Iniciativa científica de:

GECP lung cancer research

Lung Cancer UPDATES

ASCO HIGHLIGHTS

29 MAYO - 02 JUNIO 2026

Chicago, USA

#ASCOUPDATES

Iniciativa científica de:

GECP lung cancer research

Lung Cancer UPDATES

ASCO HIGHLIGHTS

29 MAYO - 02 JUNIO 2026

Chicago, USA

CNMP metastásico con Driver.

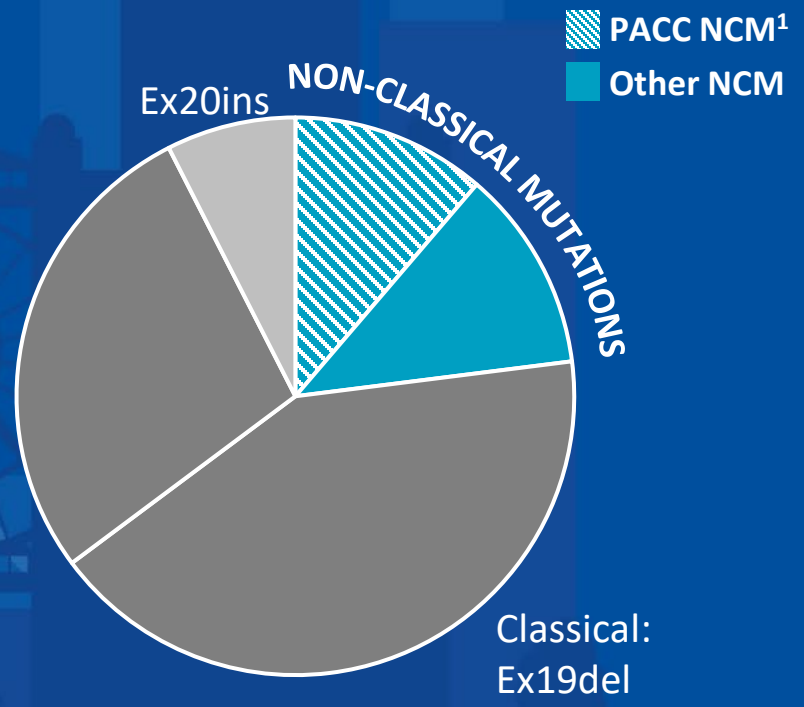
EGFR y ALK.

Dra. Eider Azkona Uribelarrea.

Iniciativa científica de:

GECP lung cancer research

mEGFR



EGFR Exon20ins

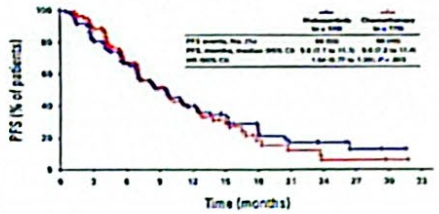
Iniciativa científica de: GECP lung cancer research

Therapeutic advances in EGFR ex20 ins mutations

Structural basis resistance to 1G EGFR TKI in Ex20 insertions Yasuda STM 2013

EXCLAIM
Accelerated approval – mobocertinib

EXCLAIM-2
Mobocertinib vs Chemo
PFS: 9.6 v **9.6 m**



CHRYSALIS
Accelerated approval – amivantamab (monotherapy)

Roubichoux et al.
Structural-functional basis classification

WU-KONG 1B
Accelerated approval
- Sunvozertinib 200 mg

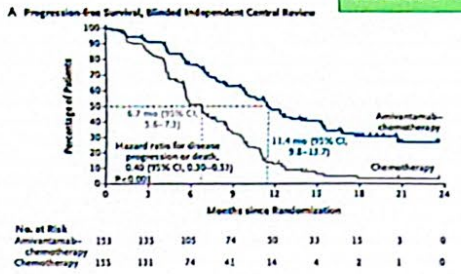
2013 2015 2017 2019 2021 2023 2024 2025 2026

Yang et al. Role of afatinib in uncommon mutations (**LUX-2, LUX-3, LUX-6**)
- 3 cohorts: Exon 20 ins/atypicals/ T790M

Limited efficacy for afatinib in exon 20 ins

Osimertinib 160 mg OM
POSITION20
ORR 28%, mPFS 6.8 m
ECOG ACRIN EA5162
ORR 24%, mPFS 9.6 m

PAPILLON
SoC chemo-amivantamab



FAVOUR
Firmonertinib
ORR 78.6%
mDoR 15.2 m

WU-KONG 28
Phase III
Sunvozertinib 300 mg vs chemo

#ASCO26

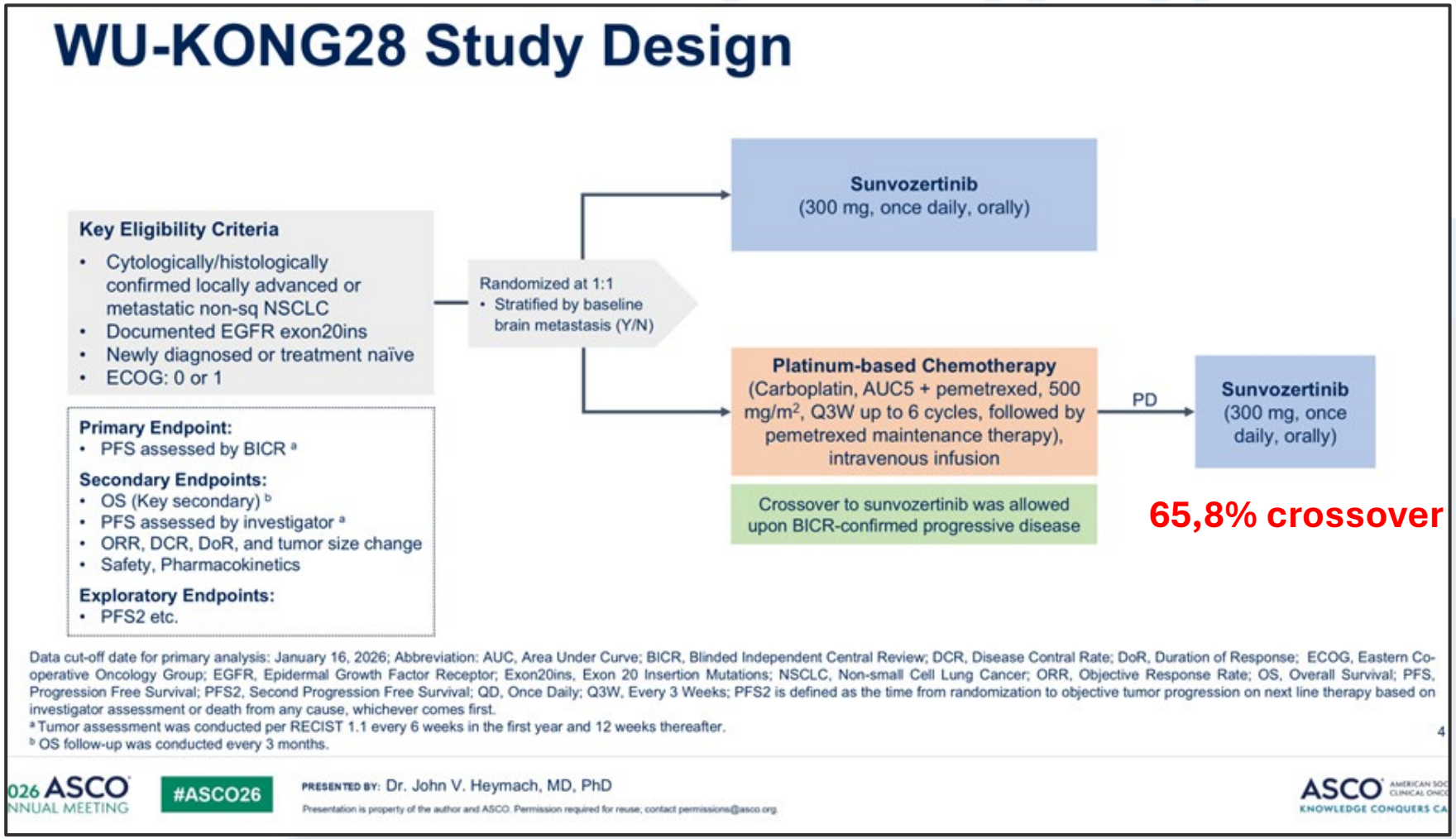
PRESENTED BY: Daniel SW Tan, National Cancer Centre Singapore

ASCO

EGFR Exon20ins

Sunvozertinib Monotherapy versus Platinum-based Chemotherapy as First-line Treatment for Advanced NSCLC with EGFR Exon20ins: Primary Analysis of A Multinational Phase 3 Randomized Study (WU-KONG28)

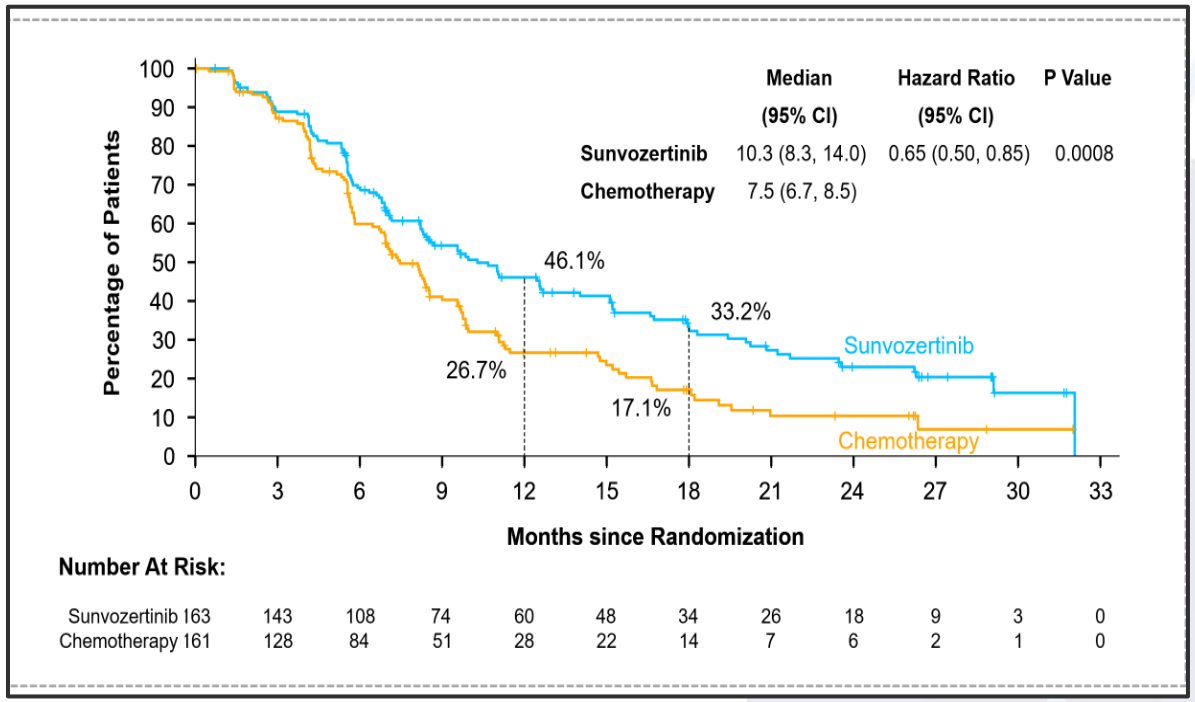
John V. Heymach, MD, PhD



EGFR exón 20 ins

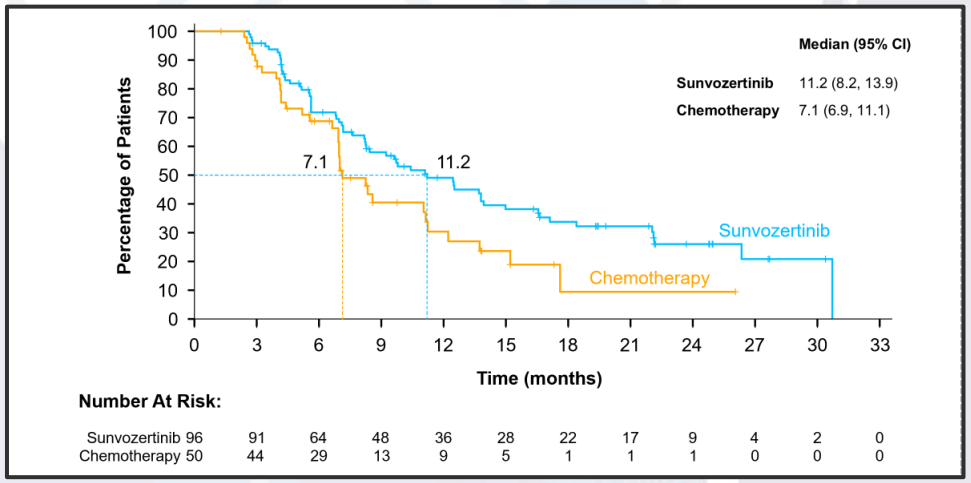
Sunvozertinib Monotherapy versus Platinum-based Chemotherapy as First-line Treatment for Advanced NSCLC with EGFR Exon20ins: Primary Analysis of A Multinational Phase 3 Randomized Study (WU-KONG28)

John V. Heymach, MD, PhD



- TR: 58,9 vs. 31,1%, p<0,0001
- TCE: 94,5 vs. 85,7%

- DoR: 11,2 vs. 7,1 m



- SLP 2: 21,7 vs. 15,5 m, HR 0,70 [0,52-0,95], p 0,0111
- SV: 29,8 vs. 28,8 m

Accelerated FDA approval *(post-chemo)*, but unavailable in US

EGFR exón 20 ins

Sunvozertinib Monotherapy versus Platinum-based Chemotherapy as First-line Treatment for Advanced NSCLC with EGFR Exon20ins: Primary Analysis of A Multinational Phase 3 Randomized Study (WU-KONG28)

Iniciativa científica de: GECP lung cancer research

John V. Heymach, MD, PhD

	Sunvozertinib All Grades	Sunvozertinib Grade ≥3	Chemotherapy All Grades	Chemotherapy Grade ≥3
Diarrhea	142 (87.1)	23 (14.1)	25 (16.7)	0
Serum creatine kinase increased	95 (58.3)	34 (20.9)	6 (4.0)	1 (0.7)
Anemia	93 (57.1)	15 (9.2)	94 (62.7)	17 (11.3)
Rash	86 (52.8)	1 (0.6)	10 (6.7)	0
Paronychia	79 (48.5)	6 (3.7)	1 (0.7)	0
Weight decreased	71 (43.6)	6 (3.7)	17 (11.3)	1 (0.7)
Decreased appetite	63 (38.7)	3 (1.8)	42 (28.0)	2 (1.3)
Serum creatinine increased	55 (33.7)	1 (0.6)	14 (9.3)	0
Nausea	46 (28.2)	3 (1.8)	69 (46.0)	2 (1.3)
Vomiting	46 (28.2)	3 (1.8)	36 (24.0)	3 (2.0)
Hypokalemia	41 (25.2)	6 (3.7)	11 (7.3)	1 (0.7)
Amylase increased	38 (23.3)	2 (1.2)	17 (11.3)	0
Lipase increased	38 (23.3)	9 (5.5)	11 (7.3)	2 (1.3)
Aspartate aminotransferase increased	36 (22.1)	4 (2.5)	56 (37.3)	1 (0.7)
Mouth ulceration	33 (20.2)	2 (1.2)	5 (3.3)	0
Alanine aminotransferase increased	29 (17.8)	3 (1.8)	52 (34.7)	2 (1.3)
Fatigue	25 (15.3)	2 (1.2)	30 (20.0)	4 (2.7)
Neutrophil count decreased	24 (14.7)	4 (2.5)	68 (45.3)	28 (18.7)
White-cell count decreased	20 (12.3)	1 (0.6)	59 (39.3)	10 (6.7)
Constipation	18 (11.0)	1 (0.6)	38 (25.3)	0
Platelet count decreased	15 (9.2)	4 (2.5)	33 (22.0)	10 (6.7)

- EAs ≥G3: 61,3 vs. 49,3%
- Disminución dosis: 40,5 vs. 24%
- Stop por EAs: 7,4 vs. 11,3%

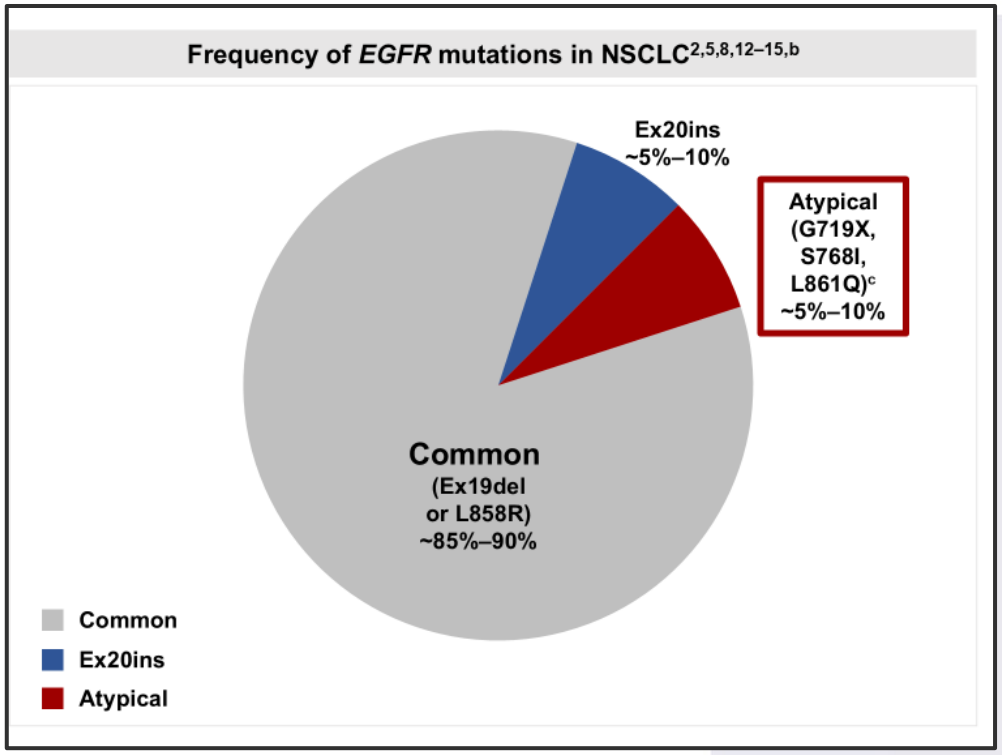
Zhou C, et al. NEJM 2026.
DOI: 10.1056/NEJMoa2604461

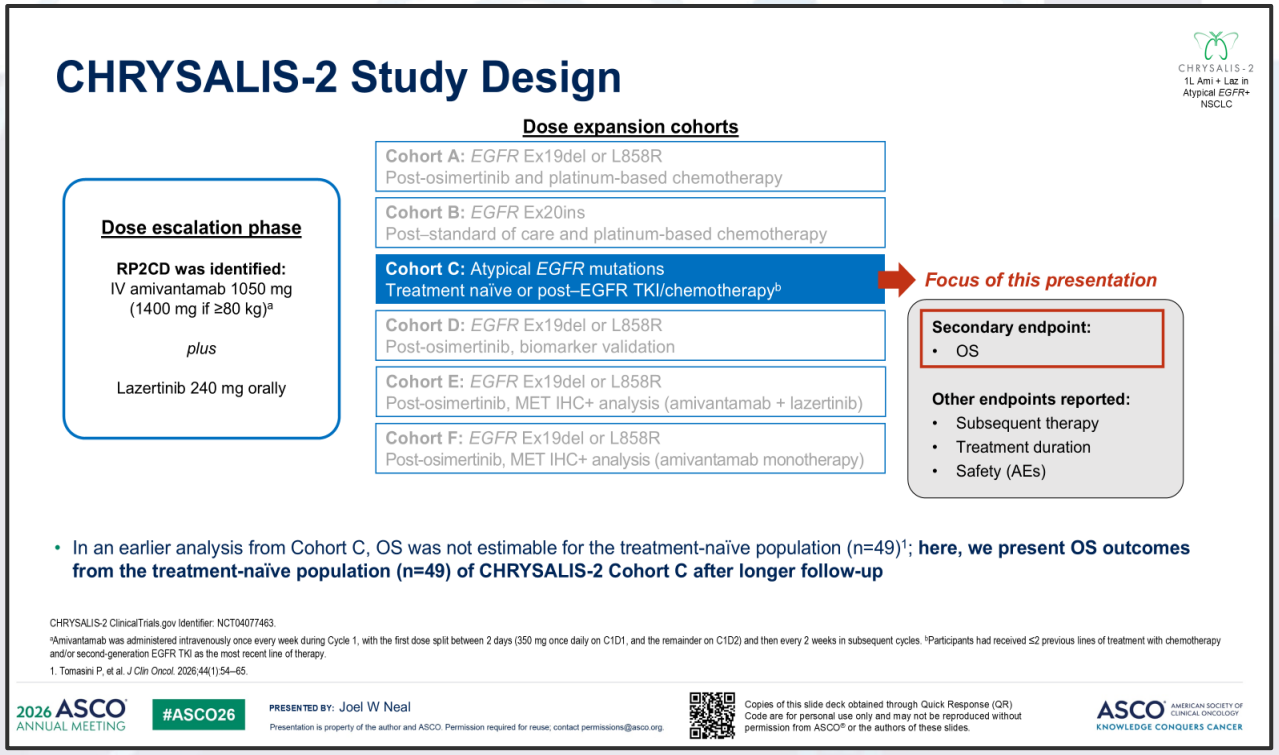
EGFR mutaciones atípicas

Overall survival of first-line amivantamab plus lazertinib in atypical EGFR-mutated advanced NSCLC. Updated results from the CHRYSALIS-2 study

Joel W. Neal, MD PhD

Iniciativa científica de: GECP lung cancer research

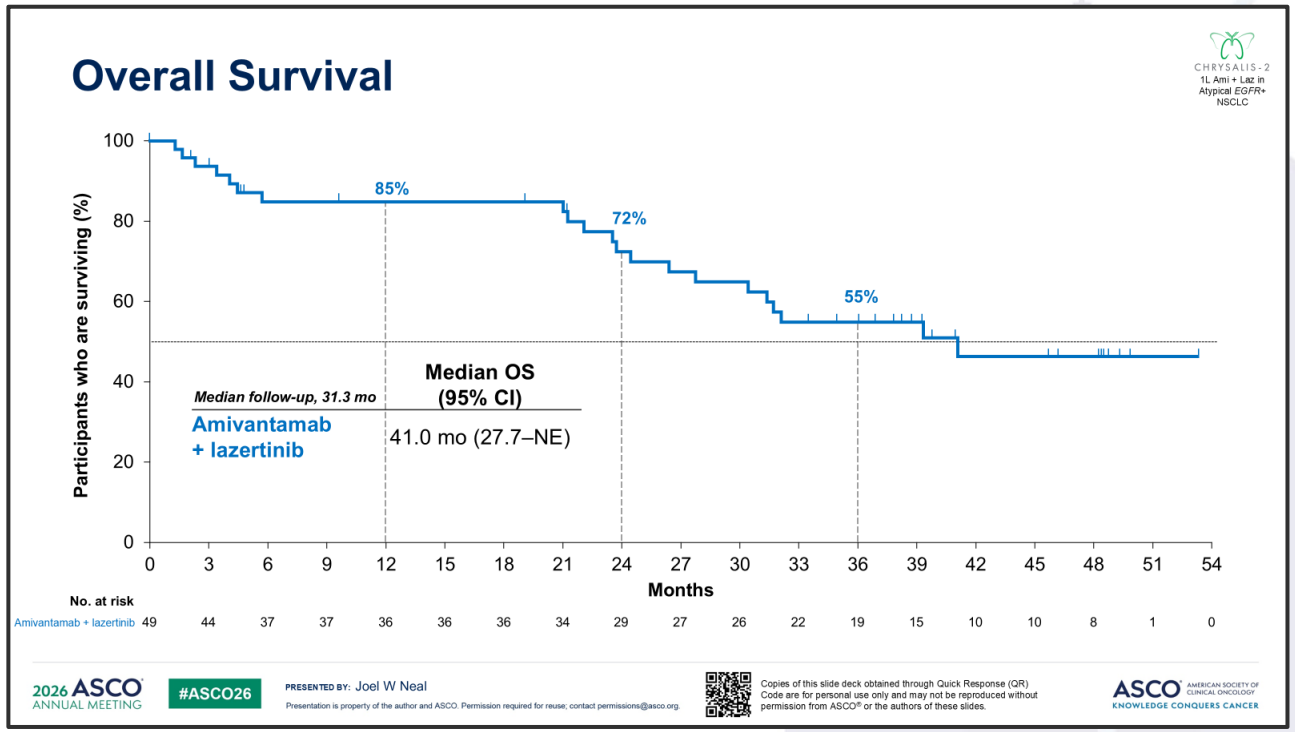




EGFR mutaciones atípicas

Overall survival of first-line amivantamab plus lazertinib in atypical EGFR-mutated advanced NSCLC. Updated results from the CHRYSALIS-2 study.

Joel W. Neal, MD PhD



- Seguimiento 31,3 m (20% siguen en tto)
  - 39% en tto >2 años (duración media: 13,3 m)
- 71% reciben tto a la PD.
- No nuevos EAs, la mayoría G1.
- EAs ≥G3: rash (14%), paroniquia (8%), reacciones infusionales (6%)

→ SV: +/- 3,5 años (41 m)

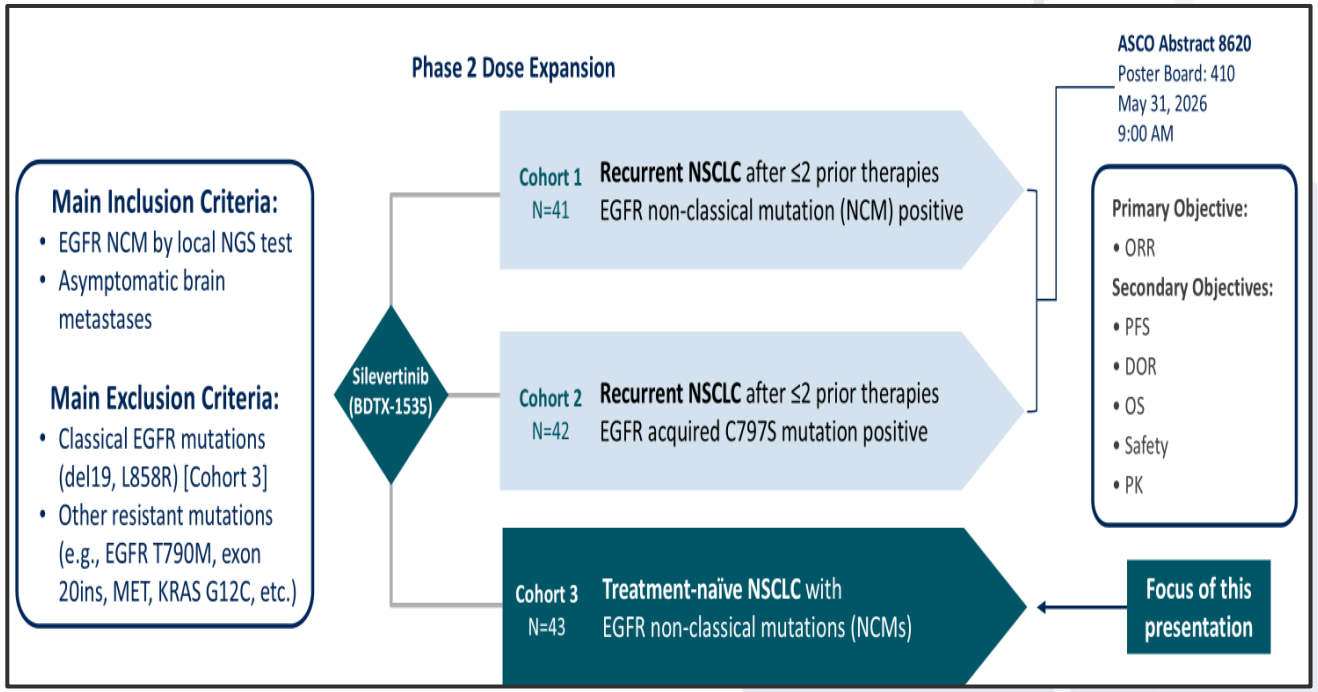
→ Respuestas duraderas indep de mutaciones y características clínico-demográficas.

→ Amivantamav-Lazertinib demuestra SV prolongada en 1ªL en mEGFR comunes y atípicas.

mEGFR atípicas

Safety and efficacy results of the Phase 2 study of silevertinib (BDTX-1535) in treatment-naïve patients with non-small cell lung cancer with non-classical EGFR mutations

Julia Rotow, MD



- TR: 60%
- SLP: 15,2 m
- DoR: NR
- icTR: 86%

Silvertinib 200 mg (n=43)	
EAs ≥G3	60%/28%
Interrupciones	88%
Disminución dosis	84%
Stop	14%

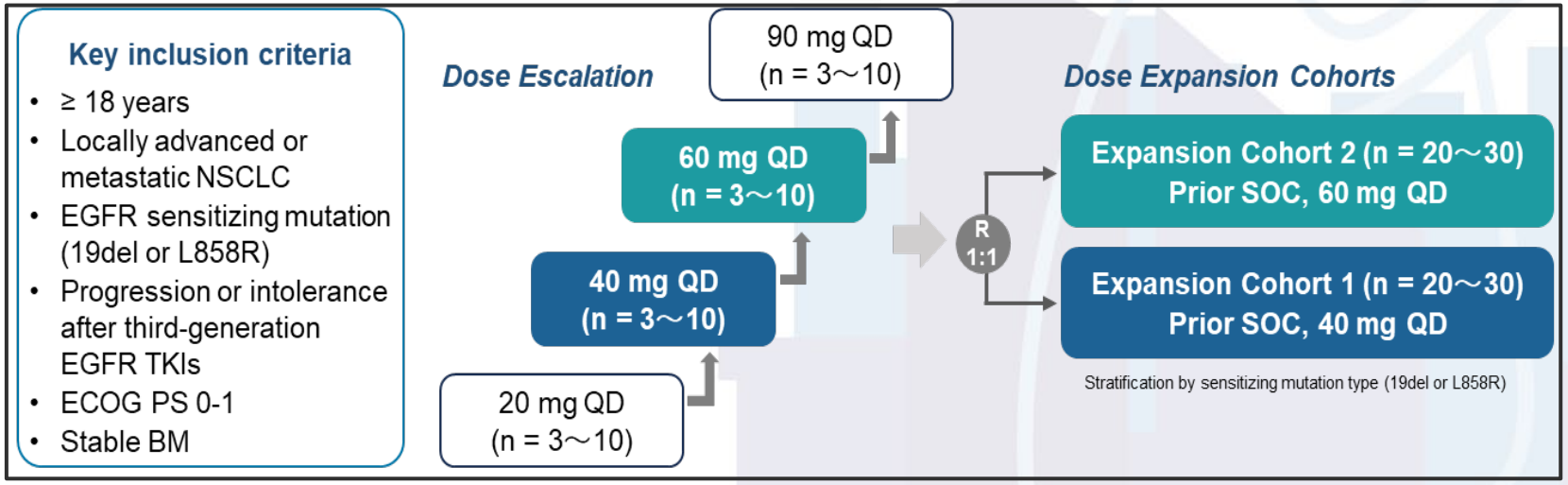
Rash 95% (≥G3: 19%), Diarrea 77% (≥G3: 19%), paroniquia 77% (≥G3: 5%), estomatitis 77% (≥G3: 9%)

EGFR C797X

DZD6008, A Fourth-generation EGFR TKI, in Pretreated NSCLC Patients with EGFR C797X Mutations: Results from Phase 1/2 Studies

Mengzhao Wang

TIAN-SHAN1/2, diseño: TIAN-SHAN1 (NCT06905197) (US/Australia) y TIAN-SHAN2 (NCT06813365; CTR20241790) (China): estudios en marcha fase 1/2 multicéntricos. Valoran seguridad, tolerancia y actividad de DZD6008 en CNMP mEGFR.



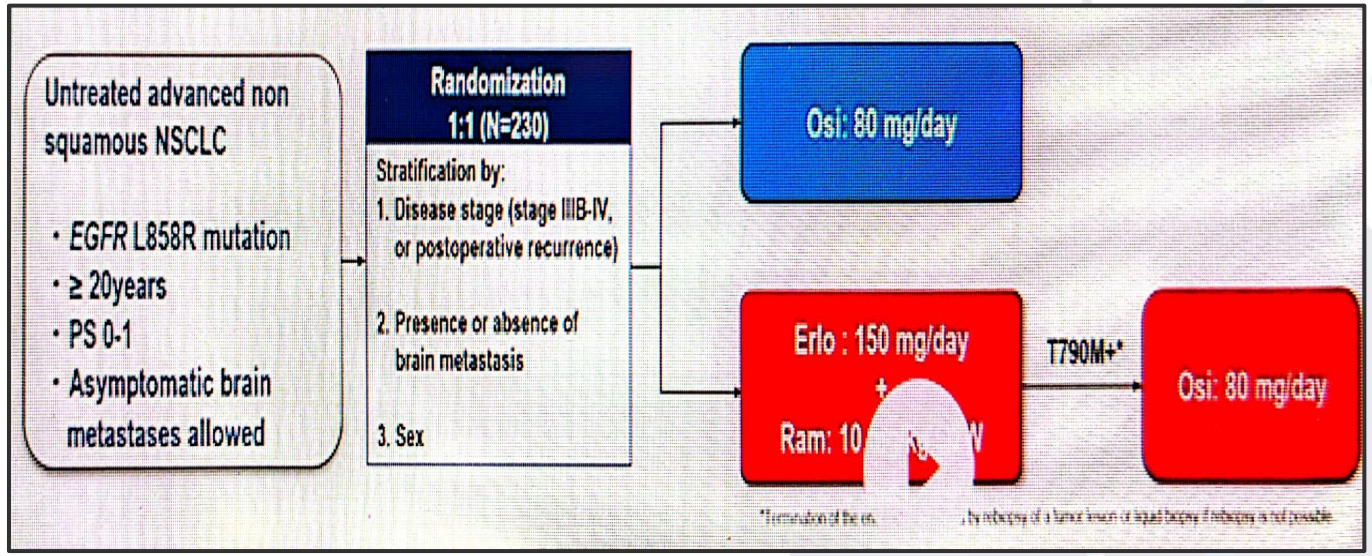
	40 mg (n=17)	60 mg (n=21)
EAs	37,5%	41,7%
Anemia G3	4,2%	16,7%
Transaminasas	0	4,2%

	40 mg (n=17)	60 mg (n=21)
TR	41,2%	42,9%
TCE	94,1%	90,5%
SLP 6 m	70,6 m	61,8 m

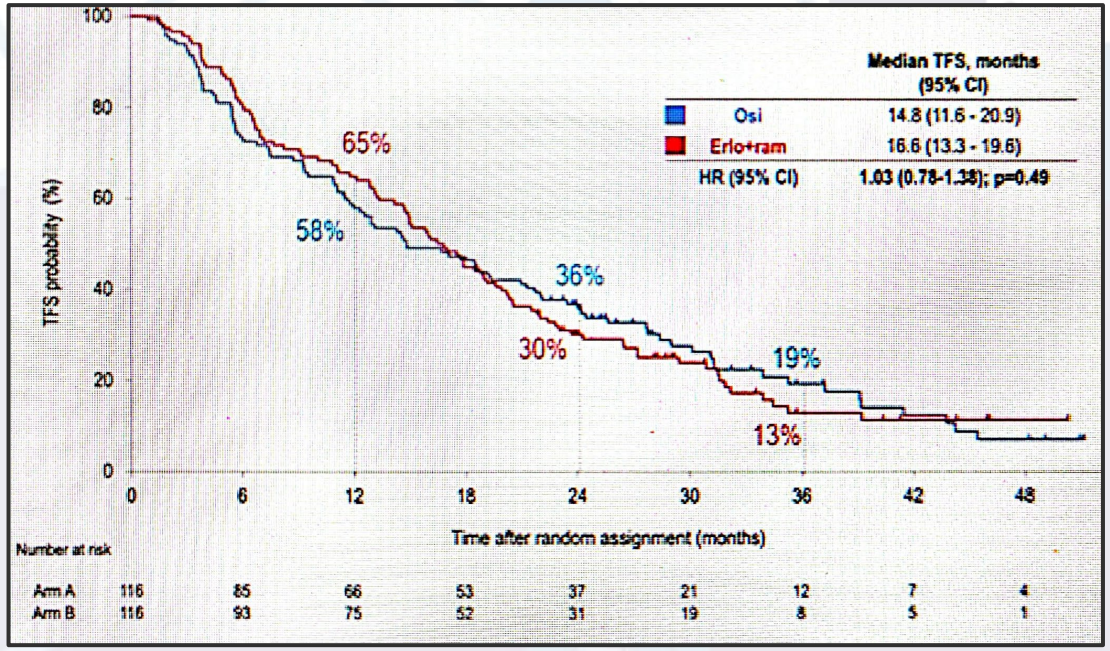
EGFR L858R

Phase 3 clinical trial of the combination of erlotinib plus ramucirumab compared with osimertinib in untreated advanced or recurrent non-small cell lung cancer with EGFR L858R mutation: The TEVIL858R trial (WJOG14420L).

Naoki Haratake, MD, PhD



TFS: 14,8 vs. 16,6 m, p 0,49

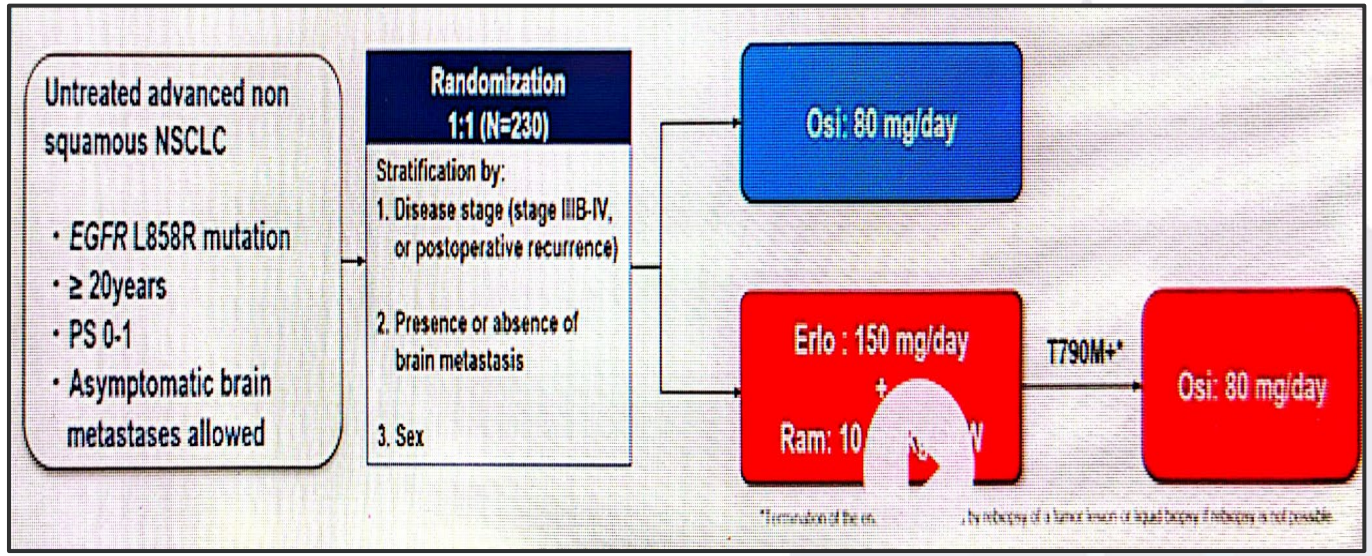


- SLP: 14,8 vs. 14,9 m
- SV: 44 vs. 38,4 m
- EAs G3: 72 vs. 44%

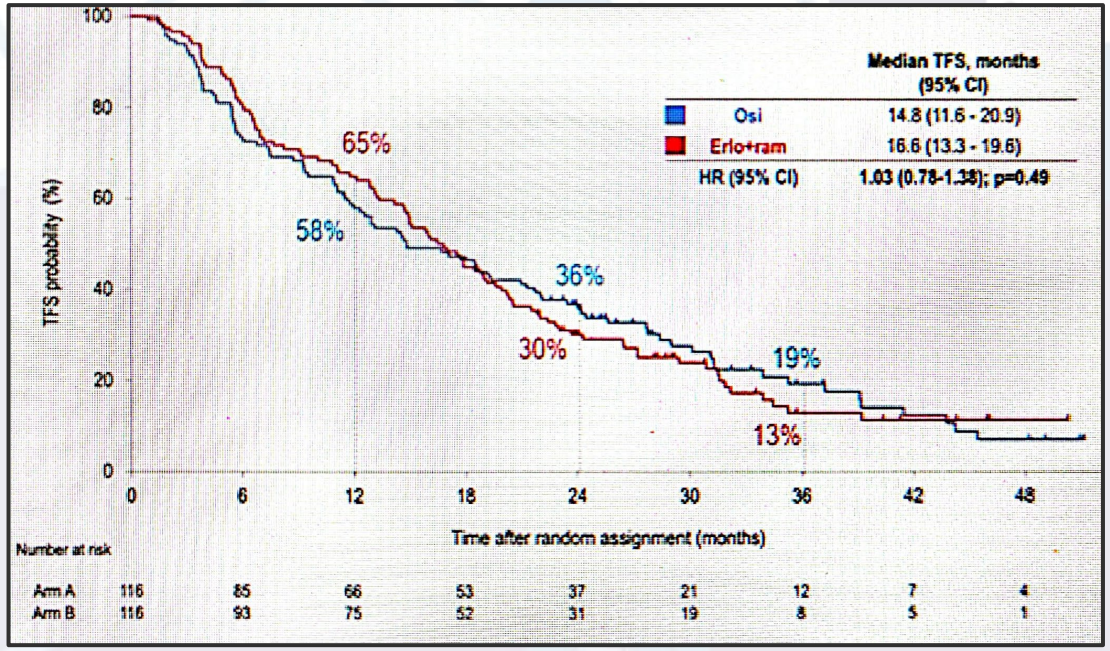
EGFR L858R

Phase 3 clinical trial of the combination of erlotinib plus ramucirumab compared with osimertinib in untreated advanced or recurrent non-small cell lung cancer with EGFR L858R mutation: The TEVIL858R trial (WJOG14420L).

Naoki Haratake, MD, PhD



TFS: 14,8 vs. 16,6 m, p 0,49



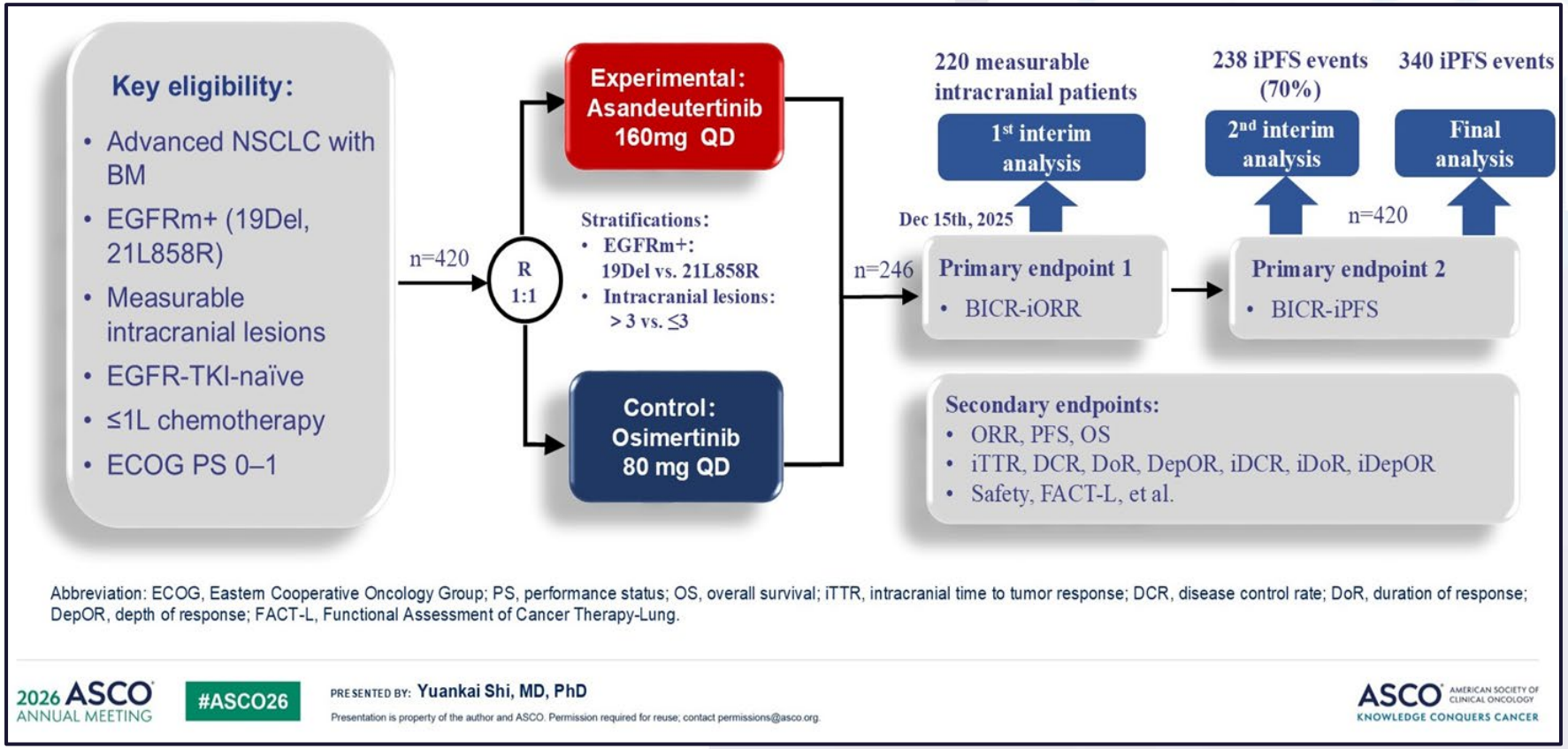
- SLP: 14,8 vs. 14,9 m
- SV: 44 vs. 38,4 m
- EAs G3: 72 vs. 44%

Negativo

EGFR 19Del, 21L858R

Efficacy and safety of asandeutertinib versus osimertinib as first-line treatment in EGFR-mutated NSCLC patients with brain metastases: Interim analysis of an open-label, multicenter, randomized, pivotal phase II study (ESAONA).

Yuankai Shi



- TR: 89,2 vs. 77,9%, p 0,0301
- SLP: NR vs. 17,22 m

HR 0,64 [0,41-1,00], p=0,0473

- EAs≥G3: 43,21 vs. 15,9%

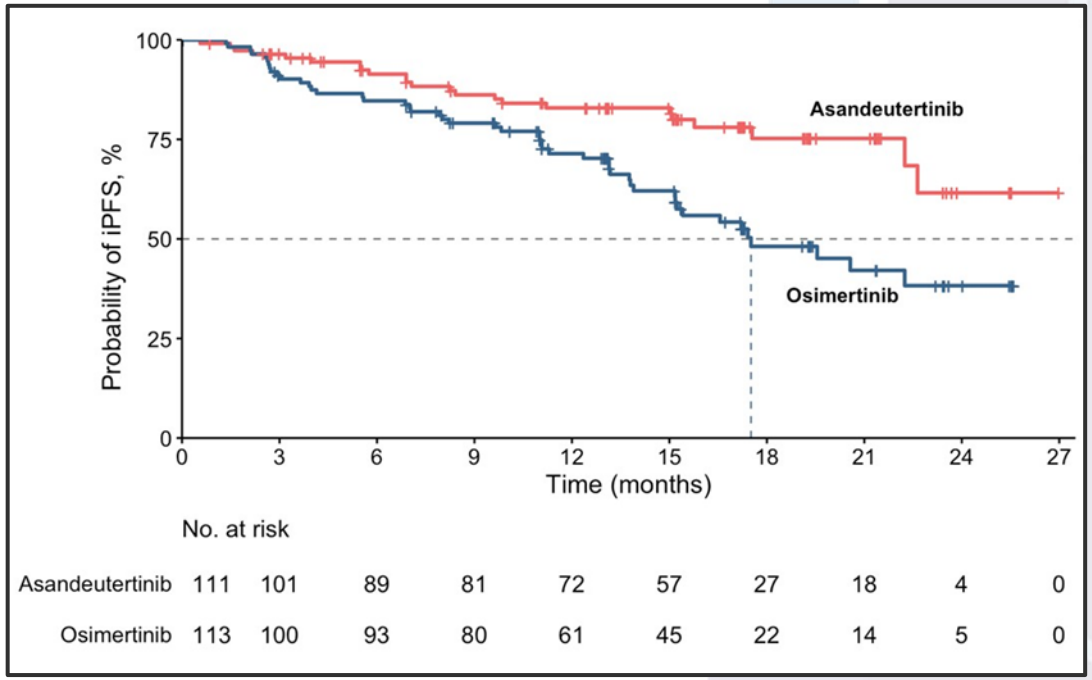
EGFR 19Del, 21L858R

Efficacy and safety of asandeutertinib versus osimertinib as first-line treatment in EGFR-mutated NSCLC patients with brain metastases: Interim analysis of an open-label, multicenter, randomized, pivotal phase II study (ESAONA).

Yuankai Shi

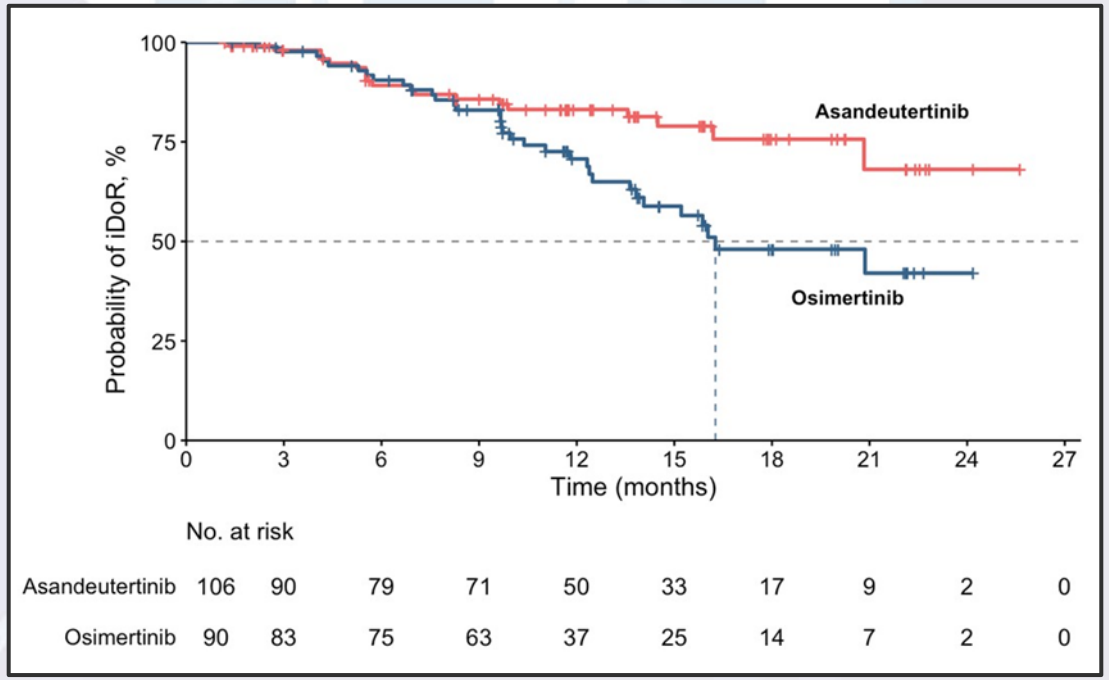
- icTR: 95,5 vs. 79,6%, p0,0004
- icSLP: NR vs. 17,51 m

HR 0,46 [0,28-0,76], p 0,0020]



- icDoR: NR vs. 16,26 m

HR 0,50 [0,28-0,88], p 0,0148



Iniciativa científica de:

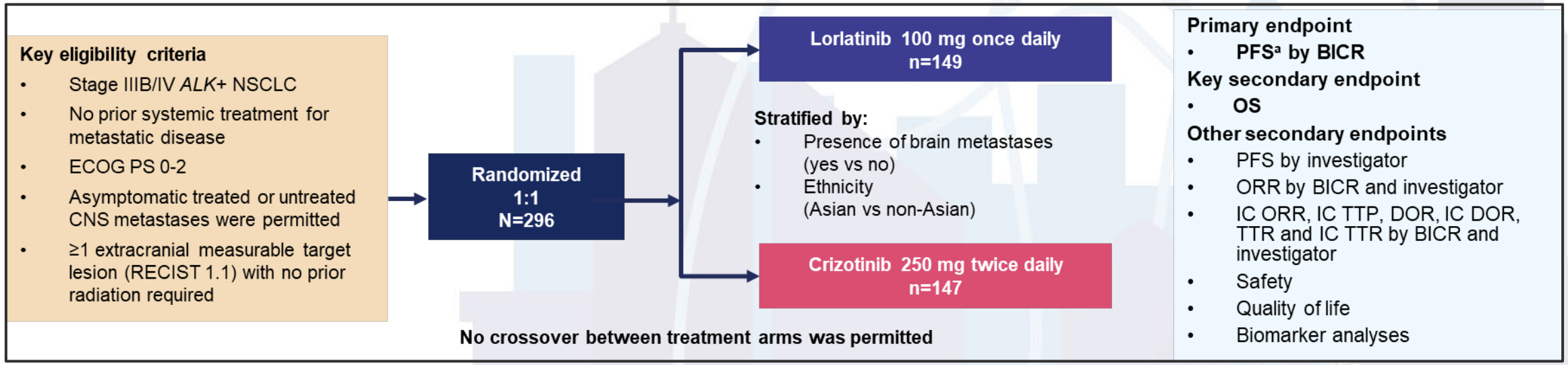
GECP lung cancer research

ALK REORDENADO

ALK

Lorlatinib vs crizotinib as first-line treatment for advanced ALK+ non-small cell lung cancer: 7-year update from the phase 3 CROWN study

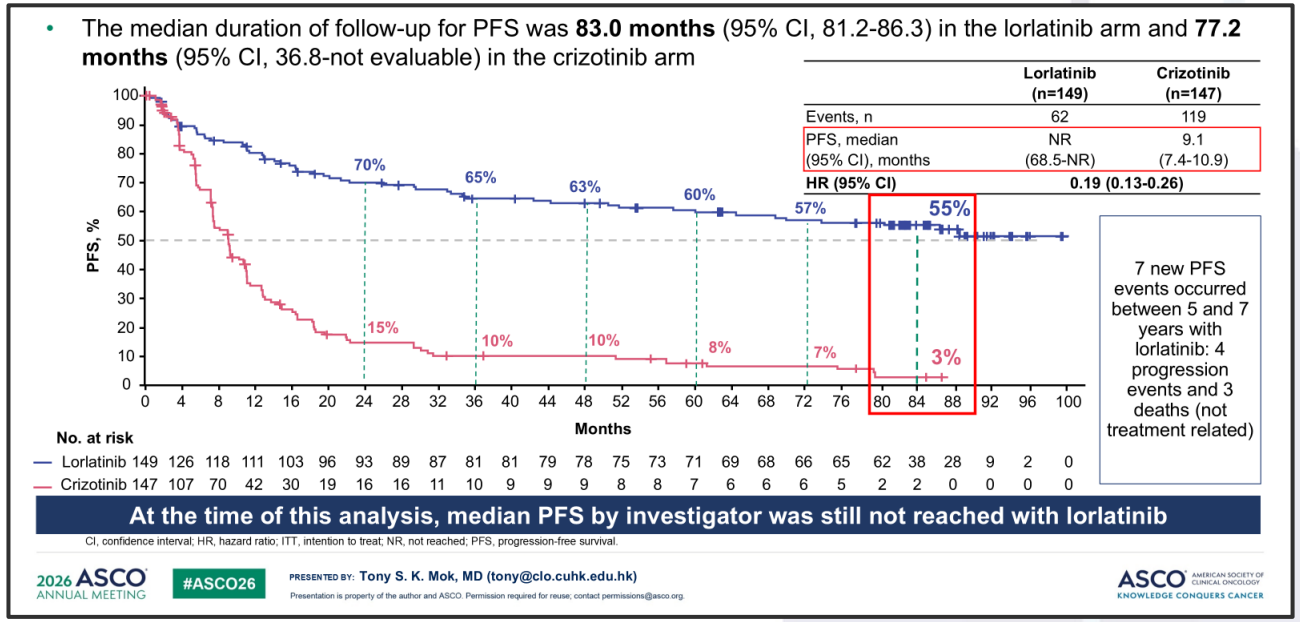
Tony S. K. Mok



ALK

Lorlatinib vs crizotinib as first-line treatment for advanced ALK+ non-small cell lung cancer: 7-year update from the phase 3 CROWN study

Tony S. K. Mok



- Sin PD a 24m → 79% de posibilidad de seguir sin EP a los 7 años.
- Beneficio en todos los subgrupos.
- T a la icPD: NR vs.16,4 m, HR 0,06 [0,05-0,12]. Sin nuevos eventos en SNC después de 30 m de tto.
- Análisis de ctDNA no detecta nuevas mutaciones de resistencia de ALK.

SLP: NR vs. 9,1 m, HR 0,19 [0,13-0,26]

SLP 7 años: 55 vs. 3%

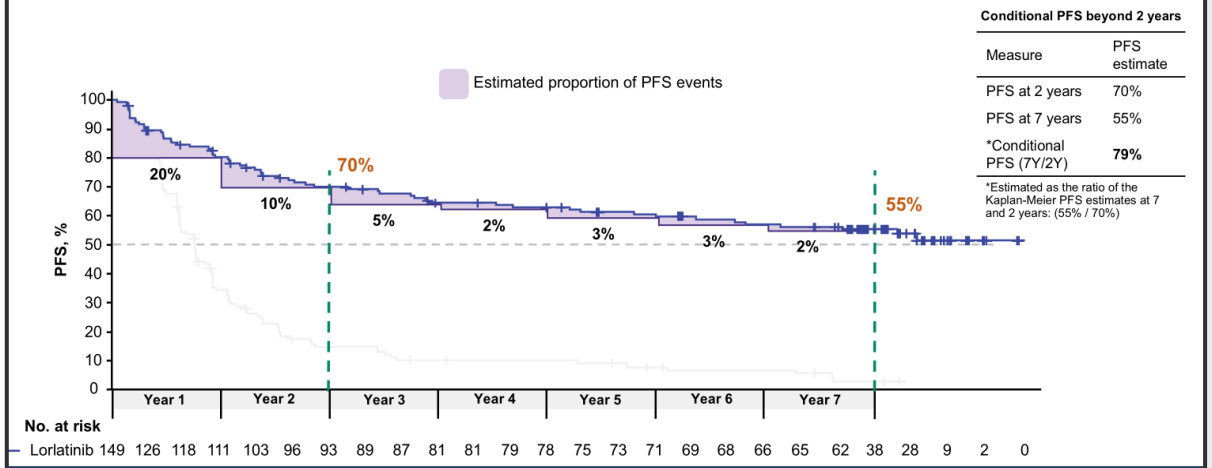
ALK

Lorlatinib vs crizotinib as first-line treatment for advanced ALK+ non-small cell lung cancer: 7-year update from the phase 3 CROWN study

Tony S. K. Mok

Iniciativa científica de: GECP lung cancer research

Estimated Proportion of PFS Events With Lorlatinib



Conditional PFS beyond 2 years

Measure	PFS estimate
PFS at 2 years	70%
PFS at 7 years	55%
*Conditional PFS (7Y/2Y)	**79%**

*Estimated as the ratio of the Kaplan-Meier PFS estimates at 7 and 2 years: (55% / 70%)

Patients without a PFS event in the first 24 months on lorlatinib have a 79%* probability of remaining alive and progression-free at 7 years

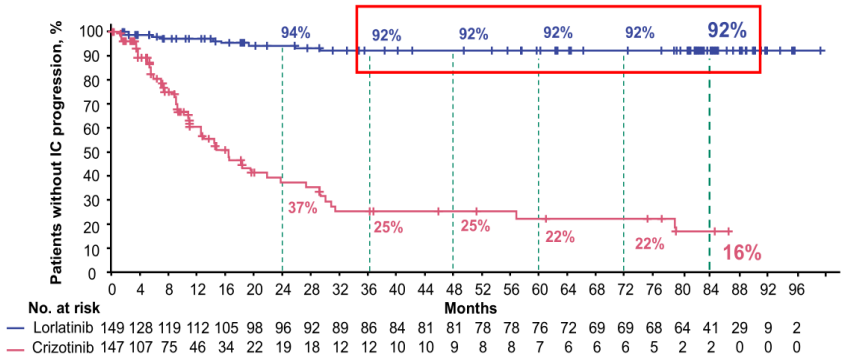
PFS, progression-free survival.

2026 ASCO ANNUAL MEETING #ASCO26

PRESENTED BY: Tony S. K. Mok, MD (tony@clo.cuhk.edu.hk)

ASCO KNOWLEDGE CONQUERS CANCER

Time to IC Progression in the ITT Population



	Lorlatinib (n=149)	Crizotinib (n=147)
Events, n	9	66
Time to IC progression, months, median (95% CI)	NR (NR-NR)	16.4 (12.7-21.9)
HR (95% CI)	**0.06 (0.03-0.12)**	

Tumor assessments, including brain MRI, have been performed every 8 weeks up to 5 years and every 16 weeks afterwards in all patients throughout the study

No new IC progression events occurred after the first 30 months on lorlatinib

CI, confidence interval; HR, hazard ratio; IC, intracranial; ITT, intention to treat; MRI, magnetic resonance imaging; NR, not reached.

2026 ASCO ANNUAL MEETING #ASCO26

PRESENTED BY: Tony S. K. Mok, MD (tony@clo.cuhk.edu.hk)

ASCO KNOWLEDGE CONQUERS CANCER

ALK

ALKOVE-1: Efficacy and safety of neladalkib in patients with advanced ALK+ NSCLC

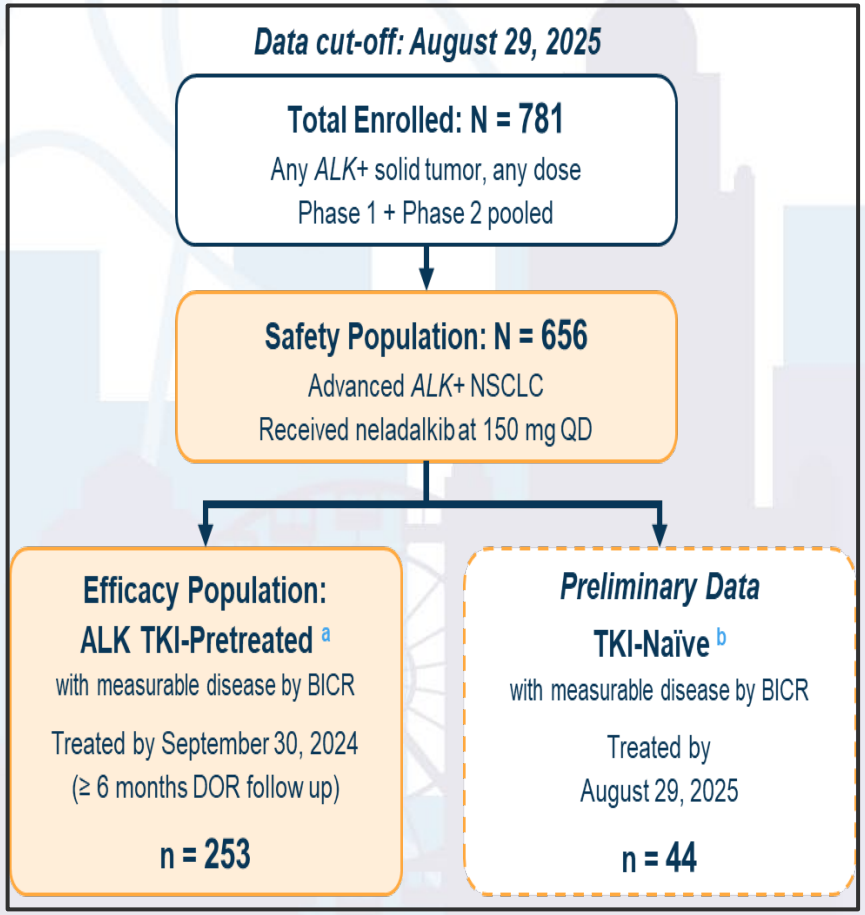
Jessica J. Lin

Iniciativa científica de: GECP lung cancer research

PHASE 1	PHASE 2: Neladalkib 150 mg QD (RP2D)			
	PATIENT POPULATION	PRIOR ALK TKI	PRIOR LINES CHEMO/I-O	PHASE 2 ENDPOINTS
Neladalkib dose escalation (15 – 200 mg QD) in patients with advanced *ALK*+ solid tumors	*ALK*+ NSCLC	1 prior 2G *(ceritinib, alectinib, or brigatinib)*	0-2	• **Primary:** ORR by BICR • **Secondary:** Additional efficacy measures (DOR, TTR, PFS, OS), intracranial activity, overall safety and tolerability, confirmation of PK profile
		2-3 prior, any generation *(crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib [a])*	0-2	
		1 prior 3G *(lorlatinib)*	≤ 1	
		None (TKI-naïve)	≤ 1	
		Any *(not eligible for other cohorts)*	Any	
	Other *ALK*+ Solid Tumors	≥ 1 prior ALK TKI or systemic therapy (or for whom no satisfactory standard therapy exists)	Any	

Neladalkib is an investigational product and has not been approved by the FDA or any other health authority.
BICR, blinded independent central review; **chemo**, chemotherapy; **DOR**, duration of response; **G**, generation; **I-O**, immunotherapy; **NSCLC**, non-small cell lung cancer; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **PK**, pharmacokinetic; **QD**, once daily; **RP2D**, recommended phase 2 dose; **TKI**, tyrosine kinase inhibitor; **TRK**, tropomyosin-related kinase; **TTR**, time to response.
[a] Excludes patients who received lorlatinib as the 1st prior ALK TKI.

2026 ASCO ANNUAL MEETING #ASCO26
PRESENTED BY: Jessica J. Lin, Mass General Brigham Cancer Institute, Boston, MA, USA



Neladalkib: inhibidor selectivo de ALK, penetra SNC. Evita EAs relacionados con TRK
Activo en M1 SNC, incluidos tratados con Lorlatinib y en portadores de mutación ALK G1202R simple o compuesta.

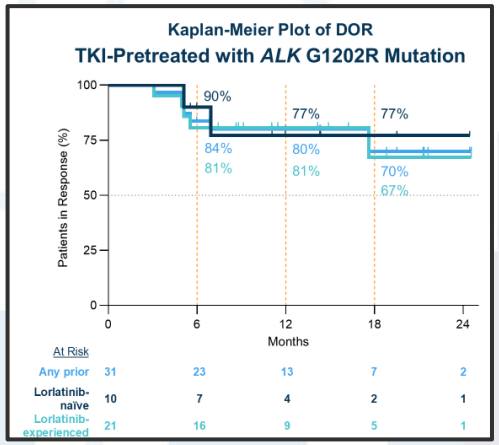
75% tras Lorlatinib

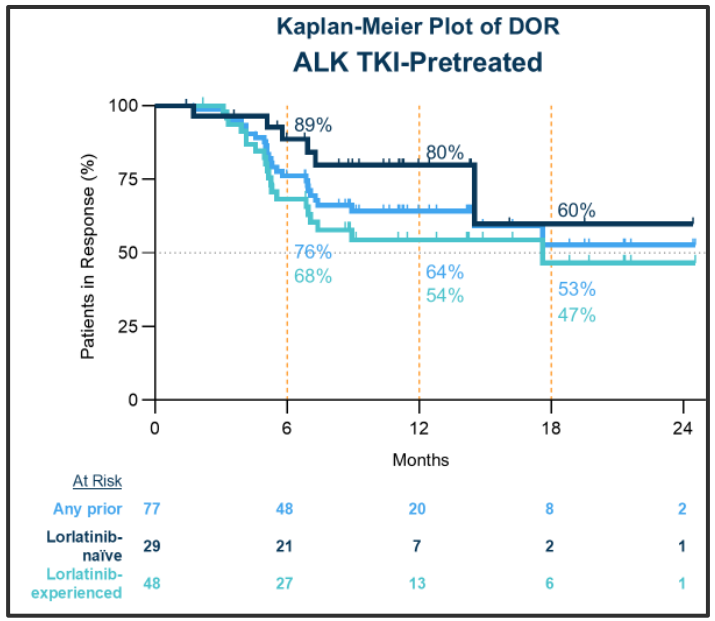
ALK

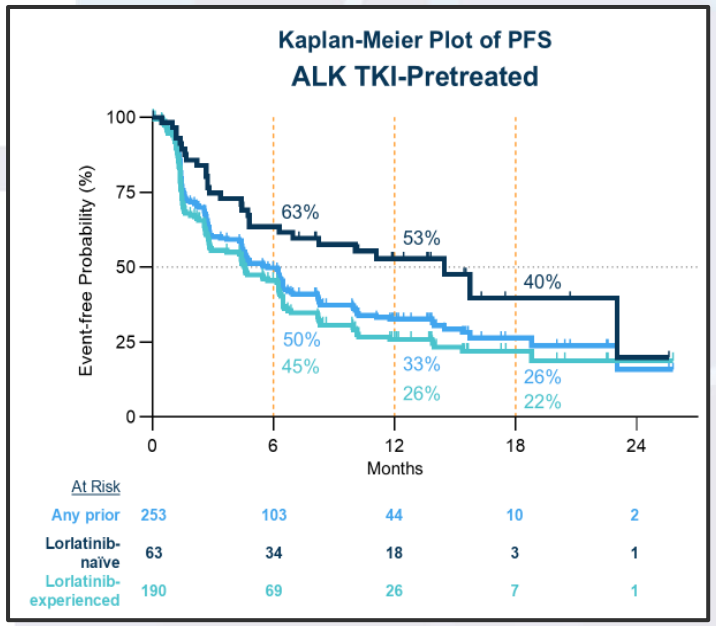
ALKOVE-1: Efficacy and safety of neladalkib in patients with advanced ALK+ NSCLC

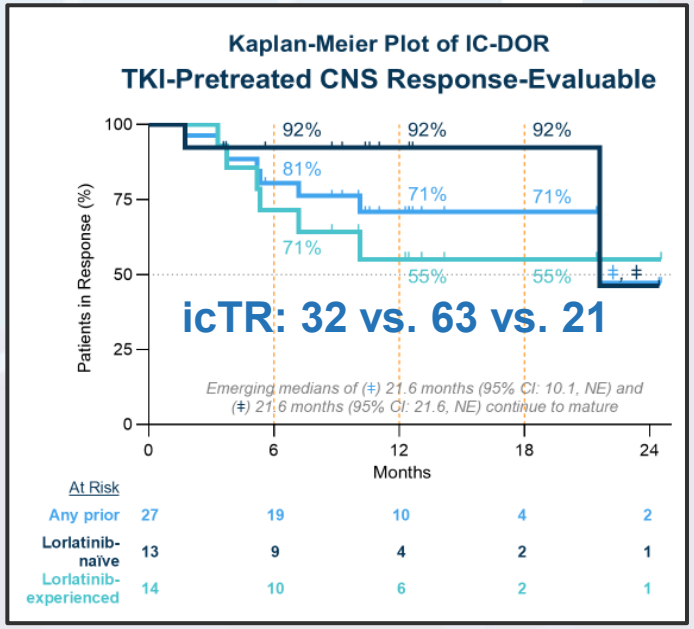
Jessica J. Lin

Advanced *ALK*+ NSCLC RECIST v1.1 by BICR	**Any prior ALK TKI** [a] (1–5 prior ALK TKIs ± chemotherapy) **N = 253**	**Lorlatinib-naive** (1–3 prior ALK TKIs ± chemotherapy) **N = 63**	**Lorlatinib-experienced** (1–5 prior ALK TKIs ± chemotherapy) **N = 190**
ORR, % (n/N) [95% CI]	**31%** (79/253) [b] [26, 37]	**46%** (29/63) [33, 59]	**26%** (50/190) [b] [20, 33]
CR, % (n/N)	2% (6/253) [c]	5% (3/63) [d]	2% (3/190) [d]









ALK

ALKOVE-1: Efficacy and safety of neladalkib in patients with advanced ALK+ NSCLC

Jessica J. Lin

1ª Línea

ALK TKI-naïve, BICR	Response-evaluable N = 44
ORR, % (n/N)	**86%** (38/44) [a]
CR, % (n/N)	9% (4/44) [b]
% DOR ≥ 12 months [95% CI] [c]	**91%** [70, 98]
DOR range	1.7+ to 14.8+ months

[a] Includes 2 single-timepoint PR pending confirmation for ongoing patients. [b] Includes 1 single-timepoint CR pending confirmation in ongoing patient with prior confirmed PR. [c] Analyses of DOR based on Kaplan-Meier estimates.

ALK TKI-naïve, BICR	CNS Response-evaluable N = 9
IC-ORR, % (n/N)	**78%** (7/9)
IC-CR, % (n/N)	44% (4/9) [d]
IC-DOR	**No CNS progression events among intracranial responders**
IC-DOR range	3.1+ to 7.0+ months

[d] Includes 1 single-timepoint IC-CR pending confirmation in ongoing patient with prior confirmed IC-PR.

- Disminución de dosis 17%: ALT y AST
- STOP por EAs: 5%
- Más frec: aumento de transaminasas (> pretratados)
- Evita neurotoxicidad relacionada con TRK

- Actividad clínica en previamente tratados y en 1ªL.
- Activo en SNC.
- Perfil de seguridad manejable.
- Fase 3 en marcha: en 1ªL, ALKAZAR trial (NCT06765109).

Wait or Treat? Managing Asymptomatic Brain Metastases in Oncogene-mutated NSCLC – Results of a Phase-III Randomized Controlled Trial

Anil Ramakant Tibdewal

Iniciativa científica de: GECP lung cancer research

Phase III, RCT, Open label, NCT05236946

Key eligibility
- Metastatic NSCLC
- EGFR or ALK mutation
- ECOG PS 0 -2
- Radiological measurable BM
- Completely Asymptomatic BM

Stratification factors
- GPA Score (0-2 vs >2)
- Synchronous vs metachronous BM

R 1:1 (n-208)

- **Upfront Cranial RT + TKIs ± Chemotherapy (n=105)**
- **Delayed Cranial RT* + TKIs ± Chemotherapy (n=103)**

Endpoints

Primary
- Intracranial PFS

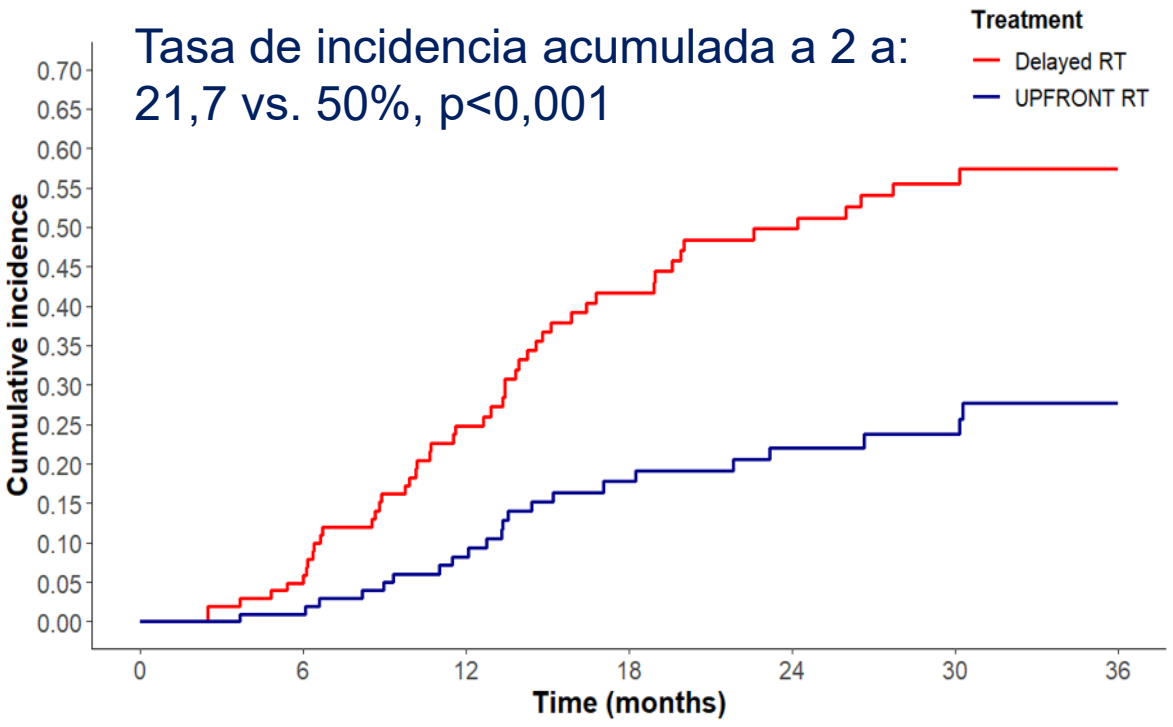
Secondary
- OS
- PFS
- Toxicity
- ORR
- Neurocognition
- PROM

*Cranial RT delivered at time of Intracranial PD or at patient's wish MRI brain every 3m for 1st year and then every 6m

2026 ASCO ANNUAL MEETING #ASCO26 PRESENTED BY: Dr. Anil Tibdewal, Wait or Treat – Managing ABM

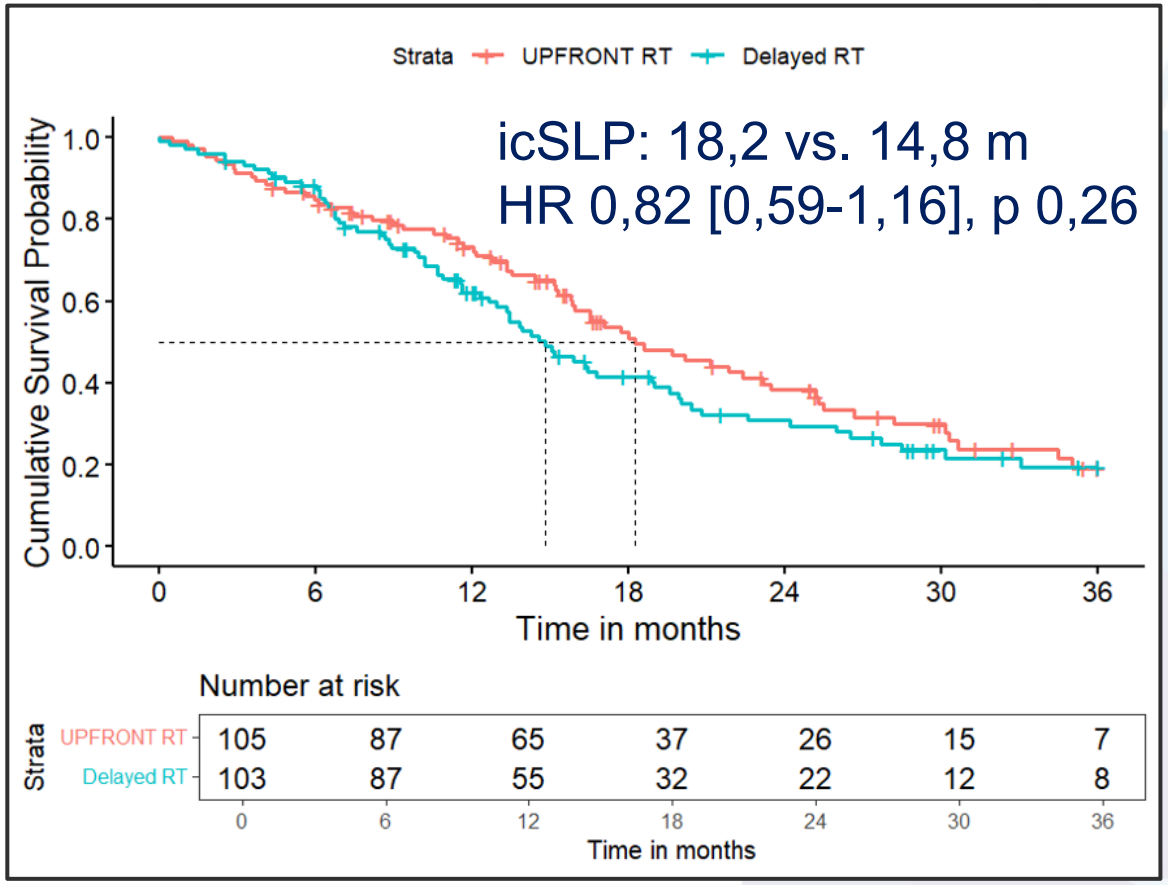
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Tasa de incidencia acumulada a 2 a: 21,7 vs. 50%, p<0,001



Wait or Treat? Managing Asymptomatic Brain Metastases in Oncogene-mutated NSCLC – Results of a Phase-III Randomized Controlled Trial

Anil Ramakant Tibdewal

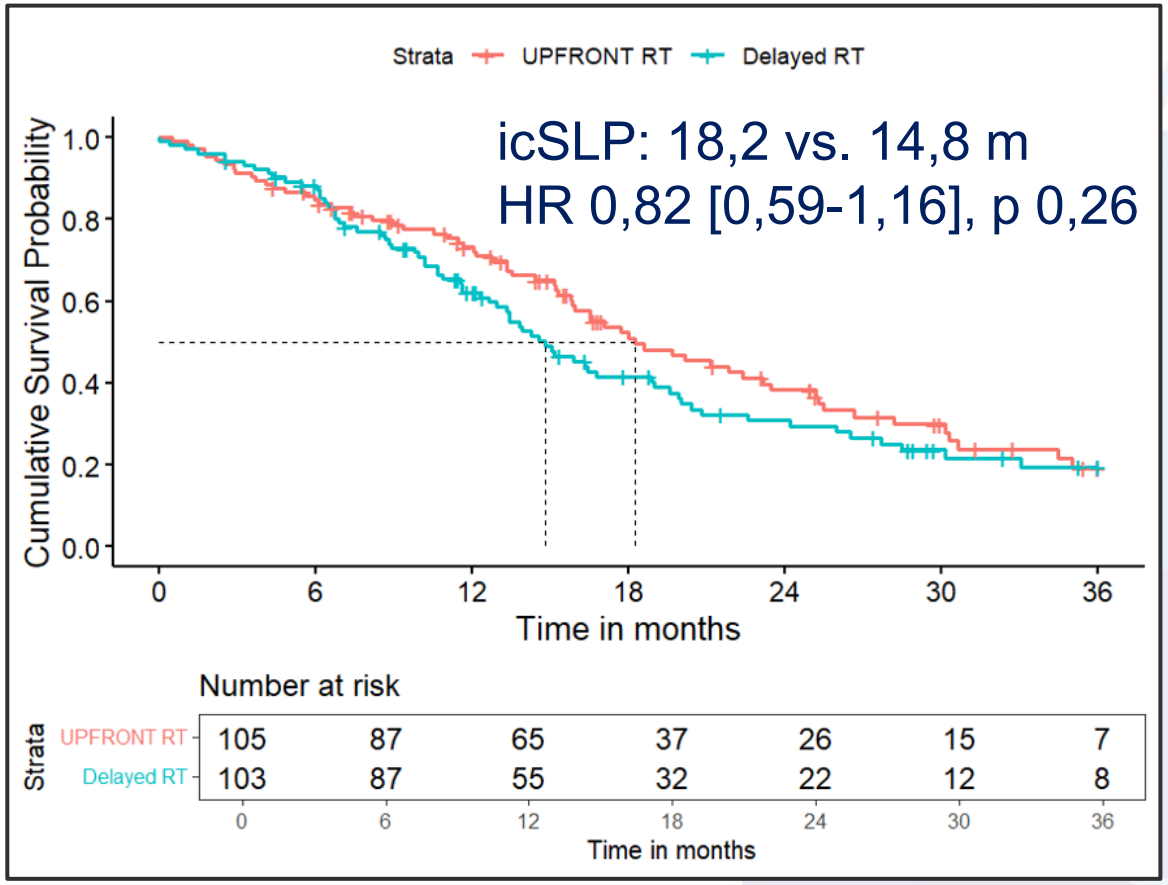


- SLP: 12,7 vs. 12 m, HR 1,05 [0,76-1,44], p0,75
- SV: 23,3 vs. 28,7 m, HR 1,45 [0,97-2,2], p 0,07
- 1ºsitio de PD:
  - SNC+EC: 11 vs. 30%
  - EC solo: 42 vs. 32%

Wait or Treat? Managing Asymptomatic Brain Metastases in Oncogene-mutated NSCLC – Results of a Phase-III Randomized Controlled Trial

Anil Ramakant Tibdewal

Iniciativa científica de: GECP lung cancer research



- SLP: 12,7 vs. 12 m, HR 1,05 [0,76-1,44], p0,75
- SV: 23,3 vs. 28,7 m, HR 1,45 [0,97-2,2], p 0,07
- 1ºsitio de PD:
  - SNC+EC: 11 vs. 30%
  - EC solo: 42 vs. 32%

→RT inicial reduce la progresión intracraneal.

→+/- 50% del grupo de tto diferido requirieron RT en un plazo de 2 años (más gfrec RT Holoc).

→El momento de la RT no afecta a la SV.

→Proporciona evidencia de nivel I para fundamentar las guías de ASCO-SNO-ASTRO.

Gracias