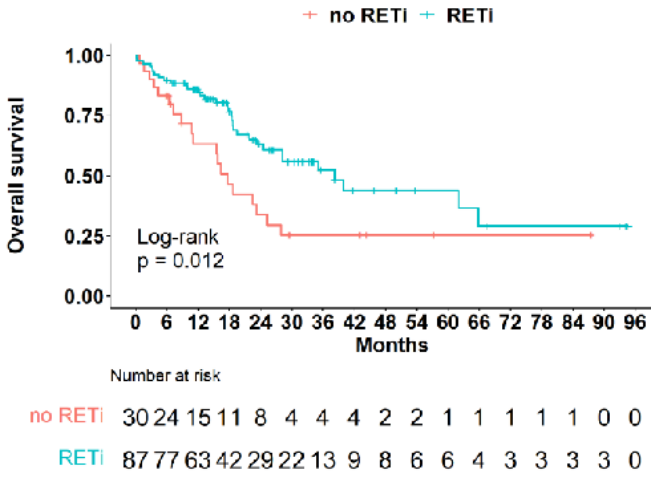
- **Chemotherapy works** [ORR~50%, mPFS~6ms, mOS~24ms]

Outcomes with 1° line CT RET Registry

Outcome	All Chemotherapy Agents (n = 108)	Platinum Doublet (n = 84)	Platinum + Pemetrexed (n = 66)
Best response (95% CI)	52% (39.8 to 64.4) 36 of 69 evaluable	51% (38.1 to 63.4) 33 of 65 evaluable	49% (35.4 to 62.9) 27 of 55 evaluable
Disease control rate (95% CI)	75% (63.5 to 84.9) 52 of 69 evaluable	75% (63.1 to 85.2) 49 of 65 evaluable	75% (61.0 to 85.3) 41 of 55 evaluable
Median PFS (95% CI)	6.6 months (5.1 to 9.3)	7.8 months (5.3 to 10.2 months)	6.4 months (4.3 to 8.8 months)
Median OS (95% CI)	23.6 months (13.6 to 30.8)	24.8 months (13.6 to 32.3 months)	23.6 months (13.4 to 33.2 months)

Drilon A et al, Ann Oncol 2016
Gautschi O et al, J Clin Oncol 2017

- Still **controversies with immunotherapy**



	Doublet CT (N=108)	Single agentCT (N=34)	CT-ICB (N=41)	ICB (N=52)	MTKi (N=21)	RETi (N=145)
ORR	55%	26%	**46%**	**23%**	37%	**76%**
mPFS	8.7	3.6	**9.6**	**3.1**	3	**16.2**

Aldea M et al, RET-MAP JTO 2023

Standard of care

Selpercatinib & Pralsetinib in 2nd line

RET

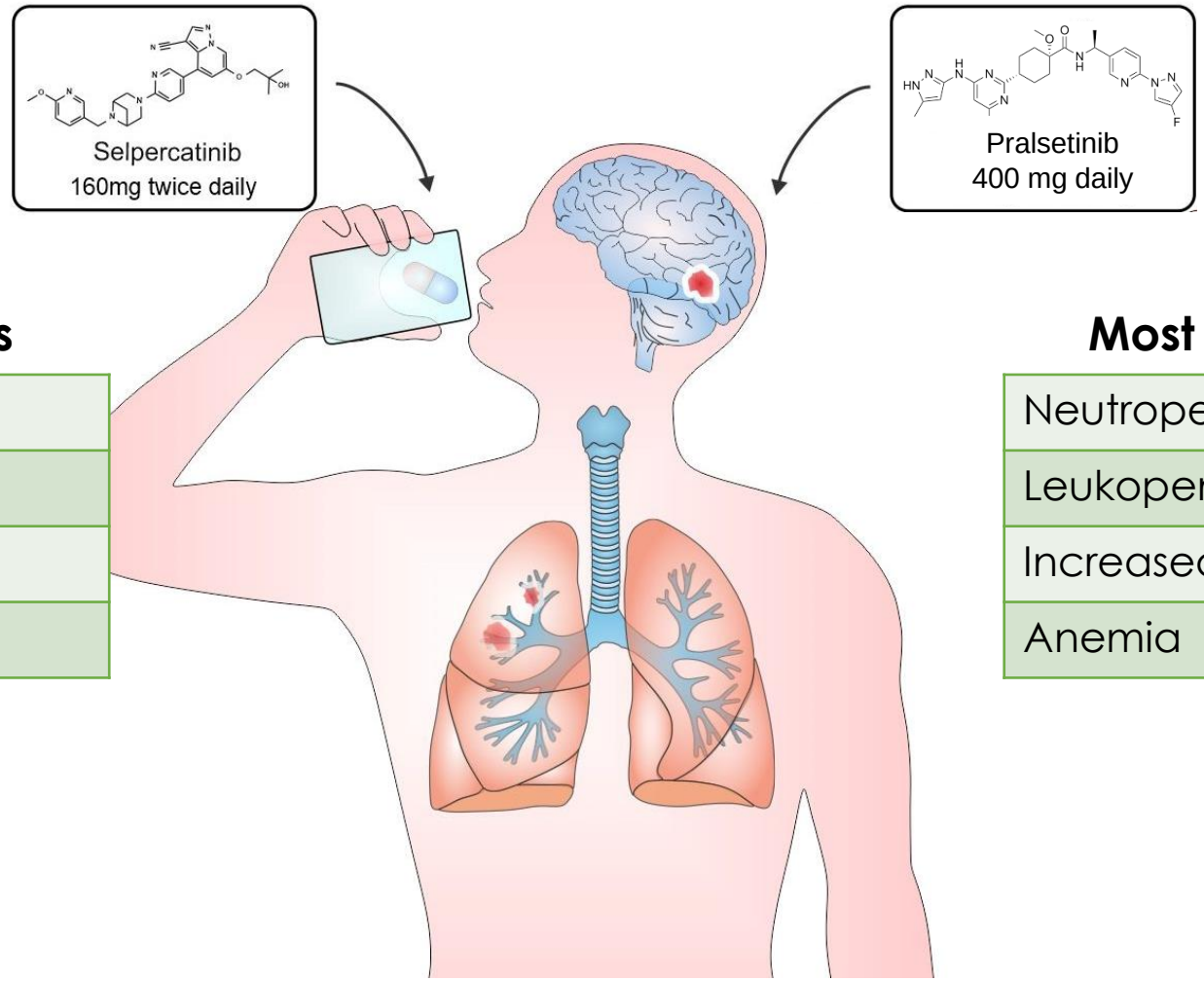
	SELPERCATINIB	PRALSETINIB
	[LIBRETTO-001]	**[ARROW]**
ORR (%, N)		
Prior platinum-based chemotherapy	**61%** (n = 247)	**59%** (n = 136)
Treatment-naïve	**84%** (n = 69)	**72%** (n = 75)
DCR (%, N)		
Prior platinum-based chemotherapy	**94%** (n = 247)	**90%** (n = 136)
Treatment-naïve	**93%** (n = 69)	**91%** (n = 75)
mPFS (months, N)		
Prior platinum-based chemotherapy	**24.9** (n = 247)	**16.5** (n = 136)
Treatment-naïve	**22.0** (n = 69)	**13.0** (n = 75)
3y-OS (%, N)		
Prior platinum-based chemotherapy	**58.5%** (n = 247)	**58%** (n = 141)
Treatment-naïve	**57.1%** (n = 69)	**58%** (n = 69)
iORR (%, N)	**85%** (n = 26)	**70%** (n = 10)
Grade ≥3 TRAEs (%, N)	**38.6%** (n = 796)	**52%** (n = 281)
Discontinuation rate (%, N)	**3%** (n = 796)	**7%** (n = 281)

Updated from Belluomini L et al, Expert Rev Anticancer Ther 2022; Drilon A et al, JCO 2022; Drilon A et al, JCO 2023; Griesinger F et al, Ann Oncol 2022; Murciano-Goroff Y et al, JTO 2023

Standard of care

Selpercatinib & Pralsetinib in 2nd line

RET



Most common TRAEs

Dry mouth	38%
Hypertension	28%
Increased ALT/AST	28%
Diarrhea	27%

Hypersensitivity

Most common TRAEs

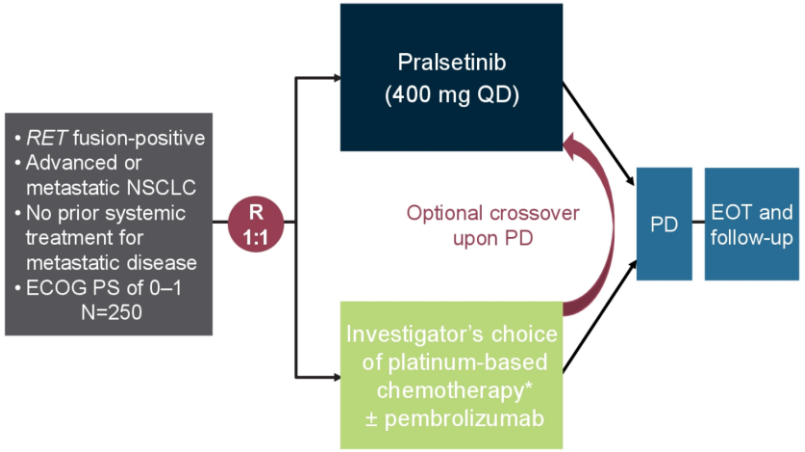
Neutropenia	46%
Leukopenia	38%
Increased ALT/AST	35%
Anemia	32%

Updated from Belluomini L et al, Expert Rev Anticancer Ther 2022; Drilon A et al, JCO 2022; Drilon A et al, JCO 2023; Griesinger F et al, Ann Oncol 2022; Murciano-Goroff Y et al, JTO 2023

Should we anticipate in 1st line RET TKIs?

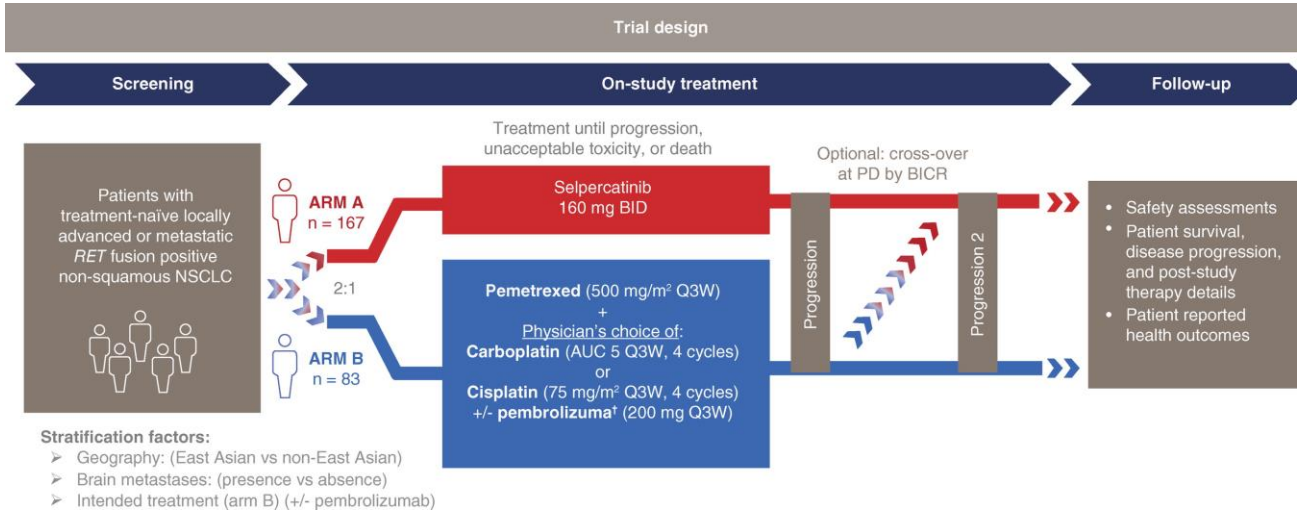
RET

AcceleRET



Besse B et al, ASCO 2020

LIBRETTO-431



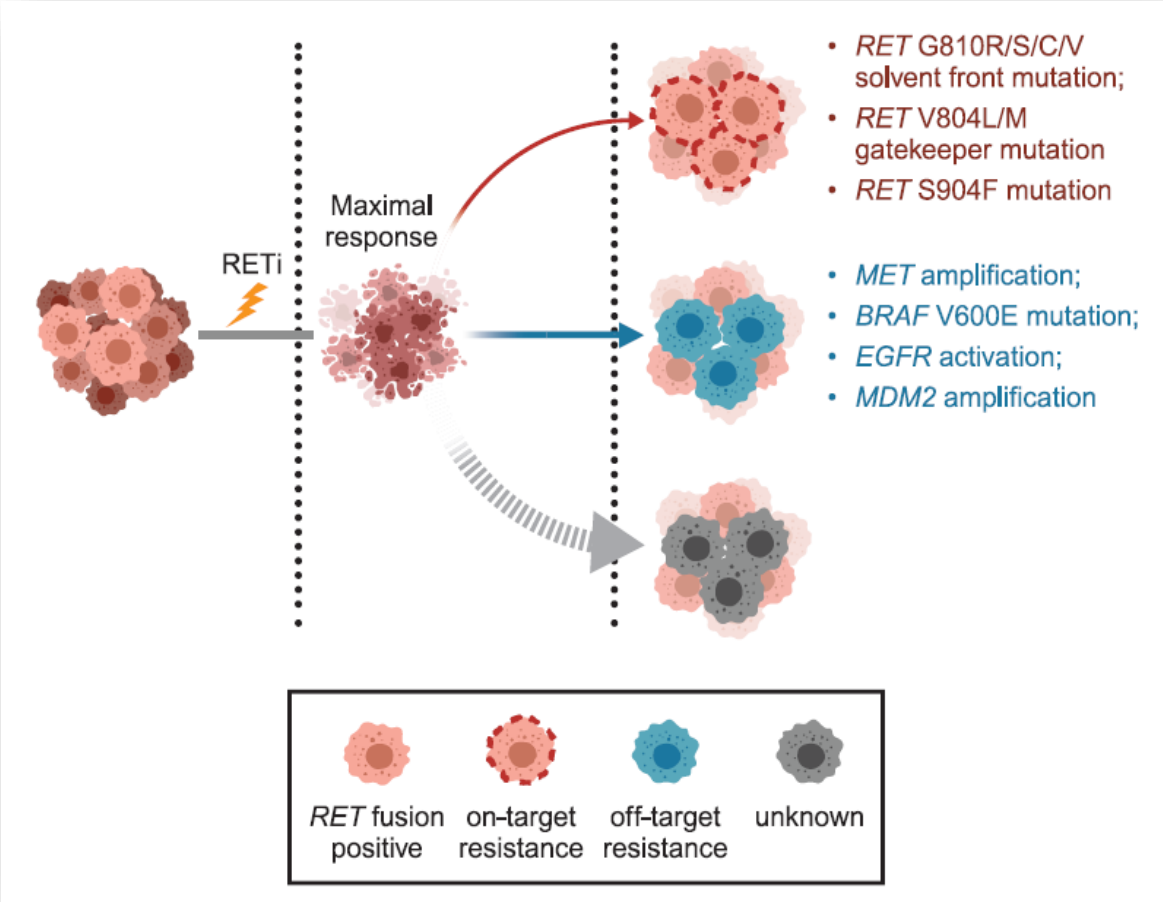
Solomon B et al, Future Oncol 2021

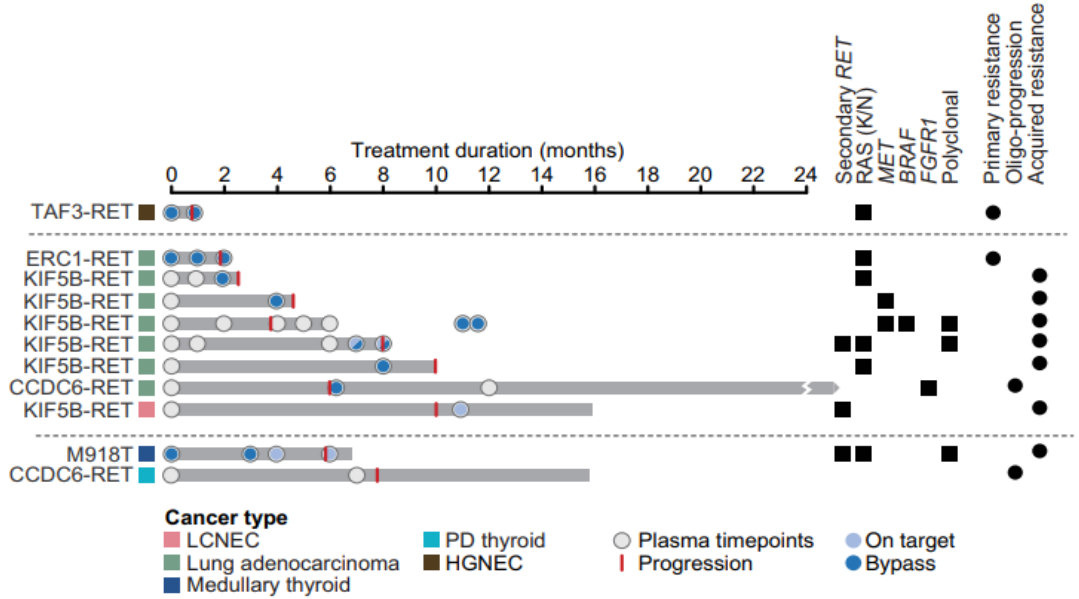
Selpercatinib is the First Targeted Therapy to Demonstrate Superior Progression-Free Survival Compared to a PD-1 Inhibitor Plus Chemotherapy for Adults with Newly-Diagnosed Advanced or Metastatic RET Fusion-Positive Non-Small Cell Lung Cancer

MADRID 2023 ESMO congress

How to manage disease PD?

RET





- **On-target:** RET kinase domain mutations occur with a low frequency based on early data
- **Off-target:** Activation of bypass pathways including MAPK pathway reactivation and MET amplifications
- Multiple distinct mechanisms are often observed in the same patient (**polyclonal resistance**)

Novello S et al, The Oncologist 2023
Rosen EY et al, Nature Communications 2022

How to manage disease PD?

RET

Retrospective study, 16 institutions

- 105 biopsies from 89 patients progressing on selective RET TKI

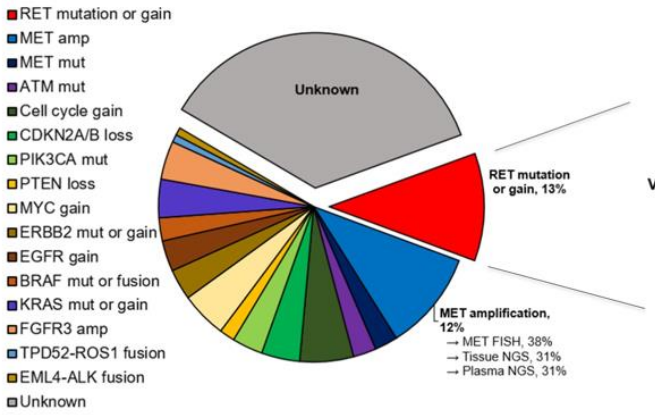


Fig. 2. Putative on- and off-target resistance mechanisms detected in post-RET TKI biopsies. The diagnostic method used for *MET* amplification detection is listed.

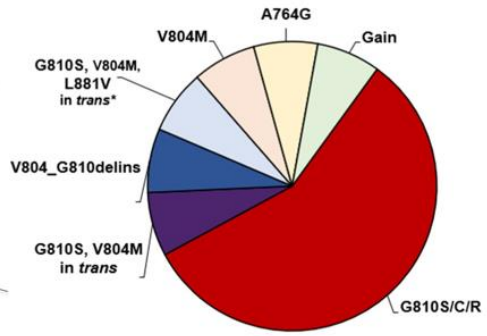
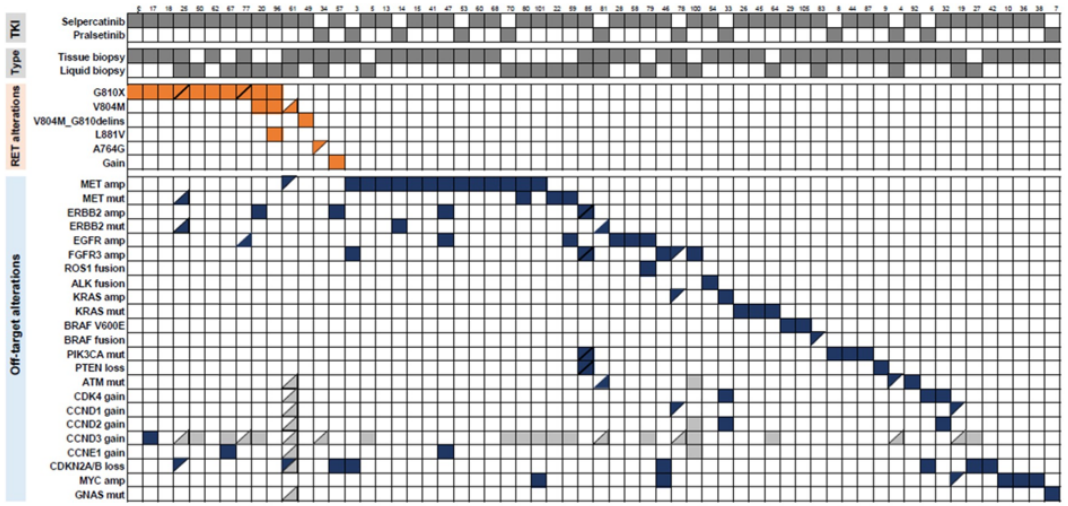


Fig. 3. On-target (*RET*) resistance alterations detected in post-RET TKI biopsies. *G810 and V804M mutations known to be in *trans*.



- Acquired RET mutations in 13% (G810X, 10%)
- Potential off target resistance alterations identified in 44% (MET amp, 12%)

Cooper AJ et al, ASCO 2023

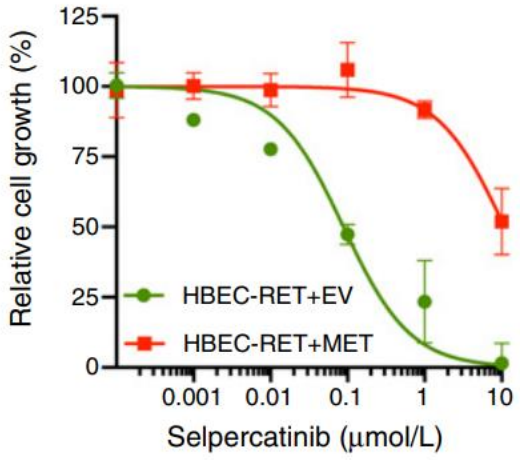
How to manage disease PD?

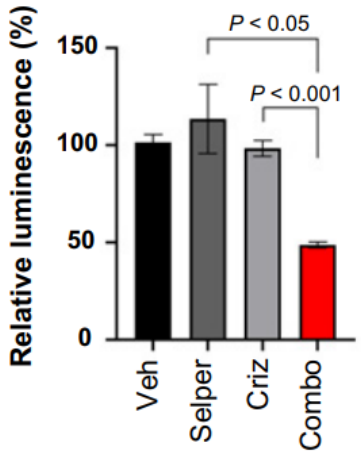
RET

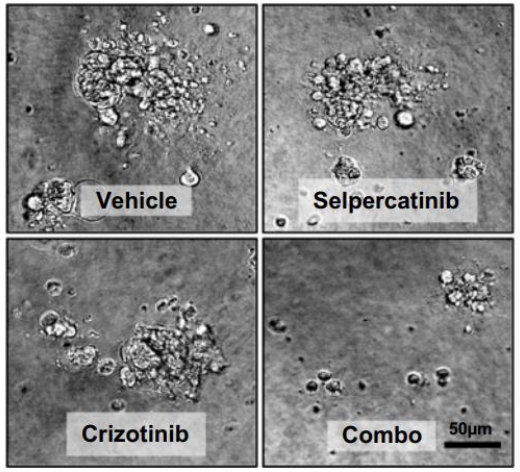
- New RET TKIs that address solvent front mediated resistance

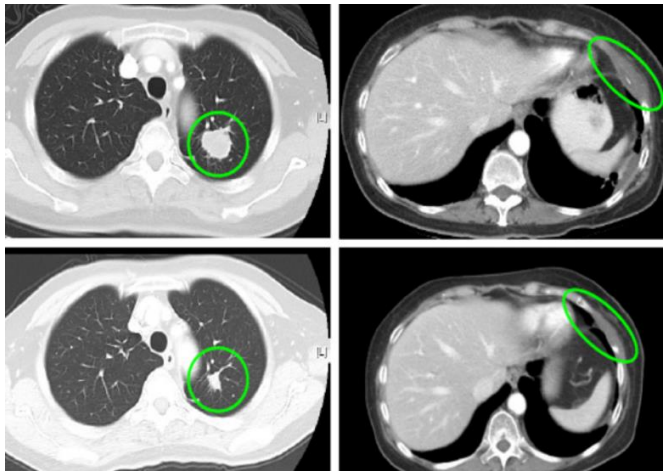
Compound	*RET* Substitution Coverage			VEGFR2	Other Non-RET Kinases	CNS?	Status
	V804X Gatekeeper	G810X Solvent Front	Other *RET* Mutation				
TPX-0046[1]	Less potent	✓	Y806N (hinge)	-	TRKA-C, SRC, FGFR1-2, FLT3, JAK2	?	Phase I/II (NCT04161391)
LOXO-260[2]	✓	✓	G810S+V804M	-	TRKC (40x selectivity)	?	Phase I/II (NCT05241834)
Vepafestinib[3,4] **(TAS0953/HM06)**	✓	✓	Y806C/N	-		✓	Phase I/II (NCT04683250)
EP0031[5] **(A400/KL590586)**	✓	✓		-	JAK1/2 (10-22x selectivity)	✓	Phase I/II (NCT05443126)
APS03118[6]	✓	✓	Y806H	-		✓	Phase I/II (NCT05653869)

- **Combos?** (+ MET inhibitors, i.e., capmatinib or cabozantinib)



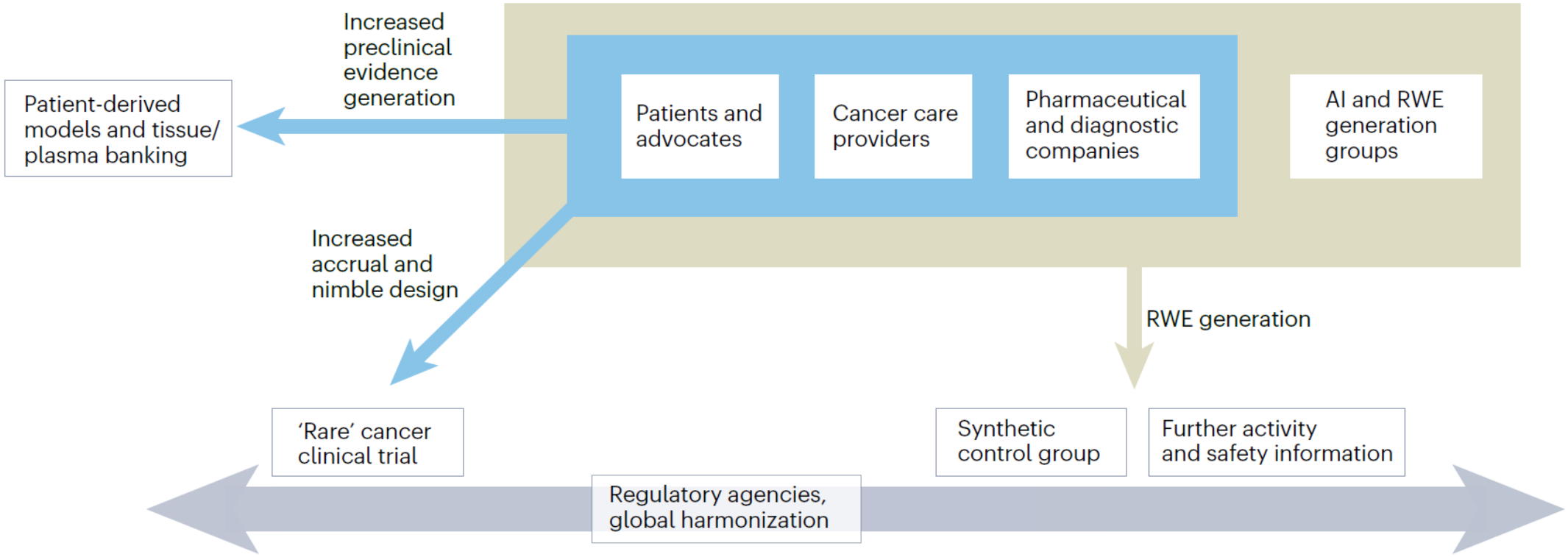






Lin JL, WCLC 2023; Rosen EY et al, CCR 2020

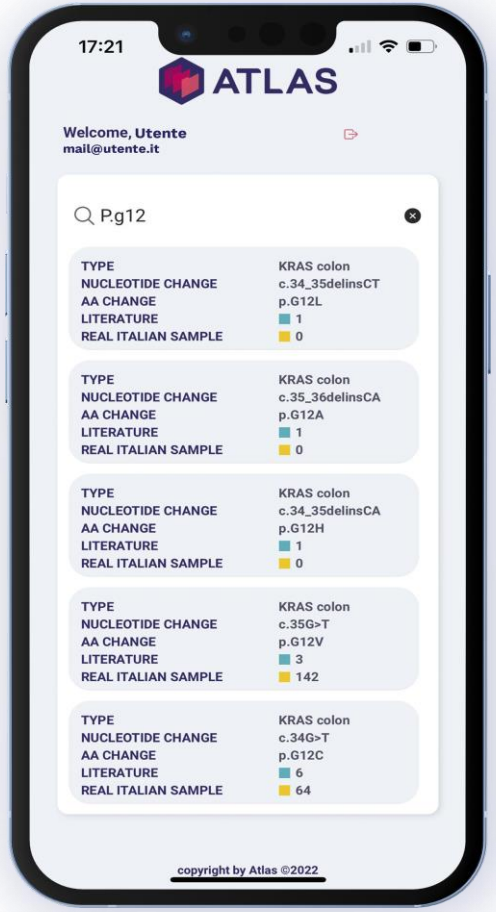
Stakeholder cooperation in Rare molecular subtypes



Patient advocates, health-care agencies, investigators and companies with an interest in diagnostics, therapeutics and real-world evidence have already taken steps to surmount the challenges associated with research into low-frequency drivers

Harada G, et al. Nat Rev Clin Oncol 2023

The value of National Platforms: ATLAS



Lo strumento innovativo a servizio della comunità degli esperti per la corretta definizione del valore clinico di ogni specifica mutazione

Malapelle U et al, Eur J Cancer 2021

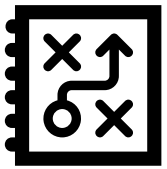
https://biomarkersatlas.com/

Conclusions

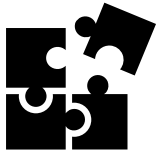
BRAF, ROS1 & RET (& beyond)

TEST!

Therapy → optimize 1st line



Strategy → address resistance (how to best sequence?)



Biology & heterogeneity → dig deep into disease details

Sessione I

NSCLC avanzato oncogene addicted

Il trattamento della malattia con alterazioni di BRAF, ROS1 & RET