Lung Cancer UPDATES
ESMO HIGHLIGTHS
19-21 SEPTIEMBRE 2020

VIRTUAL

Iniciativa científica de: GECP lung cancer research

Cáncer de pulmón no microcítico avanzado: mutaciones frecuentes.

María Guirado Risueño
HGU Elche

EGFR

ACTIVE: Apatinib plus Gefitinib versus placebo plus Gefitinib as first-line treatment for advanced epidermal growth factor receptor-mutant (EGFRm) non-small-cell lung cancer (NSCLC) : a multicenter, randomized, double-blind, placebo-controlled phase III trial (CTONG1706)

Li Zhang[1], Hongyun Zhao[2], Zhonghan Zhang[1], Wenxiu Yao[3], Xuhong Min[4], Kangsheng Gu[5], Guohua Yu[6], Chao Cheng[7], Jiuwei Cui[8], Liyun Miao[9], Xia Song[10], Li Zhang[11], Xia Yuan[12], Yong Fang[13], Xiuhua Fu[14], Chengping Hu[15], Xiaoli Zhu[16], Yun Fan[17], Qitao Yu[18]

Fase I:
TR 83,3%
TCE 91,7%
SLP 19m

VIRTUAL 2020 ESMO congress

STUDY DESIGN

- Locally advanced, metastatic or recurrent non-squamous NSCLC
- Chemo-naive
- EGFR mutation positive (exon 19 deletion or exon 21 L858R)
- ECOG PS 0-1

R 1:1

AG group (N=157): Apatinib 500mg q.d. + Gefitinib 250mg q.d.

G group (N=156): Placebo q.d. + Gefitinib 250mg q.d.

N=313

Until PD, unacceptable toxicity, study ends or withdrawal of patient's consent, whichever occurs first

Survival follow-up

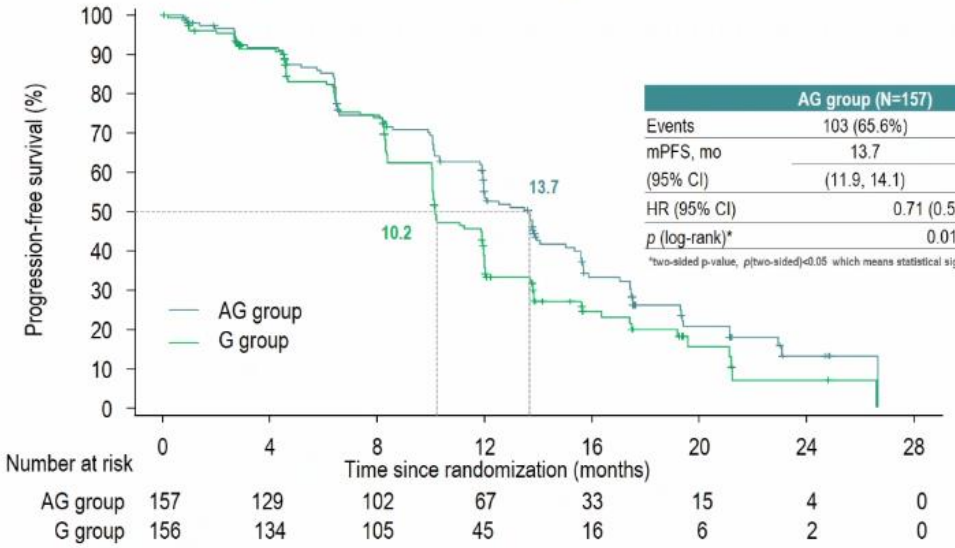
- Stratified by
  - ✓ EGFR gene mutation (exon 19 del vs. exon 21 L858R)
  - ✓ Gender (female vs. male)
  - ✓ ECOG PS (0 vs. 1)

- Primary endpoint: PFS (Independent Radiology Review Committee, IRRC)
- Secondary endpoints:
  - ✓ PFS (investigator, INV), OS, ORR, DCR, DOR, TTPD, QoL and safety
- Exploratory endpoints:
  - ✓ to analyze baseline and post-progression samples for exploring efficacy predictors and acquired resistance

EGFR

VIRTUAL 2020 ESMO congress

PRIMARY ENDPOINT: PFS BY IRRC (ITT POPULATION)



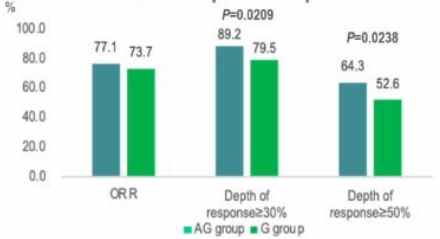
	AG group (N=157)	G group (N=156)
Events	103 (65.6%)	111 (71.2%)
mPFS, mo	13.7	10.2
(95% CI)	(11.9, 14.1)	(10.1, 11.9)
HR (95% CI)	0.71 (0.54, 0.95)	
p (log-rank)*	0.0189	

*two-sided p-value, *p*(two-sided)<0.05 which means statistical significance.

Confirmed best objective response

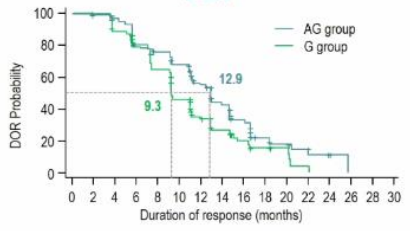
	AG group (N=157) n (%)	G group (N=156) n (%)	*p*
CR	1 (0.6)	0	
PR	120 (76.4)	115 (73.7)	
SD	12 (7.6)	22 (14.1)	
ORR	121 (77.1)	115 (73.7)	0.5572
DCR	133 (84.7)	137 (87.8)	0.3466

ORR and Depth of response



Depth of response: the best percentage change from baseline in sum of diameters of target lesions

DOR



	AG group (N=121)	G group (N=115)
Events	85 (70.2%)	83 (72.2%)
Median, mo	12.9	9.3
(95% CI)	(11.2, 14.7)	(9.2, 11.1)
HR (95% CI)	0.64 (0.47, 0.88)	
p (log-rank)	0.005	

VIRTUAL 2020 ESMO congress

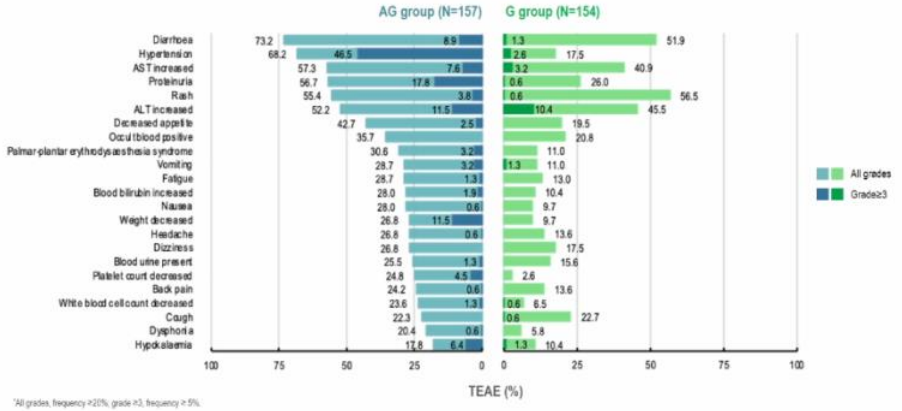
SAFETY OVERVIEW

Events	AG group (N=157) n (%)	G group (N=154) n (%)
Any TEAE	155 (98.7)	151 (98.1)
Grade ≥ 3 TEAEs	132 (84.1)	58 (37.7)
Serious TEAEs	60 (38.2)	35 (22.7)
TEAEs leading to dose interruption, any drug	94 (59.9)	35 (22.7)
TEAEs leading to dose reduction, any drug	76 (48.4)	7 (4.5)
Discontinued treatment due to TEAEs	8 (5.1)	5 (3.2)
TEAEs leading to death*	12 (7.6)	5 (3.2)

*1 death (cerebral haemorrhage) in the AG group was considered related to both Apatinib and Gefitinib.

VIRTUAL 2020 ESMO congress

MOST COMMON TEAES*

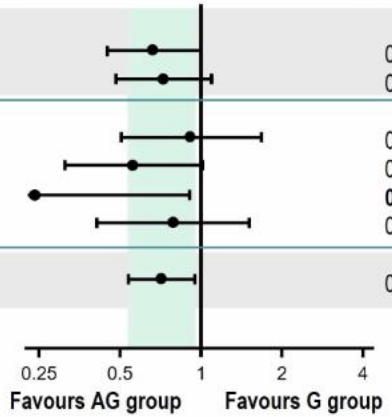


*All grades, frequency ≥20%; grade ≥3, frequency ≥ 5%.

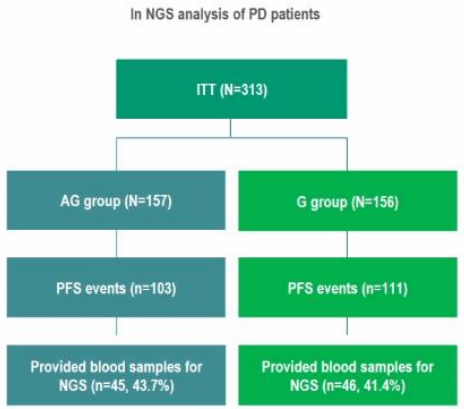
EGFR

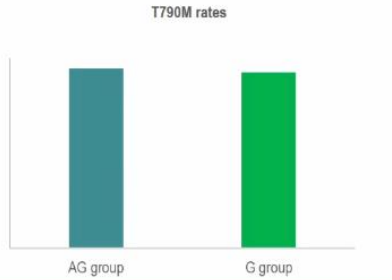
Subgroup analysis by baseline mutation status

	AG group Events/patients	G group Events/patients	Hazard ratio (95%CI)
EGFR mutation type			
Exon 19 deletion	52/81	57/83	0.67 (0.45, 0.99)
Exon 21 L858R	49/74	54/73	0.72 (0.48, 1.09)
TP53 mutation			
No	25/43	20/32	0.92 (0.50, 1.67)
Yes	23/30	31/40	0.56 (0.31, 1.01)
Exon 8	5/7	9/11	**0.24 (0.06, 0.91)**
Non-exon 8	18/23	22/29	0.79 (0.41, 1.52)
Overall	103/157	111/156	0.71 (0.54, 0.95)



RESISTANCE BIOMARKER ANALYSIS



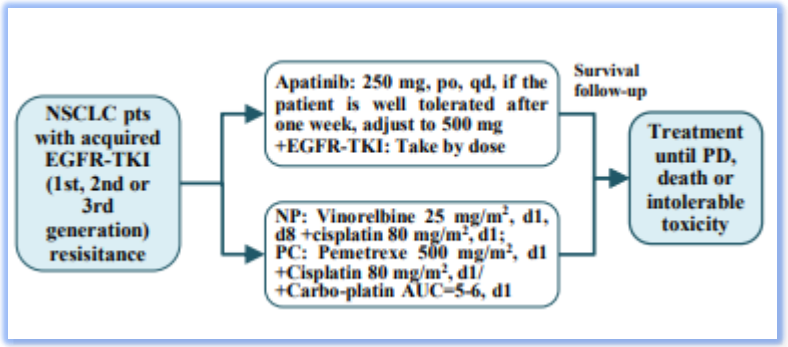


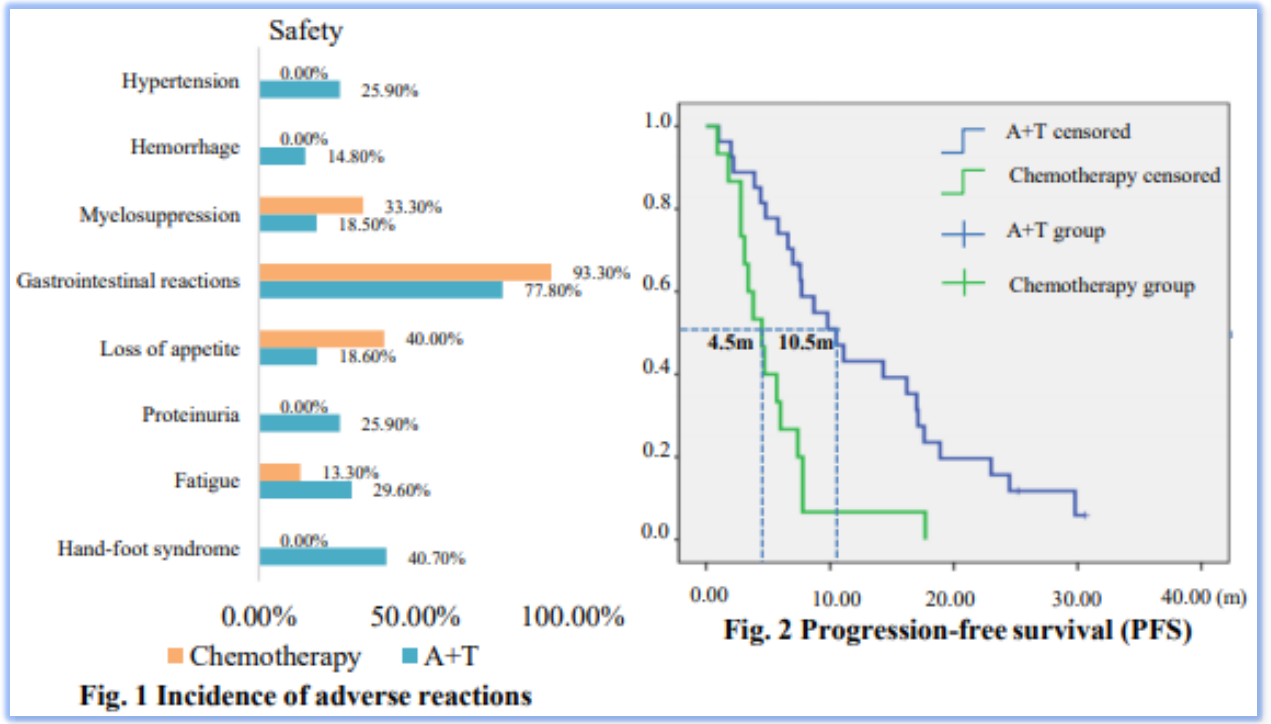
	AG group (N=45) n (%)	G group (N=46) n (%)
T790M-positive	17 (37.8)	17(37.0)
T790M-negative	28 (62.2)	29 (63.0)

EGFR

- 1366P

Efficacy and safety of apatinib plus EGFR-TKI in advanced non-small cell lung cancer with EGFR-TKI resistance (Data Updated)





EGFR

A randomized phase II study of Osimertinib with or without Bevacizumab in advanced lung adenocarcinoma patients with EGFR T790M mutation

West Japan Oncology Group 8715L

Yukihiro Toi[1], Hiroaki Akamatsu[2], Hidetoshi Hayashi[3], Daichi Fujimoto[4], Motoko Tachihara[5], Naoki Furuya[6], Sakiko Otani[7], Junichi Shimizu[8], Nobuyuki Katakami[9], Koichi Azuma[10], Naoko Miura[11], Kazumi Nishino[12], Satoshi Hara[13], Shunsuke Teraoka[2], Satoshi Morita[9], Kazuhiko Nakagawa[1], Nobuyuki Yamamoto[2]

VIRTUAL 2020 ESMO congress

WJOG8715L Study Design

Key Inclusion Criteria
- Advanced lung adeno carcinoma
- EGFR-TKI resistant
- Acquired EGFR T790M
- ECOG PS 0-1

Stratification factors
- Sex
- No. of prior chemotherapy
- Institution

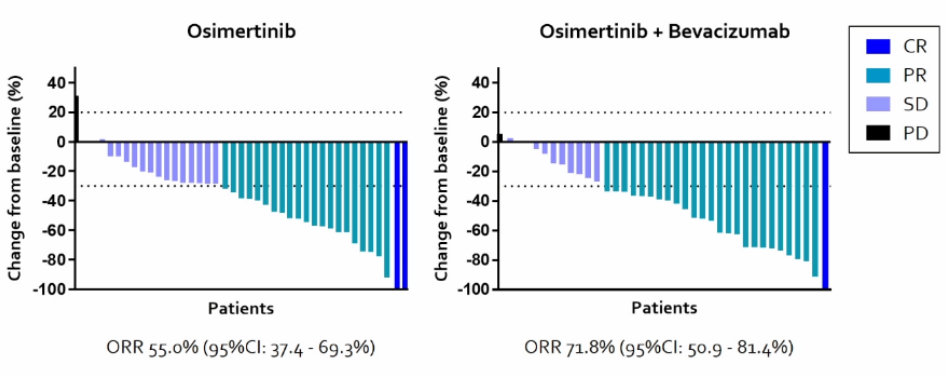
Lead-in part (N = 6) → Osi 80 mg/day + Bv 15 mg/kg, q3w until PD

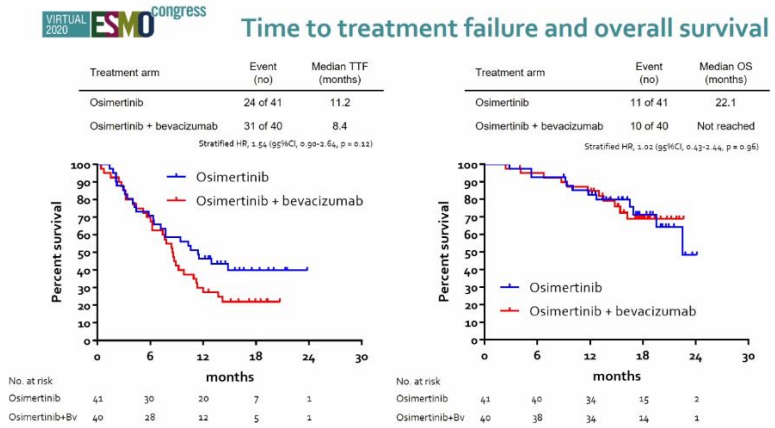
Phase II part (N = 81) → R 1:1
- Osi 80 mg/day + Bv 15 mg/kg, q3w until PD
- Osi 80 mg/day alone until PD

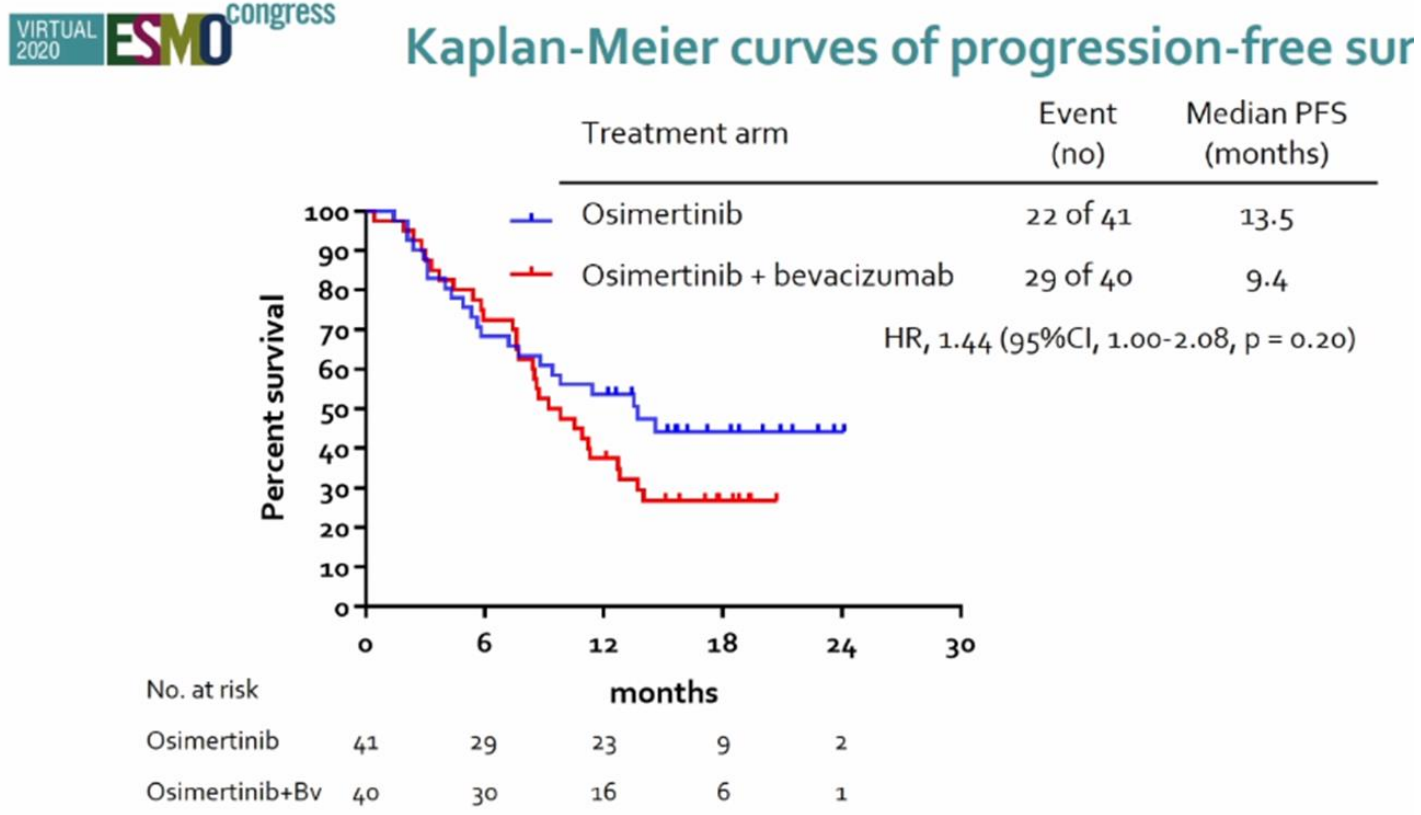
- Primary endpoint: PFS by investigator
- Secondary endpoints: overall response rate (ORR), time to treatment failure (TTF), overall survival (OS) and adverse events (Aes)

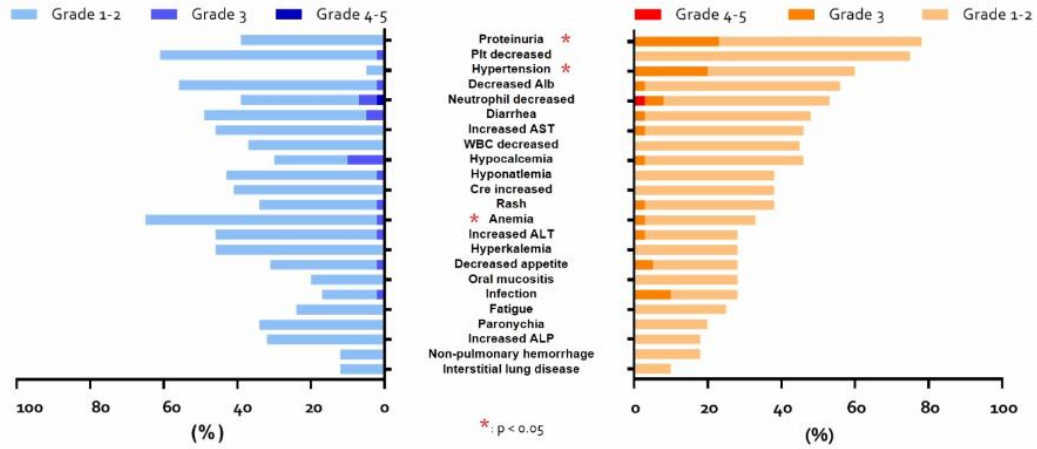
EGFR

M1 SNC	**25%**
TTO PREVIO CON ANTIANGIOGÉNICOS	10%









EGFR

- 1358P

Efficacy and toxicity of combined inhibition of EGFR and VEGFR in advanced non-small-cell lung cancer patients harboring activating EGFR mutations: A systematic review and meta-analysis

Progression Free Survival (PFS) Forest Plot

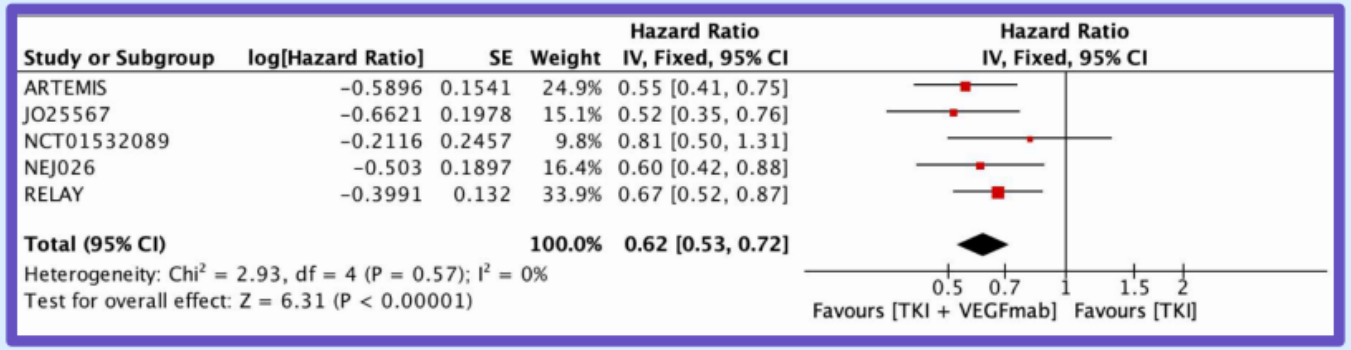


Figure 3 – Progression Free Survival (PFS) Forest Plot

Overall Survival (OS) Forest Plot

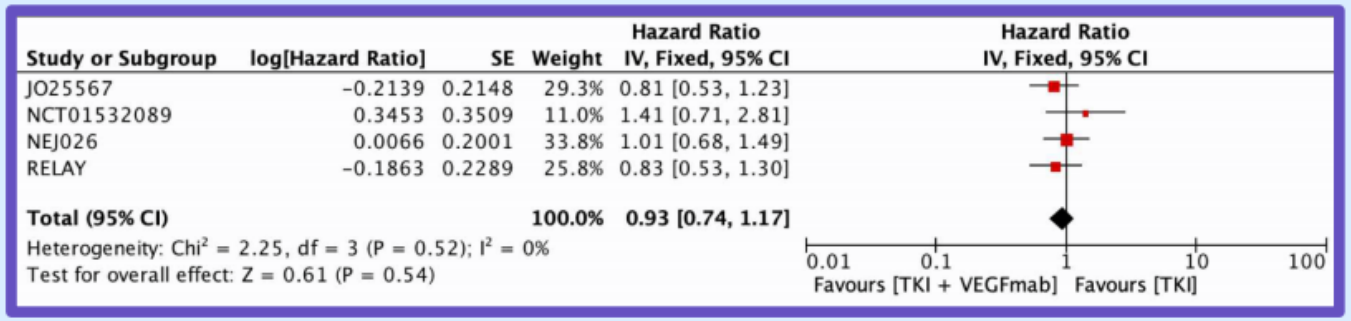


Figure 4 – 1 year Overall Survival (OS) Forest Plot

Outcome	OR/HR (95% CI)
ORR	OR= 0.86 (0.65-1.12)
DCR	OR = 0.75 (0.41-1.39)
Gr 3-4 AE (any)	OR = 3.55 (2.74-4.59)
Proteinuria	OR = 14.55 (4.47-47.4)
Hypertension	OR = 7.02 (4.73-10.43)
Diarrhea	OR = 2.70 (1.38-5.30)
Elevated ALT	OR = 0.86 (0.55-1.35)
Dermatitis	OR = 1.40 (1.00-1.95)
Stomatitis	OR = 1.02 (0.33-3.19)
Bleeding	OR = 1.40 (0.46-4.23)

NO INCLUÍDOS ESTUDIOS CON OSIMERTINIB

EGFR

CHRYSALIS Phase 1 Study: Combination Cohort Design

Key Objectives

- Establish RP2CD
- Safety and efficacy at RP2CD

Key Eligibility Criteria

- Metastatic/unresectable NSCLC
- Measurable disease (expansion cohort)
- EGFR Exon19del or L858R mutation

Dose Escalation (n=26)

- 1050/1400 mg amivantamab + 240 mg lazertinib
- 700/1050 mg amivantamab + 240 mg lazertinib

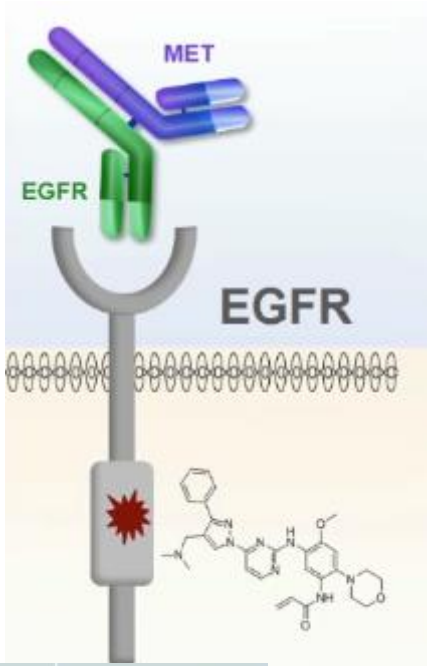
RP2CD

Amivantamab
1050 mg (<80 kg)
1400 mg (≥80 kg)
Intravenous dosing
C1 QW, C2+ Q2W
+
240 mg lazertinib
Oral daily dosing

Expansion Cohorts

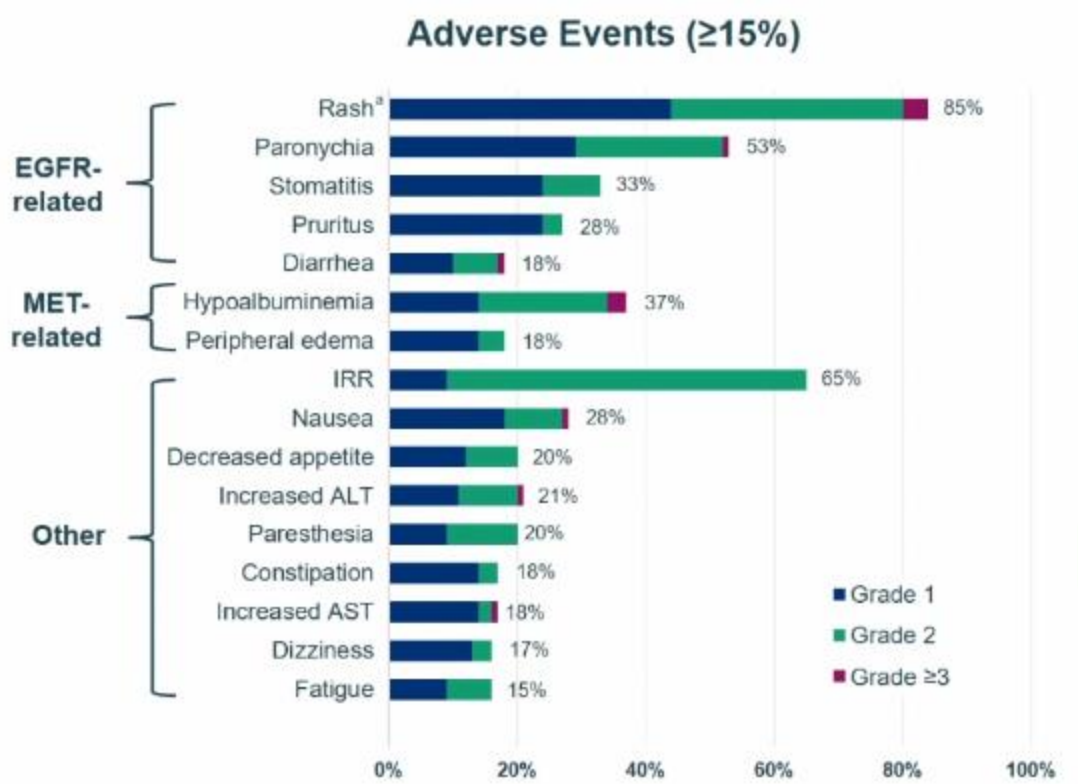
- Osimertinib-resistant, Chemo-naïve; EGFR Exon19del or L858R (n=45)
- Treatment-naïve[a]; EGFR Exon19del or L858R (n=20)

- Combination dose is at the recommended monotherapy doses of each molecule
- Proactive rash management included topical antibiotics to sun-exposed skin



Median prior lines, n (range)	2 (0–9)
No prior lines, n (%)[a]	23 (25)
Prior 1st or 2nd-gen TKI, n (%)	54 (59)
Prior 3rd-gen TKI, n (%)	53 (58)

EGFR



1ªL

- **ORR: 36% (95% CI, 22 – 51)**
  - 1 CR
  - 15 PR (1 pending confirmation)
- **CBR: 60% (95% CI, 44 – 74)**

Median follow-up: 4 mo (1 – 7)

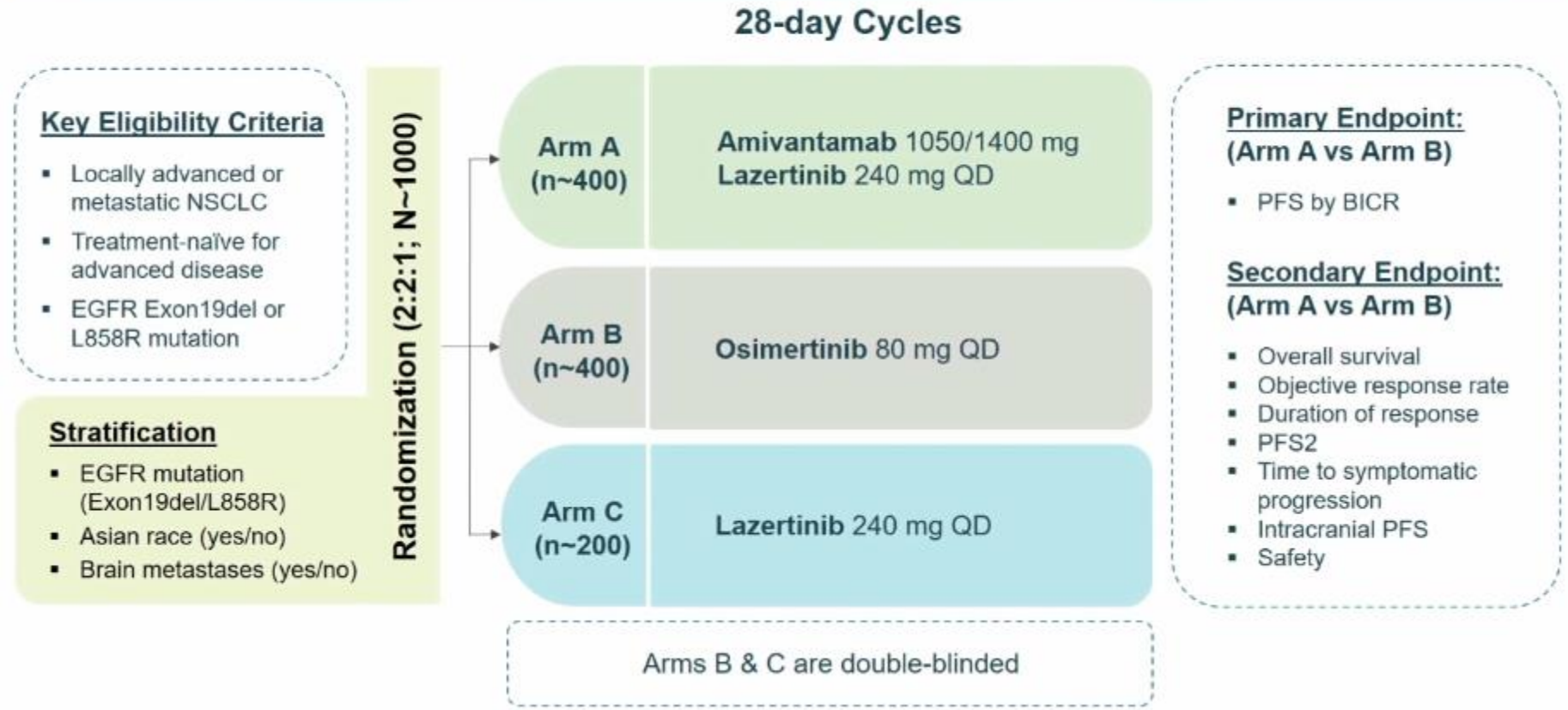
- **ORR: 100% (95% CI, 83 – 100)**
  - 20 PR
- **CBR: 100% (95% CI, 83 – 100)**
- **mDOR: not estimable**

- **Median follow-up**: 7 mo (4 – 10)
- **Median treatment duration**: 7 mo (3 – 10)

Rapid time to first response: Median 1.5 months (1.2 – 2.6)

EGFR

Phase 3 MARIPOSA Study (NCT04487080)



EGFR

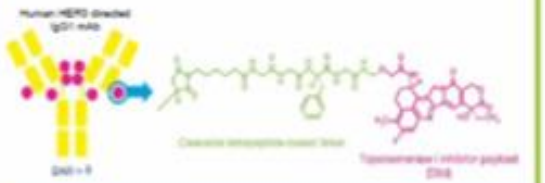
Presentation ID LBA62

Efficacy and Safety of Patritumab Deruxtecan (U3-1402), a Novel HER3 Directed Antibody Drug Conjugate, in Patients (Pts) with EGFR-mutated (EGFRm) NSCLC

Helena Yu, New York, United States

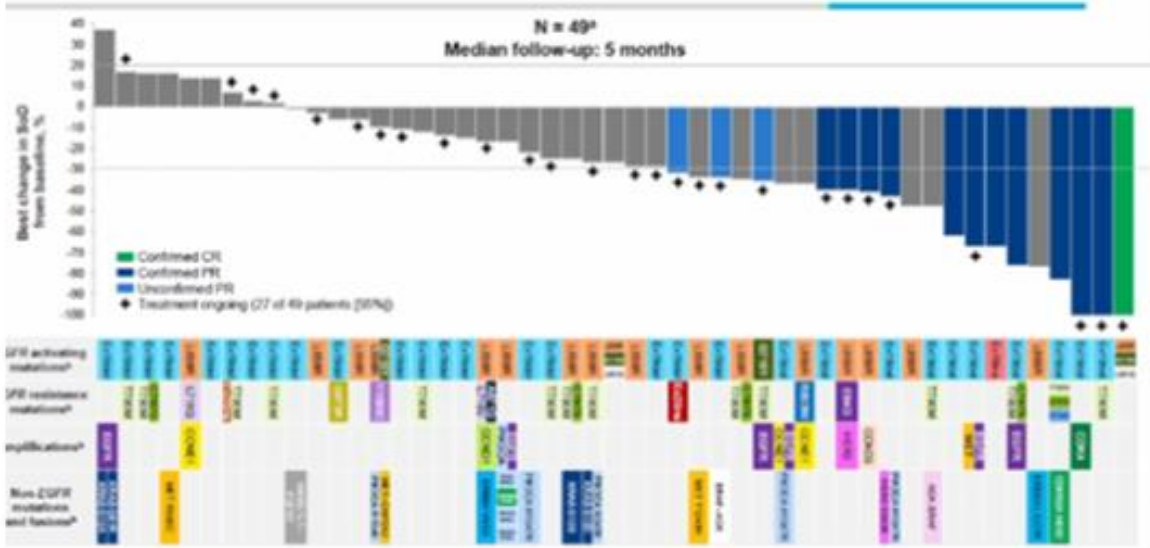
Patritumab Deruxtecan (U3-1402)

A novel HER3 directed antibody drug conjugate composed of the monoclonal antibody patritumab, a tetrapeptide-based linker, and a topoisomerase I inhibitor payload



Median number of therapies for advanced/metastatic disease (range)	4 (1-9)
Prior therapy, n (%)	
EGFR TKI	57 (100)
Osimertinib	49 (86)
Other EGFR targeted therapy	3 (5)
Platinum-based chemotherapy	51 (90)
Anti-PD-1/PD-L1	23 (40)
History of CNS metastases	27 (47)

Efficacy



ORR	**25%**
mDOR	**6.9mo**

Tox	Any Grade	G 3-4
PLT	53%	28%
ANC	33%	19%
Fatigue	58%	9%
Nausea	54%	4%

5% ILD

VIRTUAL 2020 ESMO congress

EGFR

- **1295P** **Osimertinib vs comparator EGFR-TKI as first-line treatment for EGFR mutated (EGFRm) advanced NSCLC: FLAURA China study overall survival (OS)**

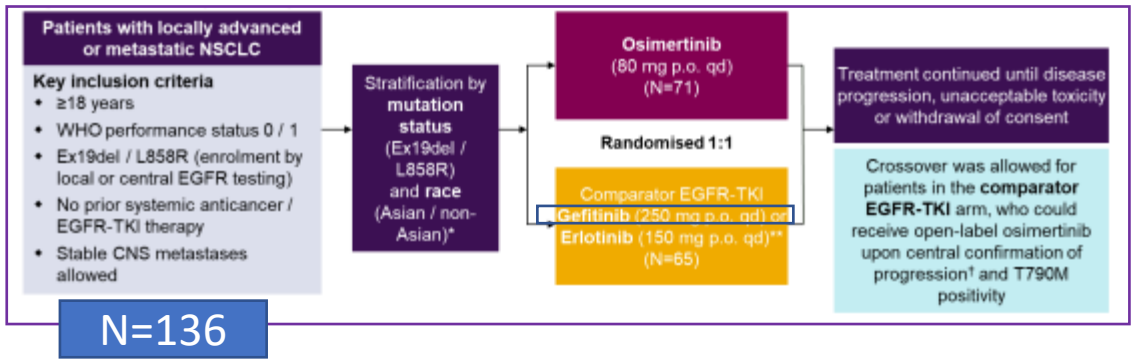
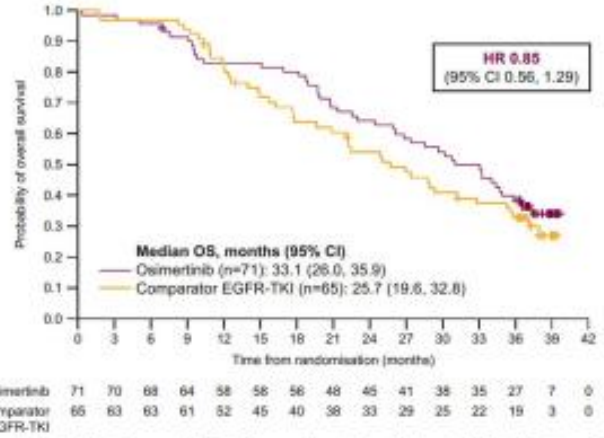
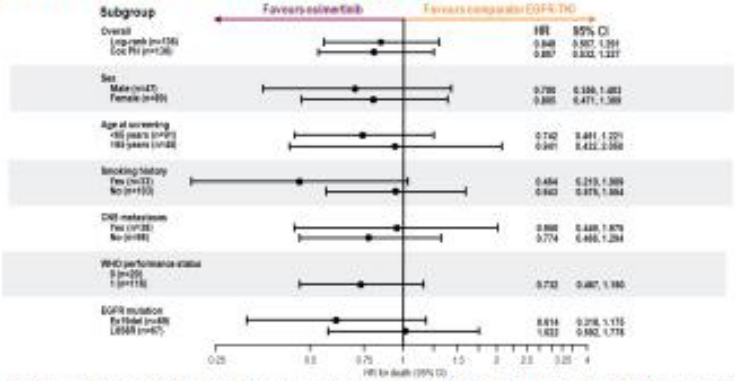


Figure 2. Kaplan-Meier plot of overall survival



Censored data are indicated by tick marks. Data from patients who had not died at the time of the analysis were censored on the basis of the last recorded date on which the patient was known to be alive.
CI, confidence interval; EGFR-TKI, epidermal growth factor receptor tyrosine kinase inhibitor; OS, overall survival.

Figure 3. Overall survival across subgroups



CI, confidence interval; CNS, central nervous system; Ex19Del, Exon 19 deletion; HR, hazard ratio; OS, overall survival; WHO, World Health Organization.

EGFR

- **1401P** **Osimertinib plus platinum-pemetrexed in newly-diagnosed EGFR mutation (EGFRm)-positive advanced NSCLC: safety run-in results from the FLAURA2 study**

Figure 1. FLAURA2 safety run-in study design

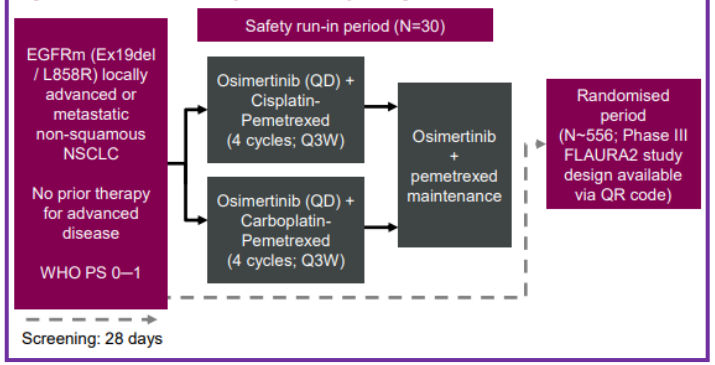
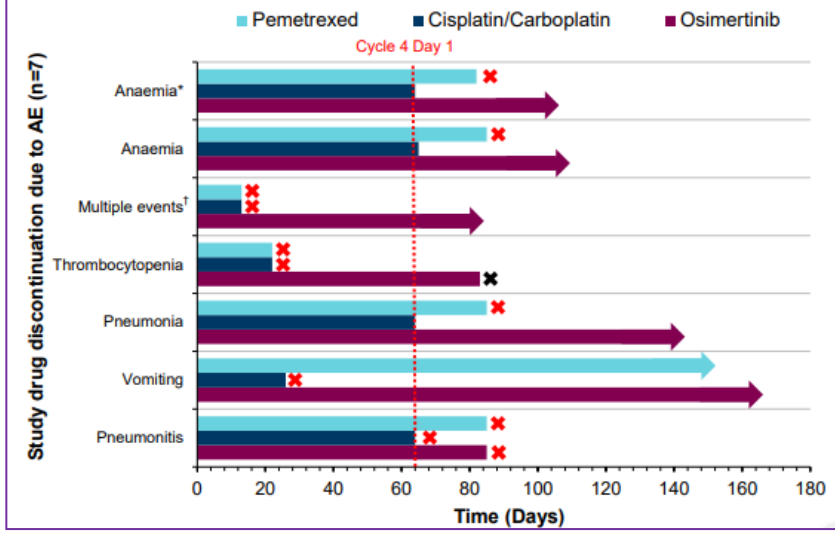


Table 2. Incidence of AEs

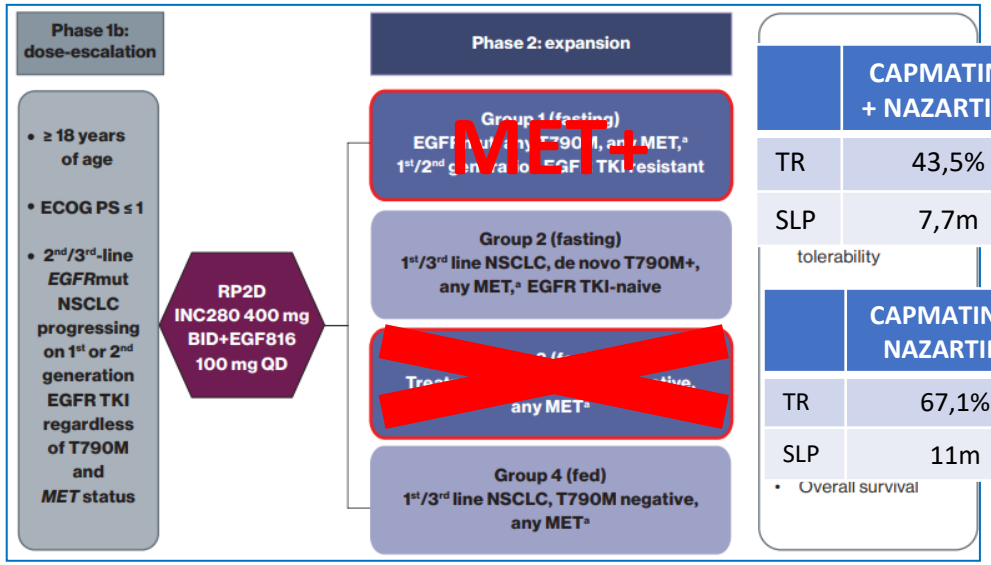
Incidence, n (%)	Osimertinib + carboplatin + pemetrexed (n=15)	Osimertinib + cisplatin + pemetrexed (n=15)	Total (N=30)
Any AE	15 (100)	12 (80)	27 (90)
Treatment-related AE	15 (100)	12 (80)	27 (90)
CTCAE grade ≥3	3 (20)	8 (53)	11 (37)
Serious AE	3 (20)	3 (20)	6 (20)
Death	1 (7)	0	1 (3)
Discontinuation of any study drug	4 (27)	3 (20)	7 (23)
Osimertinib	1* (7)	0	1 (3)
Carboplatin/cisplatin	2 (13)	2† (13)	4 (13)
Pemetrexed	3 (20)	3 (20)	6 (20)
Most common AEs (any grade)			
Constipation	9 (60)	4 (27)	13 (43)
Nausea	3 (20)	9 (60)	12 (40)
Diarrhoea	7 (47)	4 (27)	11 (37)
Rash	5 (33)	5 (33)	10 (33)
Stomatitis	6 (40)	3 (20)	9 (30)
Most common AEs (grade ≥3)			
Anaemia	1 (7)	4 (27)	5 (17)
Neutropenia	1 (7)	2 (13)	3 (10)
Thrombocytopenia	2 (13)	0	2 (7)
Nausea	0	1 (7)	1 (3)
Diarrhoea	0	1 (7)	1 (3)
Rash	0	1 (7)	1 (3)

Figure 2. Study drug discontinuations due to AEs



EGFR

- 1284P **MET Inhibitor Capmatinib Plus EGFR Tyrosine Kinase Inhibitor Nazartinib for EGFR-Mutant Non-Small Cell Lung Cancer**



	CAPMATINIB + NAZARTINIB	OSIMERTINIB + SAVOLITINIB
TR	43,5%	30-67%
SLP	7,7m	5,4-11m

	CAPMATINIB + NAZARTINIB	FLAURA
TR	67,1%	80%
SLP	11m	18,9m

Figure 3. Progression-free survival in pre-treated patients (Group 1)

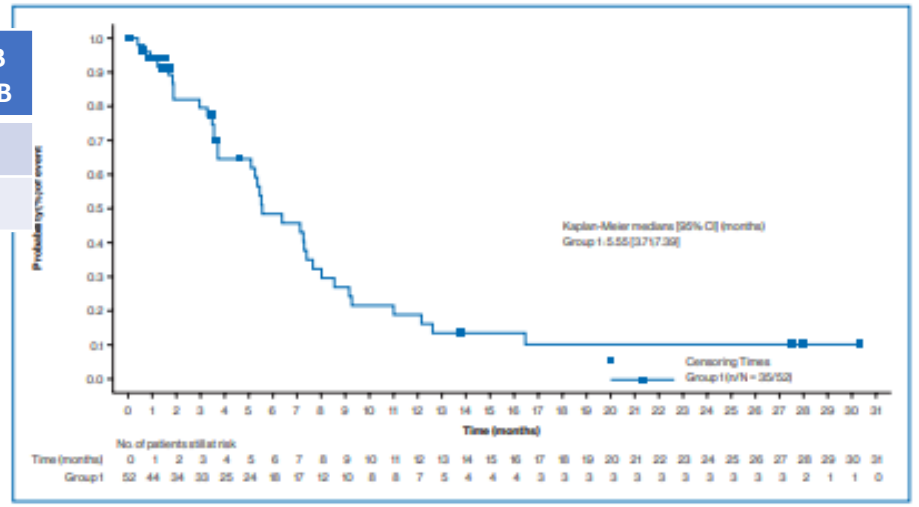


Figure 4. Progression-free survival in treatment-naive patients (Group 3)

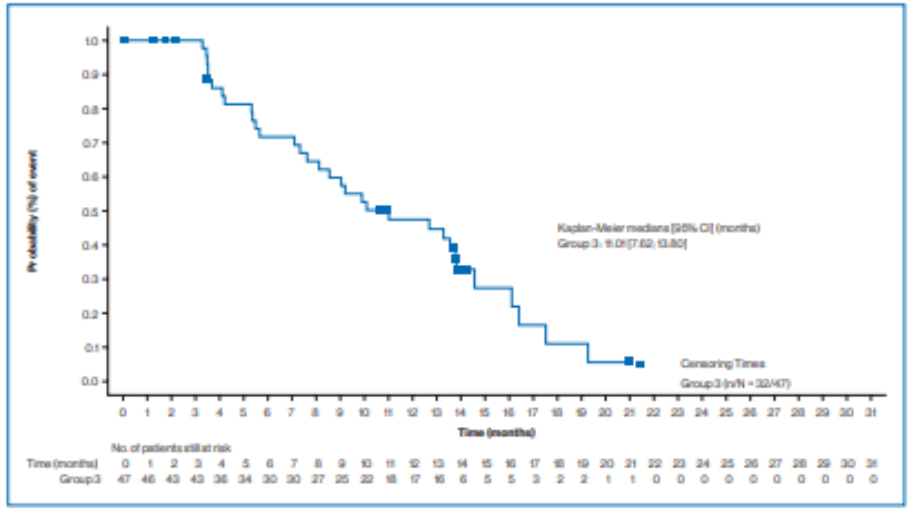


Table 6. Adverse Events Suspected to be Study Drug-Related (Any Grade Occurring in ≥20% Patients)

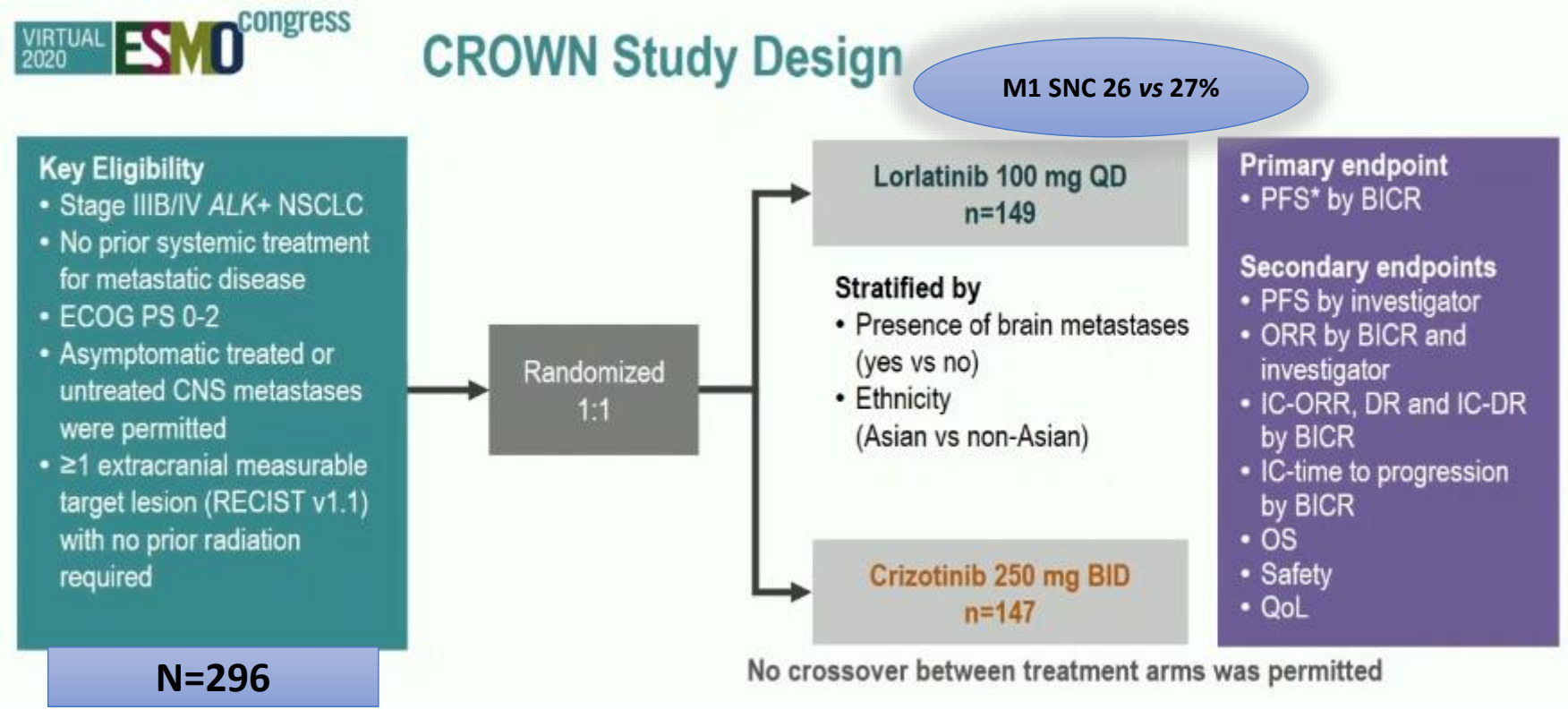
	Group 1 (Pre-treated) N = 52		Group 3 (Treatment-naive) N=47	
	All Grades n (%)	Grade 3/4 n (%)	All Grades n (%)	Grade 3/4 n (%)
Number of patients with at least one	(94.2)	30 (57.7)	46 (97.9)	27 (57.4)
Peripheral edema	(50.0)		27 (57.4)	
Nausea	(42.3)	4 (7.7)*	23 (48.9)	2 (4.3)*
Diarrhea	12 (23.1)	1 (1.9)*	22 (46.8)	0
Rash maculo-popular	12 (23.1)	8 (15.4)*	14 (29.8)	2 (4.3)*
ALT increase	7 (13.5)	3 (5.8)*	12 (25.5)	7 (14.9)
Vomiting	13 (25.0)	2 (3.8)*	11 (23.4)	1 (2.1)*
AST increased	4 (7.7)	0	11 (23.4)	5 (10.6)*
Fatigue	14 (26.9)	2 (3.8)*	6 (12.8)	0
Lipase increased	11 (21.2)	6 (11.5)	7 (14.9)	3 (6.4)*
Asthenia	5 (9.6)	1 (1.9)*	10 (21.3)	1 (2.1)*

*No grade 4 events seen
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase

ALK

Lorlatinib vs Crizotinib in the First-line Treatment of Patients with Advanced *ALK*-Positive Non-Small Cell Lung Cancer: Results of the Phase 3 CROWN Study

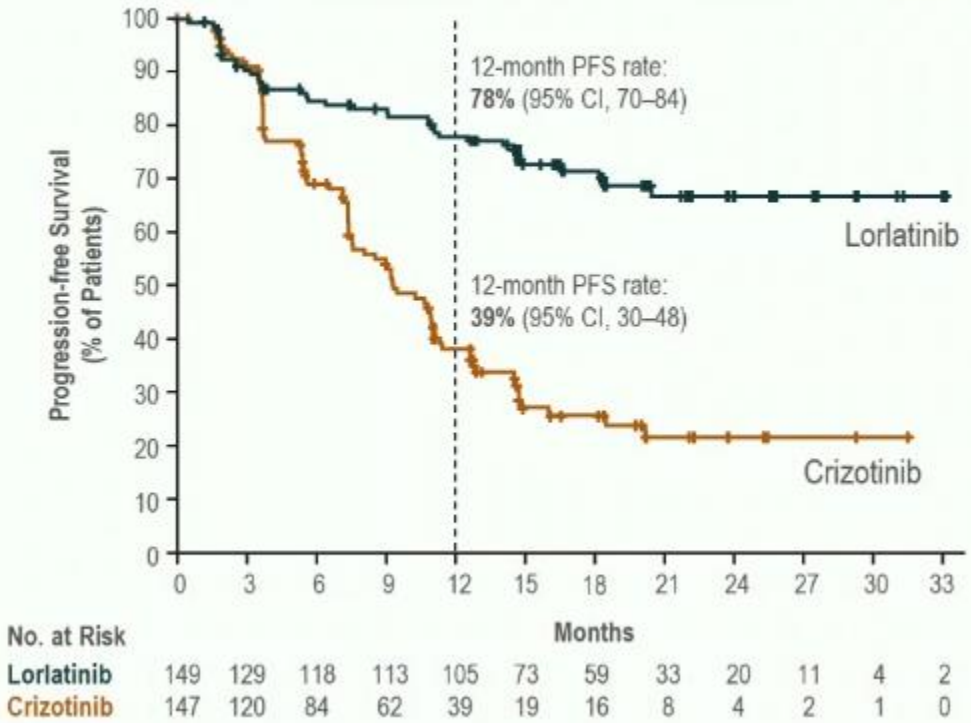
Solomon B,[1] Bauer T,[2] de Marinis F,[3] Felip E,[4] Goto Y,[5] Liu G,[6] Mazieres J,[7] Kim D-W,[8] Mok T,[9] Polli A,[10] Thurm H,[11] Calella AM,[10] Peltz G,[12] Shaw A[13]



ALK

VIRTUAL 2020 ESMO congress

Primary Endpoint: PFS by BICR



	Lorlatinib (n=149)	Crizotinib (n=147)
Patients with event, n (%)	41 (28)	86 (59)
Median PFS, months (95% CI)	NE (NE–NE)	9.3 (7.6-11.1)
HR (95% CI) 1-sided P value*	0.28 (0.19-0.41) <0.001	

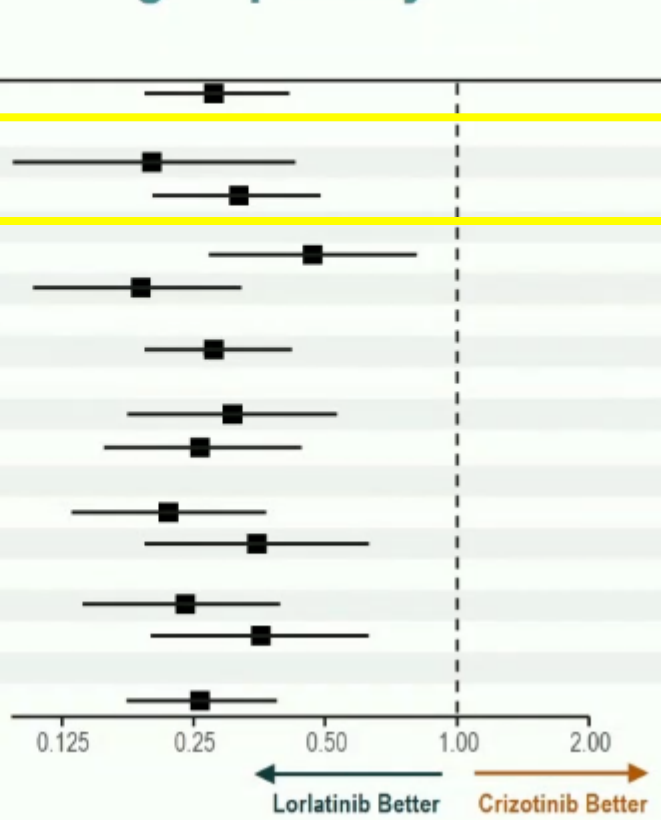
*By stratified log-rank test.

ALK

VIRTUAL 2020 ESMO congress

PFS by BICR Subgroup Analysis

Subgroup	Number of Patients (n) Lorlatinib	Crizotinib	HR (95% CI)
All patients	149	147	0.28 (0.19, 0.41)
Presence of Brain Metastases*			
Yes	38	40	0.20 (0.10, 0.43)
No	111	107	0.32 (0.20, 0.49)
Ethnic Origin			
Asian	66	65	0.47 (0.27, 0.82)
Non-Asian	83	82	0.19 (0.11, 0.32)
ECOG PS			
0/1	146	138	0.28 (0.19, 0.42)
Sex			
Male	65	56	0.31 (0.18, 0.54)
Female	84	91	0.26 (0.16, 0.44)
Age			
<65 years	90	103	0.22 (0.13, 0.37)
≥65 years	59	44	0.35 (0.20, 0.64)
Smoking Status			
Never	81	94	0.24 (0.14, 0.40)
Current/Former	68	52	0.36 (0.20, 0.63)
Histology			
Adenocarcinoma	140	140	0.26 (0.18, 0.39)



ALK

VIRTUAL ESMO 2020 congress

ORR by BICR

	Lorlatinib (n=149)	Crizotinib (n=147)
Responders, n (%)	113 (76)	85 (58)
(95% CI)	(68-83)	(49-66)
Odds ratio (95% CI)	2.25 (1.35-3.89)	
CR, n (%)	4 (3)	0 (0)
PR, n (%)	109 (73)	85 (58)
SD, n (%)	19 (13)	41 (28)
Non-CR/Non-PD, n (%)	3 (2)	3 (2)
PD, n (%)	10 (7)	7 (5)
NE, n (%)	4 (3)	11 (7)
Median DR, months (95% CI)	NE (NE-NE)	11.0 (9.0-12.9)
Median time to response, months (IQR)	1.8 (1.7-1.9)	1.8 (1.7-1.9)

- Similar response rates were obtained based on investigator assessment

ALK

VIRTUAL 2020 ESMO congress

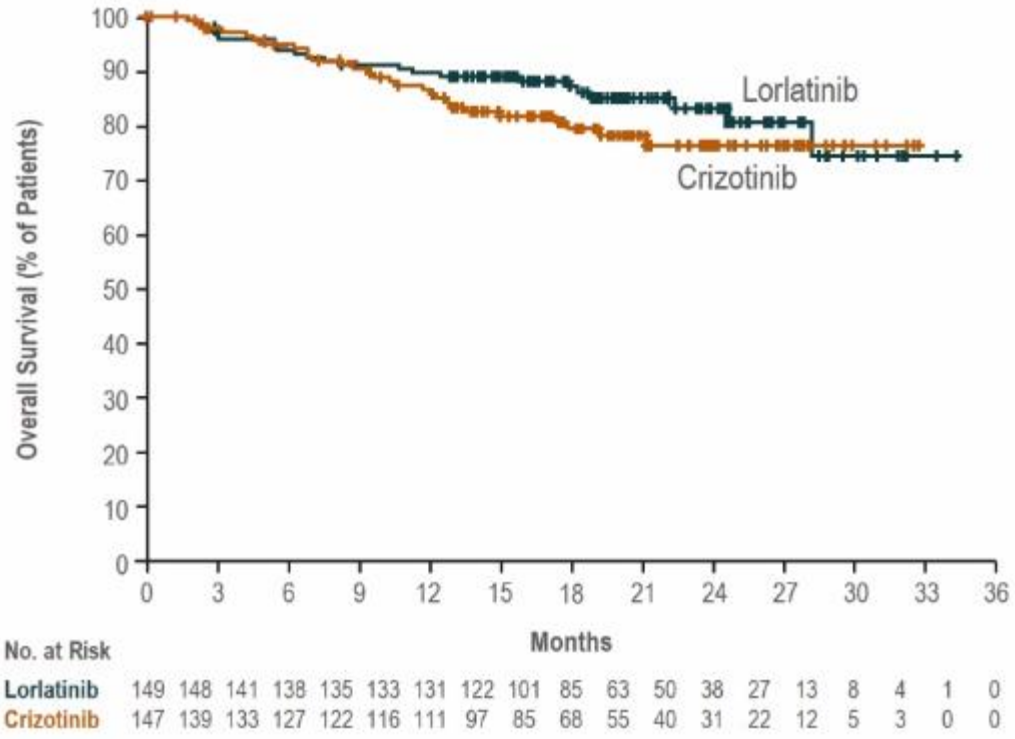
Intracranial-OR by BICR

	Patients with measurable or non-measurable brain metastases at baseline		Patients with measurable brain metastases at baseline	
	Lorlatinib (n=38)	Crizotinib (n=40)	Lorlatinib (n=17)	Crizotinib (n=13)
IC-responders, n (%)	25 (66)	8 (20)	14 (82)	3 (23)
(95% CI)	(49-80)	(9-36)	(57-96)	(5-54)
Odds ratio (95% CI)	8.41 (2.59-27.23)		16.83 (1.95-163.23)	
IC-CR, n (%)	23 (61)	6 (15)	12 (71)	1 (8)
Median DR, months (95% CI)	NE (NE–NE)	9.4 (6.0-11.1)	NE (NE–NE)	10.2 (9.4-11.1)

ALK

VIRTUAL 2020 ESMO congress

Overall Survival



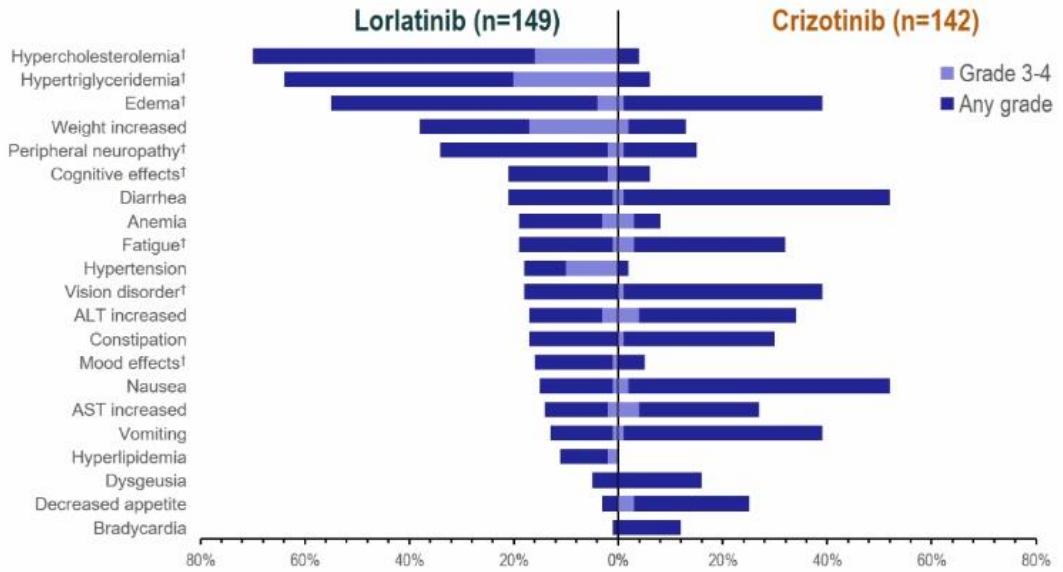
	Lorlatinib (n=149)	Crizotinib (n=147)
Patients with event, n (%)	23 (15)	28 (19)
Median OS, months (95% CI)	NE (NE–NE)	NE (NE–NE)
HR (95% CI)	0.72 (0.41-1.25)	

ALK

Safety Summary

	Lorlatinib (n=149)	Crizotinib (n=142)
Median treatment duration,* months (95% CI)	NE (NE–NE)	9.6 (7.6–11.1)
Patients with, n (%)		
Any grade AE	149 (100)	140 (99)
Grade 3/4 AE	108 (72)	79 (56)
Serious AE	51 (34)	39 (27)
Fatal AE†	7 (5)	7 (5)
AE leading to permanent treatment discontinuation	10 (7)	13 (9)
AE leading to temporary dose interruption	73 (49)	67 (47)

All Causality Adverse Events with ≥10% Difference in Frequency

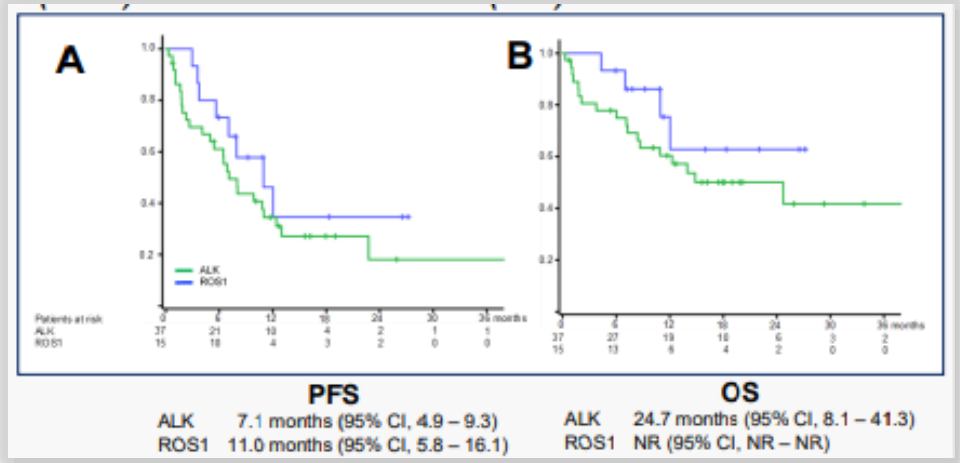


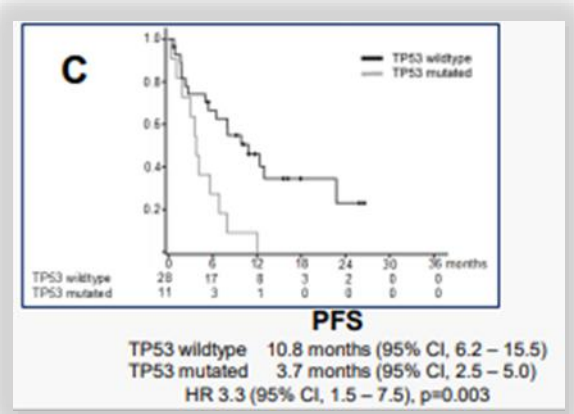
ALK

- 1368P

Lorlatinib in pretreated ALK/ROS1-positive non-small cell lung cancer (NSCLC): Results from the German early access program

M1 SNC 69%
Ca Leptomeníngea 25%

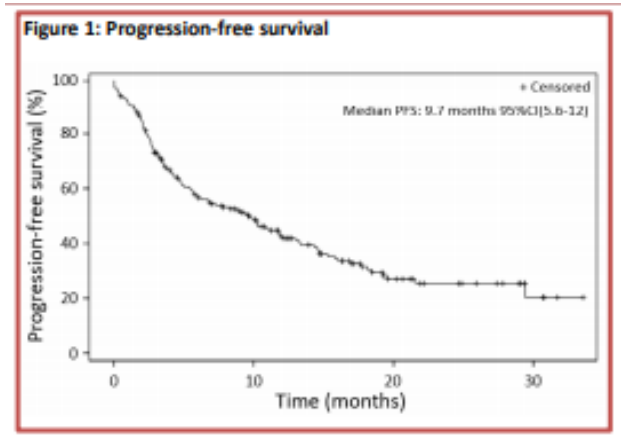


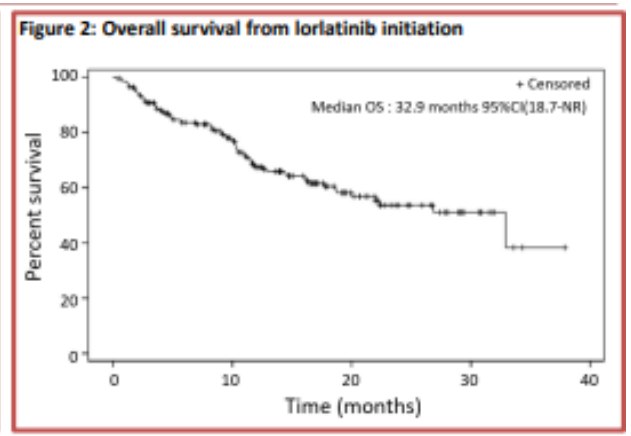


- 1303P

Lorlatinib for advanced ALK+ Non-Small Cell Lung Cancer (NSCLC): efficacy and safety data from IFCT-1803 LORLATU Expanded Access Program (EAP) cohort

M1 SNC 77%
2ª-5ªL (48% 5ªL)
Ttos previos:
-QT 77%
-ITK 1ª gen: 92,4%
-ITK 2ª gen: 92,9%





mPFS	9,7 m
mOS	32,9m
TR	50,6%
TCE	86,7%
TR SNC	42,9%

ALK

- 1302P

1302P

Lorlatinib in Patients With *ALK*+ NSCLC Treated Beyond Initial Disease Progression

Sai-Hong I. Ou,[1] Benjamin Solomon,[2] Alice Shaw,[3] Shirish M. Gadgeel,[4] Benjamin Besse,[5] Ross A. Soo,[6] Antonello Abbattista,[7] Holger Thurm,[8] Francesca Toffalorio,[7] Robin Wiltshire,[9] Alessandra Bearz[10]

[1]Chao Family Comprehensive Cancer Center, University of California Irvine, Orange County, CA, USA; [2]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [3]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [4]Henry Ford Cancer Institute/Henry Ford Hospital, Detroit, MI, USA; [5]Gustave Roussy Cancer Campus, Villejuif, France; [6]National University Hospital, Singapore; [7]Pfizer Oncology, Milan, Italy; [8]Pfizer Oncology, La Jolla, CA, USA; [9]Pfizer Oncology, Walton Oaks, UK; [10]National Institute for Cancer Research CRO-IRCCS, Aviano, Italy

Majority of patients with clinical benefit continued lorlatinib beyond progressive disease (LBPD).

Patient characteristics were broadly similar at baseline and on progression in the LBPD and non-LBPD groups.

Median OS and median OS post-PD were longer in LBPD vs non-LBPD groups.

Further evaluations to better assess the clinical benefit of continuing treatment with lorlatinib beyond RECIST-determined progression are warranted.

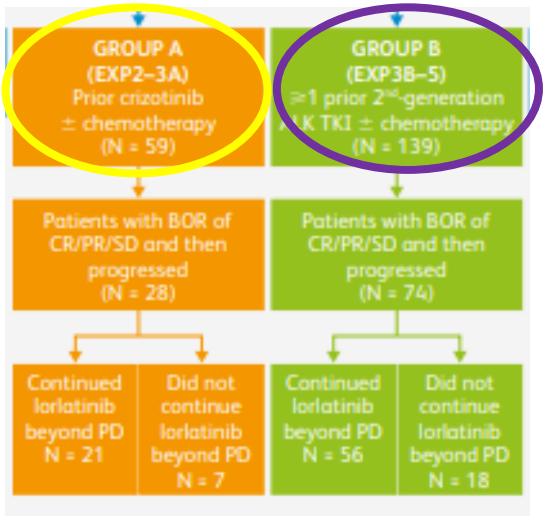
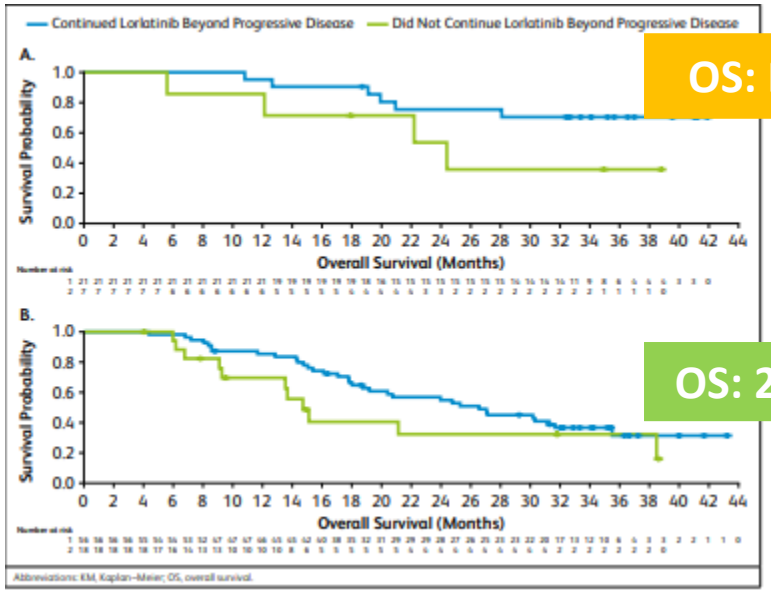


Table 2. Post-disease Progression Treatments in Patients Who Did Not Continue LBPD

	No LBPD	
	Group A (prior crizotinib) n = 7	Group B (≥1 second-generation ALK TKI) n = 18
Post-progression treatments		
ALK TKI systemic therapies	5 (71.4)	10 (55.6)
Non-ALK TKI systemic therapies	0	3 (16.7)
Radiotherapies	1 (14.3)	4 (22.2)
No subsequent treatment	2 (28.6)	5 (27.8)

Abbreviations: ALK, anaplastic lymphoma kinase; LBPD, lorlatinib beyond progressive disease; TKI, tyrosine kinase inhibitor.



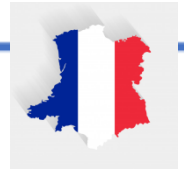
Abbreviations: KM, Kaplan–Meier; OS, overall survival.

OS: NR *vs* 26,5m

OS: 24,4 *vs* 14,7m

ALK

- **1392P** Brigatinib in patients with ALK-positive advanced non-small-cell lung cancer pretreated with sequential ALK inhibitors: a multicentric real-world study (**BRIGALK2 study**)

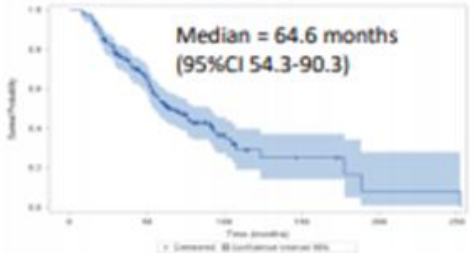


Nº ttos previos (mediana): 3
Nº ITK previos (mediana): 2
M1 SNC: 70%

Table 2: Efficacy of brigatinib

	N= 184 (ITT)
PFS, months (95%CI)	4.8 (3.8-5.6)
ORR, n (%)	73 (45,9 %)
Disease control rate, n (%)	122 (76.8%)
Duration of treatment, months (95%CI)	4.9 (4.1-5.9)
OS from brigatinib initiation, months (95%CI)	
Overall population	19.4 (15.6-24.5)
Patients with brain metastasis (BM)	21.8 (15.6-35.4)
Patients without BM	18 (12.4-24.5)

Figure 4: OS from NSCLC diagnosis



- **1350P** **Real-world treatment outcomes with brigatinib in patients with pretreated ALK+ metastatic non-small cell lung cancer**

N=104
Nº ttos previos (mediana): 1-6 (2)
M1 SNC: 62,5%

Table 3. Best response to brigatinib therapy

	N=93
CR	2 (2.2%)
PR	35 (37.6%)
SD	15 (16.1%)
PD	39 (41.9%)
Response rate	37 (39.8%)
Disease control rate	52 (55.9%)
Median duration of response, months (95% CI)	NR (19.9–NR)

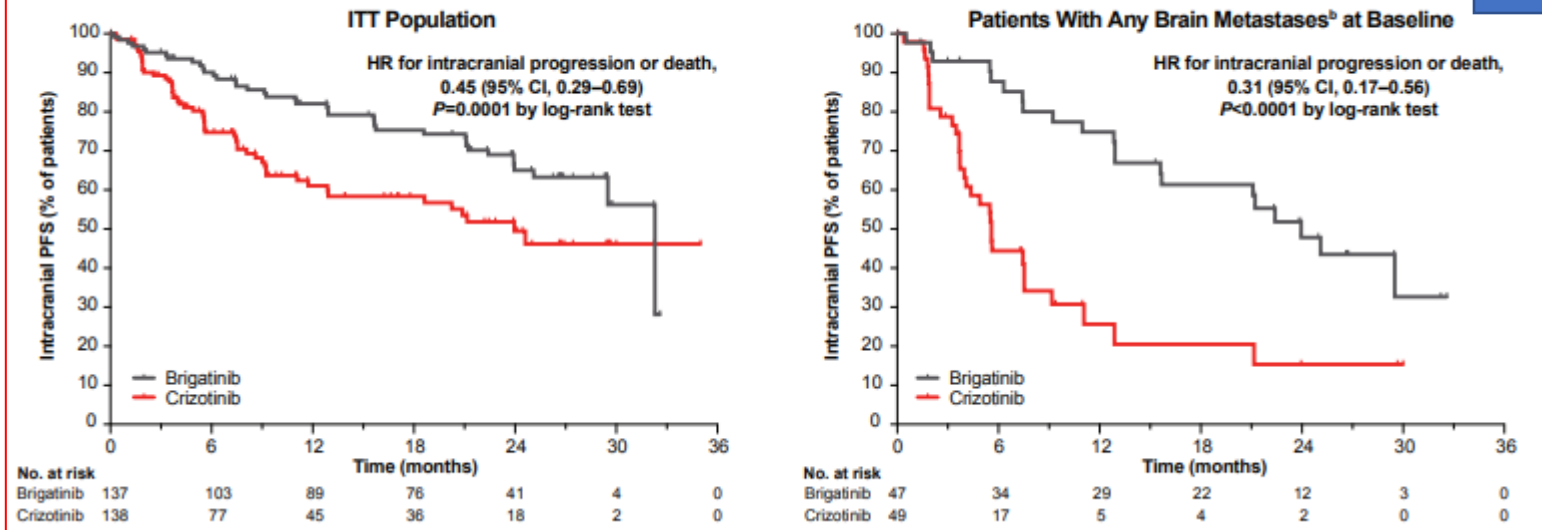
OS 23,3 m
SLP 11,3m

ALK

- 1300P

Intracranial Efficacy of Brigatinib vs Crizotinib: Updated Results From the ALTA-1L Trial

Figure 4. Updated BIRC[a]-Assessed Intracranial PFS



TR SNC: 78 *vs* 26%

- 1304P **Brigatinib vs Crizotinib in Asian vs Non-Asian Patients: Update From ALTA-1L**
- 1305P

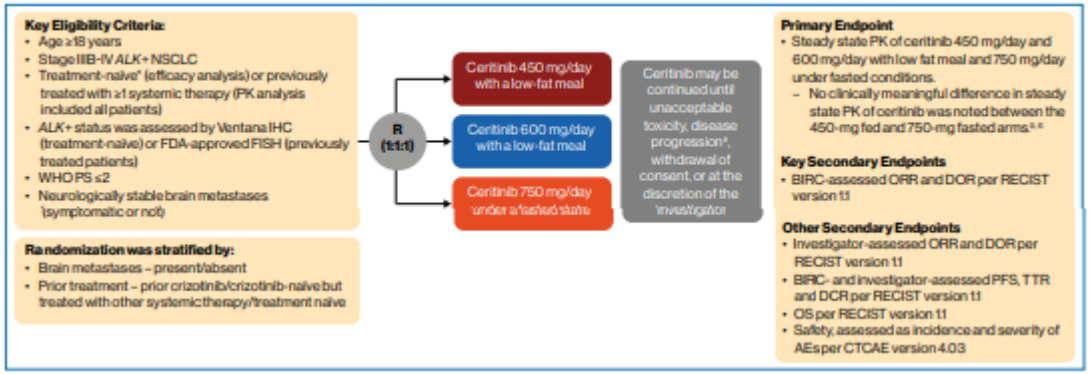
Health-Related Quality of Life in a Phase 3 Study of First-line Brigatinib vs Crizotinib in NSCLC: Updated Results From ALTA-1L

ALK

- 1348P

Efficacy and safety of ceritinib 450 mg-fed vs 750 mg-fasted in Asian patients (pts) with *ALK*+ non-small cell lung cancer (NSCLC) in the ASCEND-8 trial

Figure 1: ASCEND-8 Study Design



- 1361P

Determination of ALK rearrangements in non-small cell lung cancer: clinical and economic impact of current practice in Spain.

Figure 1. Model structure

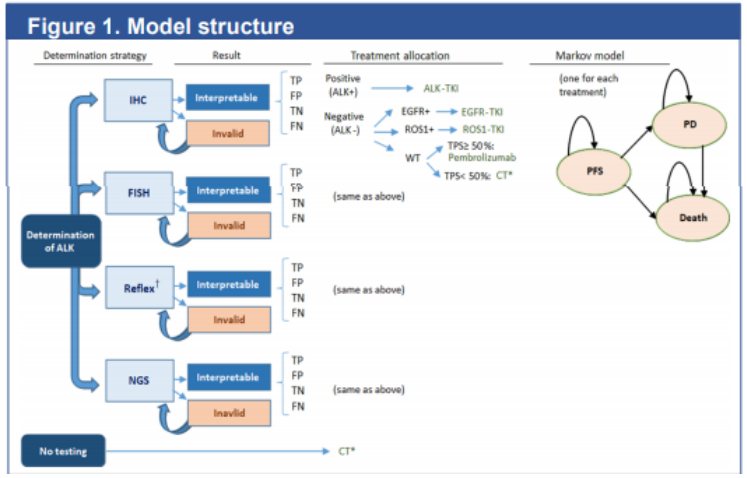


Table 3. Results for health outcomes and costs, base case

	Current scenario tested	No-testing	Difference
Cost of testing	€ 3,613,701	€ 0	€ +3,613,701
Cost of treatment	€ 854,664,411	€ 806,959,058	€ +47,705,353
Total costs	€ 858,278,111	€ 806,959,058	€ +51,319,053
LY	21,233.6	16,173.4	+5,060.1
QALYs	14,654.7	10,748.0	+3,906.6
ICER (€/LY gained)			€ 10,142 /LY
ICUR (€/QALY gained)			€ 13,136 /QALY

LY: life years; QALY: quality-adjusted life years; ICER: incremental cost-effectiveness ratio; ICUR: incremental cost-utility ratio

ROS-1

1287P

Efficacy and safety of entrectinib in locally advanced/metastatic *ROS1* fusion-positive NSCLC: an updated integrated analysis

N=161
M1 SNC 34,8%

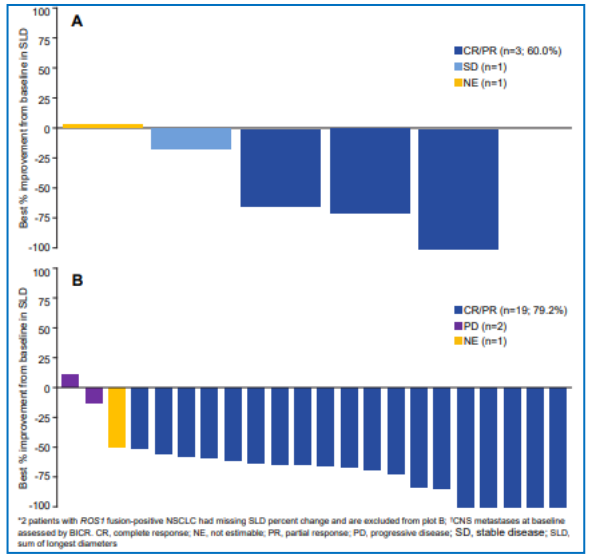
ITK naïve

	ROS1 fusion-positive NSCLC		
	Efficacy-evaluable population (N=161)	Baseline CNS metastases* (n=56)	No baseline CNS metastases* (n=105)
Objective response, % (95% CI)	**67.1** (59.3–74.3)	**62.5** (48.6–75.1)	**69.5** (59.8–78.1)
Best overall response, n (%)			
Complete response	14 (8.7)	4 (7.1)	10 (9.5)
Partial response	94 (58.4)	31 (55.4)	63 (60.0)
Stable disease	14 (8.7)	4 (7.1)	10 (9.5)
Progressive disease	15 (9.3)	9 (16.1)	6 (5.7)
Non-CR/non-PD	10 (6.2)	2 (3.6)	8 (7.6)
Missing or unevaluable†	14 (8.7)	6 (10.7)	8 (7.6)
Duration of response			
Median, months (95% CI)	**15.7** (13.9–28.6)	**14.9** (9.6–20.5)	**24.6** (13.9–34.8)
Patients with events, n (%)	48 (44.4)	17 (48.6)	31 (42.5)
6-month durable response, % (95% CI)	83 (76–90)	84 (70–97)	83 (74–92)
12-month durable response, % (95% CI)	63 (53–73)	62 (44–80)	63 (51–75)
Progression-free survival			
Median, months (95% CI)	**15.7** (11.0–21.1)	**11.8** (6.4–15.7)	**19.0** (12.0–29.6)
Patients with events, n (%)	82 (50.9)	34 (60.7)	48 (45.7)
6-month PFS, % (95% CI)	77 (70–84)	69 (57–81)	82 (74–89)
12-month PFS, % (95% CI)	55 (47–64)	47 (33–61)	60 (50–70)
Overall survival			
Median, months (95% CI)	**NE** (28.3–NE)	**28.3** (16.1–NE)	**NE** (30.8–NE)
Patients with events, n (%)	38 (23.6)	17 (30.4)	21 (20.0)
6-month OS, % (95% CI)	91 (87–96)	87 (78–96)	93 (88–98)
12-month OS, % (95% CI)	81 (74–87)	75 (63–88)	84 (76–91)

*CNS disease at baseline as judged per investigator (RECIST version 1.1).

1288P

Efficacy of entrectinib in patients with *NTRK* or *ROS1* fusion-positive NSCLC with CNS metastases at baseline



*2 patients with *ROS1* fusion-positive NSCLC had missing SLD percent change and are excluded from plot B; †CNS metastases at baseline assessed by BICR. CR, complete response; NE, not estimable; PR, partial response; PD, progressive disease; SD, stable disease; SLD, sum of longest diameters

Intracranial **ORR** in *NTRK* fusion-positive NSCLC **62.5%**

In patients with measurable CNS metastases at baseline: **60.0%**

Intracranial **ORR** in *ROS1* fusion-positive NSCLC **52.2%**

In patients with measurable CNS metastases at baseline: **79.2%**

Median intracranial PFS

8.9 months (*NTRK*)
8.3 months (*ROS1*)

Few patients with *ROS1* fusion-positive NSCLC **without baseline CNS** metastases experienced **CNS progression**

540P

Entrectinib in patients with *ROS1* fusion-positive non-small cell lung cancer (NSCLC) or *NTRK* fusion-positive solid tumours: analysis of response by line of therapy

	Prior LOT: 0*	Prior LOT: 1	Prior LOT: 2	Prior LOT: ≥3
***NTRK*+ solid tumours†**				
ORR, % (n/N)	80.0 (16/20)	61.9 (13/21)	65.0 (13/20)	38.5 (5/13)
95% CI	56.3–94.3	38.4–81.9	40.8–84.6	13.9–68.4
Median DoR, months (responders n/N)	NE (16/20)	15.1 (13/21)	11.1 (13/20)	9.4 (5/13)
95% CI	5.6–NE	10.4–15.1	7.9–15.0	2.8–NE
***ROS1*+ NSCLC‡**				
ORR, % (n/N)	71.7 (43/60)	60.9 (39/64)	66.7 (12/18)	73.7 (14/19)
95% CI	58.6–82.6	47.9–72.9	41.0–86.7	48.8–90.9
Median DoR, months (responders n/N)	16.5 (43/60)	14.8 (39/64)	28.6 (12/18)	15.7 (14/19)
95% CI	11.0–NE	9.2–NE	24.6–28.6	9.1–20.5

ROS-1

- 1349P

Lorlatinib for advanced ROS1+ Non-Small Cell Lung Cancer (NSCLC): efficacy and safety data from IFCT-1803 LORLATU Expanded Access Program (EAP) cohort

Table 2: Characteristics at lorlatinib initiation

Characteristics	ROS1+ (n=71)
Performance status	
0-1	*49 (79%)*
≥2	13 (21%)
Unknown	9
Previous lines	
1	22 (31%)
2	19 (26.8%)
3	12 (16.9%)
≥4	*18 (25.4%)*
Previous treatment	
Chemotherapy	47 (66.2%)
1st generation ALK TKI	*71 (100%)*
2nd generation ALK TKI	*14 (19.7%)*
Brain radiotherapy	23 (32.4%)
Brain metastasis	
Present	*45 (63.4%)*
Absent	26 (36.6%)

Table 3: Overall response to lorlatinib

	ROS1+ (n=71)
Best overall response	
Number of patients with available data	66 (92.9%)
Complete response	0 (0.0%)
Partial response	30 (45.5%)
Stable disease	26 (39.4%)
Progressive disease	8 (12.1%)
Objective response	*30 (45.5%)*
Disease control	*56 (84.8%)*
Not evaluable	2 (3%)
Central nervous system objective response rate (available data; %)*	*28 (/67; 41.8%)*
Median duration of response (range, months)	*6.1 (0-34.5)*
Median follow up (IC95%, months)	14.8 (12.5-25.7)
Median lorlatinib duration (range, months)	7.4 (0.49-34.7)
Median lorlatinib duration beyond progression (range, months)	0.7 (0.03-25.3)

* Defined as the rate of intracracnial tumor response according RECIST v1.1

Figure 1: Progression-free survival

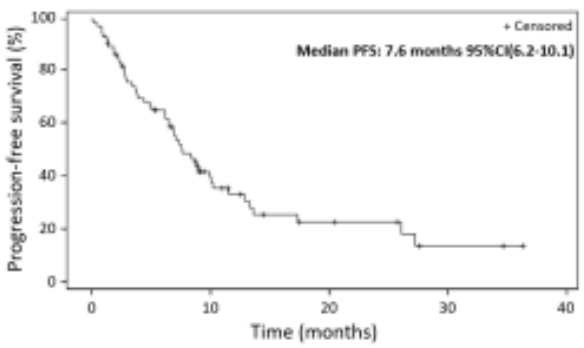
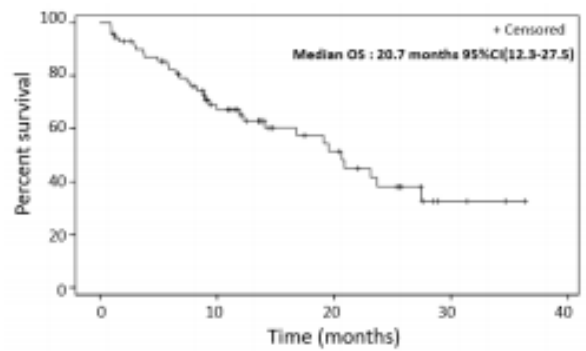


Figure 2: Overall survival from lorlatinib initiation



Lung Cancer UPDATES
ESMO HIGHLIGTHS
19-21 SEPTIEMBRE 2020

VIRTUAL

Iniciativa científica de: GECP lung cancer research

Cáncer de pulmón no microcítico avanzado: mutaciones frecuentes.

María Guirado Risueño
HGU Elche