Lung Cancer UPDATES
ESMO HIGHLIGTHS
19-21 SEPTIEMBRE 2020

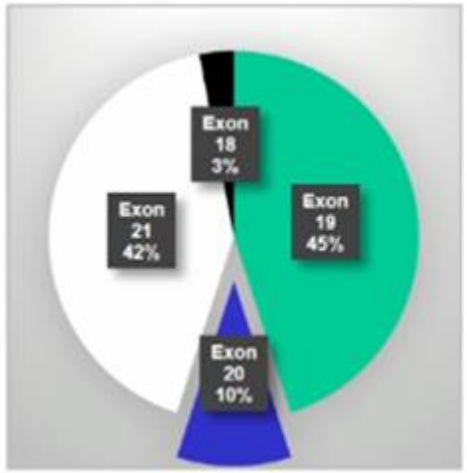
VIRTUAL

Iniciativa científica de: GECP lung cancer research

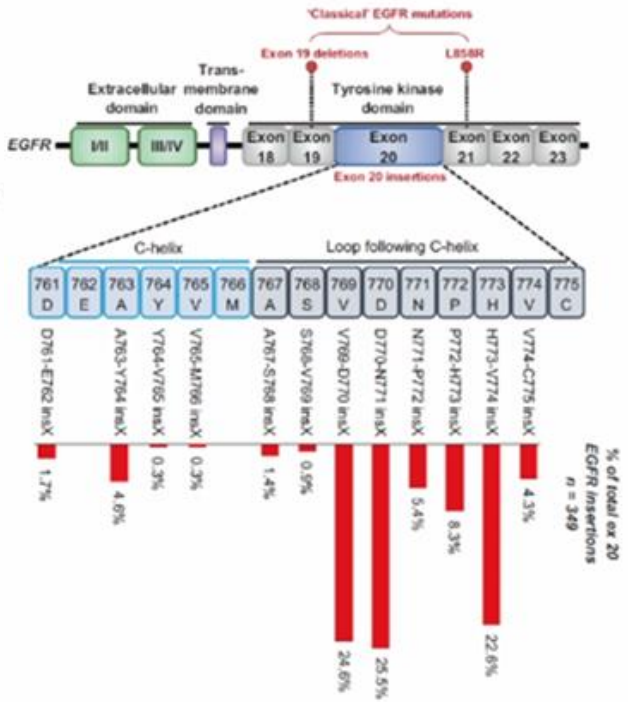
Cáncer de pulmón no microcítico avanzado con mutaciones infrecuentes.

María Guirado Risueño
HGU Elche

EGFR INSERCIÓN 20



- Insertions – 6%
- S768I 1%
- T790M DE novo 5%



Vyse et al, Signal Transduction and Targeted Therapy 2019 ; Kobayashi et al, Cancer Science 2016 ; Yasuda et al, Lancet Oncol 2012

Drug	Group	ORR	PFS (mo)
Gefitinib/erlotinib	1st gen *EGFR* TKI	8-27%	-
Afatinib	2nd gen *EGFR/HER2* TKI	8%	2.7
Osimertinib	3rd gen *EGFR* TKI	5%	3.6
Cetuximab +afatinib	Anti-*EGFR* Ab+ TKI	3/4 pts	-

Vyse et al, Signal Transduction and Targeted Therapy 2019 ; NCT 03414814 ; Van Veggel et al, Lung Cancer 2020

EGFR INSERCIÓN 20

Updated results from a phase I/II study of mobocertinib (TAK-788) in NSCLC with EGFR exon 20 insertions (exon20ins)

Gregory Riely, New York, United States

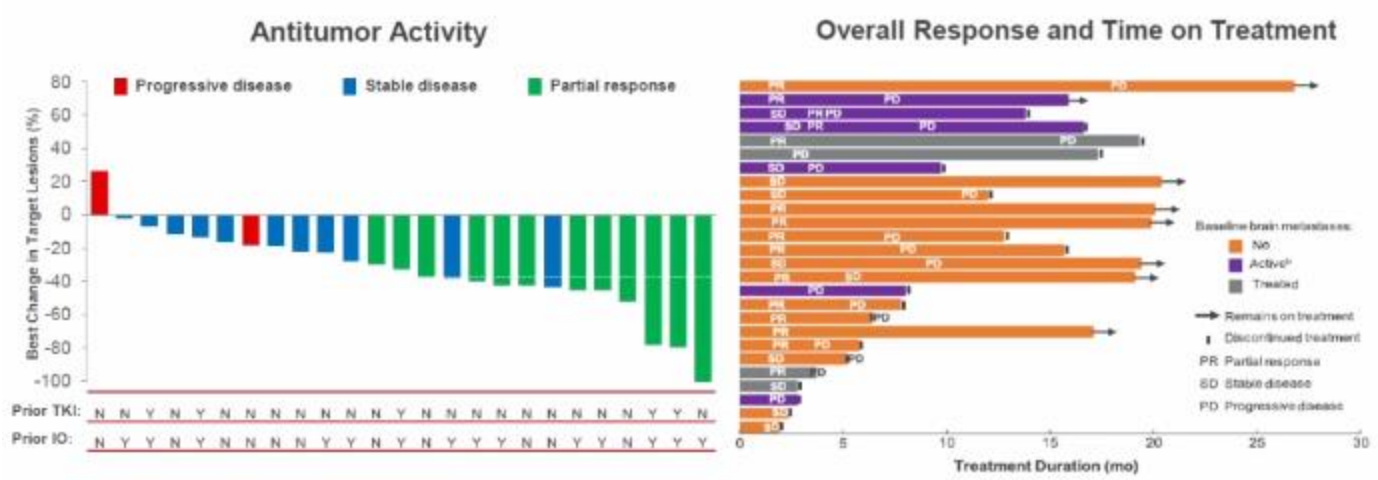
Expansio
160 mg q
in *EGFR*
exon 20
with prio
therapy

DLTs During Dose Escalation	Dose
Missed >25% of planned dose due to drug-related AEs	180 mg
Grade 3	
Diarrhea	180 mg
Mucositis	160 mg
Pneumonitis	80 mg
Grade 5	
Pneumonitis	120 mg; 1

Any grade: ≥20% of all patients Grade ≥3: ≥5% of all patients	Patients With *EGFR* Exon 20 Insertions Treated at 160 mg qd (n=28)	
	Any Grade, %	Grade ≥3, %
Diarrhea	82	32
Nausea	39	11
Rash	46	0
Vomiting	36	7
Decreased appetite	39	0
Dry skin	18	0
Fatigue	14	4
Baseline brain metastases, n (%)	12 (43)	

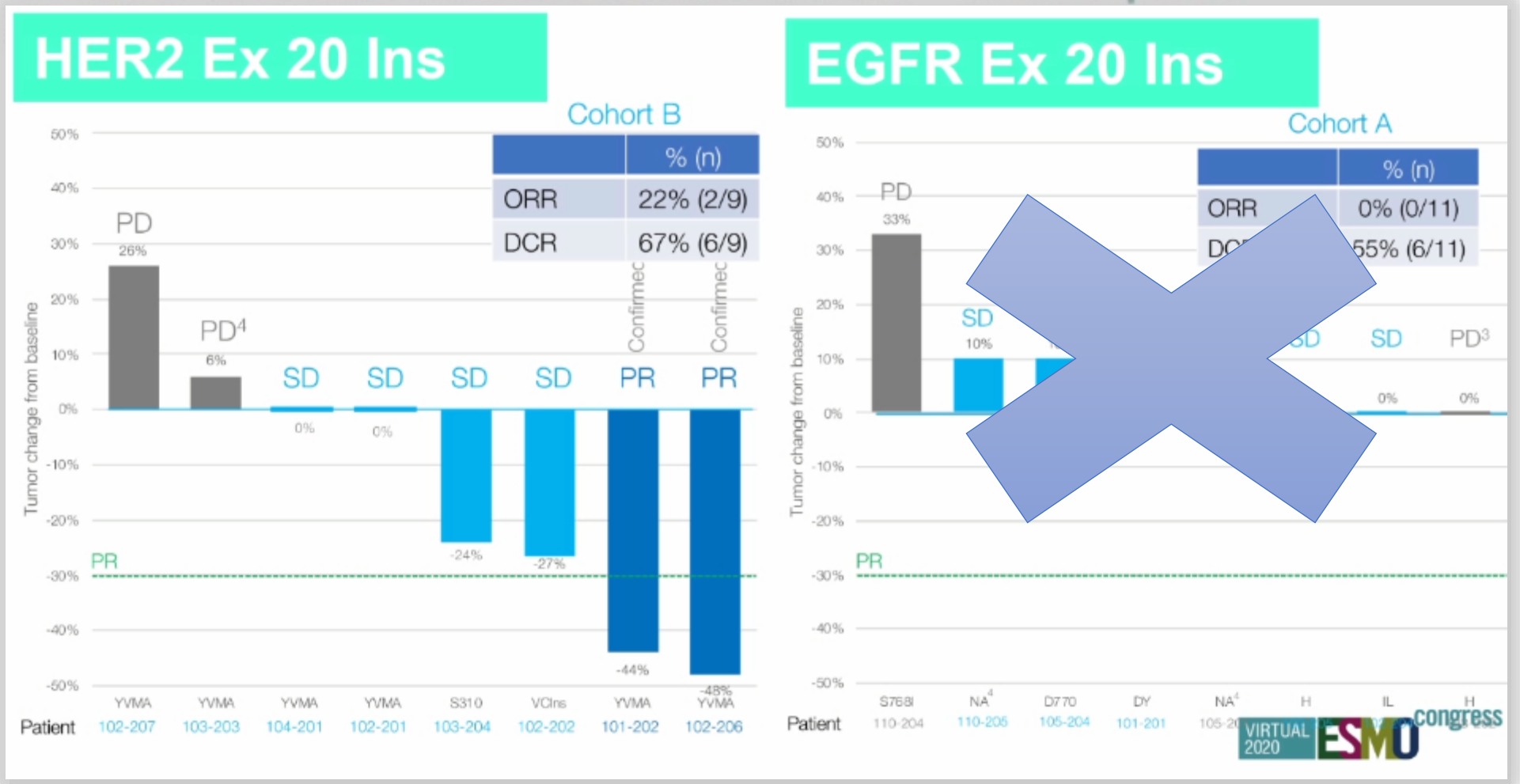
ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; *EGFR*, epidermal growth factor rece

N=28	
TR	43%
EE	43%
TCE	86%
mDoR	13,9
mPFS	7,3m



EGFR/HER2 INSERCIÓN 20

Tarloxotinib - *EGFR* Ex 20 Ins, *HER2*-Activating Mutations & Other Solid Tumors with *NRG1/ERBB* Gene Fusions – First report

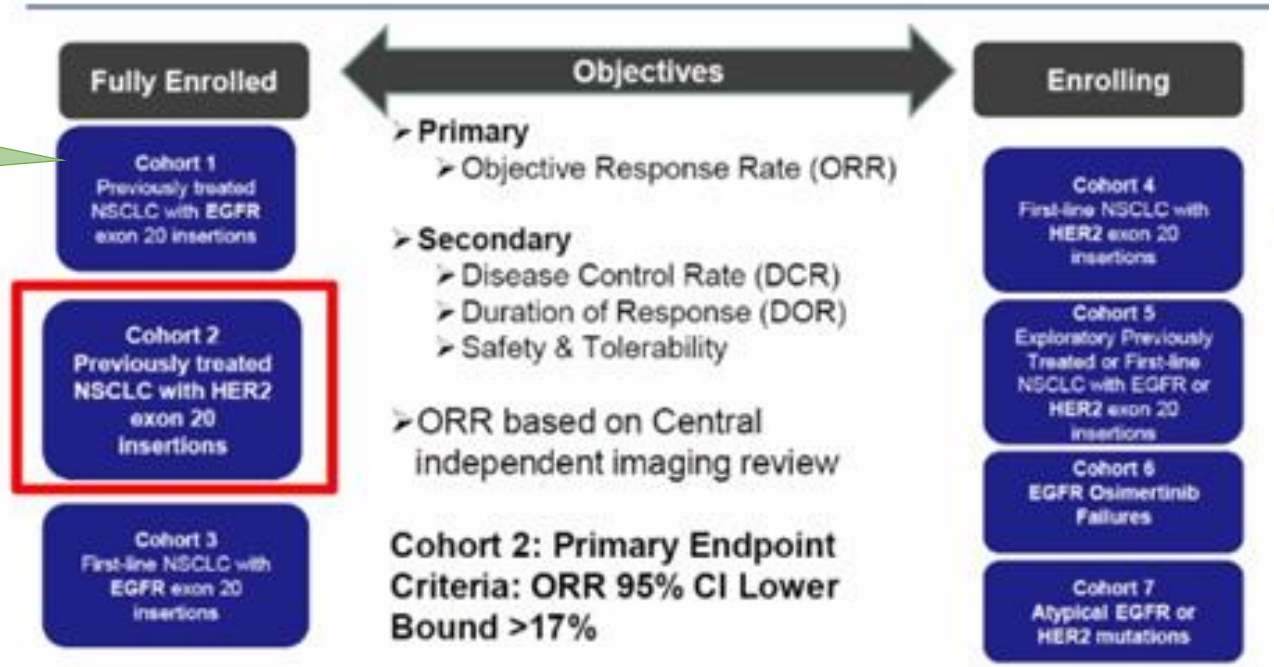


EGFR HER 2 INSERCIÓN 20

ZENITH20, a multinational, multi-cohort Phase 2 study of poziotinib in NSCLC patients with EGFR or HER2 exon 20 insertion mutations

Mark Socinski, Orlando, United States

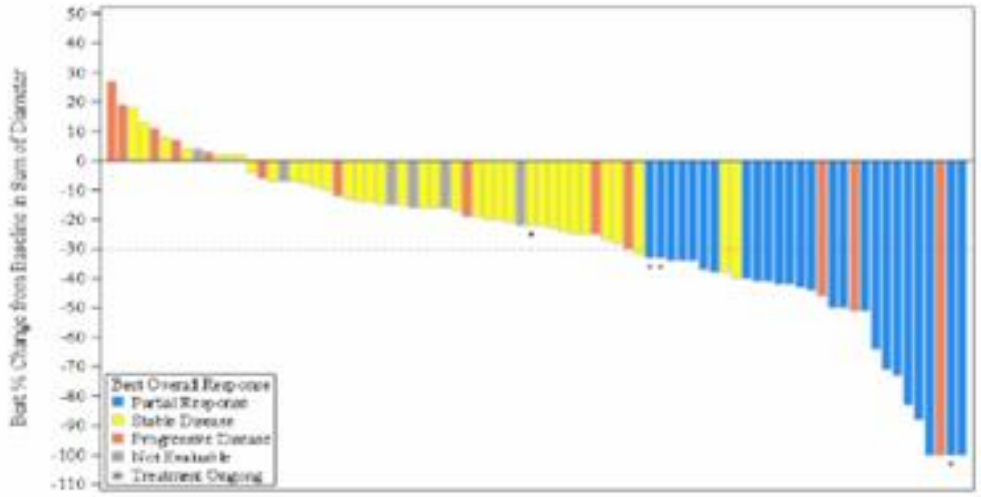
ASCO 2020:
TR 14.9%
mPFS 4,2m



Disposition	N=90, n (%)
Treated	90 (100)
Number of therapies, median (range)	2 (1-6)
Chemotherapy only	22 (24)
Chemo / IO checkpoint inhibitors	41 (46)
Chemo / HER2 therapy / IO checkpoint inhibitors	17 (19)
Others	10 (11)
Mutations: A775_G776insYVMA / Others, n	61 / 29

EGFR HER2 INSERCIÓN 20

	As-Treated (N=90)	Evaluable (N= 74)
ORR, n (%)	25 (27.8)	26 (35.1)
PFS (months)	5.5 (0 - 13.1+)	5.5 (1 - 13.1+)



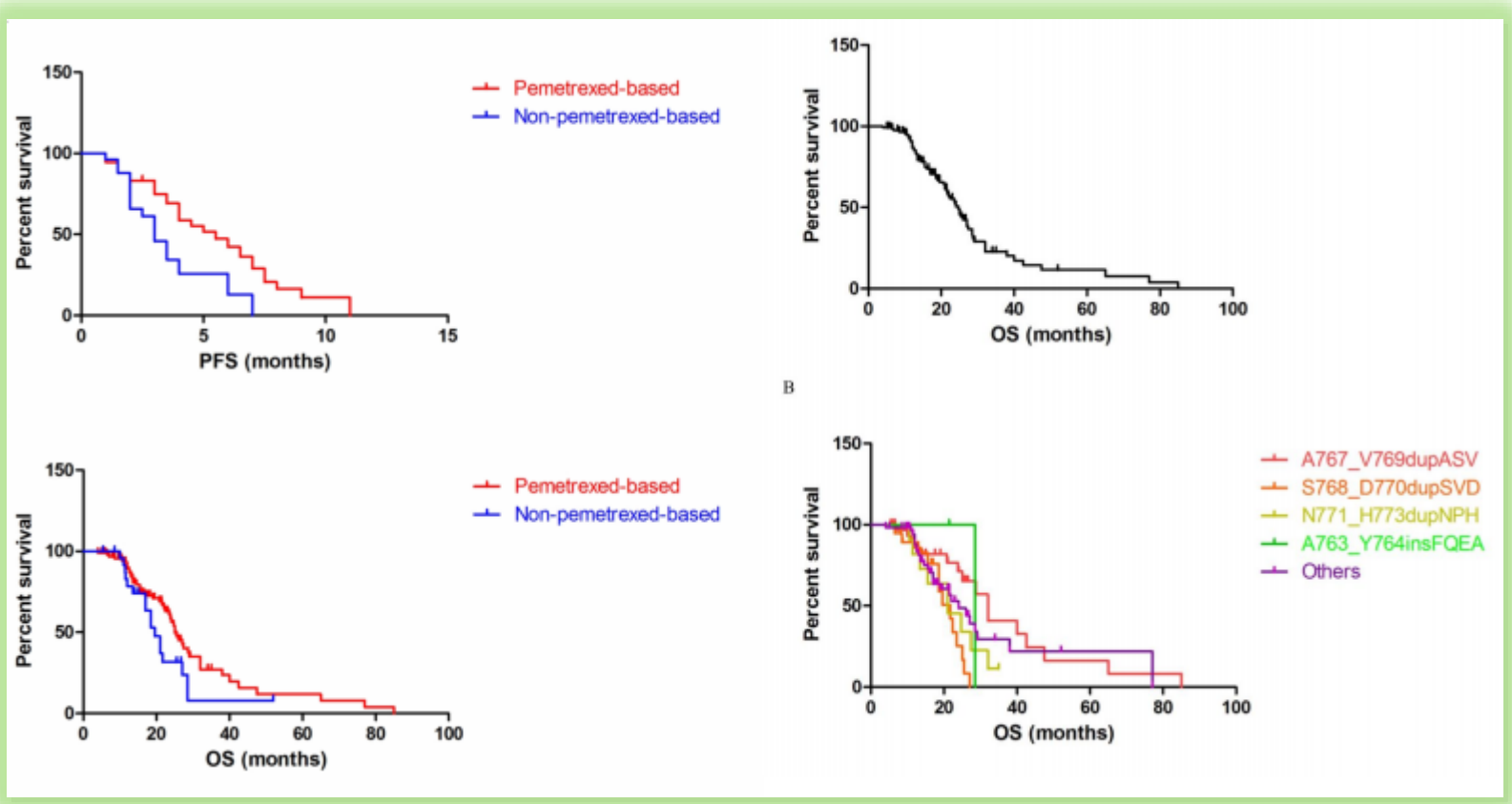
	N=90, n (%)
Treatment-related AE	88 (98)
Dose interruptions	78 (87)
Dose reductions	70 (78)

Preferred Term (PT)	N=90, n (%)		
	Any Grade	Grade 3	G4
Diarrhea	74 (82)	23 (26)	0
Rash	61 (68)	27 (30)	0
Stomatitis	59 (66)	20 (22)	1 (1)
Paronychia	34 (38)	1 (1)	0
Pneumonitis	1 (1)	0	0

EGFR INSERCIÓN 20

Patients with EGFR exon 20 insertion mutation non-small-cell lung cancer benefit from pemetrexed-based chemotherapy: A multicenter study

N=119

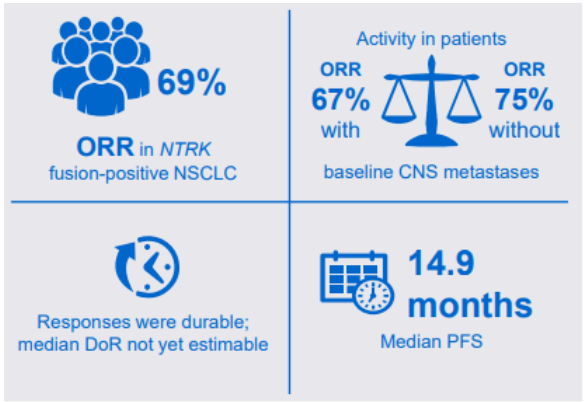


NTRK

543P

Entrectinib in *NTRK* fusion-positive NSCLC: updated integrated analysis of STARTRK-2, STARTRK-1 and ALKA-372-001

Endpoint	All patients with *NTRK*-fp NSCLC (N=13)	Patients with *NTRK*-fp NSCLC with baseline CNS metastases* (n=9)	Patients with *NTRK*-fp NSCLC without baseline CNS metastases* (n=4)
ORR, % (95% CI)	**69.2** (38.6–90.9)	**66.7** (29.9–92.5)	**75.0** (19.4–99.4)
CR, n (%)	1 (7.7)	0	1 (25.0)
PR, n (%)	8 (61.5)	6 (66.7)	2 (50.0)
SD, n (%)	2 (15.4)	2 (22.2)	0
PD, n (%)	0	0	0
Missing/unevaluable, n (%)	2 (15.4)	1 (11.1)	1 (25.0)
Median PFS, months (95% CI)	14.9 (4.7–NE)	6.5 (4.5–NE)	NE (14.9–NE)
Median OS, months (95% CI)	14.9 (5.9–NE)	8.9 (5.6–NE)	NE (14.9–NE)
Median DoR, months (95% CI)	NE (5.6–NE)†	NE (3.6–NE)‡	NE (10.4–NE)§



1193P

Clinical validity of FoundationOne Liquid CDx (F1L CDx) assay as an aid in selecting patients for treatment with entrectinib

NTRK-rp		CTA		
		Detected	**Not detected**	**Total**
F1L CDx	**Detected**	18	0	18
	Not detected	20	47	67
	Total	38	47	85

ROS1-rp		CTA		
		Detected	**Not detected**	**Total**
F1L CDx	**Detected**	20	0	20
	Not detected	11	54	65
	Total	31	54	85

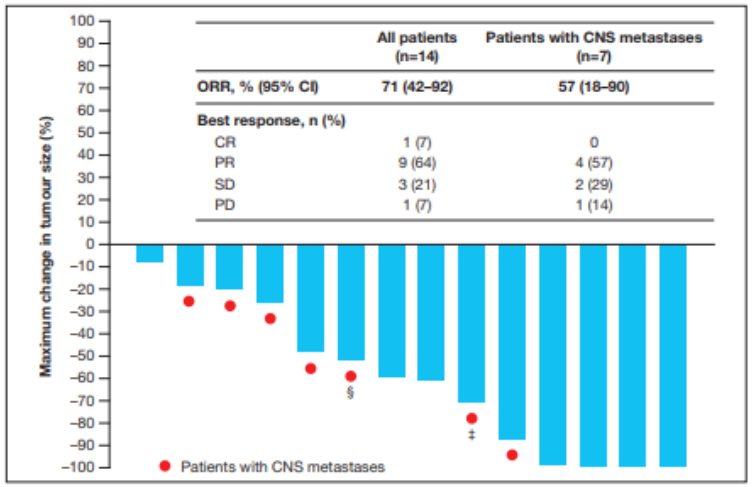
CTA, clinical trial assays; F1L CDx, FoundationOne Liquid CDx; *NTRK*/*ROS1*-rp, *NTRK*/*ROS1* rearrangement-positive

	NTRK-rp ORR (95% CI), n	*ROS1*-rp ORR (95% CI), n
CTA+*	57.4 (43.2–70.8), n=54	78.4 (64.8–88.7), n=51†
CTA+ FL1 CDx+	72.2 (46.5–90.3), n=18	72.2 (46.5–90.3), n=18
CTA+ F1L CDx-	55.0 (31.5–76.9), n=20	72.7 (39.0–94.0), n=11
CTA+ F1L CDx unknown	43.8 (19.8–70.1), n=16	86.4 (65.1–97.1), n=22

NTRK

- 1289P

Efficacy and safety of larotrectinib in patients with tropomyosin receptor kinase (TRK) fusion lung cancer

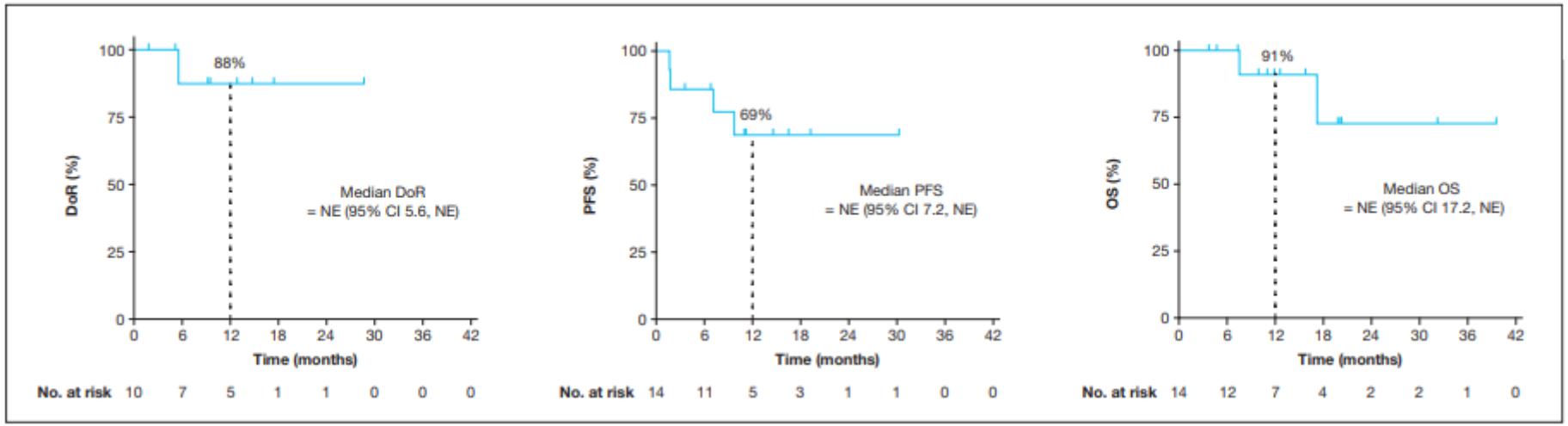


	All patients (n=14)	Patients with CNS metastases (n=7)
ORR, % (95% CI)	71 (42–92)	57 (18–90)
Best response, n (%)		
CR	1 (7)	0
PR	9 (64)	4 (57)
SD	3 (21)	2 (29)
PD	1 (7)	1 (14)

N=14

Nº ttos previos (mediana): 3

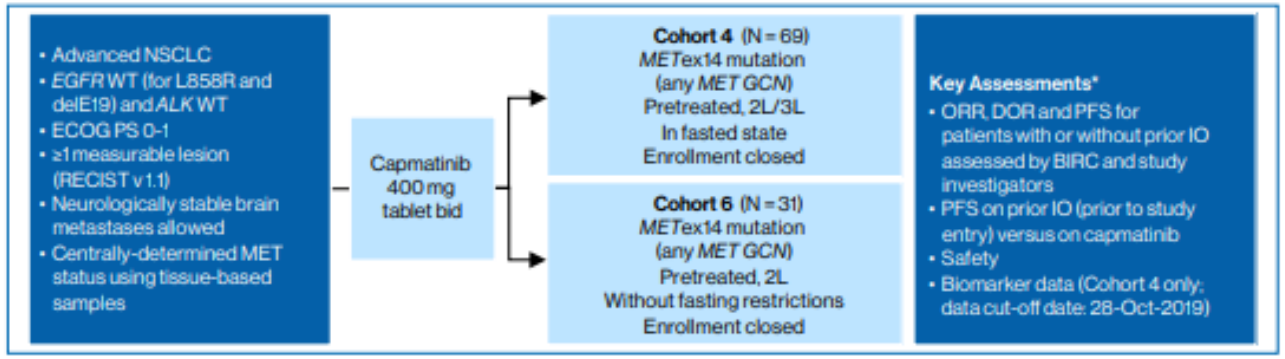
Number of prior therapies, n (%)	
0	1 (7)
1	4 (29)
2	2 (14)
≥3	7 (50)



MET

- 1285P

Capmatinib in Patients With *METex14*-Mutated Advanced NSCLC Who Received Prior Immunotherapy: Results From the Phase 2 GEOMETRY Mono-1 Study



	Patients With Prior IO N = 32		Patients Without Prior IO N = 68	
	BIRC	Investigator	BIRC	Investigator
Best Overall response, n (%)				
Complete Response (CR)	0	0	0	1 (1.5)
Partial Response	20 (62.5)	17 (53.1)	23 (33.8)	25 (36.8)
Stable Disease	7 (21.9)	8 (25.0)	30 (44.1)	27 (39.7)
Non-CR/Non-PD	1 (3.1)	2 (6.3)	1 (1.5)	1 (1.5)
Progressive Disease (PD)	1 (3.1)	3 (9.4)	5 (7.4)	4 (5.9)
Not evaluable[a]	3 (9.4)	2 (6.3)	9 (13.2)	10 (14.7)
Overall response rate, % (95% CI)	62.5 (43.7,78.9)	53.1 (34.7,70.9)	33.8 (22.8,46.3)	38.2 (26.7,50.8)
Disease control rate, % (95% CI)	87.5 (71.0,96.5)	84.4 (67.2,94.7)	79.4 (67.9,88.3)	79.4 (67.9,88.3)
Responders, n (%)[b]				
With event (progression/death)	14 (70.0)	12 (70.6)	17 (73.9)	20 (76.9)
Without event	6 (30.0)	5 (29.4)	6 (26.1)	5 (19.2)
Median duration of response, months (95% CI)[b]	9.95[c] (5.55, 19.52)	11.20[c] (4.34, 21.65)	6.93 (4.17, 11.14)	7.16 (4.17, 10.87)
Patients with DOR ≥ 6 months, n (%)[b]	12 (60.0)	9 (52.9)	12 (52.2)	15 (57.7)
Patients with DOR ≥ 12 months, n (%)[b]	5 (25.0)	5 (29.4)	5 (21.7)	5 (19.2)
PFS events, n (%)	24 (75.0)	23 (71.9)	54 (79.4)	56 (82.4)
Median PFS, months (95% CI)	8.34[c] (4.17, 12.58)	6.90 (4.70, 19.81)	5.39 (4.17, 6.93)	5.42 (4.17, 7.39)

	Patients With Prior IO N = 32		Patients Without Prior IO N = 68	
	All Grades, n (%)	Grade 3/4, n (%)	All grades, n (%)	Grade 3/4, n (%)
Any AE	32 (100)	24 (75.0)	66 (97.1)	45 (66.2)
Treatment-related AEs	23 ([illegible])	17 ([illegible])	59 (86.8)	30 (44.1)
SAEs	16 (50.0)	13 (40.6)	29 (42.6)	25 (36.8)
Treatment-related SAEs	8 (25.0)	5 (15.6)	9 (13.2)	8 (11.8)
AEs requiring dose adjustment	13 (40.6)	5 (15.6)	19 (27.9)	6 (8.8)
AEs leading to drug discontinuation	8 (25.0)	5 (15.6)	9 (13.2)	6 (8.8)
Most common AEs regardless of causality (≥ 10%, all grades in either of subgroup)				
Peripheral edema	20 (62.5)	6 (18.8)	38 (55.9)	8 (11.8)
Nausea	16 (50.0)	1 (3.1)	26 (38.2)	0
Vomiting	12 (37.5)	0	14 (20.6)	0
Fatigue	10 (31.3)	2 (6.3)	17 (25.0)	4 (5.9)
Dyspnea	8 (25.0)	2 (6.3)	13 (19.1)	5 (7.4)
Back pain	7 (21.9)	1 (3.1)	12 (17.6)	1 (1.5)
Increased blood creatinine	7 (21.9)	0	23 (33.8)	0
Cough	7 (21.9)	1 (3.1)	10 (14.7)	0
Pyrexia	6 (18.8)	1 (3.1)	5 (7.4)	1 (1.5)
Increased Alanine aminotransferase	5 (15.6)	3 (9.4)	8 (11.8)	4 (5.9)
Decreased appetite	5 (15.6)	0	14 (20.6)	1 (1.5)
Diarrhea	5 (15.6)	0	9 (13.2)	0
Headache	5 (15.6)	0	5 (7.4)	0
Abdominal pain upper	4 (12.5)	0	1 (1.5)	0
Dizziness	4 (12.5)	0	7 (10.3)	0
Hypoalbuminaemia	4 (12.5)	0	6 (8.8)	0
Nasopharyngitis	4 (12.5)	0	2 (2.9)	0
Pneumonia	4 (12.5)	3 (9.4)	5 (7.4)	2 (2.9)
Rash	4 (12.5)	0	5 (7.4)	0
Pruritus	3 (9.4)	1 (3.1)	10 (14.7)	0
Weight decreased	3 (9.4)	0	7 (10.3)	0
Amylase increased	2 (6.3)	0	9 (13.2)	5 (7.4)
Lipase increased	2 (6.3)	2 (6.3)	8 (11.8)	7 (10.3)
Anaemia	1 (3.1)	0	8 (11.8)	2 (2.9)
Constipation	1 (3.1)	0	10 (14.7)	2 (2.9)

MET

Tepotinib in patients with advanced NSCLC with *MET* exon 14 skipping: Overall efficacy results from VISION Cohort A

Julien Mazieres,[1] Paul Paik,[2] Enriqueta Felip,[3] Remi Veillon,[4] Hiroshi Sakai,[5] Alexis B. Cortot,[6] Santiago Viteri,[7] Marina Chiara Garassino,[8] Jan Van Meerbeeck,[9] Jo Raskin,[9] Michael Thomas,[10] Masahiro Morise,[11] Byoung Chul Cho,[12] Pierfranco Conte,[13] Rolf Bruns,[14] Tim Demuth,[15] Karl Maria Schumacher,[15] Xiuning Le[16]

		N=146	
		IRC	INV
ORR, % (95% CI)		45.2 (37.0, 53.6)	54.1 (45.7, 62.4)
Best overall response, n (%)	Complete response	0	3 (2.1%)
	Partial response	66 (45.2%)	76 (52.1%)

mDoR	11,1m
mPFS	8,9m

Activity of tepotinib in brain metastases: Preclinical models and clinical data from patients with *MET* exon 14 skipping NSCLC

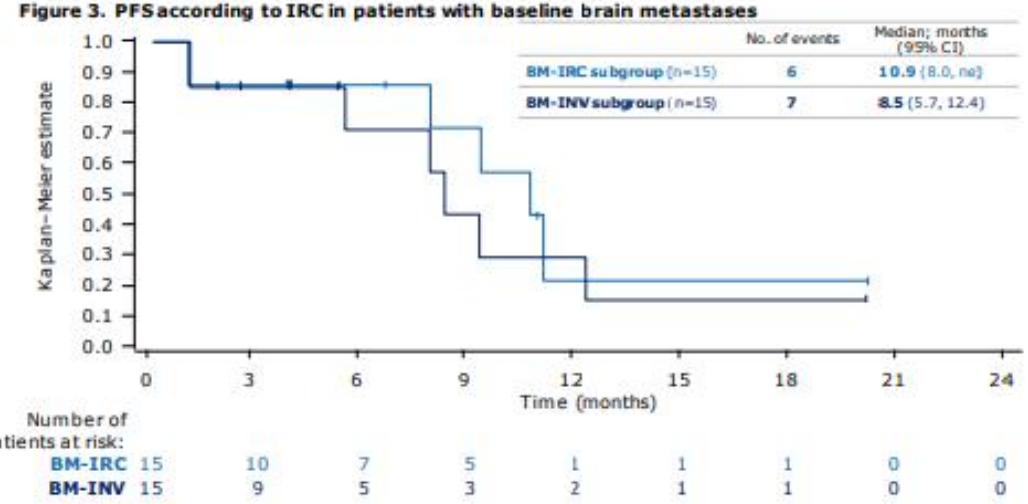
Santiago Viteri,[1] Julien Mazieres,[2] Remi Veillon,[3] Enriqueta Felip,[4] Xiuning Le,[5] Marina Chiara Garassino,[6] Thomas Stanton,[7] Masahiro Morise,[8] Jong-Seok Lee,[9] Shingo Matsumoto,[10] Filippo De Marinis,[11] Thomas Wehler,[12] Anderson Clark,[13] Manja Friese-Hamim,[14] Christopher Stroh,[14] Rolf Bruns,[15] Gordon Otto,[16] Paul Paik[17]

Table 2. Clinical efficacy of tepotinib in patients with baseline brain metastases

		BM-IRC	BM-INV
Patients with brain metastases; n	Non-target lesions*	14	12
	Target lesions†	0	1
Objective response rate; % (95% CI)		57.1% (28.9, 82.3)	53.8% (25.1, 80.8)
Best overall response; n	Partial response	8	7
	Stable disease	3	3

- PFS (95% CI) was 10.9 months (8.0, ne) for the BM-IRC subgroup and 8.5 months (5.7, 12.4) for the BM-INV subgroup (**Figure 3**)

Figure 3. PFS according to IRC in patients with baseline brain metastases



RET

- 1413P

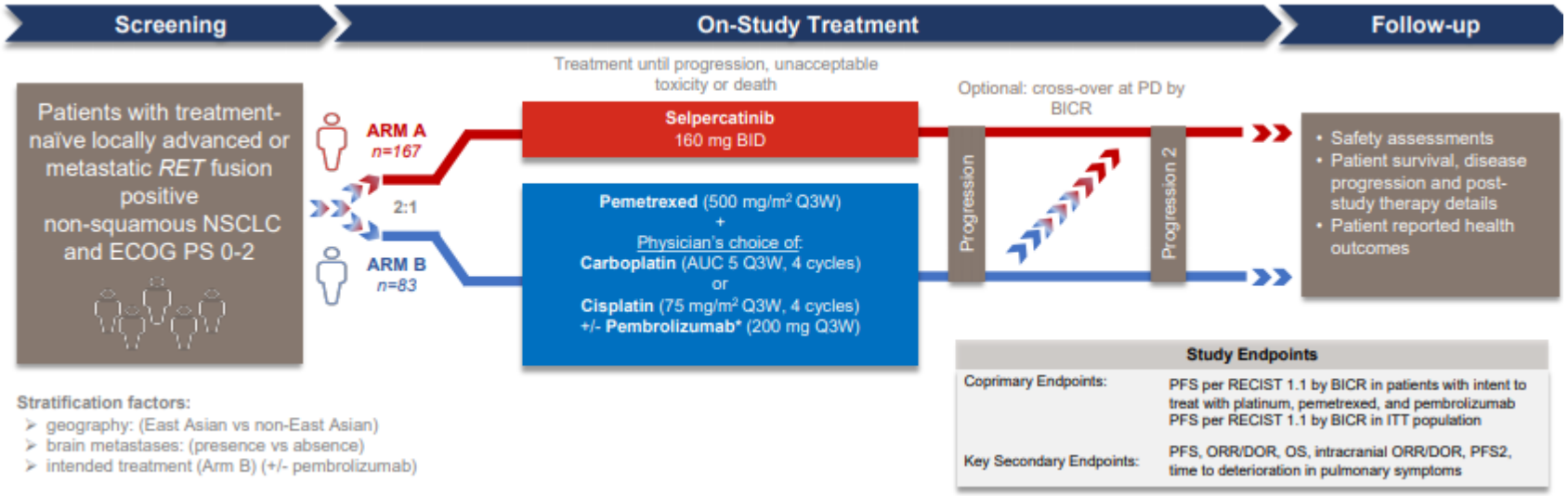
LIBRETTO-431: Selpercatinib in Treatment (Tx)-Naïve Patients with *RET* Fusion-Positive (*RET*+) Non-Small Cell Lung Cancer (NSCLC)

Ph I

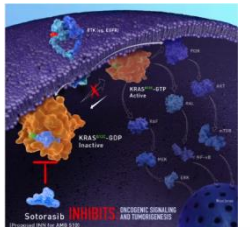
- Platinum chemotherapy pretreated *RET*-fusion positive NSCLC (n=105) ORR 64% (95% CI: 54-73)
- Platinum chemotherapy naïve *RET*-fusion positive NSCLC (n=39): ORR 85% (95% CI: 70-94)
- Intracranial CNS (n=10/11): ORR 91% (95% CI: 59-100)

Hypersensitivity Reactions to Selpercatinib Following Chemoimmunotherapy

- 1291P



KRAS



VIRTUAL 2020 ESMO congress

The NEW ENGLAND JOURNAL of MEDICINE

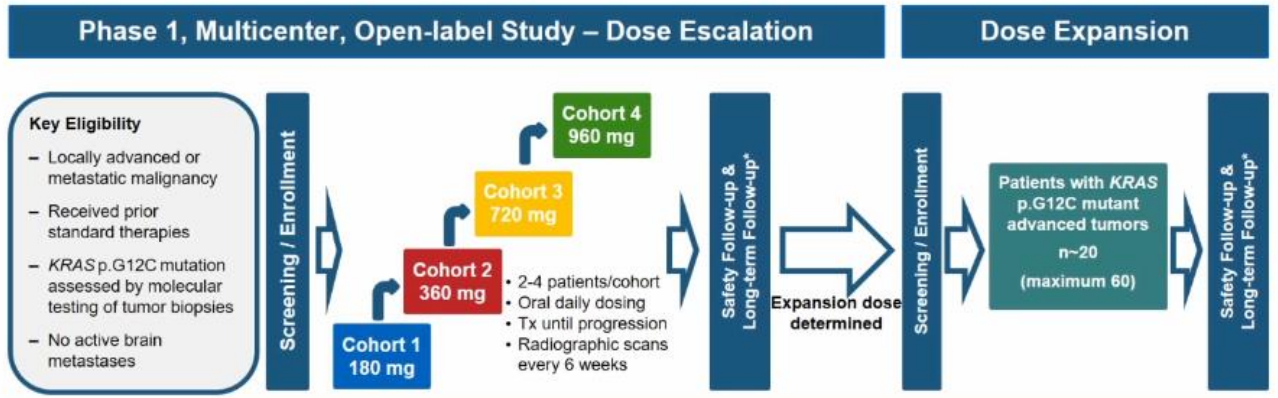
Durability of clinical benefit and biomarkers in patients with advanced non-small cell lung cancer (NSCLC) treated with AMG 510 (sotorasib): CodeBreaK 100

David S. Hong†, Yung-Jue Bang, Fabrice Barlesi, Gregory A. Durm, Gerald S. Falchook, Ramaswamy Govindan, Grace K. Dy, Keunchil Park, John H. Strickler, Timothy F. Burns, June Kim, Agnes Ang, J. Russell Lipford, Gataree Ngarmchamnanrith, Abraham Anderson, Bob T. Li

†Deputy Chair of the Department of Investigational Cancer Therapeutics, Phase I Clinical Trials Program, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

VIRTUAL 2020 ESMO congress

Phase 1 study design (CodeBreaK100: NCT03600883)



Primary endpoint: safety
Secondary endpoints include: PK, ORR, DOR, DCR, PFS, duration of SD

Median prior systemic anticancer therapy for metastatic disease – n (range)	2 (0–10)	3 (0–10)
Prior systemic anticancer therapy – n (%)		
0	2 (5.9)	2 (3.4)
1	12 (35.3)	13 (22.0)
2	8 (23.5)	14 (23.7)
3	6 (17.7)	11 (18.6)
≥ 4	6 (17.7)	19 (32.2)
Brain metastasis	12 (35.3)	18 (30.5)

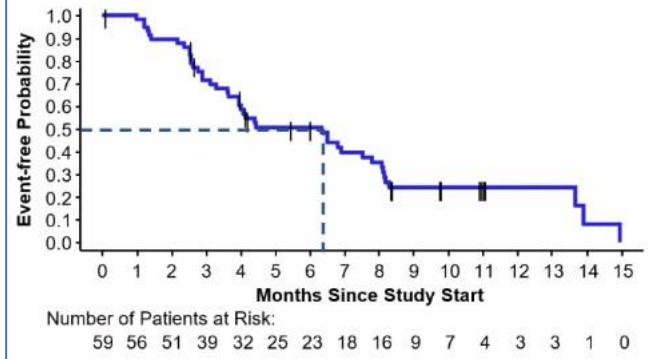
KRAS

Treatment-related Adverse Events	All Patients (N = 59) n (%)		
	Any Grade	Grade ≥3	Grade ≥4
Any	39 (66.1)	11 (18.6)	1 (1.7)
Diarrhea	15 (25.4)	3 (5.1)	0 (0.0)
ALT increased			
AST increased			
Fatigue			
Nausea	6 (10.2)	0 (0.0)	0 (0.0)
Alkaline phosph increased			
Decreased appetite	4 (6.8)	0 (0.0)	0 (0.0)

Sotorasib demonstrates clinical activity across a range of *KRAS* p.G12C MAFs, PD-L1 tissue expression levels, and plasma TMB levels

Sotorasib demonstrates clinical activity across a range of tissue co-mutational profiles. No clear tissue co-mutational profile correlates with response to sotorasib.

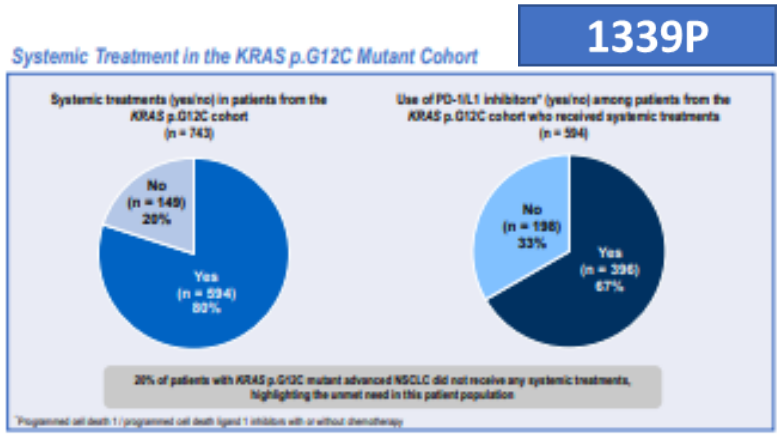
	960 mg (n = 34)	All patients (N = 59)
Best Overall Response per Investigators' Assessment, n (%)		
Confirmed Partial Response	12 (35.3)	19 (32.2)
Stable Disease	19 (55.9)	33 (55.9)
	9)	5 (8.5)
	9)	1 (1.7)
	0)	1 (1.7)
Confirmed Objective Response	35.3	32.2
Disease Control Rate‡, % (95% CI)	(76.3, 98.1)	(77.1, 95.1)



Median PFS: 6.3 (range 0.0+ to 14.9) months

KRAS

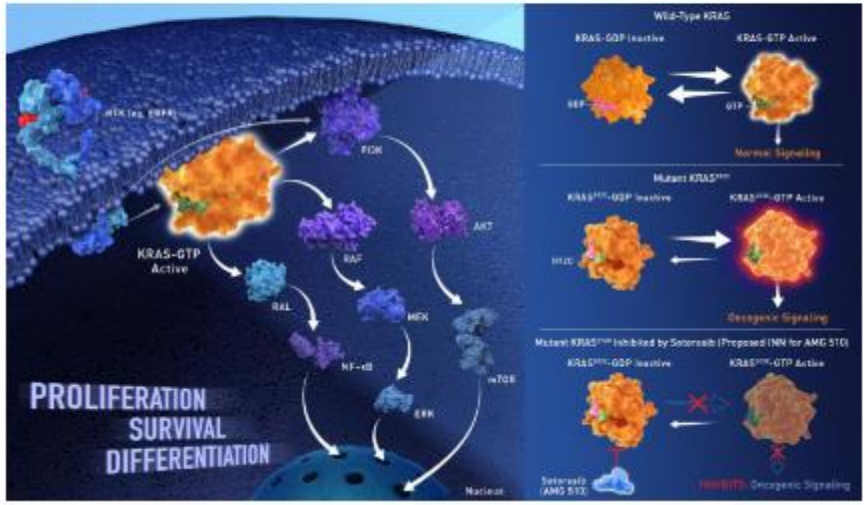
1339P



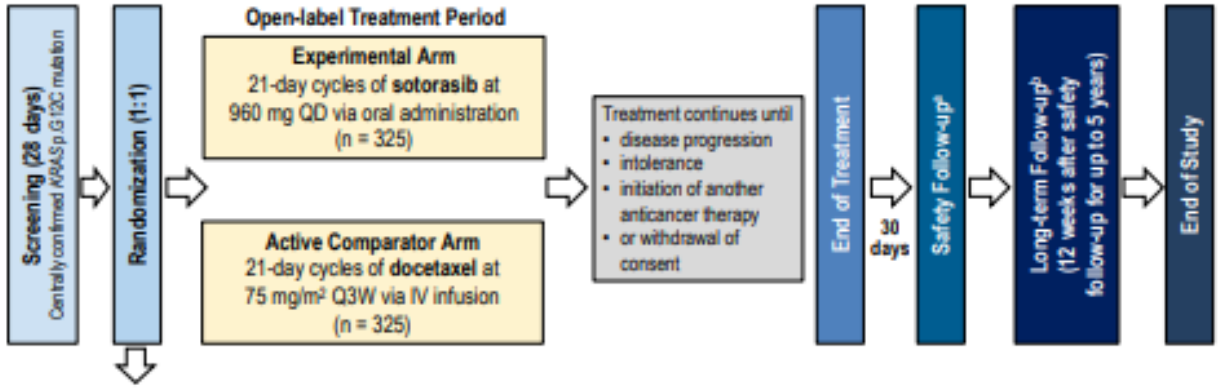
CodeBreaK 200: A Phase 3, Multicenter Study of Sotorasib, a KRAS^{G12C} Inhibitor, Versus Docetaxel in Patients With Previously Treated Advanced Non–Small-Cell Lung Cancer Harboring *KRAS* p.G12C Mutation

MECHANISM OF ACTION

Sotorasib Locks KRAS^{G12C} in the Inactive State, Inhibiting Oncogenic Signaling



STUDY DESIGN

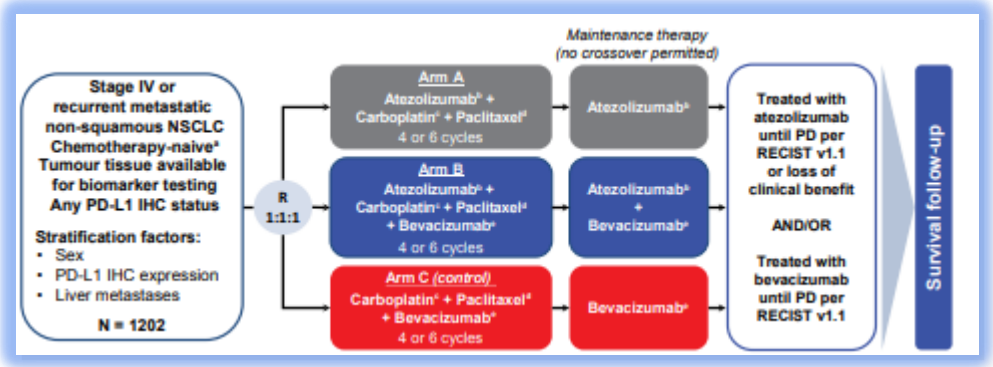


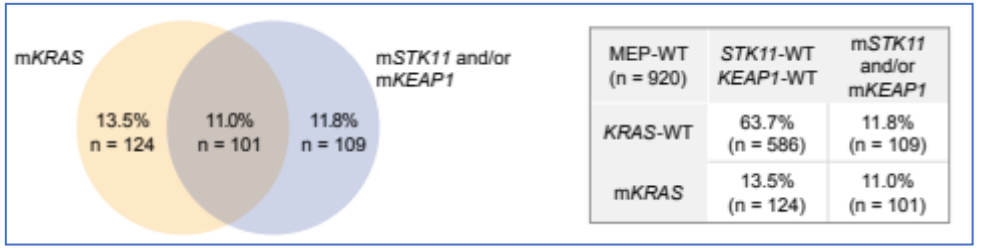
Patient Stratification
- Number of prior lines of therapy (1 vs 2 vs > 2)
- Race (Asian vs non-Asian)
- History of central nervous system involvement (present vs absent)

QD: once daily; Q3W: once every three weeks; IV: intravenous
†Upon permanent discontinuation from the study treatment for any reason, a safety follow-up visit will be conducted 30 days (± 7 days) after the end of last dosing of investigational treatments.
‡For patients who discontinued treatment without disease progression or start of subsequent anticancer therapy, tumor assessment will continue at the same frequency during long-term follow-up. Patients who had disease progression or start of subsequent anticancer therapy will be followed up via telephone or clinic visit every 12 weeks (± 4 weeks) for assessment of survival and documentation of anticancer therapy.

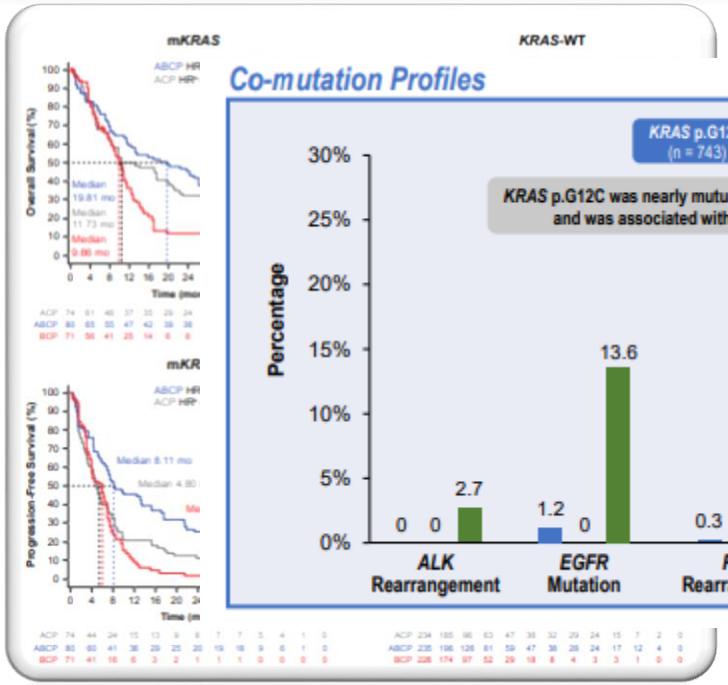
KRAS

IMpower150: A Post Hoc Analysis of Efficacy Outcomes in Patients With *KRAS*, *STK11* and *KEAP1* Mutations





MEP-WT (n = 920)	*STK11*-WT *KEAP1*-WT	m*STK11* and/or m*KEAP1*
KRAS-WT	63.7% (n = 586)	11.8% (n = 109)
m*KRAS*	13.5% (n = 124)	11.0% (n = 101)



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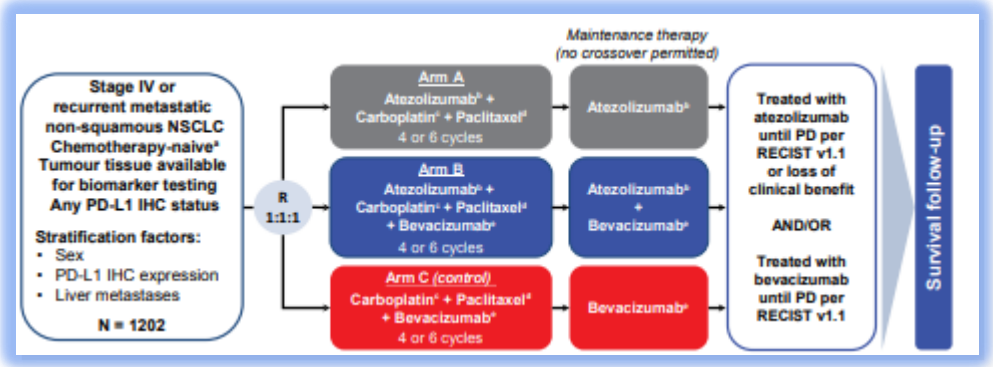

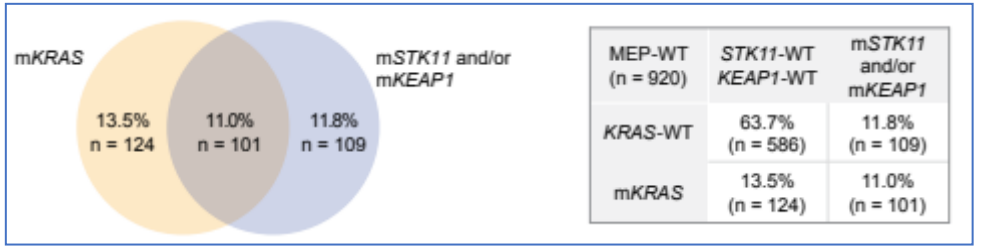

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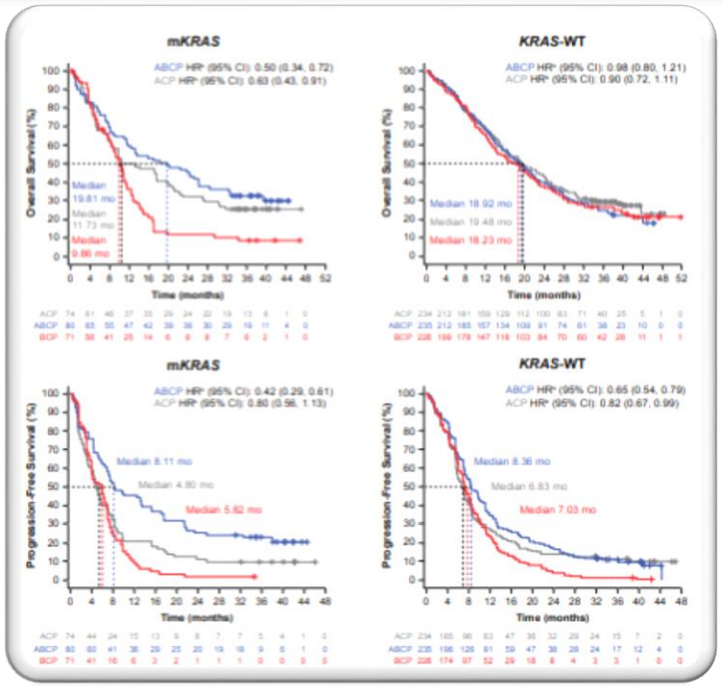
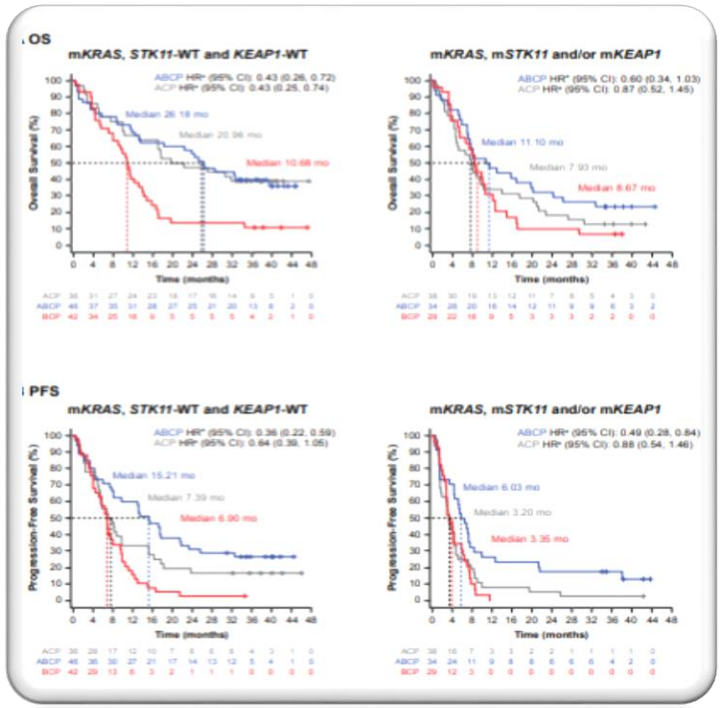




KRAS

Impact of *KRAS* Mutations and Subtypes on Efficacy of Immune-Checkpoint Inhibitors (ICI) in Non-Small Cell Lung Cancer (NSCLC).

N=913
(421 KRASm)

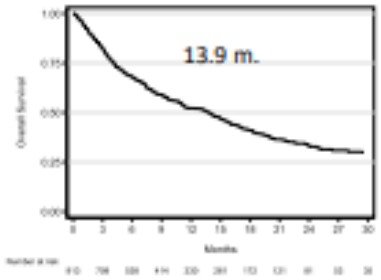
III. OUTCOMES according to KRAS

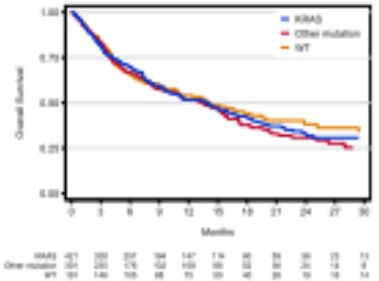
Whole population

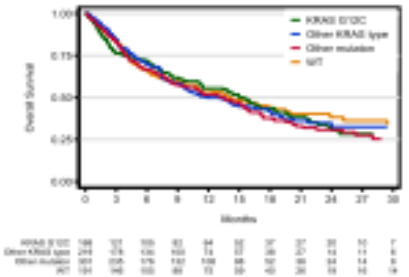
According to mutation group
(KRAS vs other mut vs WT)

According to mutation sub group
(G12C vs other KRAS mut vs other mut vs WT)

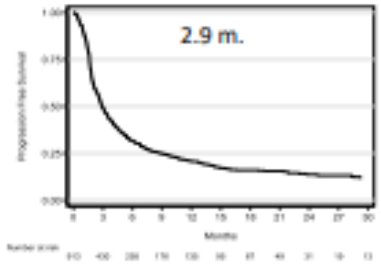
Overall Survival

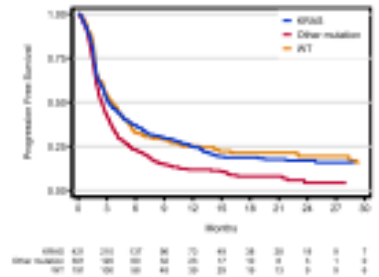


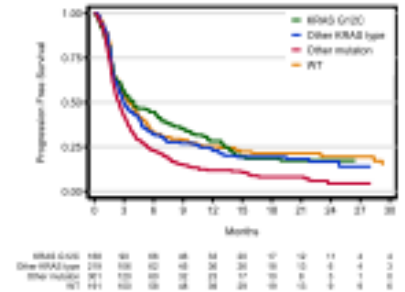




Progression free survival



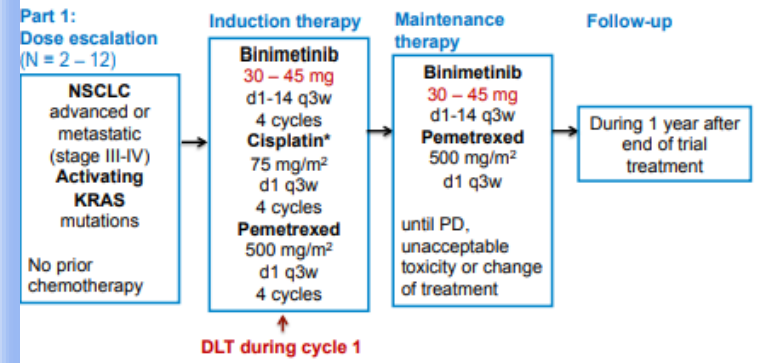




KRAS

Binimetinib, pemetrexed and cisplatin, followed by maintenance of binimetinib and pemetrexed in patients with advanced non-small cell lung cancer (NSCLC) and KRAS mutations. The phase 1B SAKK 19/16 trial.

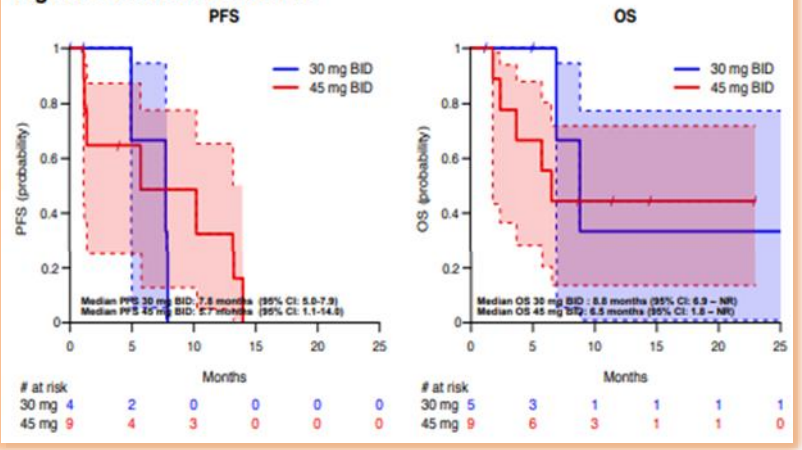
Figure 1 Phase IB Trial design



Part 2: Dose expansion (N = max. 6): Follow the same schedule and medications as in part 1 with the maximum tolerated dose of Binimetinib.

Adverse event	N= 16 (%)	Possible related*	Probable related*	Definite related*
Lung infection	4 (25%)	1	-	-
Anemia	3 (19%)	1	1	-
Fatigue	3 (19%)	-	3	-
Nausea	2 (12%)	-	-	2
Hypertension	2 (12%)	-	-	-
Hyponatremia	2 (12%)	1	1	-
Thromboembolic event	2 (12%)	2	-	-
General worsening of health status	2 (12%)	-	-	-

Figure 2 Survival outcomes



Response (N=14*)	No. of patients (%)	
	Cisplatin** 75mg/m², pemetrexed 500mg/m² with **Binimetinib 30 mg (N=5)**	Cisplatin**75mg/m², pemetrexed 500mg/m² with **Binimetinib 45 mg (N=9)**
Overall response rate	**20%**	**33%**
Complete response	0	0
Partial response	1 (20%)	3 (33%)
Stable disease	3 (60%)	2 (22%)
Progressive disease	0	3 (33%)
Not assessed	1 (20%)	1 (11%)

Lung Cancer UPDATES
ESMO HIGHLIGTHS
19-21 SEPTIEMBRE 2020

VIRTUAL

Iniciativa científica de: GECP lung cancer research

Cáncer de pulmón no microcítico avanzado con mutaciones infrecuentes.

María Guirado Risueño
HGU Elche