Lung Cancer UPDATES
IASLC HIGHLIGTHS
28-31 ENERO 2021
VIRTUAL

Iniciativa científica de:
GECP lung cancer research

TRATAMIENTO DIRIGIDO EN CPCNP – II (OTRAS MUTACIONES)

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Hospital de la Santa Creu i Sant Pau

MUTACIÓN o SOBREEXPRESIÓN DE *HER2*

rastuzumab Deruxtecan in HER2-Overexpressing Metastatic Non–Small Cell Lung Cancer (NSCLC): Interim Results of DESTINY-Lung01

ko Nakagawa,[1] Misako Nagasaka,[2] Enriqueta Felip,[3] Jose M. Pacheco,[4] Christina Baik,[5] Yasushi Goto,[6] Andreas Saltos,[7] Bob T. Li,[8] Hibiki Udagawa,[9] Shirish Gadgeel,[10] Haruyasu Murakami,[11] David Planchard,[12] Lyudmila Bazhenova,[13] az-Ares,[14] Maurice Perol,[15] Julien Mazieres,[16] Fabrice Barlesi,[17] Kapil Saxena,[18] Ryota Shiga,[18] Suddhasatta Acharyya,[18] Yingkai Cheng,[18] Javad Shahidi,[18] Pasi A. Jänne,[19] Egbert F. Smit[20]

On behalf of the DESTINY-Lung01 investigators

Trastuzumab Deruxtecan in HER2-Mutated Metastatic Non–Small Cell Lung Cancer (NSCLC): Interim Results of DESTINY-Lung01

Egbert F. Smit,[1] Kazuhiko Nakagawa,[2] Misako Nagasaka,[3] Enriqueta Felip,[4] Yasushi Goto,[5] Bob T. Li,[6] Jose M. Pacheco,[7] Haruyasu Murakami,[8] Fabrice Barlesi,[9] Andreas Saltos,[10] Maurice Perol,[11] Hibiki Udagawa,[12] Kapil Saxena,[13] Ryota Shiga,[13] Ferdinand Guevara,[13] Suddhasatta Acharyya,[13] Javad Shahidi,[13] David Planchard,[14] Pasi A. Jänne[15]

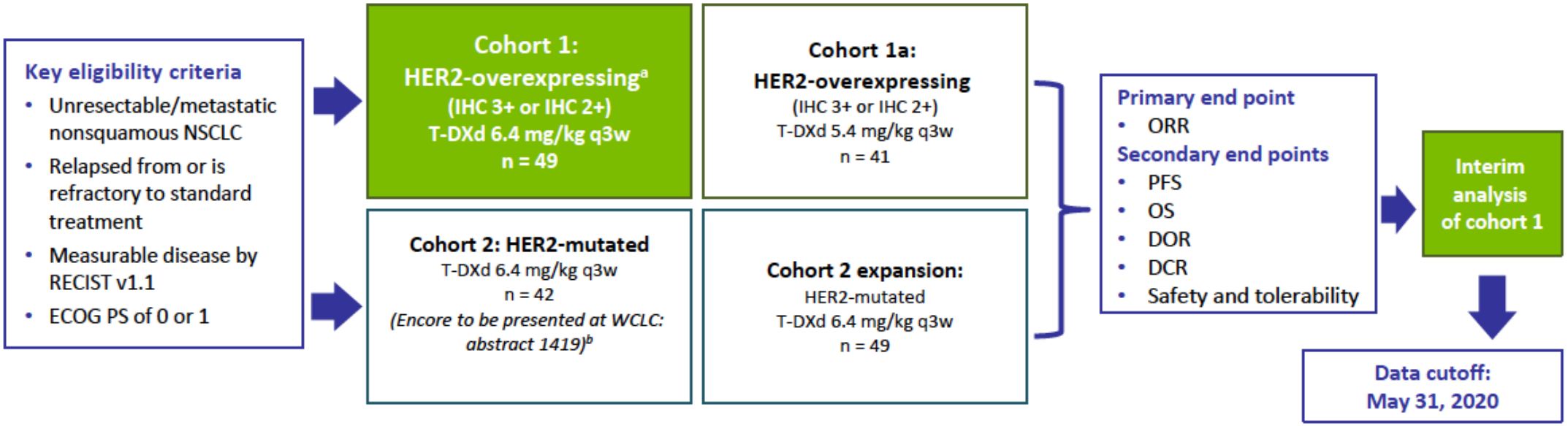
On behalf of the DESTINY-Lung01 investigators

ZENITH20 Trial: A Phase 2 International Trial

Updated efficacy, safety, and dosing management of poziotinib in previously treated EGFR and HER2 exon 20 NSCLC patients

R Cornelissen[1], MC Garassino[2], X Le[3], J Clarke[4], N Tchekmedyian[5], J Goldman[6], F Lebel[7], G Bhat[7], MA Socinski[8]

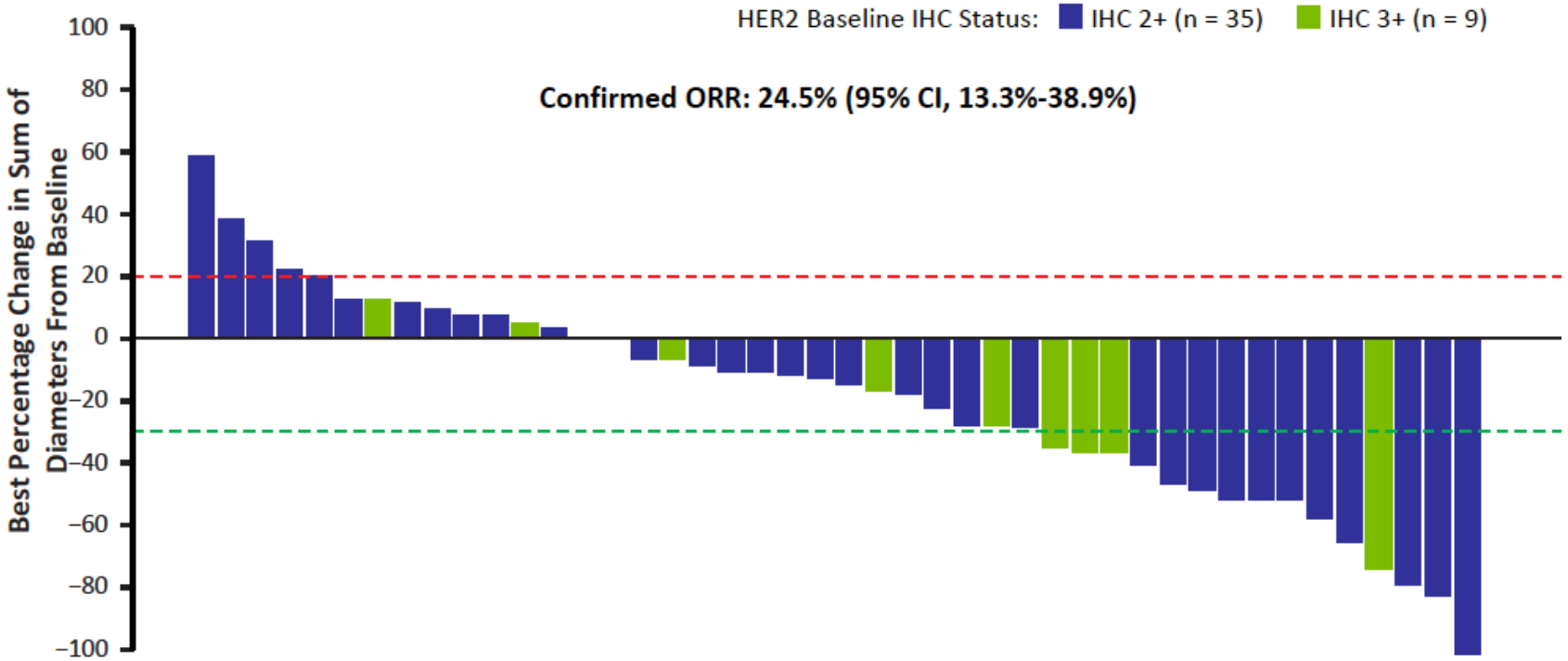
Phase 2 study of T-DXd, a novel antibody-drug conjugate, in patients with HER2-overexpressing or HER2-mutated metastatic NSCLC (NCT03505710)



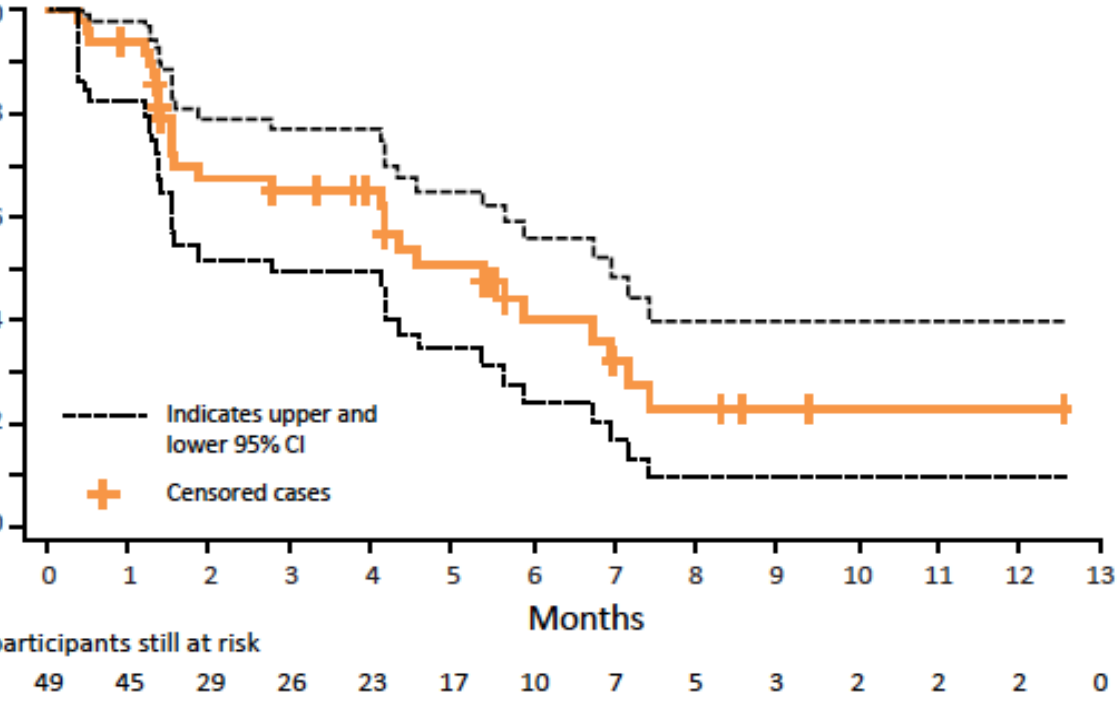
Demographics and Baseline Characteristics	Patients (N = 49)
Age, median (range), years	63.0 (37-85)
<65 years, n (%) | ≥75 years, n (%)	27 (55.1%) | 2 (4.1%)
Female, n (%)	19 (38.8%)
Region, n (%)	
Asia	12 (24.5%)
North America	19 (38.8%)
Europe	18 (36.7%)
HER2 IHC status, n (%)	
IHC 3+	10 (20.4%)
IHC 2+	39 (79.6%)
IHC 1+ | IHC 0 | missing	0 | 0 | 0

Demographics and Baseline Characteristics	Patients (N = 49)
Other gene abnormality status, n (%)	
EGFR/ALK/ROS1/BRAF	3 (6.1%)
No EGFR/ALK/ROS1/BRAF	14 (28.6%)
Not reported	32 (65.3%)
ECOG performance status, n (%) 0 | 1	14 (28.6%) | 35 (71.4%)
Presence of CNS metastases, n (%)	17 (34.7%)
Prior therapies, n (%)	49 (100.0%)
Platinum-based Anti–PD-1/PD-L1 Docetaxel	45 (91.8%) 36 (73.5%) 12 (24.5%)
Median number of prior lines of therapies (range)	3 (1-8)

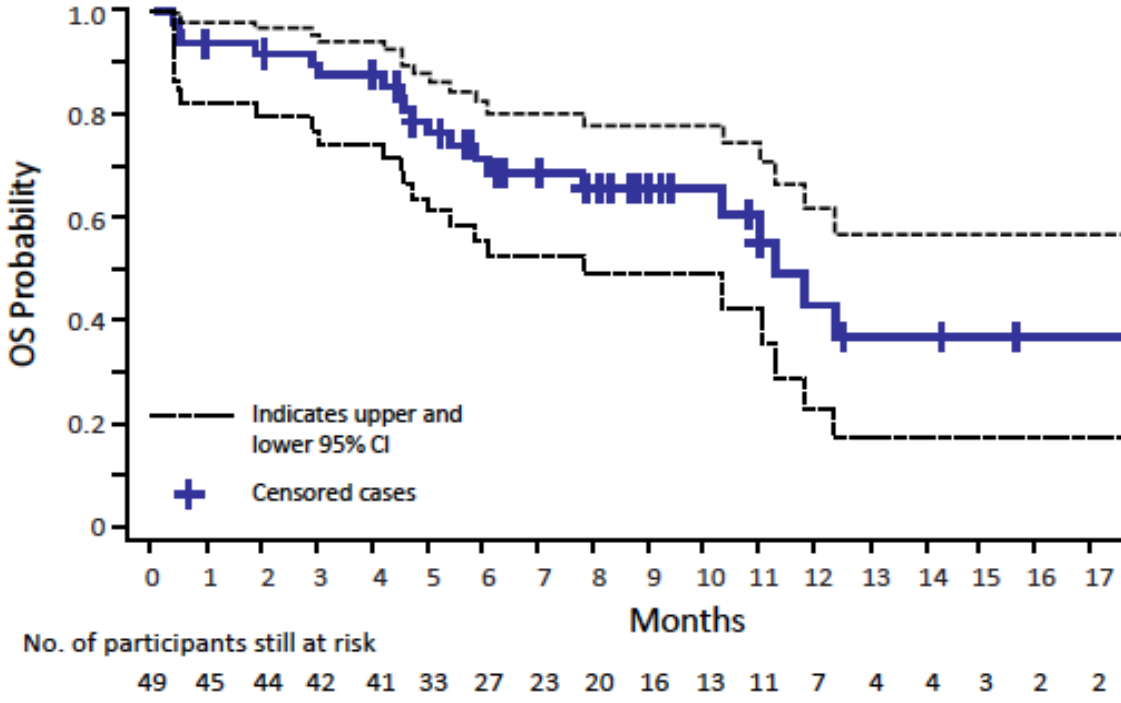
Response Assessment by ICR	IHC 3+ (n = 10)	IHC 2+ (n = 39)	Overall (N = 49)
Confirmed ORR, n (95% CI)	**20.0%** 2 (2.5-55.6)	**25.6%%** 10 (13.0-42.1)	**24.5%** 12 (13.3-38.9)
CR, n (%)	0	1 (2.6%)	1 (2.0%)
PR, n (%)	2 (20.0%)	9 (23.1%)	11 (22.4%)
SD, n (%)	6 (60.0%)	16 (41.0%)	22 (44.9%)
PD, n (%)	1 (10.0%)	10 (25.6%)	11 (22.4%)
Not evaluable, n (%)	1 (10.0%)	3 (7.7%)	4 (8.2%)
DCR, n (95% CI)	**80.0%** 8 (44.4-97.5)	**66.7%** 26 (49.8-80.9)	**69.4%** 34 (54.6-81.8)
Median DOR, months (95% CI)	**6.0 (NE-NE)**	**5.8 (3.2-NE)**	**6.0 (3.2-NE)**

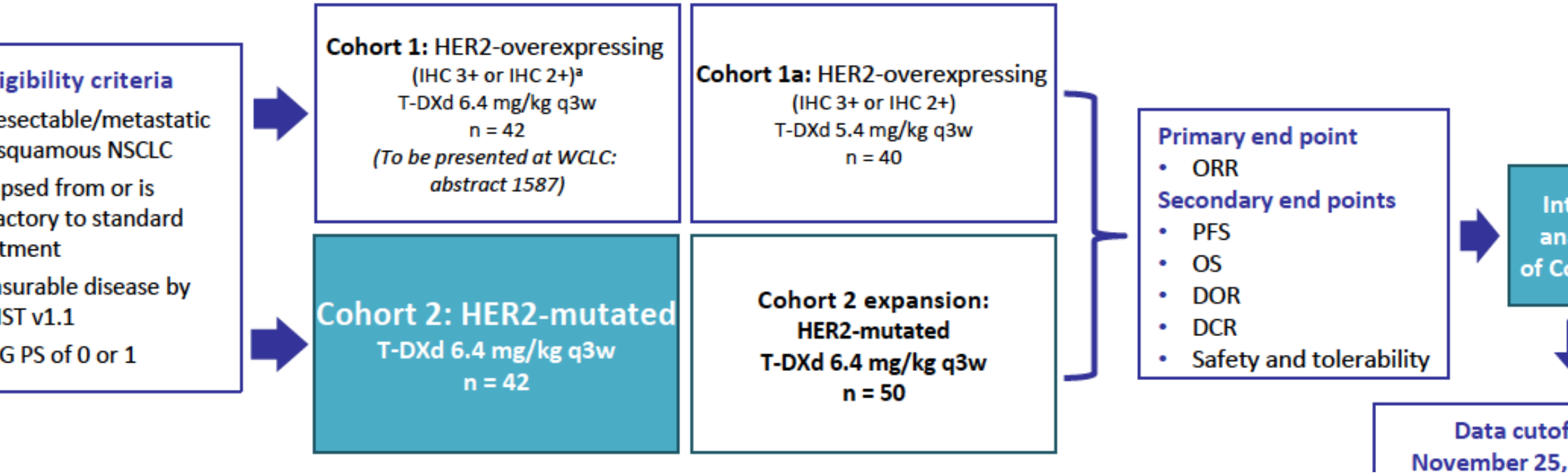


PFS (N = 49)
Median: 5.4 months (95% CI, 2.8-7.0 months)

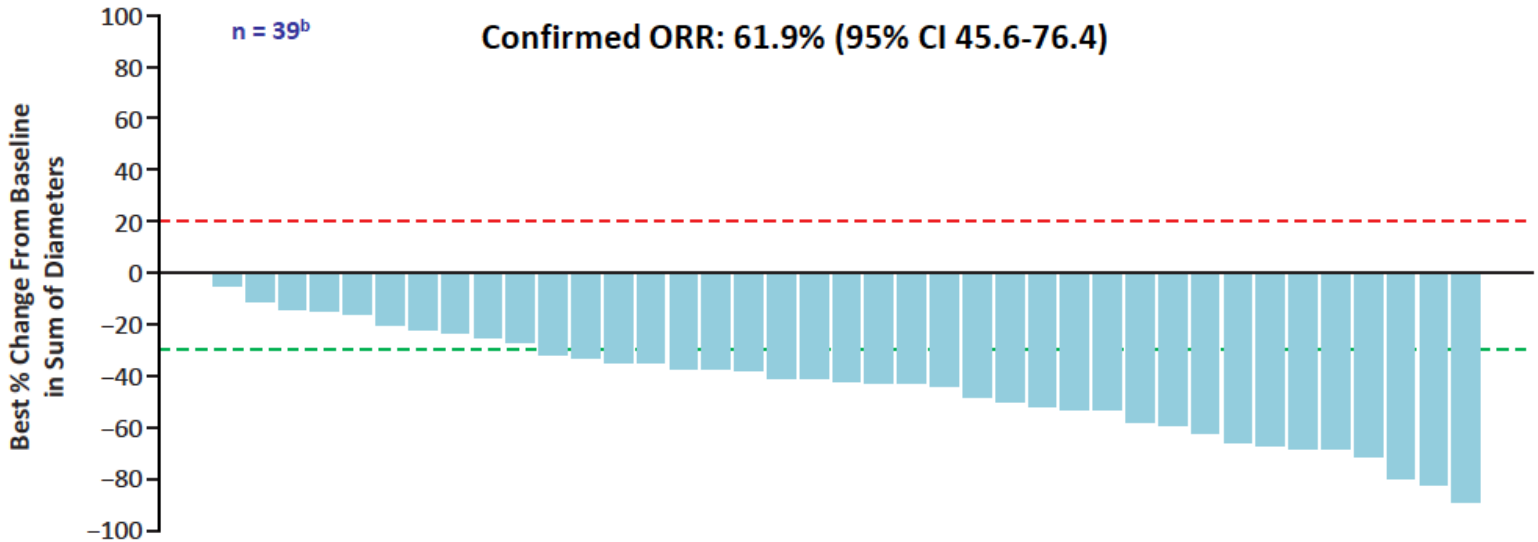


OS (N = 49)
Median: 11.3 months (95% CI, 7.8-NE)





Assessment by ICR	Patients (N = 42)
ORR	**61.9%** 26 (45.6-76.4)
%)	1 (2.4%)
%)	25 (59.5%)
%)	12 (28.6%)
%)	2 (4.8%)
aluable, n (%)	2 (4.8%)
	90.5% 38 (77.4-97.3)
OR, months (95% CI)	NE (5.3-NE)
S, months (95% CI)	14 (6.4-14.0)
S, months (95% CI)	NE (11.8-NE)



Es of Special Interest: ILD

All Patients (N = 49)						
)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/Tot
dicated drug-ted ILD[a]	2 (4.1%)	3 (6.1%)	0	0	3 (6.1%)	8 (16.3%)

dicated drug-related ILDs[b]

- edian time to onset was 64.5 days (range, 2-126 days)
- patients had drug withdrawn
- eroid treatment was used in patients who had grade 2 = 3) and those who had grade 5 ILDs (n = 3)
- atients recovered (grade 1 [n = 1] and grade 2 [n = 2]) and atients had not recovered by data cutoff (grade 1 [n = 1] d grade 2 [n = 1])
- f 8 patients had immune checkpoint inhibitors included in eir prior lines of therapy

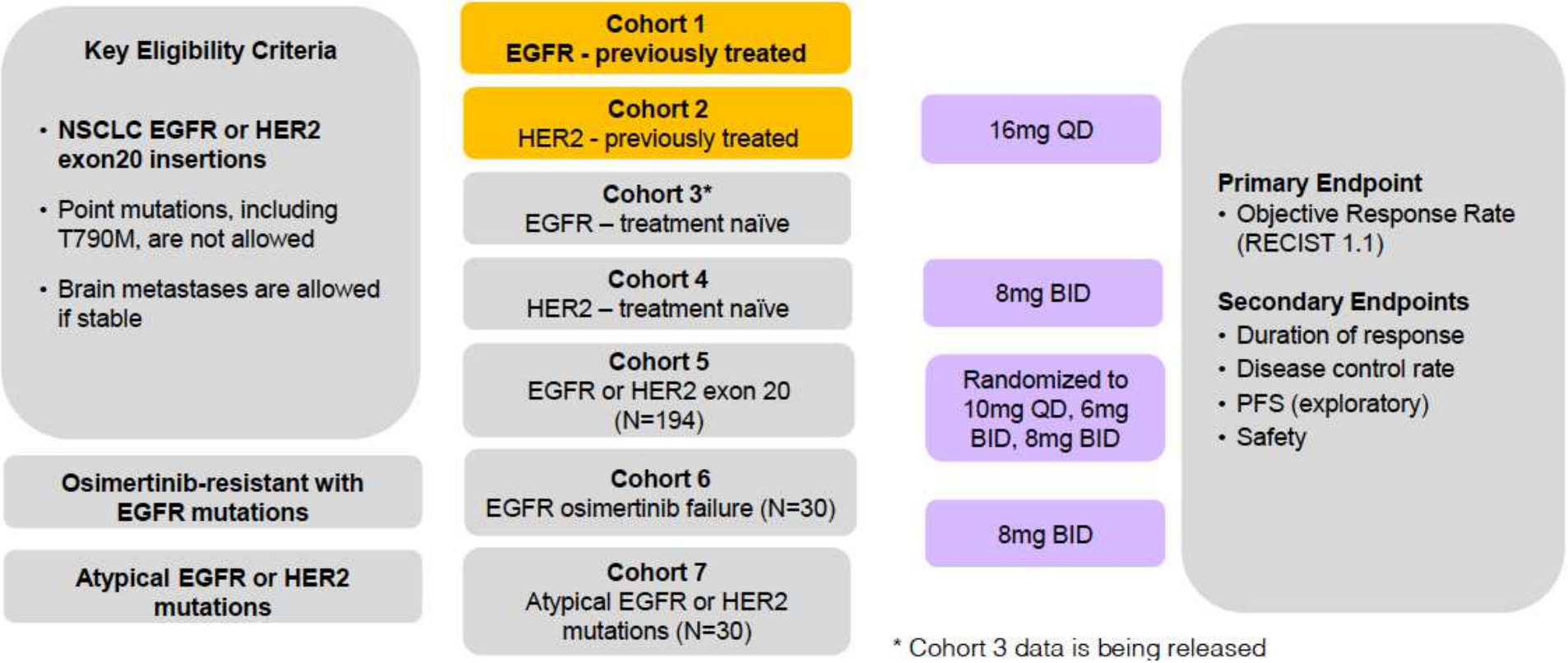
Grade 5 ILD[c] events

- Medical history of the 3 patients included
  1. Pulmonary embolism, productive cough, dyspnea, pleural effusion, and lobectomy; 4 prior lines of therapy
  2. Cough, dyspnea, pleural effusion, and pulmonary embolism; 5 prior lines therapy
  3. Dyspnea, SLE without lung involvement, and TTP; 1 prior line of therapy
- Steroid treatment was initiated within 5 days after the event wa reported by the investigator[d]
- All had previously received immune checkpoint inhibitors
- Primary cause of death was PD in 2 patients and pneumonitis in patient

ZENITH20 Trial: A Phase 2 International Trial

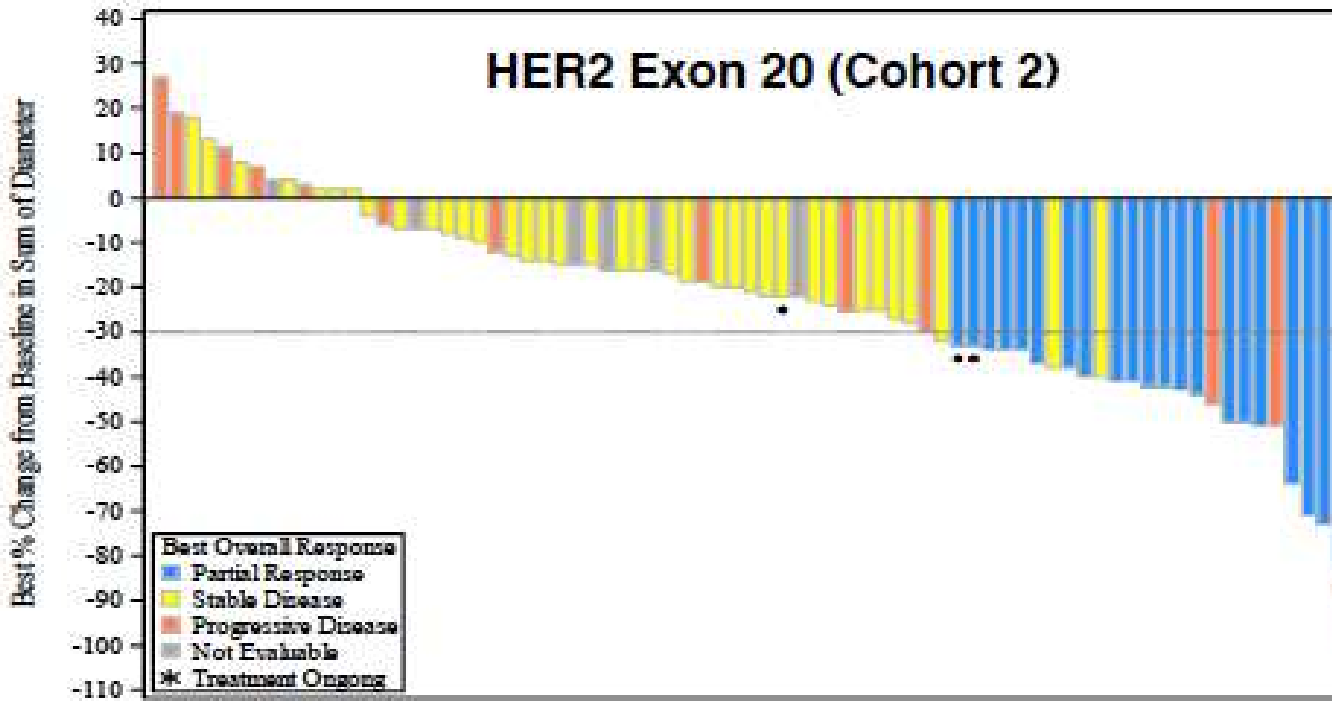
Updated efficacy, safety, and dosing management of poziotinib in previously treated EGFR and HER2 exon 20 NSCLC patients

R Cornelissen[1], MC Garassino[2], X Le[3], J Clarke[4], N Tchekmedyian[5], J Goldman[6], F Lebel[7], G Bhat[7], MA Socinski[8]



* Cohort 3 data is being released

	2L HER2 Exon 20 (N=90)
(n), [95% CI]	**27.8%** (25) [18.9, 38.2%]
nfirmed ORR (n), CI]	**31.1%** (28) [21.8, 41.7%]
(n), CI]	**70.0%** (63) [59.4, 79.2%]
median (months), CI]	**5.1** [4.2, 5.5]
median (months), CI]	**5.5** [3.9, 5.8]



Abstract 3255

Phase 1/2 TRIDENT-1 Study of Repotrectinib in Patients with *ROS1*+ or *NTRK*+ Advanced Solid Tumors

Byoung Chul Cho,[1] Robert C. Doebele,[2] Jessica J. Lin,[3] Misako Nagasaka,[4] Christina Baik,[5] Anthonie J. van der Wekken,[6] Vamsidhar Velcheti,[7] Ki Hyeong Lee,[8] Stephen V. Liu,[9] Benjamin Solomon,[10] Steven Kao,[11] Matthew G. Krebs,[12] Viola Zhu,[13] Shanna Stopatschinskaja,[14] D. Ross Camidge,[15] Alexander Drilon[16]

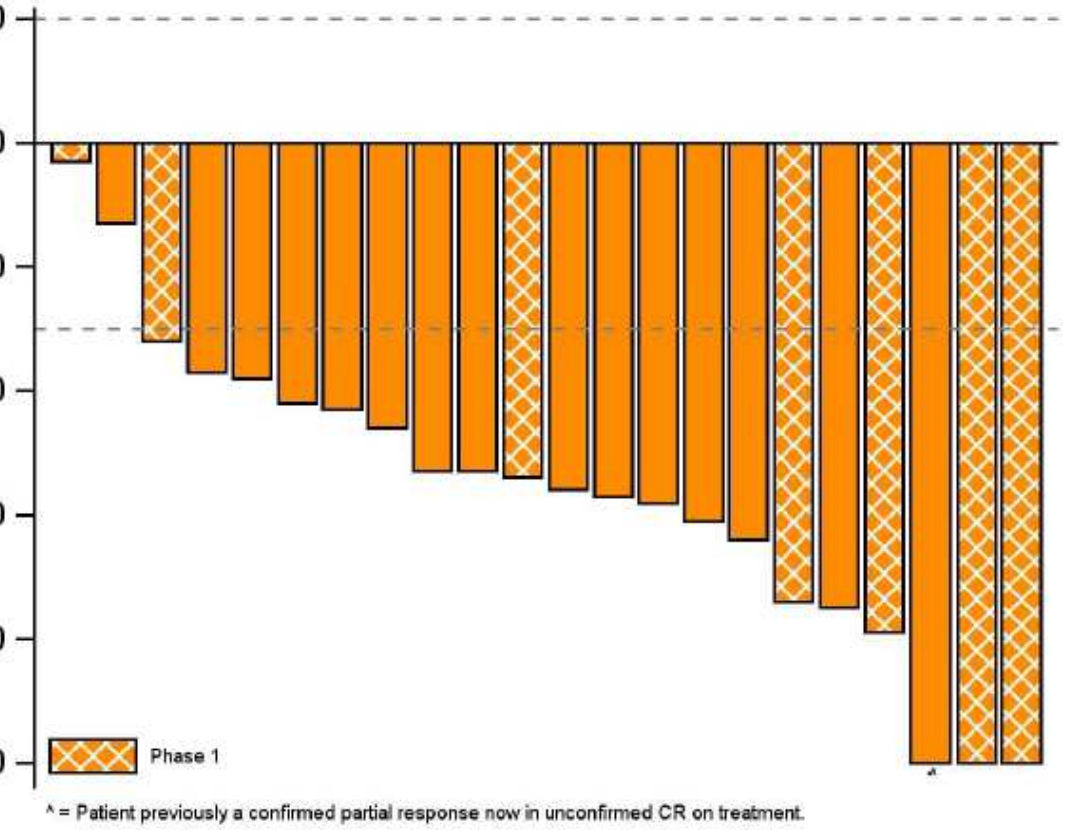
TRIDENT-1 Study Design and Early Interim Phase 2 Data as of August 2020

ROS1+ Advanced NSCLC				*NTRK*+ Advanced Solid Tumors	
EXP-1 ROS1 TKI naïve (n=55)	**EXP-2** 1 prior ROS1 TKI AND 1 platinum-based chemotherapy (n=60)	**EXP-3** 2 prior ROS1 TKIs AND No prior chemotherapy (n=40)	**EXP-4** 1 prior ROS1 TKI AND No prior chemotherapy (n=60)	**EXP-5** TRK TKI naïve (n=55)	**EXP-6** TRK TKI pretreated (n=40)
ORR **86% (6/7)** 95% CI, 42–100	**ORR** **40% (2/5)** 95% CI, 5–85	**ORR** **40% (2/5)** 95% CI, 5–85	**ORR** **67% (4/6)** 95% CI, 22–96	**Not Reported**	**ORR** **50% (3/6)** 95% CI, 12–88

Today's presentation will focus on UPDATED Phase 2 EXP-1 data (N=15) utilizing a data cutoff of 31 December 2020:
- Median age 58 (range 30-76); ECOG PS 1 = 60%; Prior Chemotherapy Use = 20%

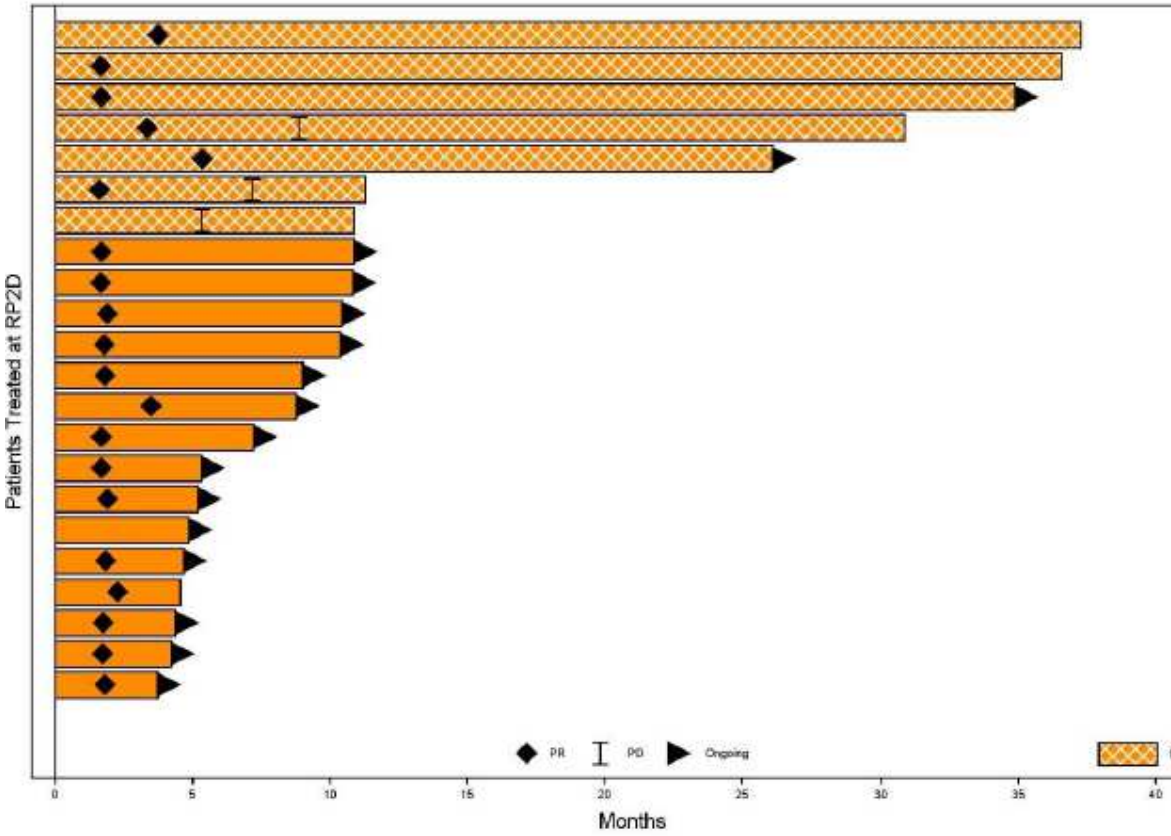
Previously reported Phase 1 *ROS1*+ TKI-Naïve results (N=11) based on data cutoff by BICR of 22 July 2019:
- ORR: 91% (10/11) (95% CI: 59 – 100)
  - ORR 86% (6/7) at or above the Phase 2 recommended dose
- Median DOR (95% CI): 23.1 months (5.6 - NR)
- Median PFS (95% CI): 24.6 months (7.2 - NR)

Overall Response (N=22)



^ = Patient previously a confirmed partial response now in unconfirmed CR on treatment.

Duration of Treatment (N=22):†



	Phase 2 N=15	Phase 1+2 N=22
Confirmed ORR, % (95% CI)	93% (68–100)	91% (71–99)

	Phase 1 n=7	Phase 2 n=15
Remaining on treatment, n (%)	2 (29)	14 (93)
On treatment >30 months, n (%)	4 (57)	–
Median Time on treatment, months (range)	30.9 (10.9–37.3)	5.3 (3.7+–10.9+)

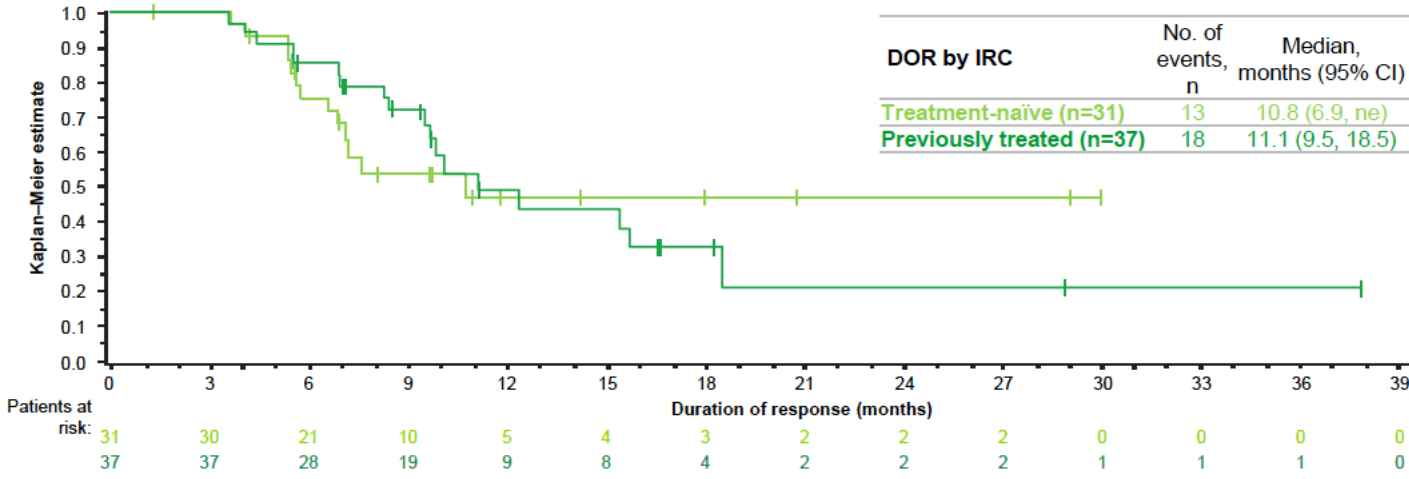
Tepotinib in patients with *MET* exon 14 (*MET*ex14) skipping advanced NSCLC: Updated efficacy results from VISION Cohort A

Paul K. Paik,[1,2] Hiroshi Sakai,[3] Enriqueta Felip,[4] Remi Veillon,[5] Marina Chiara Garassino,[6] Jo Raskin,[7] Santiago Viteri,[8] Julien Mazieres,[9] Alexis B. Cortot,[10] Egbert Smit,[11] Michael Thomas,[12] Byoung Chul Cho,[13] Pierfranco Conte,[14] James Chih-Hsin Yang,[15] Masahiro Morise,[16] Yuh-Min Chen,[17] Keunchil Park,[18] Maya Gottfried,[19] Christian Britschgi,[20] Rolf Bruns,[21] Gordon Otto,[22] Andreas Johne,[22] Xiuning Le[23]

ficacy cording to C	Treatment-naïve (n=69)	Previously treated (n=83)	Overall (N=152)
RR, (95% CI)	**44.9** (32.9, 57.4)	**44.6** (33.7, 55.9)	**44.7** (36.7, 53.0)
DR, n (%)			
CR	0	0	0
PR	31 (44.9)	37 (44.6)	68 (44.7)
SD	16 (23.2)	23 (27.7)	39 (25.7)
PD	13 (18.8)	13 (15.7)	26 (17.1)
NE	9 (13.0)	10 (12.0)	19 (12.5)
edian DOR, onths (95% CI)	10.8 (6.9, ne)	11.1 (9.5, 18.5)	11.1 (8.4, 18.5)
edian PFS, onths (95% CI)	8.5 (6.8, 11.3)	10.9 (8.2, 12.7)	8.9 (8.2, 11.2)

ata cut-off: July 1, 2020.

Responses to tepotinib treatment were durable and consistent irrespective of therapy line



- Overall, median DOR (95% CI) was 11.1 months (8.4, 18.5)

Efficacy and Safety of Larotrectinib in Patients With Tropomyosin Receptor Kinase (TRK) Fusion Lung Cancer

Daniel S. W. Tan
National Cancer Center, Singapore

On behalf of:
Daniel S. W. Tan,[1] Anna F. Farago,[2] Shivaani Kummar,[3] Victor Moreno,[4] Jyoti Patel,[5] Ulrik Lassen,[6] Benjamin Solomon,[7] Lee Rosen,[8] Serge Leyvraz,[9] John A. Reeves,[10] Nicoletta Brega,[10] Laura Dima,[10] Barrett H. Childs,[10] Alexander Drilon[11]

Adult phase I trial (NCT02122913)
- Age ≥18 years
- Advanced solid tumors

n=1

Adult/adolescent phase II basket trial (NAVIGATE, NCT02576431)
- Age ≥12 years
- Advanced solid tumors
- TRK fusion cancer

n=13

14 patients with TRK fusion lung cancer

Patient characteristics

Median age, range	52 (25–76)
Sex, n (%)	
Male	8 (57)
Female	6 (43)
***NTRK* fusion, n (%)**	
NTRK1	11 (79)
NTRK2	0
NTRK3	3 (21)
CNS metastases at baseline, n (%)	
Yes	7 (50)
No	7 (50)
Number of prior systemic therapies, median (range)†	3 (0–5)
Number of prior systemic therapies, n (%)	
0	1 (7)
1	4 (29)
2	2 (14)
≥3	7 (50)

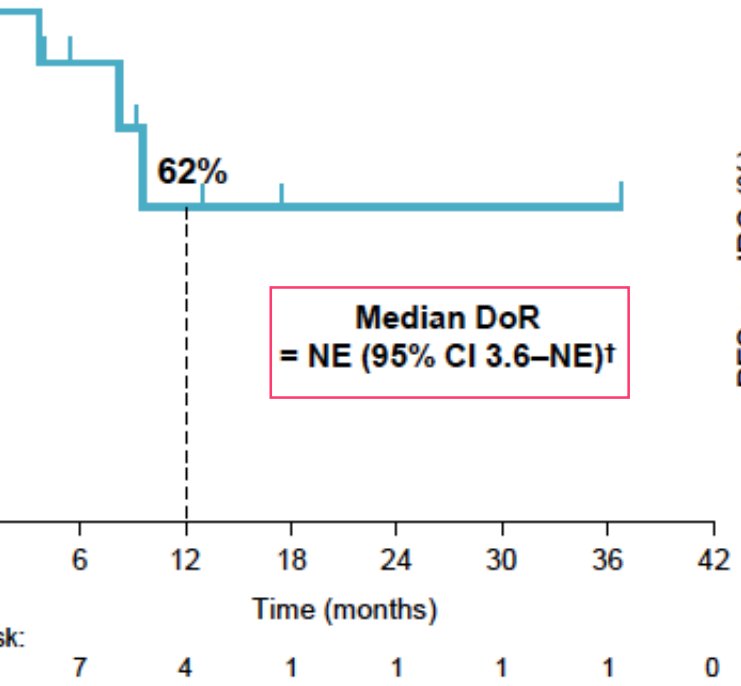
Dosing
- Larotrectinib, 100 mg BID continuously
- 28-day cycles

Endpoints
- **Primary**
  - Best ORR per IRC and INV (RECIST v1.1)
- **Secondary**
  - DoR
  - PFS
  - OS
  - Safety

Data cut-off: July 15, 2019

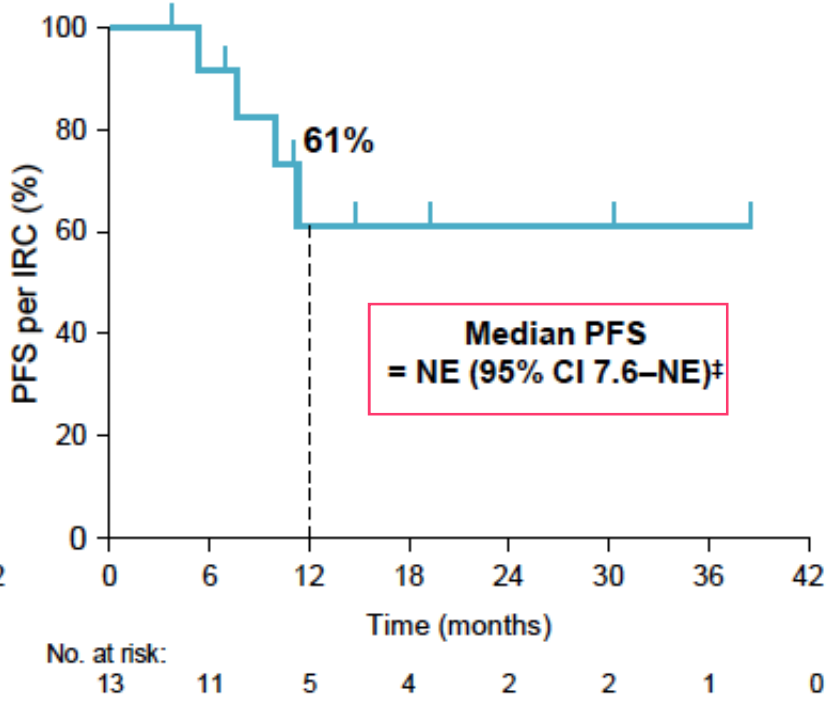
†Median prior systemic therapies for CNS metastases patients = 1 (range 0–4). The best overall response to prior therapy was PR in two patients, SD in two patients and PD in one patient. Responses were unavailable for two patients.
BID, twice daily; CNS, central nervous system; DoR, duration of response; INV, investigator; IRC, independent review committee; *NTRK*, neurotrophic tyrosine receptor kinase; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST, response evaluation criteria in solid tumors; SD, stable disease; TRK, tropomyosin receptor kinase.

DoR per IRC in all lung cancer patients



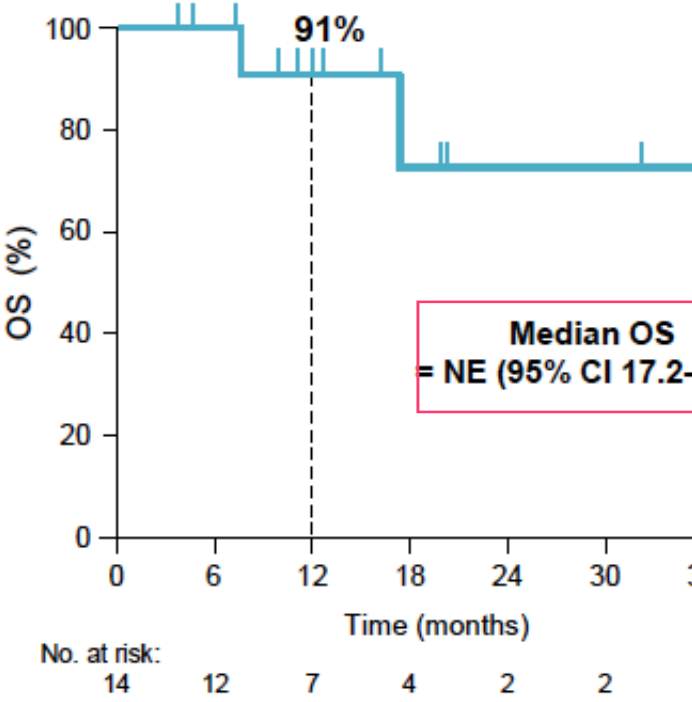
CNS metastases subset (n=7):
Median DoR = 9.5 months (95% CI 3.6–NE)

PFS per IRC in all lung cancer patients



In CNS metastases subset (n=7):
- Median PFS = 9.9 months (95% CI 5.3–NE)

OS in all lung cancer patients



In CNS metastases subset (n=7):
- Median OS = 17.2 months (95% CI 7.6

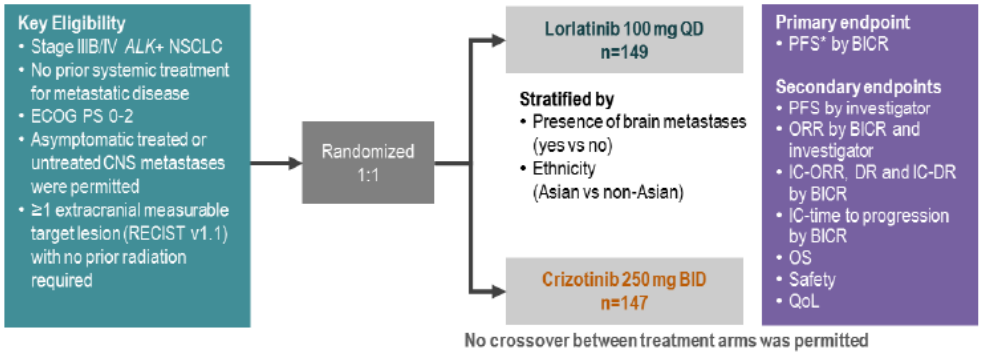
edian follow-up of 12.9 months. ‡At a median follow-up of 19.3 months. §At a median follow-up of 12.6 months.
nfidence interval; CNS, central nervous system; DoR, duration of response; INV, investigator; IRC, independent review committee; NE, not estimable; OS, overall survival; PFS, progression-free survival.

Patient-reported outcomes from the randomized Phase 3 CROWN study of first-line lorlatinib versus crizotinib in *ALK*+ NSCLC

Julien Mazieres,[1] Laura Iadeluca,[2] Alice T. Shaw,[3] Benjamin Solomon,[4] Todd M. Bauer,[5] Filippo de Marinis,[6] Enriqueta Felip,[7] Yasushi Goto,[8] Dong-Wan Kim,[9] Tony Mok,[10] Arlene Reisman,[2] Holger Thurm,[11] Anna Polli,[12] Geoffrey Liu[13]

INTRODUCTION

- Lorlatinib, a 3rd-generation ALK inhibitor, significantly improved progression-free survival compared with crizotinib in the CROWN Phase 3 study in patients with previously untreated advanced *ALK*-positive NSCLC (NCT03052608)



No crossover between treatment arms was permitted

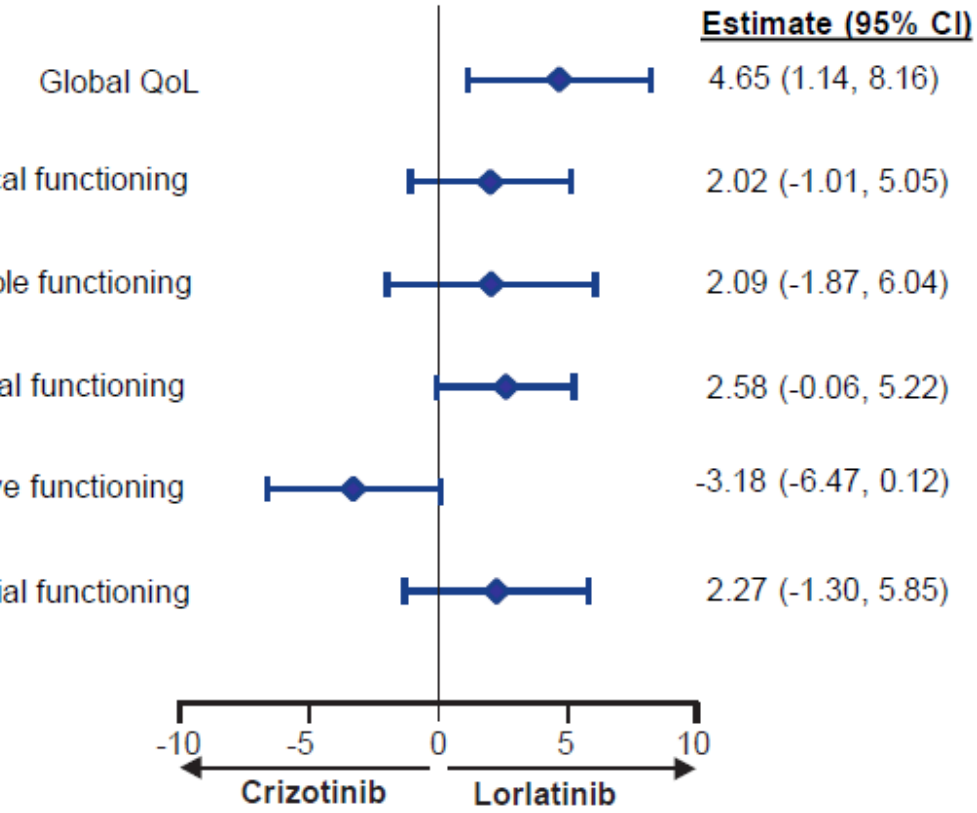
- Improvement in global quality of life (QoL) was greater in patients receiving lorlatinib versus crizotinib
- Here, we report additional patient reported outcomes (PROs) from the CROWN Phase 3 study

METHODS

- Patients (n=296) with *ALK*+ NSCLC were randomized to receive either lorlatinib or crizotinib
- PROs were assessed using the EORTC QLQ-C30 and QLQ-LC13 at baseline, then on the first day of each cycle (28 days) through end of treatment (EOT)
- A longitudinal random-intercept, random-slope, mixed-effect model was used to assess score change from baseline. Longitudinal mean score changes from baseline were compared between treatment arms (≥10-point difference considered clinically meaningful). No adjustments were made for multiple comparisons
- Time to deterioration (TTD) in the composite endpoint of pain in chest, dyspnea, and cough, and in global QoL, was compared between treatment arms using a 1-sided log-rank test stratified by randomization stratification factors. The treatment effect was estimated using a Cox Proportional Hazard model

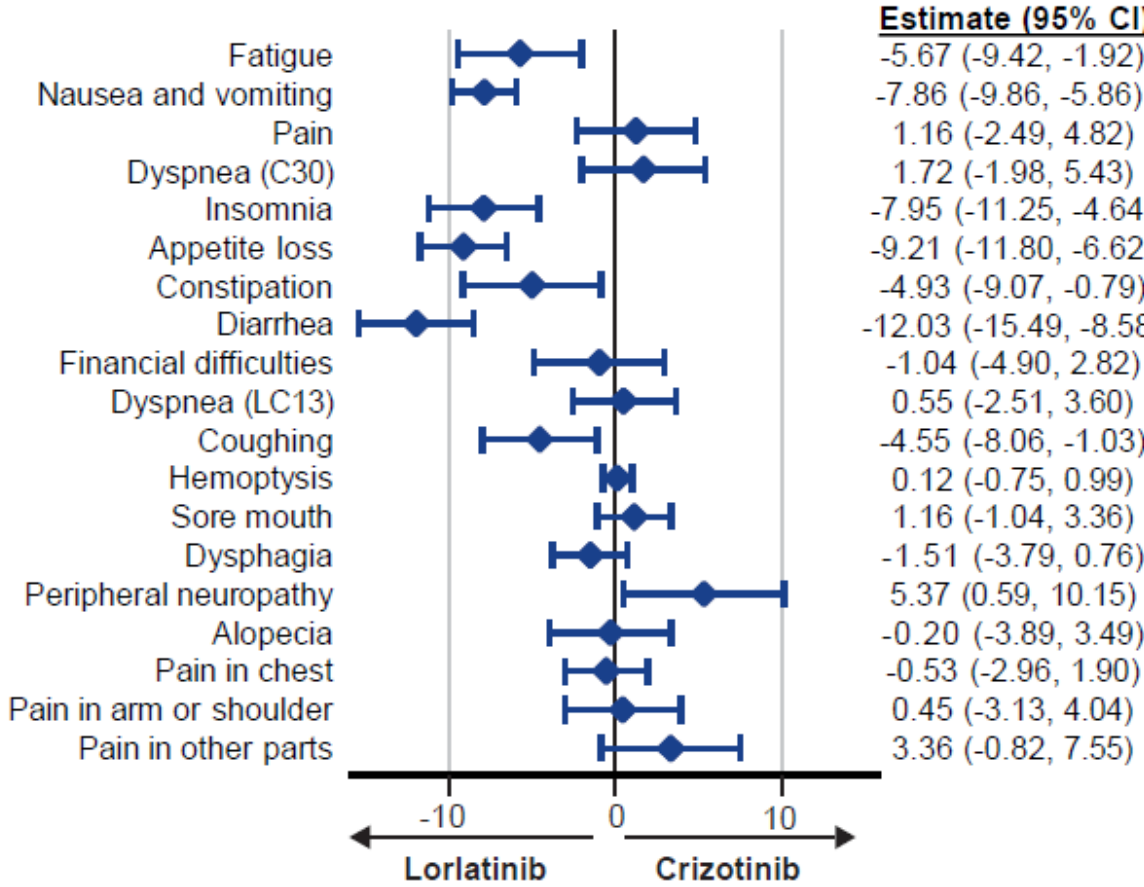
FFERENCES IN CHANGE FROM BASELINE UP TO BUT NOT INCLUDING EOT (MIXED MODE

EORTC QLQ-C30
(Global QoL and Functioning[a])



There were no differences between treatment arms in any functioning domain

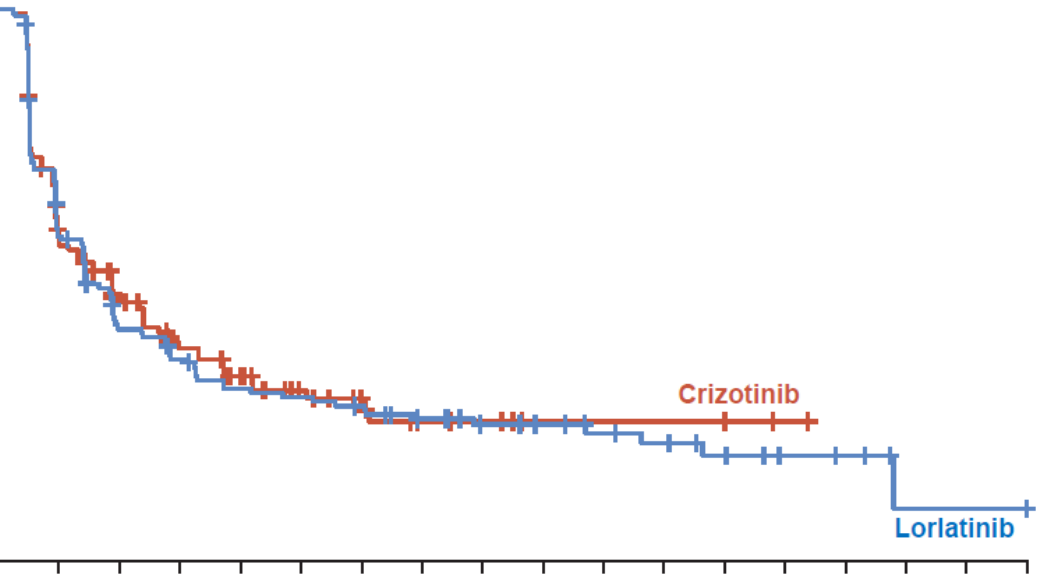
EORTC QLQ-C30 and LC13
(Symptoms[b])



For diarrhea there was both a clinically meaningful and statistica significant difference favoring lorlatinib

ients in the EORTC QLQ-C30 PRO analysis set with a score at baseline and post-baseline assessment. Analysis based on random-intercept, random-slope, mixed-effects model with an intercept term, trea ontinuous variable), treatment-by-time, baseline and randomization stratification factors as covariates. Analysis model included post-baseline assessments up to EOT, but not including EOT

TO DETERIORATION IN COMPOSITE ENDPOINT*

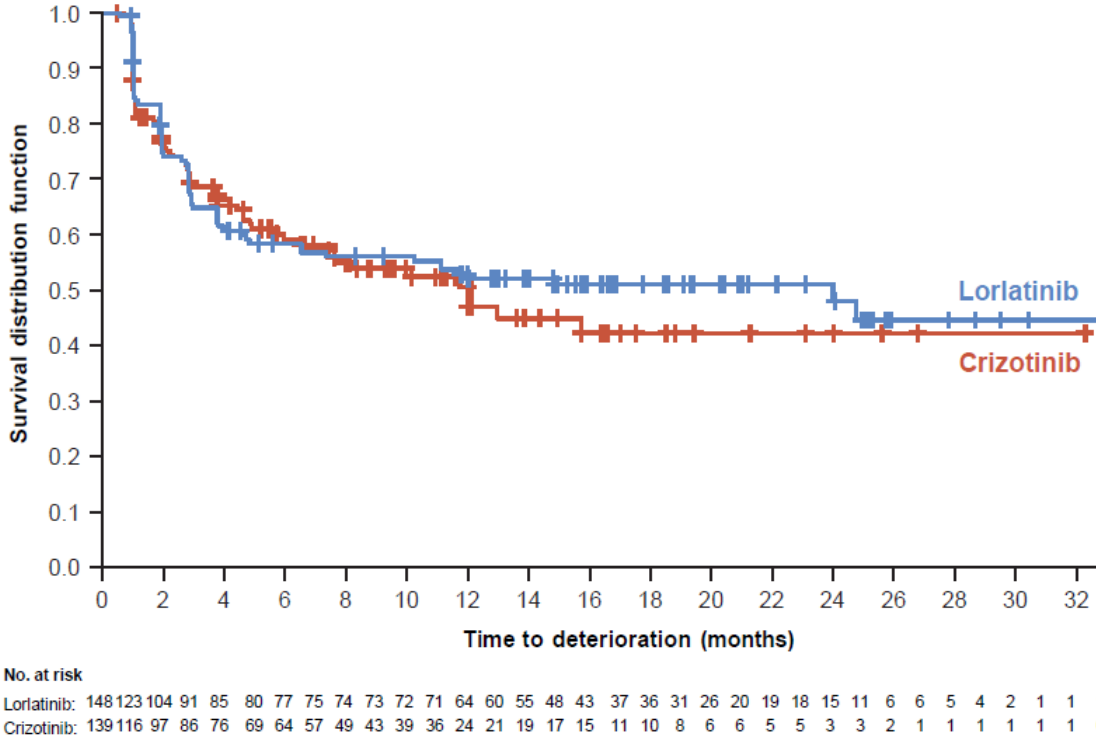


endpoint of lung cancer symptoms: cough, dyspnea, and pain in chest

Lorlatinib: Median 3.3 months (95% CI 2.1–4.7)
Crizotinib: Median 3.7 months (95% CI 2.0–5.5)

Hazard Ratio: **1.09** (95% CI 0.822–1.444)
1-sided *P* = 0.7293

TIME TO DETERIORATION IN GLOBAL QoL



Lorlatinib: Median 24 months (95% CI 6.5–NE)
Crizotinib: Median 12 months (95% CI 6.5–NE)

Hazard Ratio: **0.92** (95% CI 0.650–1.294)
1-sided *P* = 0.3127