

Selpercatinibe: Uma nova perspectiva para pacientes com NSCLC RET+ no Brasil

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O conteúdo desta apresentação reflete o ponto de vista do palestrante e, não necessariamente, o da Lilly.
Material destinado exclusivamente a profissionais prescritores ou dispensadores de medicamentos. PP-SE-BR-0077 – Mar/2024



Retsevmo[®]
(selpercatinibe)

Lilly

Retsevmo phase III data and clinical case

Maximilian J. Hochmair
Klinik Floridsdorf
Wien, Austria



Wiener Gesundheitsverbund

Klinik Floridsdorf



Disclosure – Maximilian Hochmair

- Honoraria from AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Eli Lilly, Merck Sharp & Dohme, Pfizer and Roche
- Consulting or advisory roles with Boehringer Ingelheim, Merck Sharp & Dohme, Eli Lilly, Novartis, Pfizer, Roche

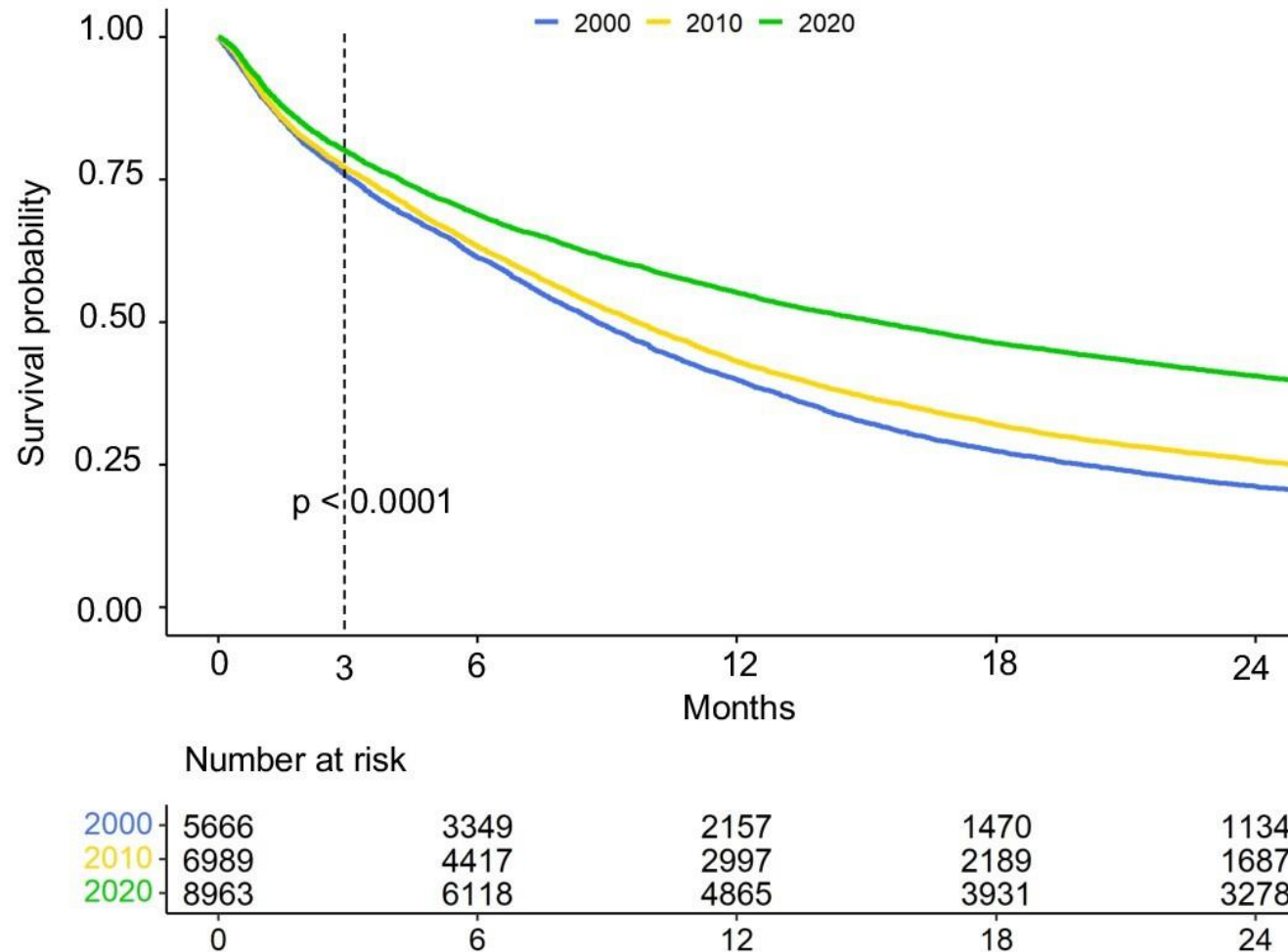
Two-year lung cancer survival between 2000 to 2020: Results from 3 French nationwide cohorts

Debieuvre D¹, Monnet I², Bylicki O³, Schneider S⁴, Goupil F⁵, Godbert B⁶, Dussopt C⁷, Pegliasco H⁸, Portel H⁹, Chikouche R¹⁰, Masson P¹¹, Jaafar M¹², Marty C¹³, El Khanjari F¹⁴, Obert J¹⁵, Picaud M¹⁶, Bravard As¹⁷, Le Floch H¹⁸, Letierce A¹⁹, Morel H²⁰

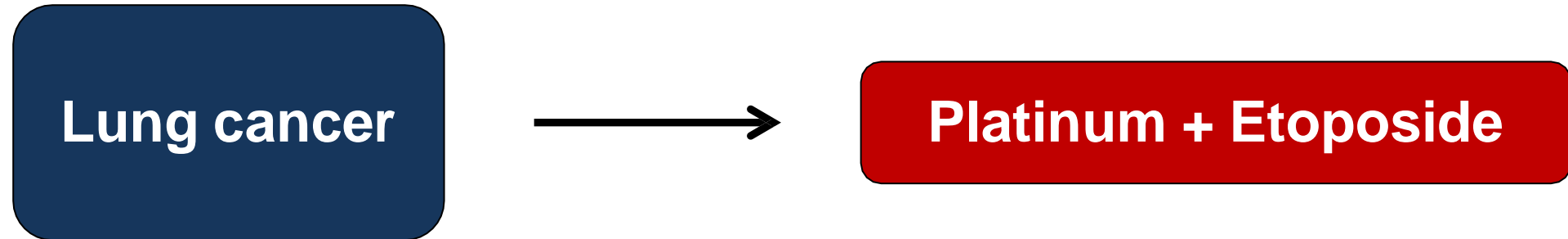
1- Respiratory Medicine Department, Groupe Hospitalier de la Région Mulhouse Sud-Alsace (GHRMSA), Hôpital Emile Muller, Mulhouse, France ; 2- Centre Hospitalier Intercommunal, Créteil, France ; 3- Hôpital d'Instruction des Armées Ste Anne, Toulon, France ; 4- Centre Hospitalier de la Côte Basque, Bayonne, France ; 5- Centre Hospitalier, Le Mans, France ; 6- CHR Metz-Thionville, Metz, France ; 7- Hôpitaux Nord-Ouest, Villefranche-sur-Saône, France ; 8- Hôpital Européen, Marseille, France ; 9- Centre Hospitalier Robert Boulin, Libourne, France ; 10- Centre Hospitalier d'Auxerre, Auxerre, France ; 11- Centre Hospitalier De Cholet, Cholet, France ; 12- Centre Hospitalier Eure-Seine, Evreux, France ; 13- Centre Hospitalier Saint Nazaire, Saint-Nazaire, France ; 14- Centre Hospitalier de Blois, Blois, France ; 15- Groupe Hospitalier Intercommunal Le Raincy Montfermeil, Montfermeil, France ; 16- Centre Hospitalier de Tourcoing, Tourcoing, France ; 17- Centre Hospitalier de Granville, Granville, France ; 18- HIA Percy, Clamart, France ; 19- Qualitystat, Morangis, France ; 20- Centre Hospitalier Régional D'orléans Hôpital de La Source, Orléans, France.

Poster
#169

Figure 2: 2-year survival curve total population (Kaplan-Meier)

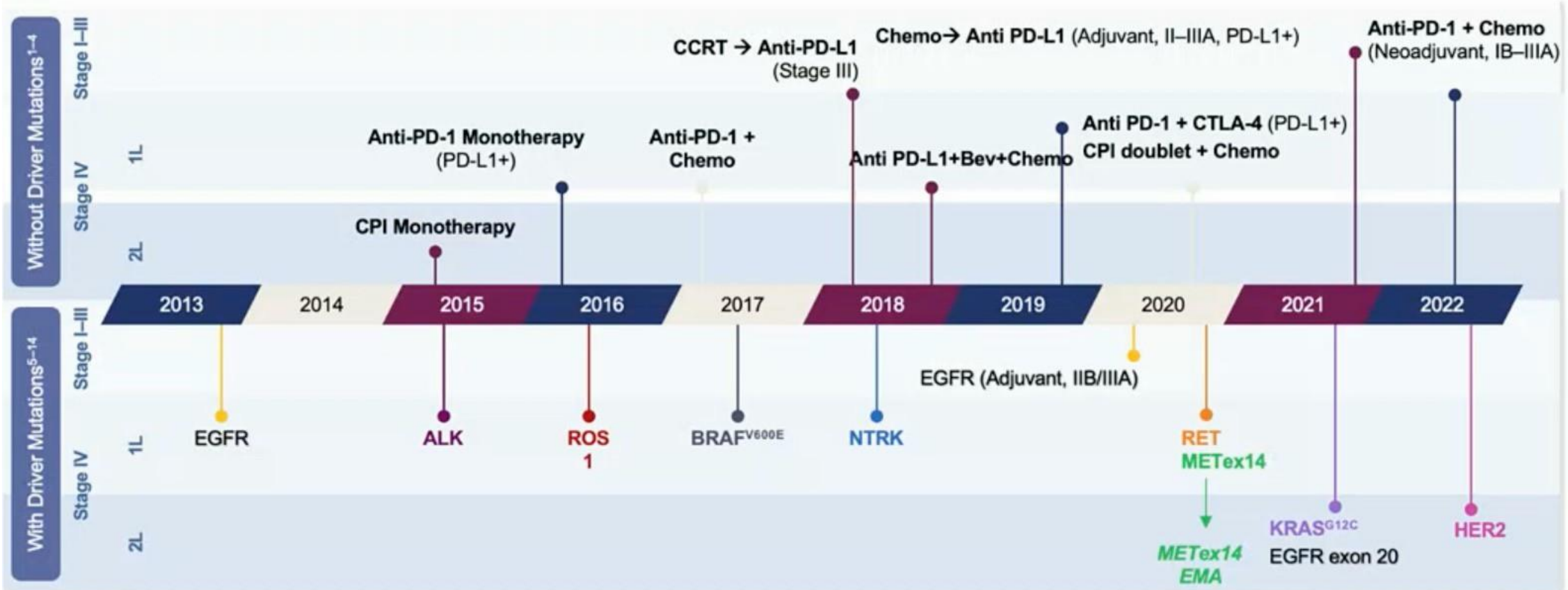


1990's: A thoracic oncologist's life was simple...

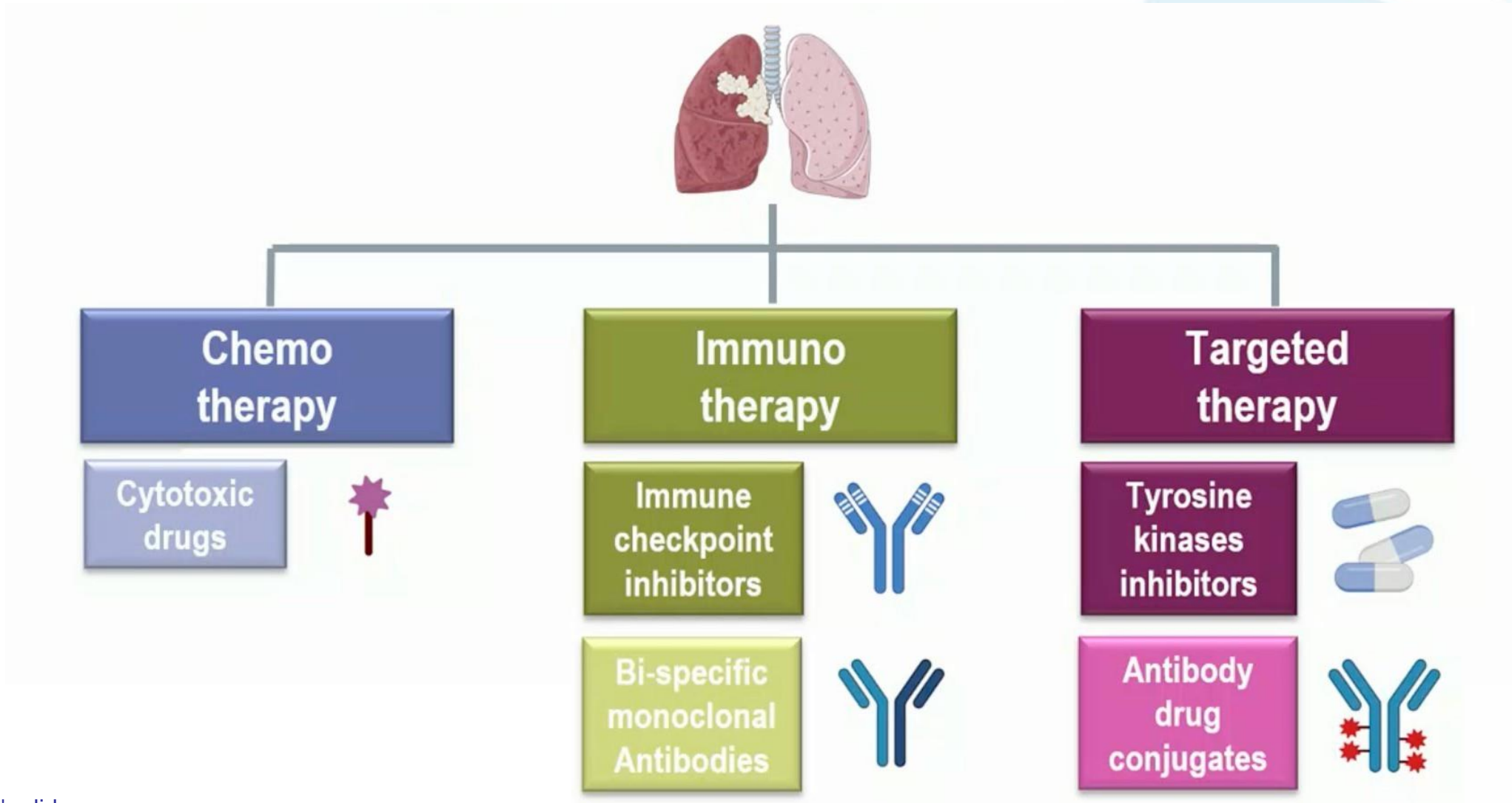


→ Very few treatment options

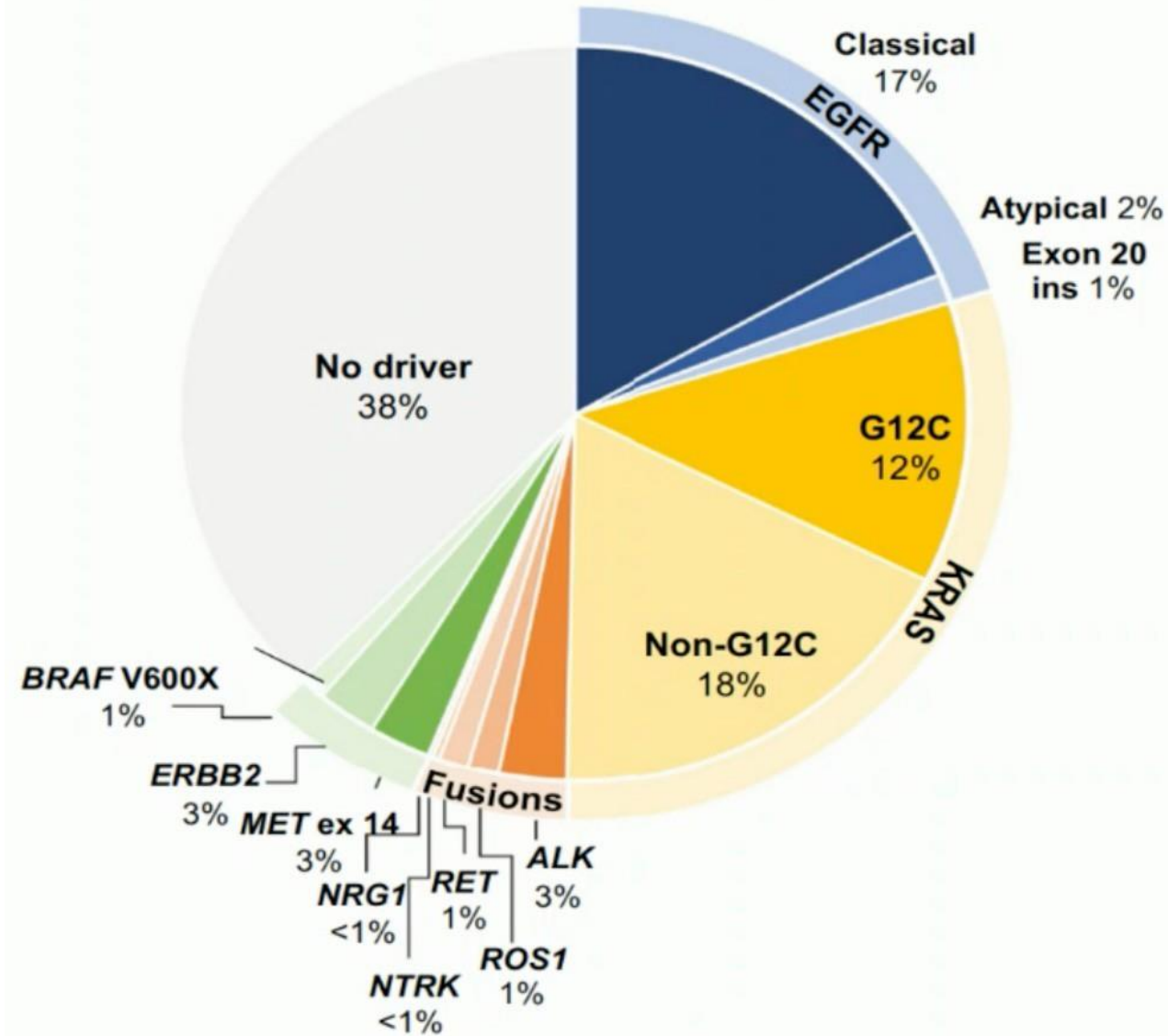
Very fast developments in the last years



Treatment today and near future



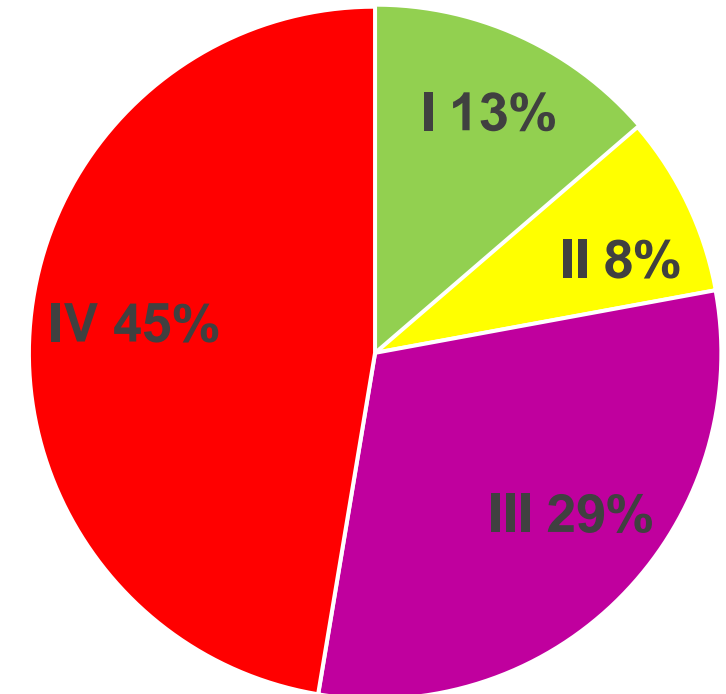
Drugable Targets 2023



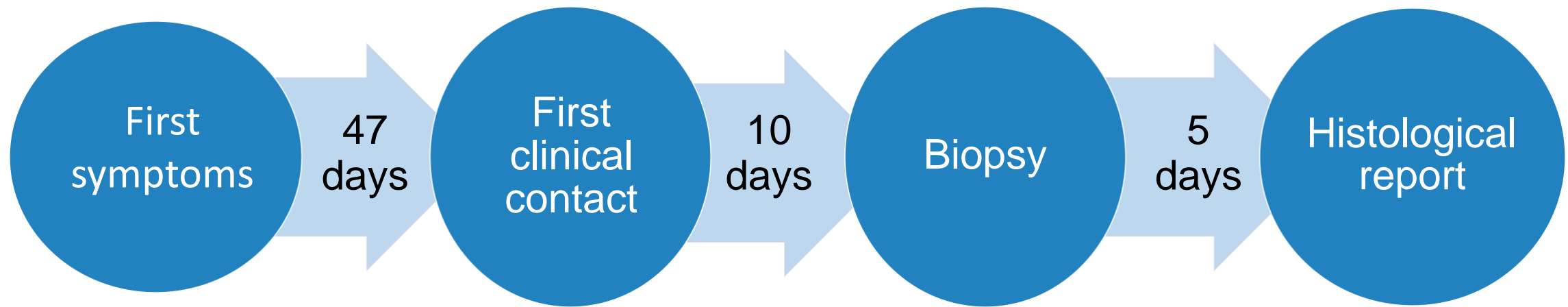
LALUCA REGISTRY - Staging

PARAMETER	VALUES	PERCENTAGE ¹
Pack years	0 Y	10 %
	1-10 Y	3 %
	11-30 Y	13 %
	31-50 Y	32 %
	51-70 Y	24 %
	>70 Y	16 %
	Unknown	2 %
Staging at Initial Diagnosis	Stage IA	8 %
	Stage IB	3 %
	Stage IIA/B	8 %
	Stage IIIA	12 %
	Stage IIIB	12 %
	Stage IIIC	5 %
	Stage IVA/B	45 %
	Indetermined	7 %
Location of Metastases at Initial Diagnosis²	No distant metastasis	51 %
	Pleural effusion	16 %
	Bone	10 %
	Brain	9 %
	Unknown	8 %
	Liver	6 %
	Adrenal Gland	5 %
	Lymph nodes (distant)	5 %
	Other	4 %

Distribution of different stages

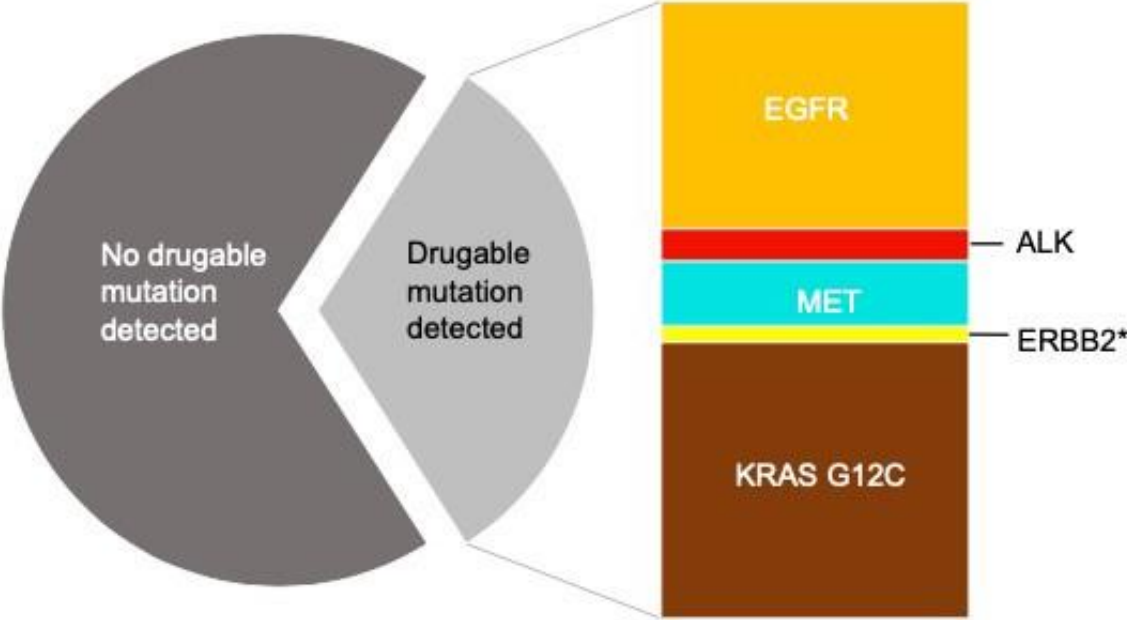


Time from symptoms to diagnosis

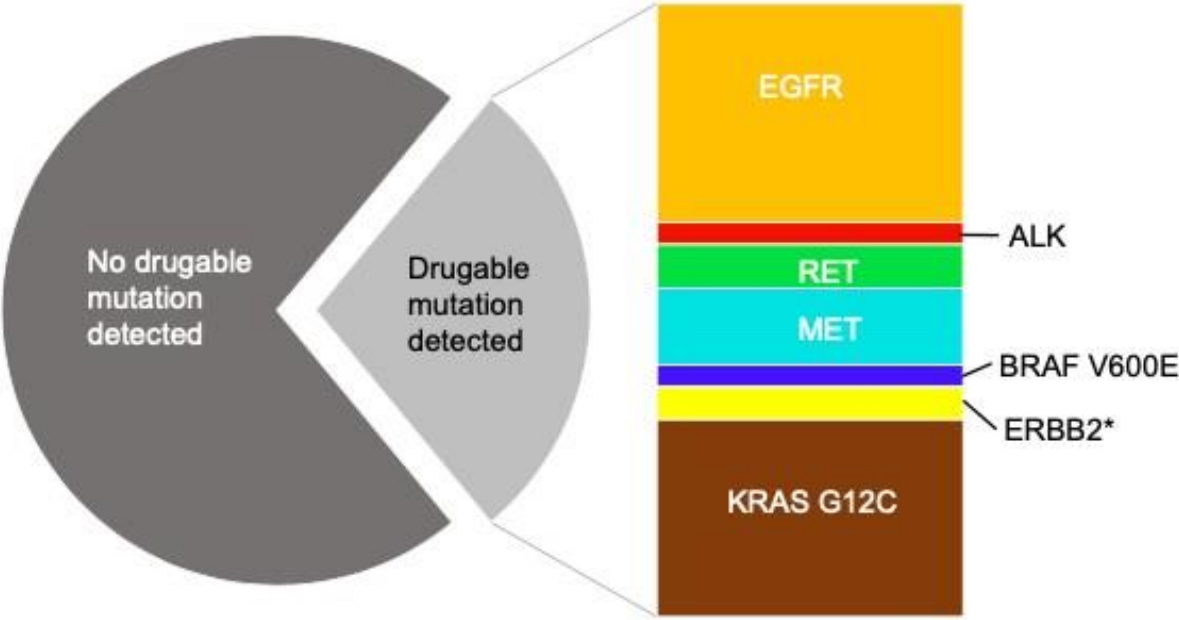


No difference between early vs later stage

Early-stage, n=119



Advanced-stage, n=200



Different mutations in the LALUCA registry

N=800

KRAS	28,2 %
EGFR	10,3 %
MET14	4,4 %
BRAF	3,4 %
ALK	1,4 %
RET	0,8%
ROS1, NTRK, HER2	0%
None	51,5%

All lungcancer patients are all different

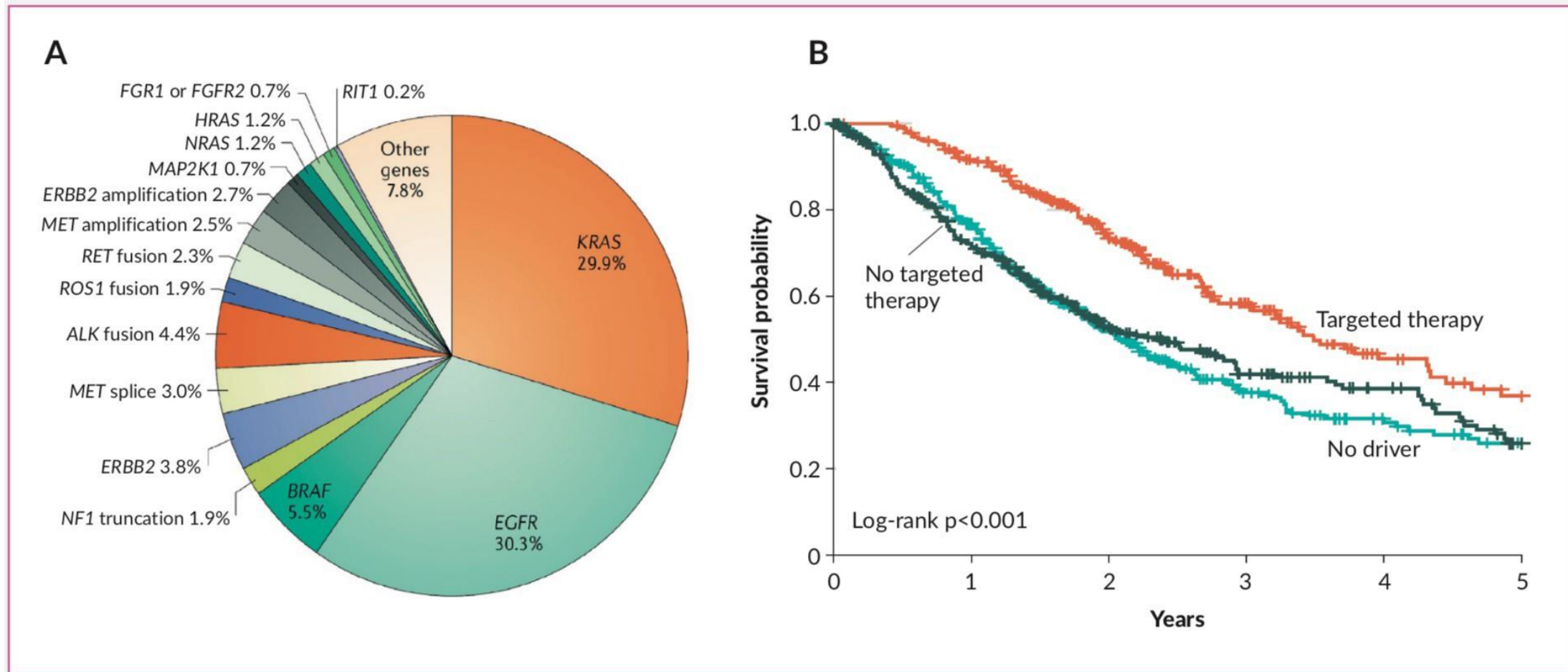


Figure 1. A) Distribution of oncogenic driver mutations in NSCLC (adapted from Skoulidis F et al. 2019¹); **B) OS targeted versus non-targeted treatment** (adapted from Kris MG et al. 2014²); and **C) History of EGFR-mutant positive (EGFR M+) NSCLC** (adapted from Rotow J et al. 2017³³).

RET activation as oncogenic driver in NSCLC

historical data

Activating RET rearrangements and mutations are actionable drivers of oncogenesis in several tumor types including NSCLC¹⁻⁶

- At least 45 *RET* gene fusion partners have been identified in lung cancers,⁷ but the clinical significance of specific fusion partners is not yet defined⁸



Historical 1L standard of care

Non-RET selected mNSCLC (RCT, N=616): **Pembrolizumab + platinum + pemetrexed vs placebo + platinum + pemetrexed⁹**

- **mOS 22.0 mo** **HR 0.56** (95% CI 0.46-0.69)
- **mPFS 9.0 mo** **HR 0.49** (95% CI 0.41-0.59)

Most common Gr 3-4 AEs: Neutropenia (17.9%); anemia (12.5%); asthenia (7.1%).
Gr3-4 IMAEs included severe skin reactions (n=2); colitis/ hypothyroidism/ myocarditis/ type 1 diabetes mellitus (n= 1 each).

RET rearranged aNSCLC (Phase 2 single arm, N=26, 25 response-evaluable): **Cabozantinib¹⁰**

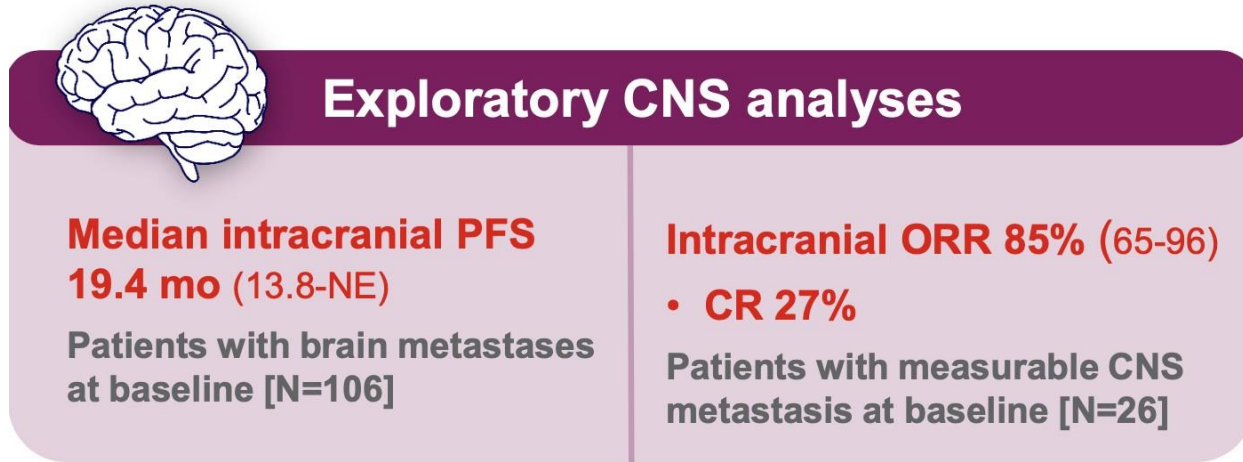
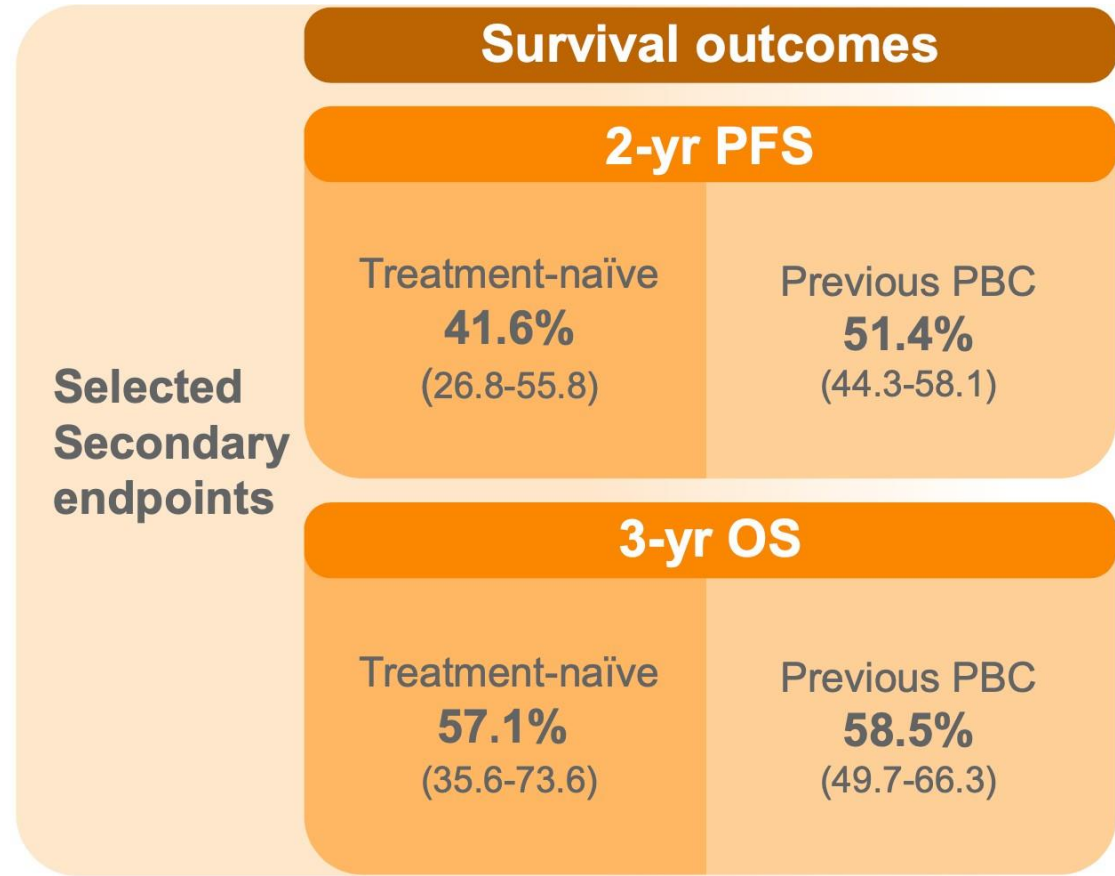
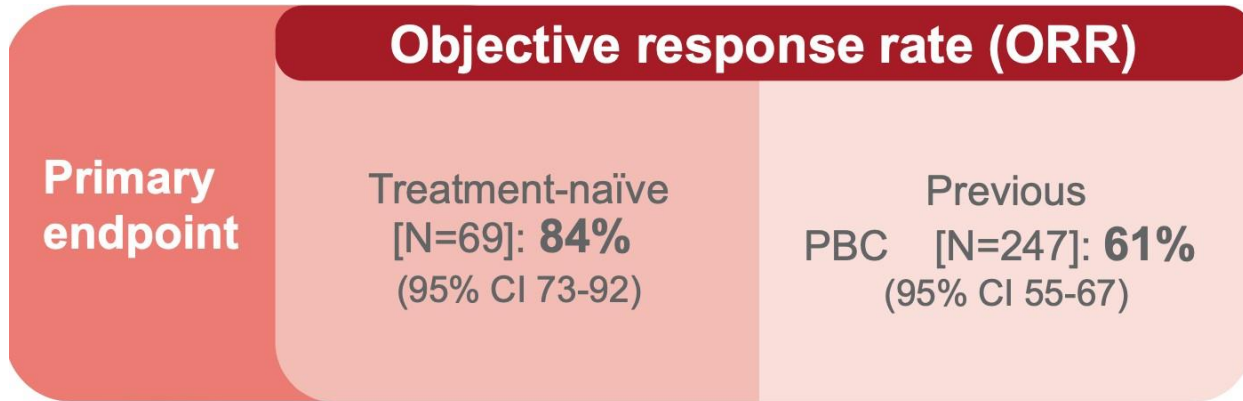
- **mOS 9.9.mo** (95% CI 8.1-NR)
- **mPFS 5.5 mo** (95% CI, 3.8-8.4)

Most common Gr 3 TRAEs: Asymptomatic lipase elevation (n=2, 15%); increased ALT (n=2, 8%); increased AST (n=2, 8%); thrombocytopenia (n=2, 8%); hypophosphatemia (n=2, 8%).

1L, first line; AEs, adverse events; ALT, alanine transaminase; aNSCLC, advanced non-small cell lung cancer; AST, aspartate aminotransferase; CI, confidence interval; Gr, grade; HR, hazard ratio; IMAEs, immune-mediated adverse events; mNSCLC, advanced non-small cell lung cancer; mOS, median overall survival; mPFS, median progression-free survival; NR, not reached; RCT, randomized controlled trial; *RET*, rearranged during transfection; TRAEs, treatment-related adverse events

1. Lipson D, et al. *Nat Med*. 2012; 18, 382–384; 2. Regua AT, et al. *Front Oncol*. 2022;12:932353; 3. Drilon A, et al. *Nat Rev Clin Oncol*. 2018 Mar;15(3):151–167; 4. Kohno T, et al. *Nat Med*. 2012; 18, 375–377; 5. Takeuchi K, et al. *Nat Med*. 2012; 18, 378–381; 6. Cancer Genome Atlas Research. *Nature* 2014; 511, 543–550; 7. Ou S-H, et al. *JTO Clin Res Reports* 2020; 1(2):1–7; 8. Novello S, et al. *Oncologist*. 2023; 28(5): 402–413; 9. Rodriguez-Abreu D, et al. *Ann Oncol*. 2021; 32(7): 881–895; 10. Drilon A, et al. *Lancet Oncol*. 2016; 17(12): 1653–1660.

LIBRETTO-001 (selpercatinib): Phase I/II single arm trial with a RET fusion-positive advanced NSCLC cohort



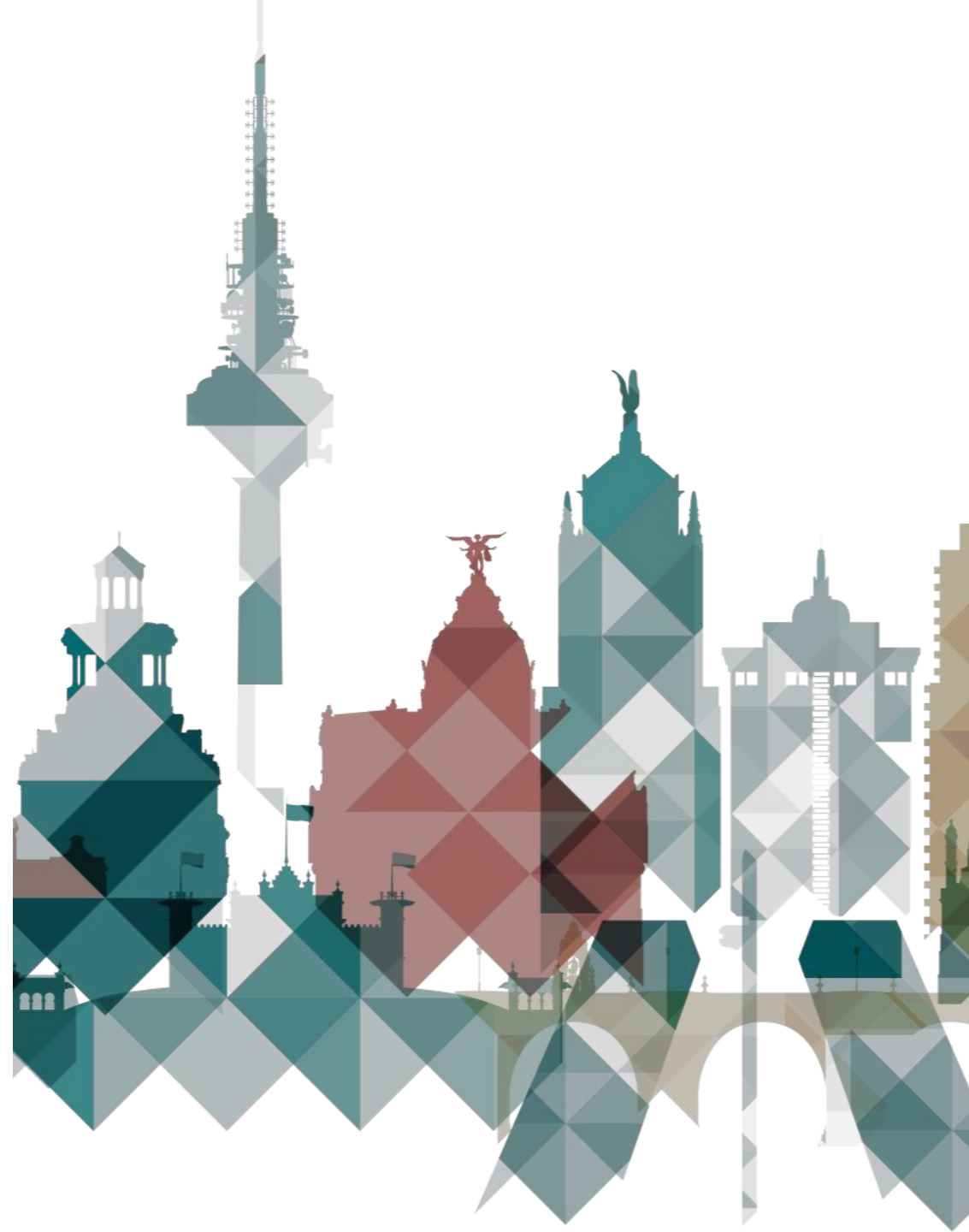
CI, confidence interval; CNS, central nervous system; CR, complete response; HR, hazard ratio; ITT, intent-to-treat; mo, months; NE, not evaluable; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PBC, platinum-based chemotherapy; PFS, progression-free survival

Randomized Phase 3 Study of First-line Selpercatinib versus Chemotherapy and Pembrolizumab in *RET* Fusion-positive NSCLC

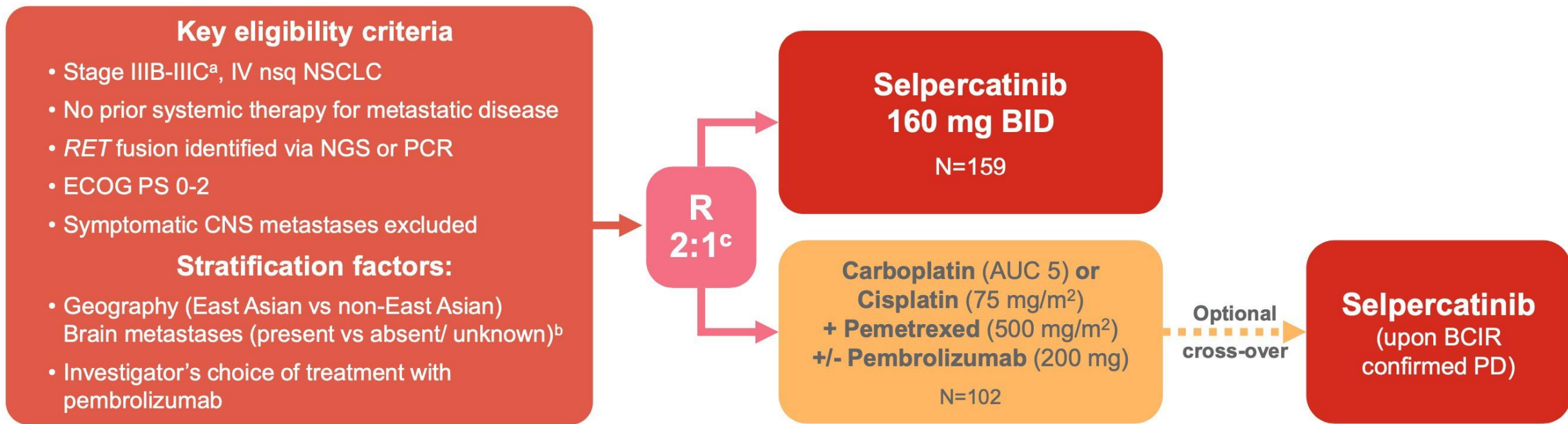
LIBRETTO-431 (NCT04194944)

Herbert H. Loong, Koichi Goto, Benjamin J. Solomon, Keunchil Park, Maurice Pérol, Edurne Arriola, Silvia Novello, Ying Cheng, Andrea Ardizzoni, Milena P. Mak, Fernando C. Santini, Yasir Y. Elamin, Alexander Drilon, Jürgen Wolf, Baohui Han, Hongmei Han, Minji K. Uh, Tarun Puri, Viktoriya Soldatenkova, Caicun Zhou

Madrid, Spain, October 21st, 2023



LIBRETTO-431: Randomized Phase 3 Study of First-line Selpercatinib versus Chemotherapy and Pembrolizumab in RET fusion-positive advanced NSCLC



Gated Primary Endpoints: PFS by blinded independent central review (BICR) in ITT-Pembrolizumab^d and ITT population

Secondary Endpoints:

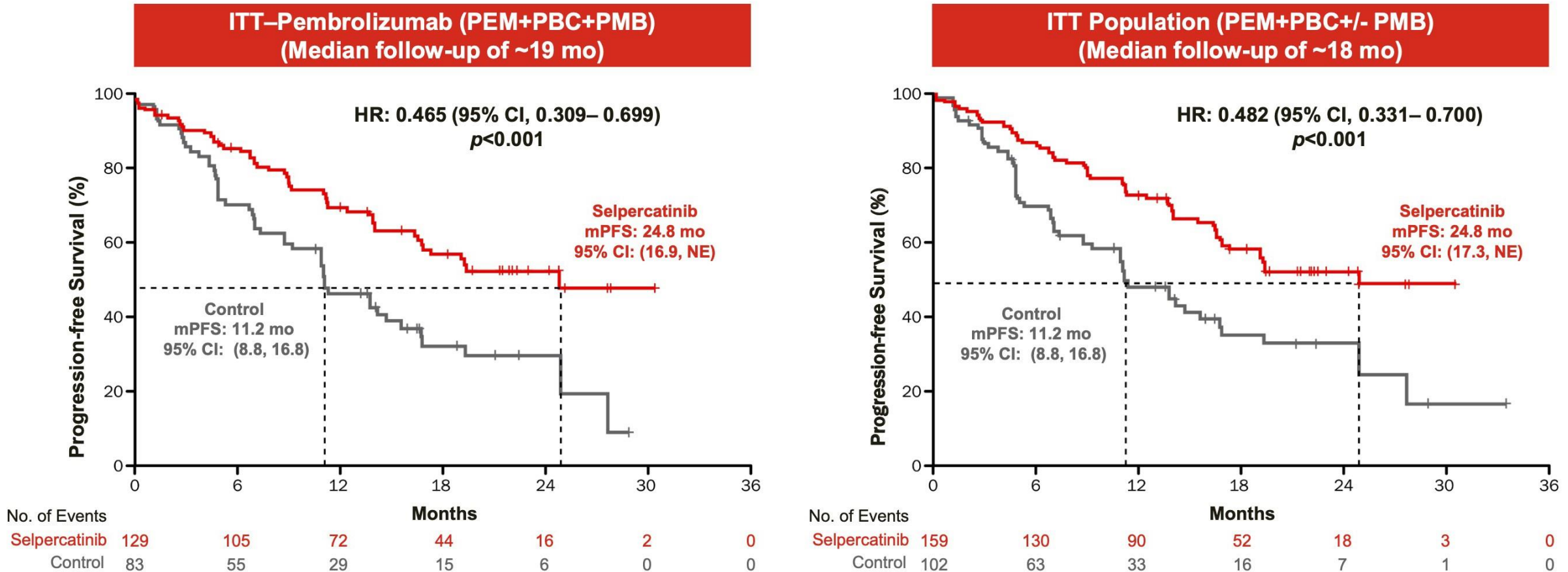
- Efficacy ([OS, ORR, DOR], CNS [ORR, DOR, time to progression]^e)
- Safety
- Patient Reported Outcomes (NSCLC-SAQ [tertiary endpoint EORTC QLQ-C30])

^a Not suitable for radical surgery or radiation therapy.
^b Investigator assessed.
^c The initial randomization ratio was 1:1, but amended to 2.1, hence the final ratio was 1:6:1.
^d ITT-Pembrolizumab are patients stratified with investigator intent to receive chemotherapy with pembrolizumab and per protocol had to be at least 80% of the ITT population.
^e Baseline and longitudinal intracranial scans were required for all patients following an amendment. Prior to the amendment, longitudinal intracranial scans were required if patients had known CNS metastases at baseline.

AUC, area under curve; BCIR, blinded central independent review; BID, twice daily; CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Group Performance Status; EORTC QLQ, European Organisation for Research and Treatment Quality of Life Questionnaire; ITT, intent-to-treat; nsq, nonsquamous; NSCLC, non-small cell lung cancer; NGS, next generation sequencing; NSCLC-SAQ, non-small cell lung cancer Symptoms Assessment Questionnaire; ORR, overall response rate; OS, overall survival; PCR, polymerase chain reaction; PD, progressive disease; PFS, progression-free survival; R, randomization; *RET*, rearranged during transfection

LIBRETTO-431: Progression-free survival (PFS) assessed by BICR

A protocol-specified interim analysis was conducted after 98 BICR PFS events were observed in the ITT-Pembrolizumab population. Data cutoff date: 1 May 23



BCIR, blinded central independent review; CI, confidence interval; HR, hazard ratio; ITT, intent to treat; NE, not estimable; mPFS, median progression-free survival; PBC, platinum-based chemotherapy; PEM, pemetrexed; PMB, pembrolizumab
1. Loong HHF, et al. Abstract LBA4 presented at ESMO Congress, 2023.

LIBRETTO-431: ORR, DoR, OS and intracranial outcomes

Systemic Outcomes		
	Selpercatinib N=129	Control N=83
ORR, %	83.7	65.1
Median DOR, mo (95% CI)	24.2 (17.9, NE)	11.5 (9.7, 23.3)
Overall Survival immature (censoring rate ~80%) and confounded by crossover (75% effective rate) ^a ; HR 0.961 (95% CI 0.503, 1.835)		
Intracranial Outcomes ^b		
	Selpercatinib N=17	Control N=12
Intracranial ORR, %	82.4	58.3
Intracranial CR, %	35.3	16.7
12-mo Intracranial DOR Rate, % (95% CI)	76.0 (42.2, 91.6)	62.5 (14.2, 89.3)
Median Intracranial PFS, mo (95% CI)	16.1 (8.8, NE)	10.4 (3.8, NE)

^a Effective crossover rate: patients who discontinued from control treatment and received a selective *RET* inhibitor on or off study

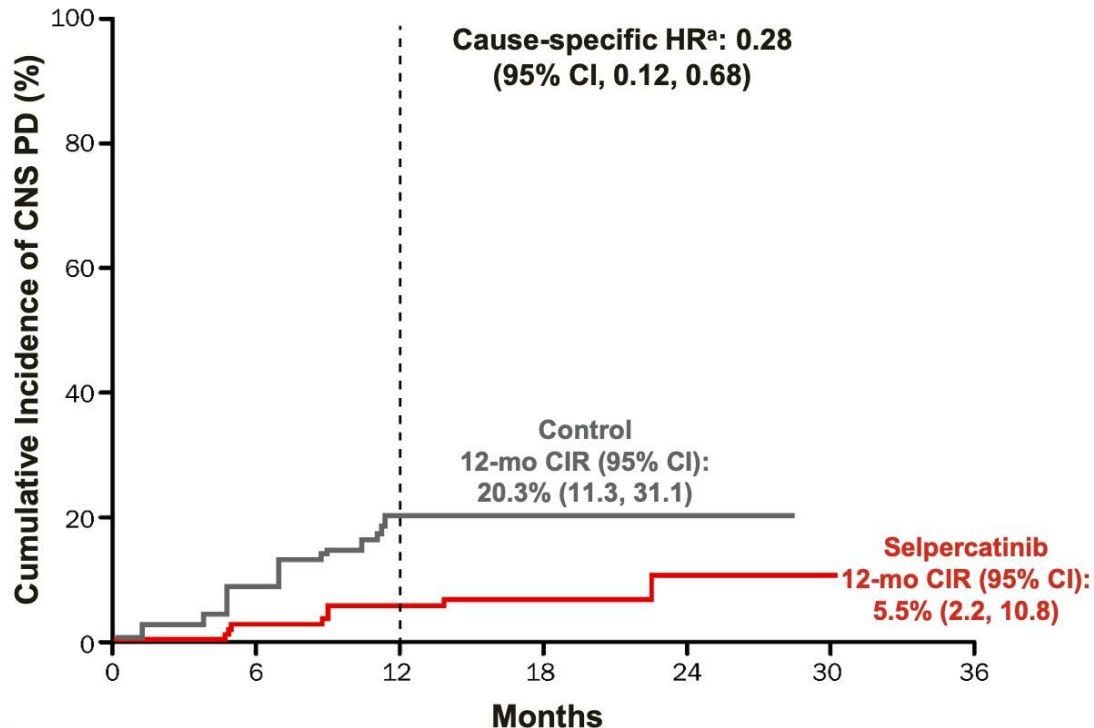
^b In patients with measurable CNS disease at baseline.

BCIR, blinded central independent review; CI, confidence interval; CNS, central nervous system; CR, complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Group Performance Status; HR, hazard ratio; mo, months; NE, not estimable; ORR, objective response rate; PD-L1, programmed death-ligand 1; PFS, progression-free survival; *RET*, rearranged during transfection

1. Loong HHF, et al. Abstract LBA4 presented at ESMO Congress, 2023.

LIBRETTO-431: Cumulative incidence rate of CNS progression

Patients with and without Baseline CNS Metastases (N=192)



No. of Events	0	3	6	7	8	8	8
Selpercatinib	0	3	6	7	8	8	8
Control	0	6	13	13	13	13	13

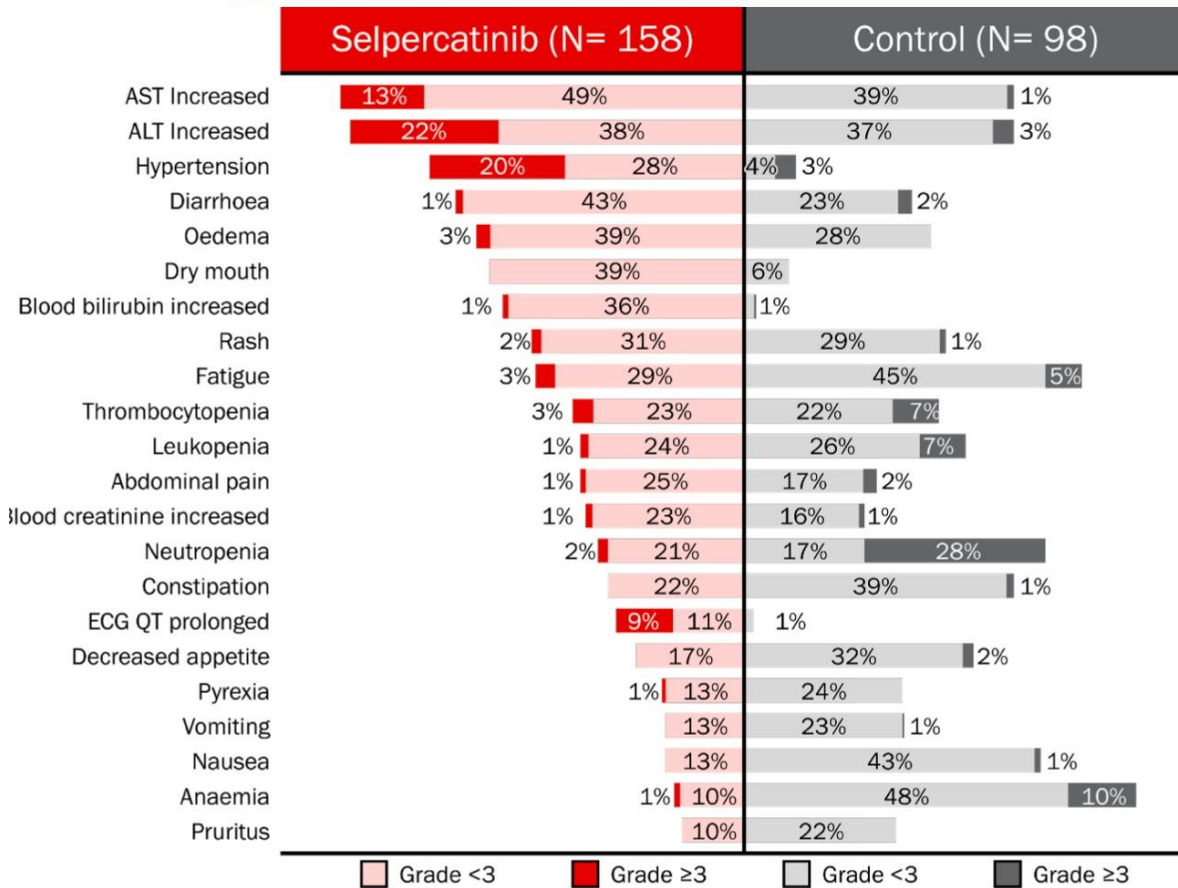
Risk of CNS Progression

Without CNS Metastases at Baseline	Selpercatinib N=99	Control N=51
12-month CIR, % (95% CI)	1.1% (0.1, 5.2)	14.7% (5.7, 27.6)
Cause-specific HR ^a (95% CI)	0.17 (0.04, 0.69)	
With CNS Metastases at Baseline	Selpercatinib N=21	Control N=21
12-month CIR, % (95% CI)	25.7% (8.8, 46.7)	33.3% (14.3, 53.8)
Cause-specific HR ^a (95% CI)	0.61 (0.19, 1.92)	

^aCause-specific HR for CNS progression, accounting for the competing risks of non-CNS PD and death
CI, confidence interval; CIR: Cumulative incidence rate; CNS, central nervous system; HR, hazard ratio; PD, progressive disease
1. Loong HHH, et al. Abstract LBA4 presented at ESMO Congress, 2023.

LIBRETTO-431: Safety in the planned interim analysis

Any grade treatment-emergent adverse events (TEAEs) occurring in ≥20% of patients in either study arm



	Selpercatinib N=158	Control N=98
Median time on treatment, months ± SD	16.7 ± 8.3	9.8 ± 7.2
Any AE, n (%)	158 (100.0)	97 (99.0)
AE Grade ≥3	111 (70.3)	56 (57.1)
Deaths due to AE, n (%)	7 (4.4)	0
Related AE (malnutrition and sudden death)	2 (1.3)	0
AEs leading to discontinuation, n (%)	16 (10.1)	2 (2.0)
AEs leading to any dose adjustment, n (%)	123 (77.8)	74 (75.5)
AEs leading to dose reduction	81 (51.3)	28 (28.6)

Data shown are from all patients who received at least one dose of study treatment.

AE, adverse event; ALT, alanine transaminase; AST, aspartate aminotransferase; ECG QT, electrocardiogram QT interval; SD, standard deviation; TEAEs, treatment-emergent adverse events

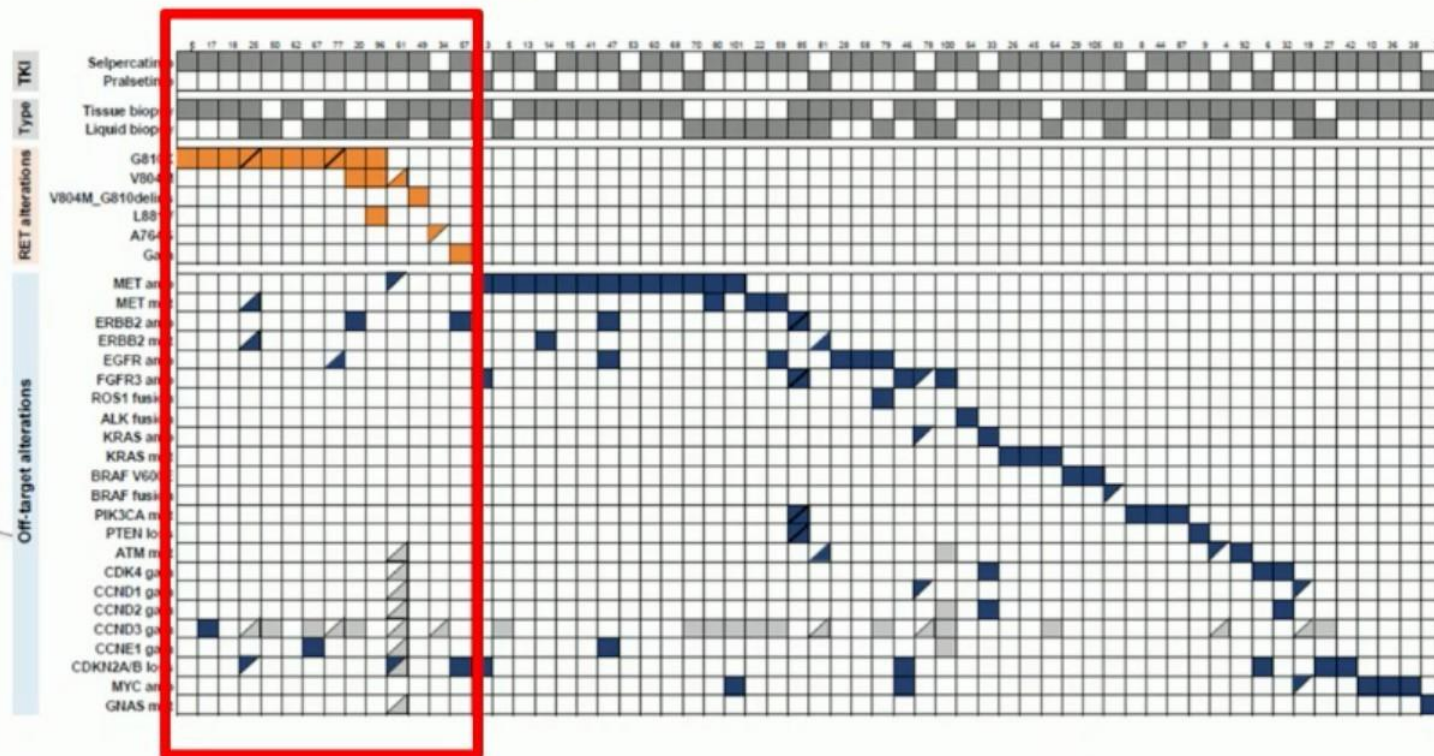
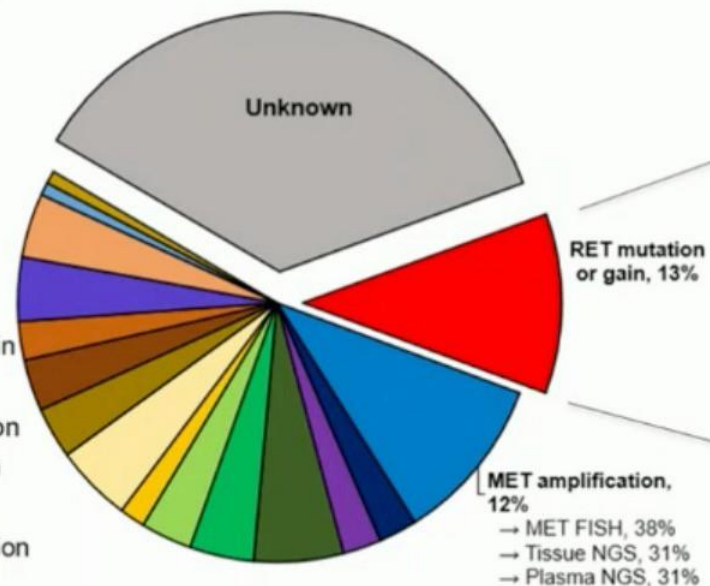
1. Loong HHF, et al. Abstract LBA4 presented at ESMO Congress, 2023.

RET resistance

On / Off target resistance mutations post selpercatinib or pralsetinib

Acquired RET mutations in < 13% of cases

- RET mutation or gain
- MET amp
- MET mut
- ATM mut
- Cell cycle gain
- CDKN2A/B loss
- PIK3CA mut
- PTEN loss
- MYC gain
- ERBB2 mut or gain
- EGFR gain
- BRAF mut or fusion
- KRAS mut or gain
- FGFR3 amp
- TPD52-ROS1 fusion
- EML4-ALK fusion
- Unknown




Selective 2nd gen RETi


Next gen RET inhibitors

Several ongoing trials + pre-clinical data on new molecules



Drug	Company	Status	Activity
LOXO-260	LOXO-Lilly	Phase I	Active against solvent front and gatekeeper mutations
SY-5007	Shouyao Holdings	Phase I completed (ASCO 2023): ORR 62%, DCR 94% Phase II ongoing	Selective RET inhibitor
TPX-0046	Turning Point Therapeutics	Phase I/II	RET/SRC inhibitor, active against solvent front mutations
TY-1091	TYK Medicines	Phase I/II	Active against solvent front and gatekeeper mutations
TAS0953/HM06	Helsinn Healthcare	Phase I/II	Active against solvent front and gatekeeper mutations

SIREN: Real world data from the NPP

 *Advances in Treatment of Lung Cancer
Patients with Targetable Mutations* **Special Collection**

 *Therapeutic Advances in Medical Oncology* *Original Research*

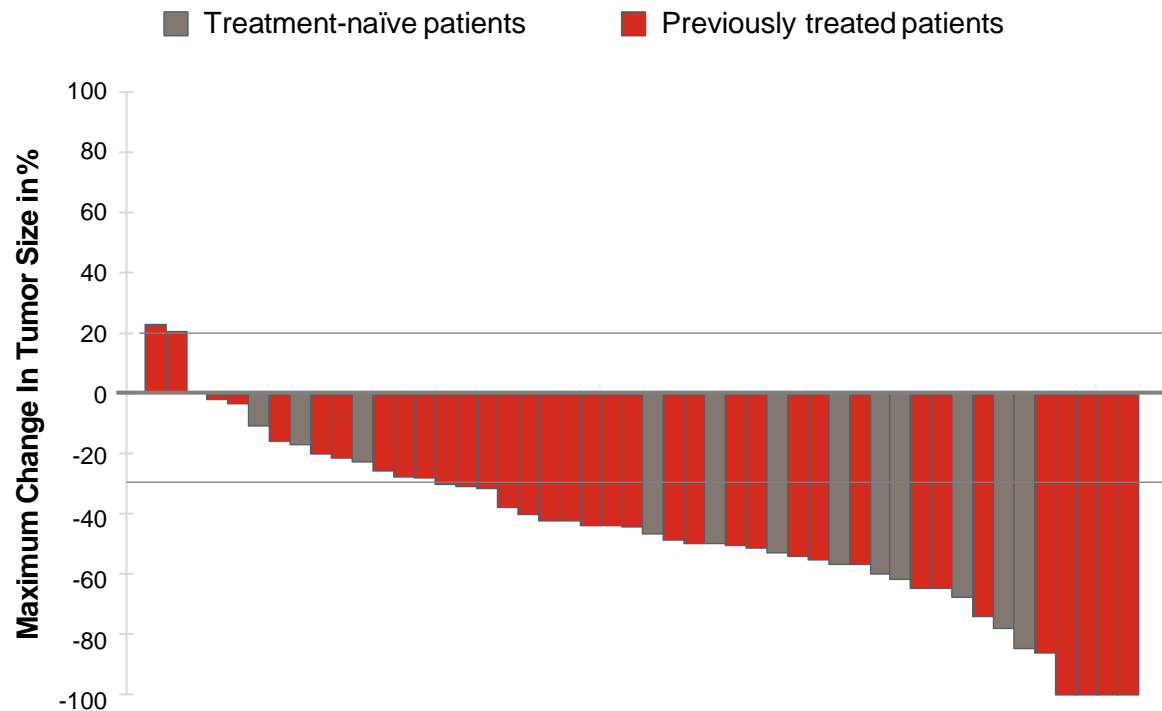
Selpercatinib in RET fusion-positive non-small-cell lung cancer (SIREN): a retrospective analysis of patients treated through an access program

Oliver Illini^{*}, Maximilian Johannes Hochmair^{*}, Hannah Fabikan, Christoph Weinlinger, Amanda Tufman, Aurélie Swalduz, Kristina Lamberg, Sayed M. S. Hashemi, Florian Huemer, Anders Vikström^{*}, Martin Wermke, Gudrun Absenger, Alfredo Addeo, Shantanu Banerji, Antonio Calles^{*}, Stephen Clarke, Massimo Di Maio, Alice Durand, Michaël Duruisseaux, Malinda Itchins, Okko-Sakari Kääränen, Florian Krenn, Eckart Laack, Adrianus Johannes de Langen, Katja Mohorcic, Georg Pall, Antonio Passaro^{*}, Gerald Prager, Achim Rittmeyer, Jeffrey Rothenstein, Michael Schumacher, Ewald Wöll and Arschang Valipour

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Maximilian Johannes

Maximum Change in Tumor Size: Overall Population



2 patients were excluded due to no measurable lesions at baseline

Non-responders:

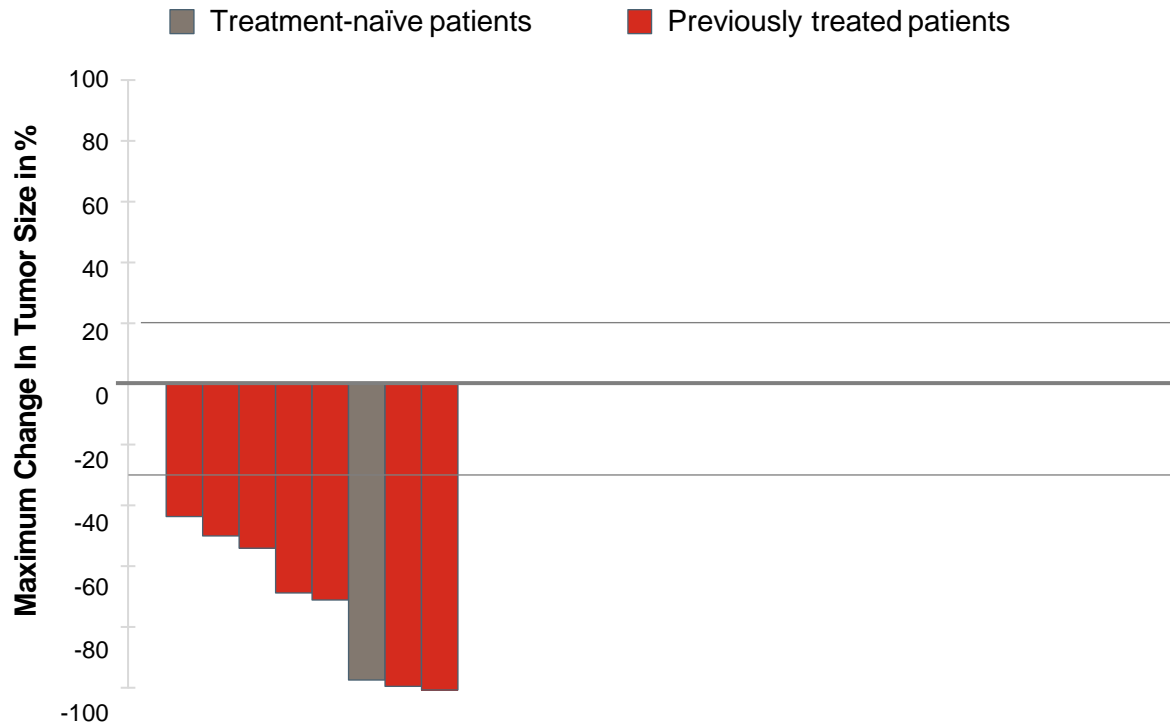
- Stable disease: 12 patients (24%)
 - Treatment-naïve: 3 patients (23%)
 - Pretreated: 9 patients (24%)
- Progressive disease: 2 patients (4%)
 - Treatment-naïve: 0 patients
 - Pretreated: 2 patients (5%)

68% of patients (n=34) experienced a tumor shrinkage

Objective response rate, % (95% CI)

- All patients: 68 (53-81)
 - Treatment-naïve: 69 (39-91)
 - Pretreated: 68 (50-82)

Intracranial Response

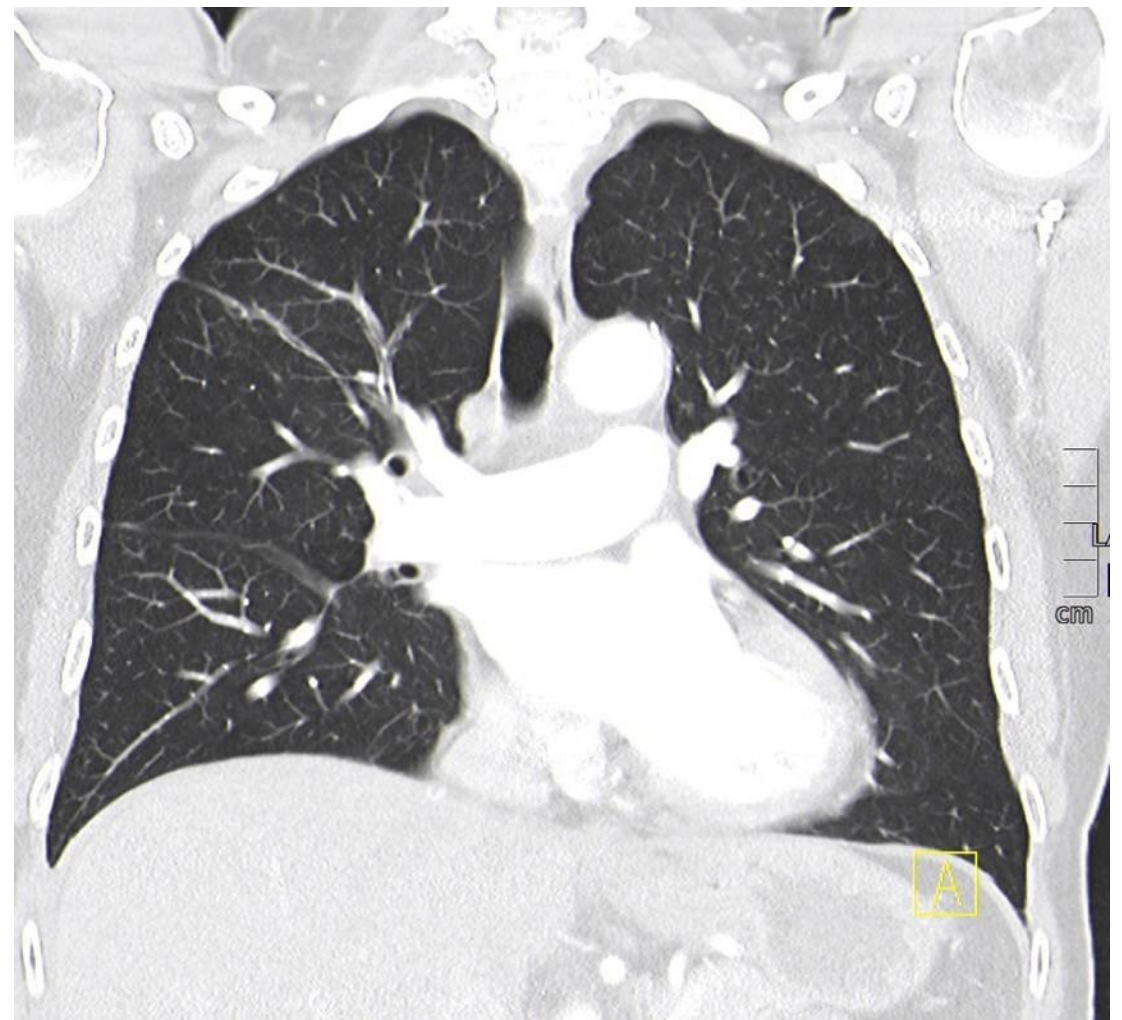
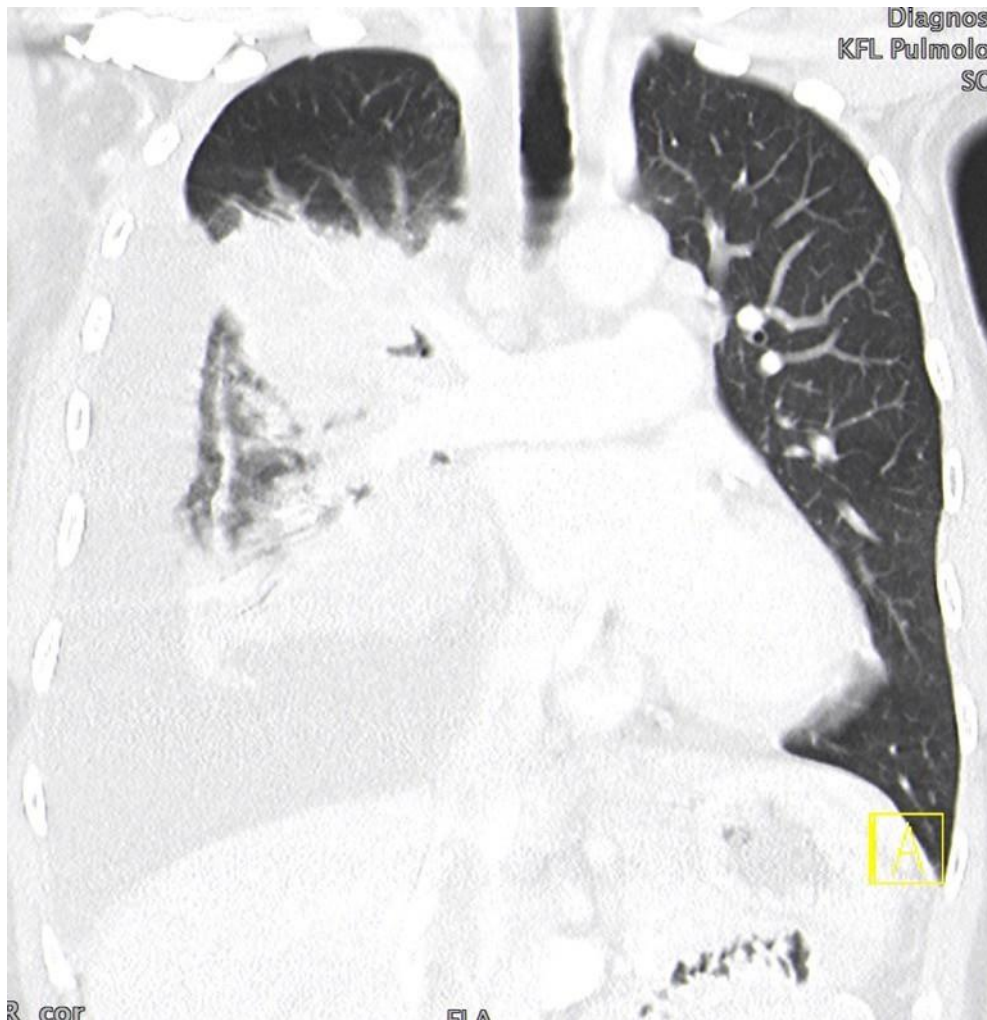


Requirements for intracranial response assessment

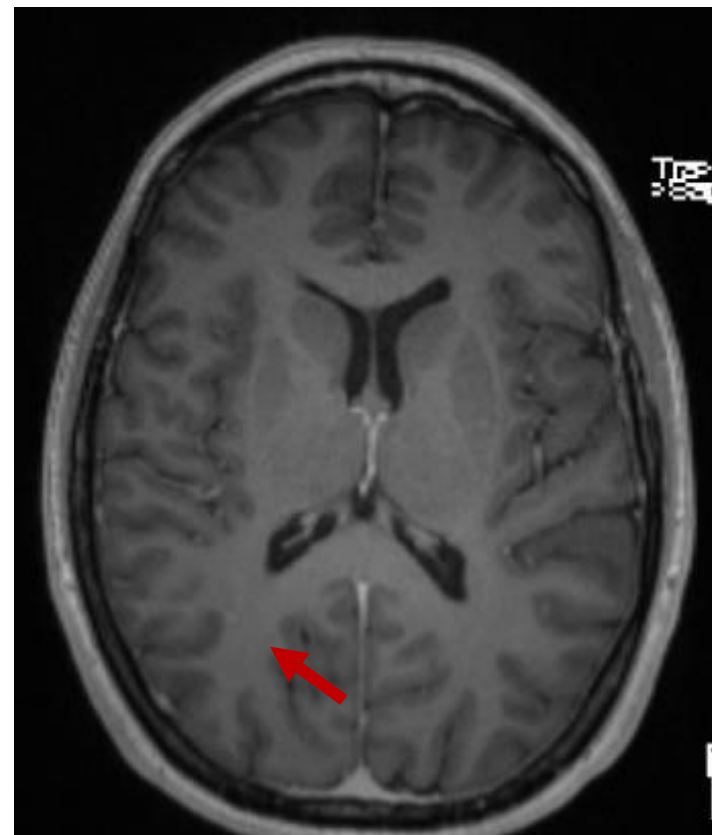
- Untreated/previously progressed
 - Measurable brain lesions
- **8 patients**

- 7 assessed with MRI
- 1 assessed with CT
- 100% intracranial ORR

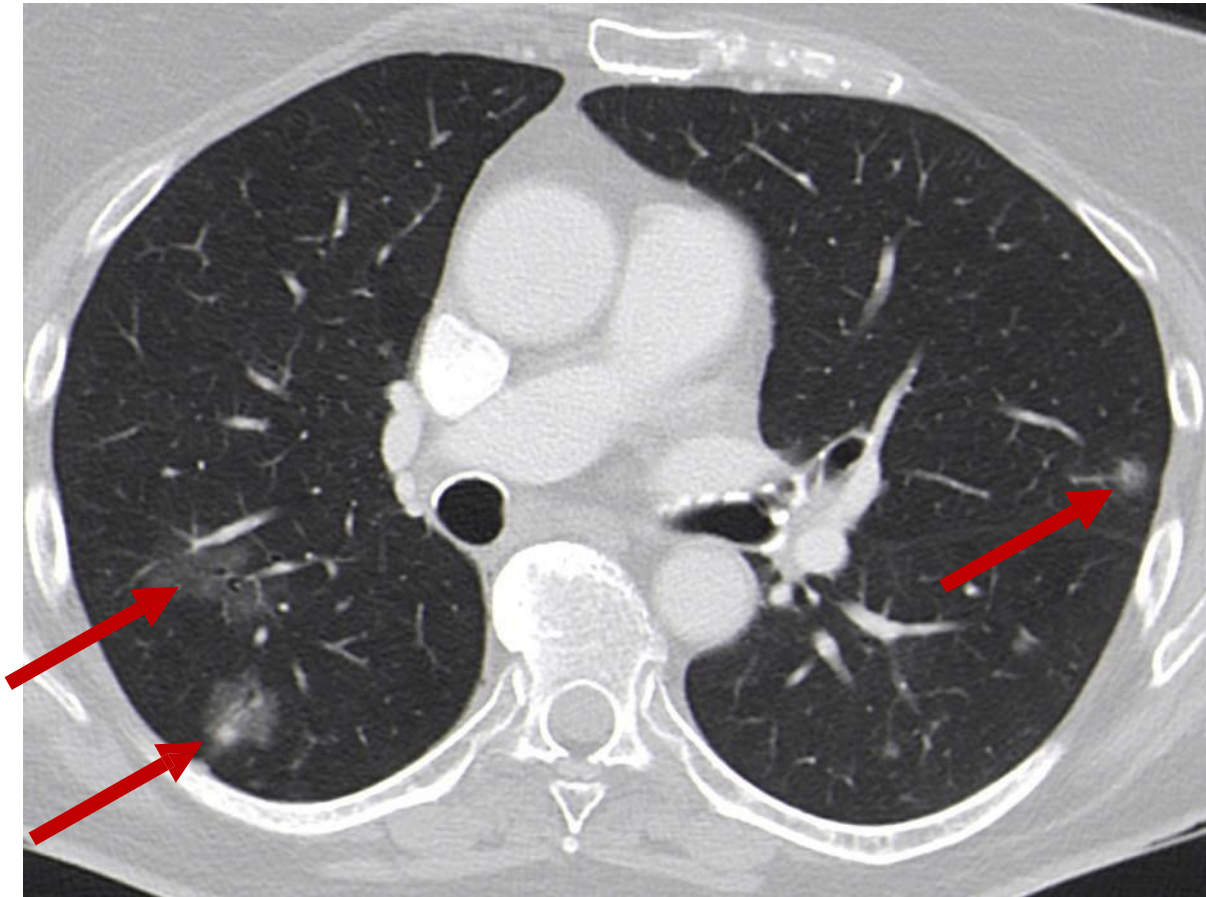
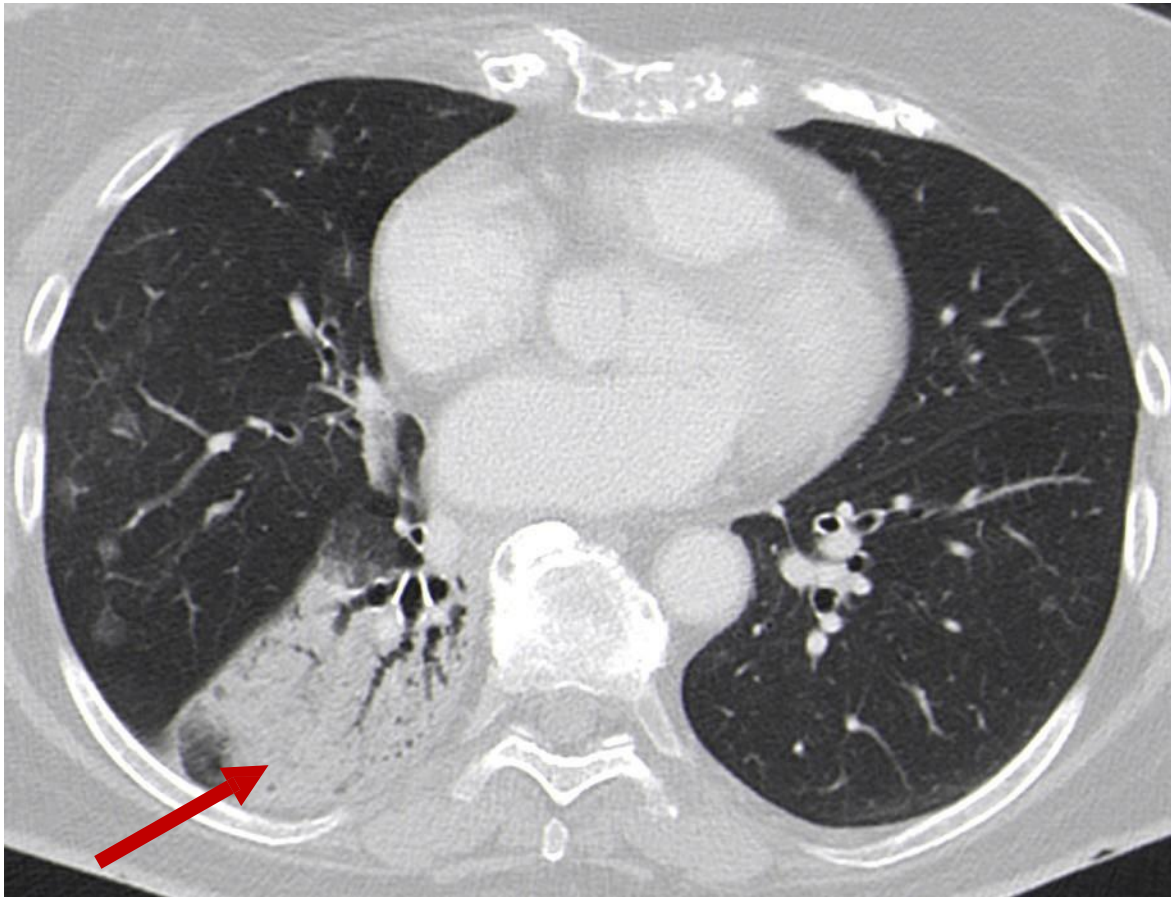
NSCLC RET+ Diag in 1/2020, 58 a since 1/2020 on Selpercatinib



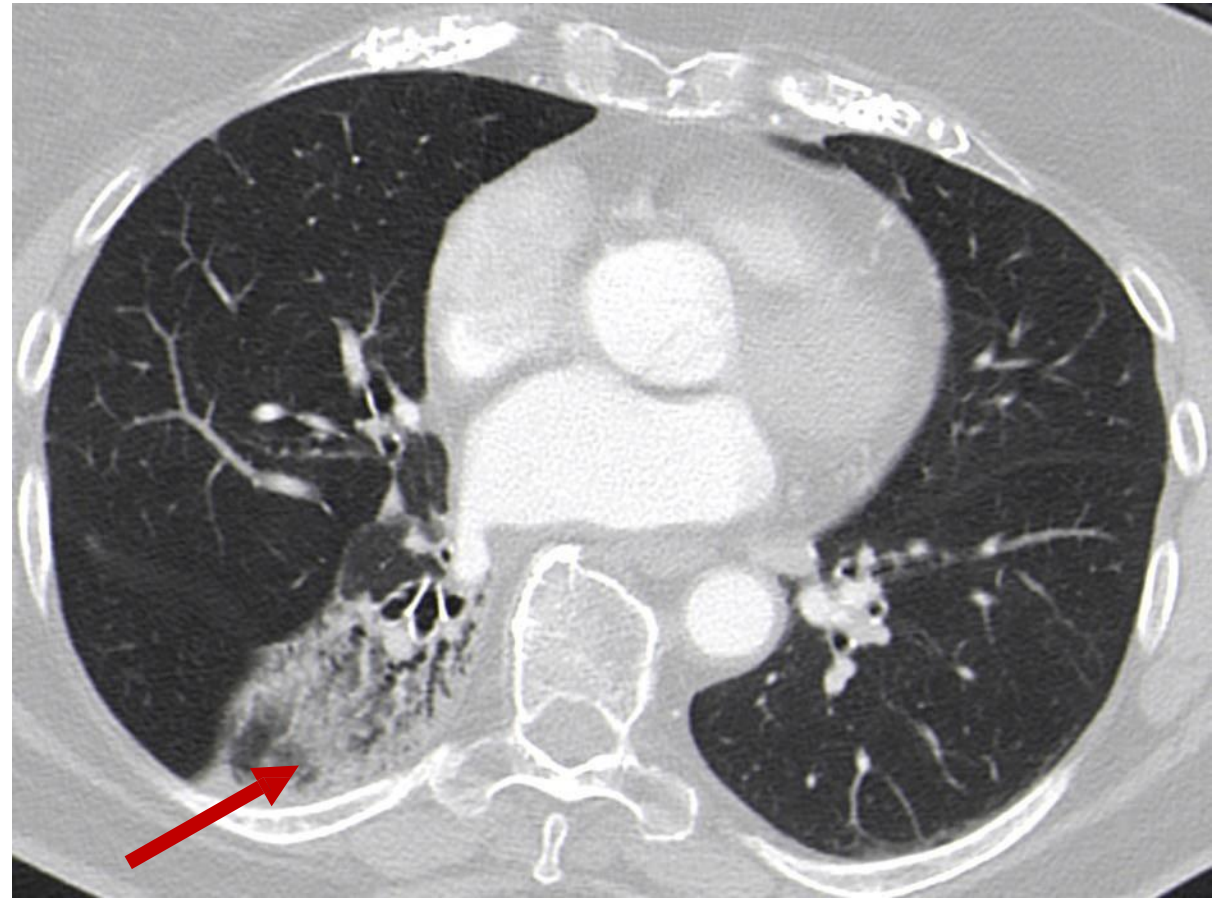
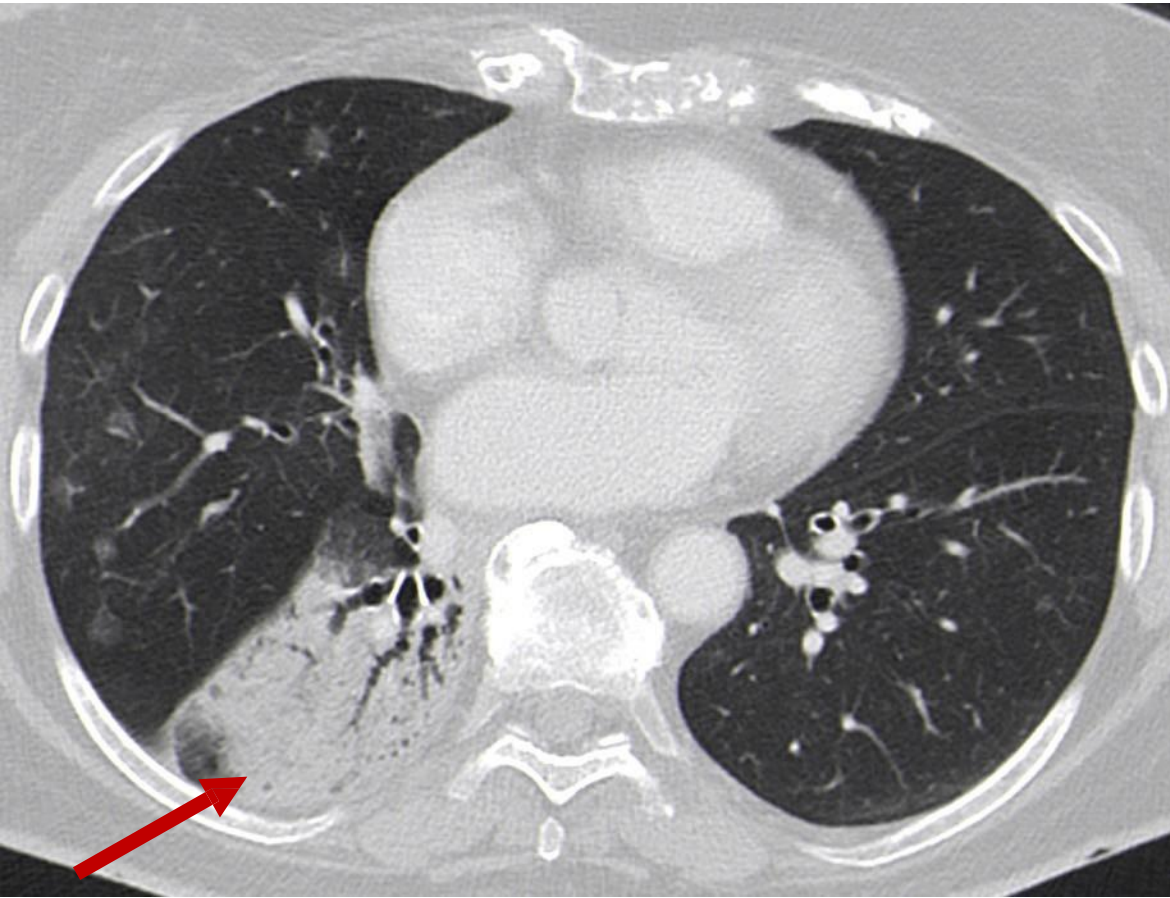
NSCLC RET+ Diag in 1/2020, 58 a since 1/2020 on Selpercatinib



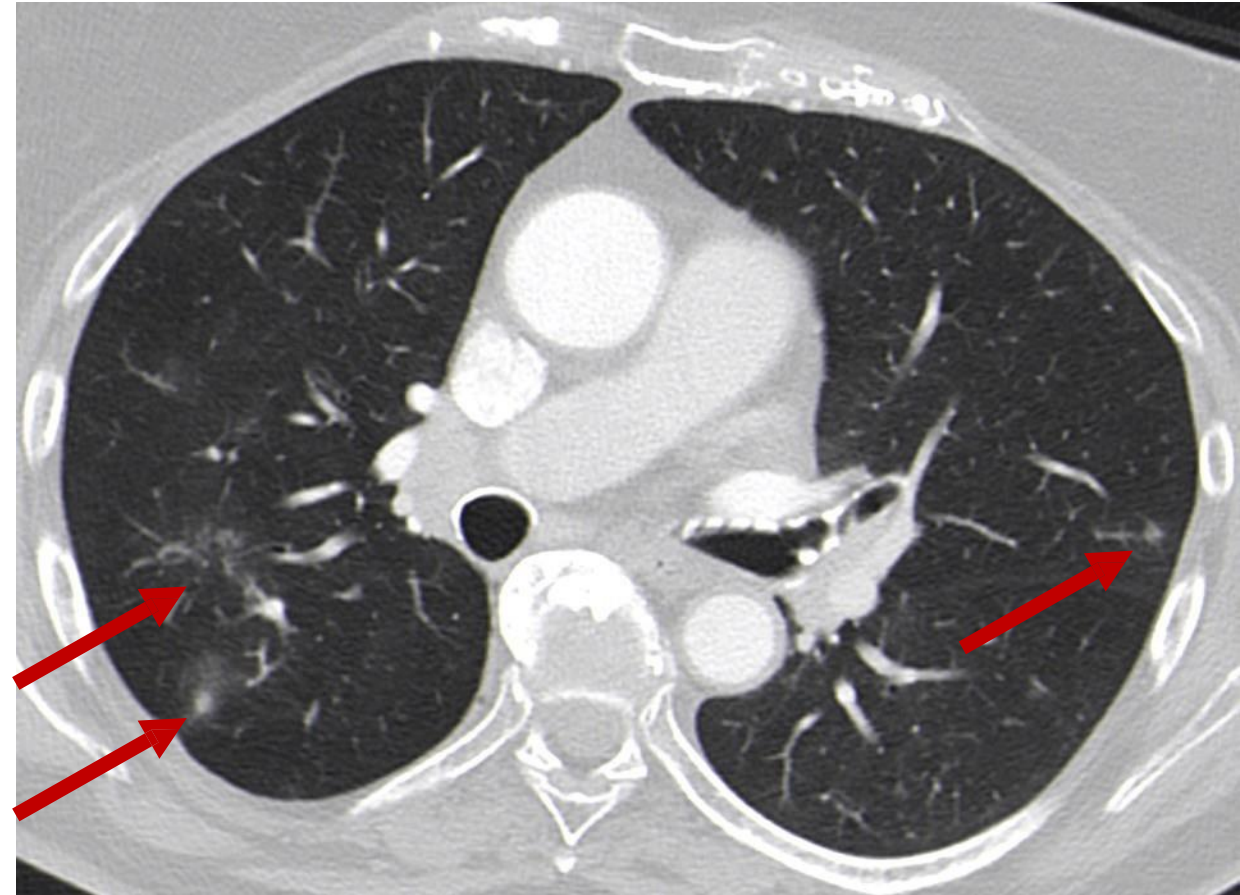
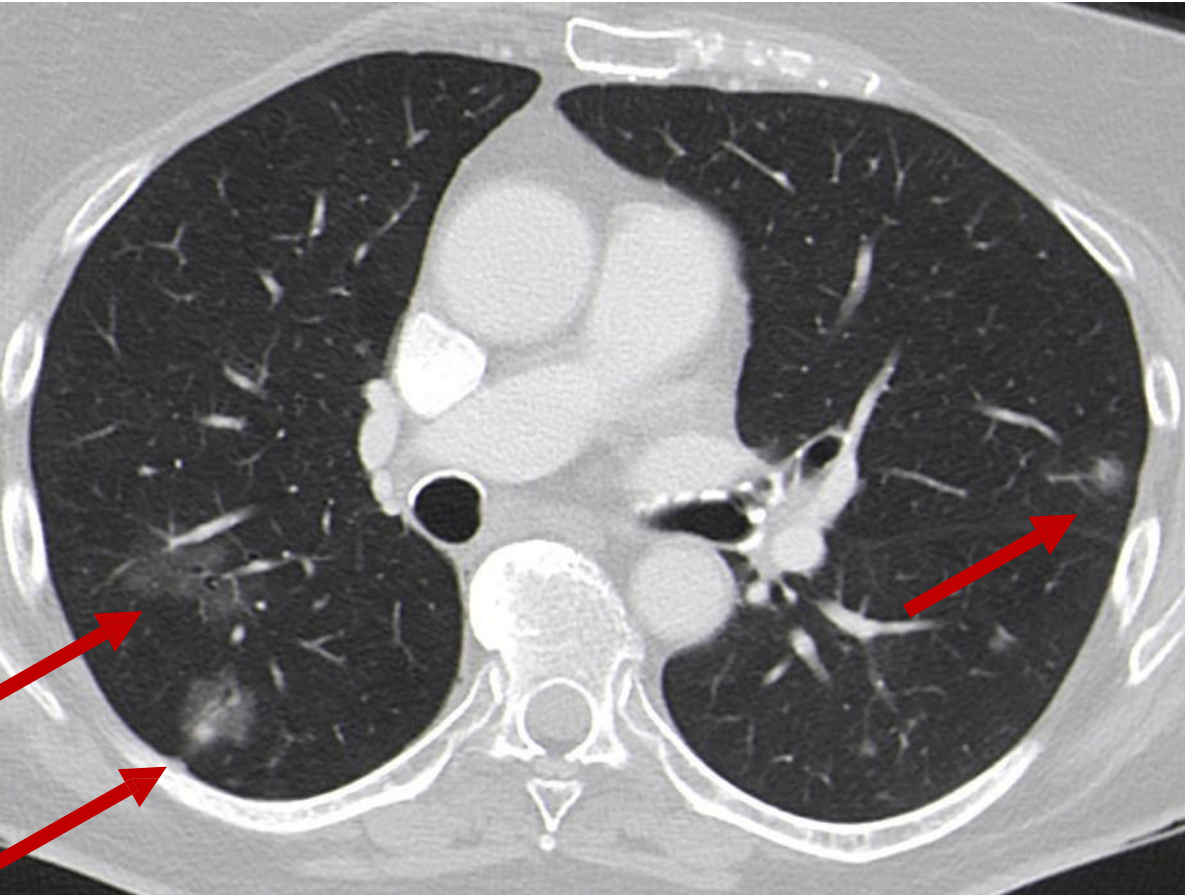
**81 a, NSCLC non-squamous, never smoker, PDL1 80%
local biomarker neg → Foundation one showed RET
fusion – Diagnosis in October 2019**



CT scan Oct 2019 → Oct 2023



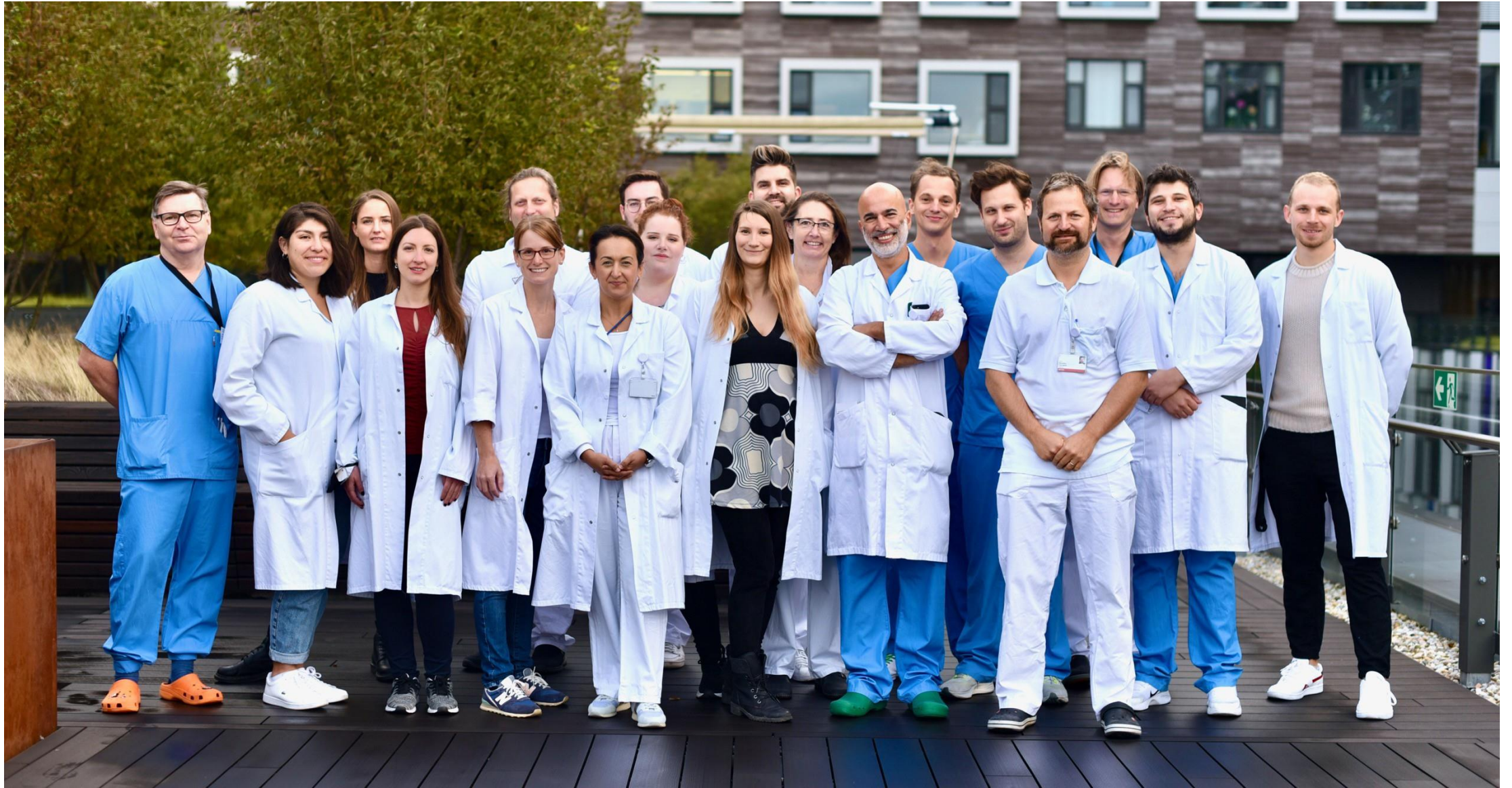
CT scan Oct 2019 → Oct 2023



Summary

- Lung Cancer treatment is not a one-size-fits-all
- Each case is unique and needs individualized treatment based on NGS, PDL1 Status, comorbidities and patient preferences
- Phase III data in LIBRETTO-431 demonstrated a statistically significant improvement in PFS for selpercatinib vs PD-L1 inhibitor + chemotherapy in RET pos NSCLC
- NSCLC underscores the importance of early RET testing at the time of diagnosis

DANKE SCHÖN aus der Klinik Floridsdorf



Disclosure of potential conflicts of interest

Guilherme Harada

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Oncologista Clínico

Hospital Sírio Libanês, SP

Category	Sponsor
Speakers' bureau	Pfizer, MSD, AstraZeneca, Bayer, Lilly

Q&A

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CRM: SP162463
Oncologista Clínico
Hospital Sírio Libanês, SP



Retsevmo[®]
(selpercatinibe)

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Indicações: RETSEVMO é indicado para o tratamento de câncer de pulmão de não-pequenas células (NSCLC) avançado com fusão no gene RET em pacientes adultos não tratados anteriormente com um inibidor de RET e que requerem terapia sistêmica. RETSEVMO é indicado para o tratamento de câncer de tireoide avançado com fusão no gene RET em pacientes adultos e pediátricos com 12 anos ou mais que requerem terapia sistêmica após tratamento prévio com sorafenibe ou lenvatinibe e que são refratários ao iodo radioativo (se o iodo radioativo for apropriado). RETSEVMO é indicado para o tratamento de câncer de tireoide medular avançado com mutação no gene RET em pacientes adultos e pediátricos com 12 anos ou mais que requerem terapia sistêmica. RETSEVMO é indicado para o tratamento de tumores sólidos metastáticos com fusão no gene RET em pacientes adultos que não possuem outras opções terapêuticas satisfatórias. Contraindicações: RETSEVMO é contraindicado em pacientes com hipersensibilidade grave conhecida a selpercatinibe ou a qualquer um de seus componentes. Advertências e Precauções: Monitorar os pacientes quanto a sintomas pulmonares indicativos de DPI (doença pulmonar intersticial)/pneumonite, tratar conforme apropriado e com base na gravidade, pode ser necessária a interrupção de RETSEVMO. Monitorar a ALT e AST antes do início da terapia com RETSEVMO, a cada 2 semanas durante os primeiros 3 meses de tratamento, mensalmente durante os próximos 3 meses de tratamento e de outra forma conforme clinicamente indicado. Com base no nível das elevações de ALT ou AST, pode ser necessário modificar a dose. A pressão arterial do paciente deve ser controlada antes de iniciar o tratamento e monitorada durante o tratamento com RETSEVMO, pois pode ser necessário modificar a dose ou descontinuar o tratamento permanentemente se a hipertensão não puder ser controlada com anti-hipertensivo. Utilizar com cuidado em pacientes com doenças como síndrome do QT longo congênito ou síndrome do QT longo adquirido ou outras condições clínicas que predispõem a arritmias. Monitorar através de eletrocardiogramas e eletrólitos séricos em todos os pacientes após 1 semana de tratamento com RETSEVMO, pelo menos mensalmente durante os primeiros 6 meses de tratamento. Pode ser necessário suspender ou ajustar a dose. Monitorar os pacientes quanto a hipotireoidismo. Descontinuar RETSEVMO permanentemente em pacientes com hemorragia grave ou de ameaça à vida. Suspender RETSEVMO caso ocorra hipersensibilidade e inicie o tratamento com esteroide. Dependendo do grau pode ser necessário ajustara dose de RETSEVMO e descontinuar em caso de recorrência. Pacientes com fatores de risco para Síndrome da lise tumoral devem ser monitorados de perto e tratados conforme indicação clínica, e a profilaxia apropriada deve ser considerada. RETSEVMO tem o potencial de afetar adversamente a cicatrização de feridas. Suspender RETSEVMO por pelo menos 7 dias antes da cirurgia eletiva, não administrar por pelo menos 2 semanas após uma cirurgia de grande porte e até a cicatrização adequada da ferida. Monitorar os pacientes quanto a sintomas indicativos de deslizamento da epífise da cabeça do fêmur/epifisiólise do fêmur e trate conforme apropriado do ponto de vista médico e cirúrgico. Aconselhar mulheres com potencial reprodutivo a utilizar contracepção eficaz durante o tratamento e por pelo menos 2 semanas após a última dose de RETSEVMO. RETSEVMO pode prejudicar a fertilidade em homens e mulheres. Este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista. Aconselhar as lactantes a descontinuar a amamentação durante o tratamento com RETSEVMO e por pelo menos 2 semanas após a última dose de RETSEVMO. Interações medicamentosas: Evitar o uso concomitante de inibidores potentes de CYP. Se inevitável, reduzir a dose atual de RETSEVMO em 50%. Evitar o uso concomitante de indutores potentes de CYP. Administrar RETSEVMO com alimento quando usado com um inibidor de bomba de prótons. Administrar RETSEVMO 2 horas antes dos antagonistas do receptor H2. Administrar RETSEVMO 2 horas antes ou 2 horas após antiácidos de ação local. Reações adversas: Muito comum ($\geq 1/10$) nos estudos Libretto-001 e Libretto-431: hipotireoidismo, diarreia, boca seca, dor abdominal, constipação, náusea, vômito, estomatite, edema, fadiga, piroxia, infecção do trato urinário, QT prolongado no eletrocardiograma, hipertensão, apetite diminuído, cefaleia, erupção cutânea, AST e ALT aumentadas, cálcio diminuído, albumina diminuída, contagem de linfócitos diminuída, creatinina sérica aumentada, contagem de células brancas diminuída, sódio diminuído, fosfatase alcalina aumentada, plaquetas diminuídas, magnésio diminuído, hemoglobina diminuída, bilirrubina total aumentada, contagem de neutrófilos diminuída e potássio diminuído. Muito comum ($\geq 1/10$) no estudo Libretto-001: pneumonia, tosse, dispneia, tontura e hemorragia. Comum ($\geq 1/100$ a $<1/10$) no estudo Libretto-001: Ascite quilosa, hipersensibilidade, DPI/pneumonite e quilotórax. Comum ($\geq 1/100$ a $<1/10$) no estudo Libretto-431: Ascite quilosa, hipersensibilidade, pneumonia, tontura e DPI/pneumonite. Outras reações adversas: deslizamento da epífise da cabeça do fêmur/epifisiólise do fêmur em pacientes pediátricos (comum). Posologia: A dose recomendada para pacientes abaixo de 50 kg, é 120 mg, duas vezes ao dia. Para pacientes com 50 kg ou mais, 160 mg, duas vezes ao dia. O tratamento deve ser continuado até a progressão da doença ou toxicidade inaceitável. Seguir orientação para modificação de dose devido às reações adversas e pacientes com insuficiência hepática. Venda sob prescrição. Registro: 1.1260.0204. Documentação científica e/ou informações adicionais à classe médica sobre o produto mediante solicitação. Para mais informações, consulte a bula completa do produto ou o Serviço de Atendimento ao Cliente Lilly SAC 0800 701 0444, e-mail: sac_brasil@lilly.com, 22/01/2024.

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