EGFR-mutated Non-Small Cell Lung Cancer: Update from WCLC Singapore

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DISCLOSURES

Commercial Interest	Relationship(s)
Genentech	Research Grant (Institutional)
Amgen	Research Grant (Institutional)
Astra Zeneca	Consultant (Institutional)
IO Biotech	Consultant (Institutional)
Guardant Health	Consultant (Institutional)
Oncocyte	Consultant (Institutional)
Roche Genentech	Advisory Board
Merck	Advisory Board
Novartis	Advisory Board
Boehringer Ingelheim	Advisory Board
Amgen	Advisory Board

EGFR-mutated NSCLC: Overview for Advanced Stage Disease in March 2021

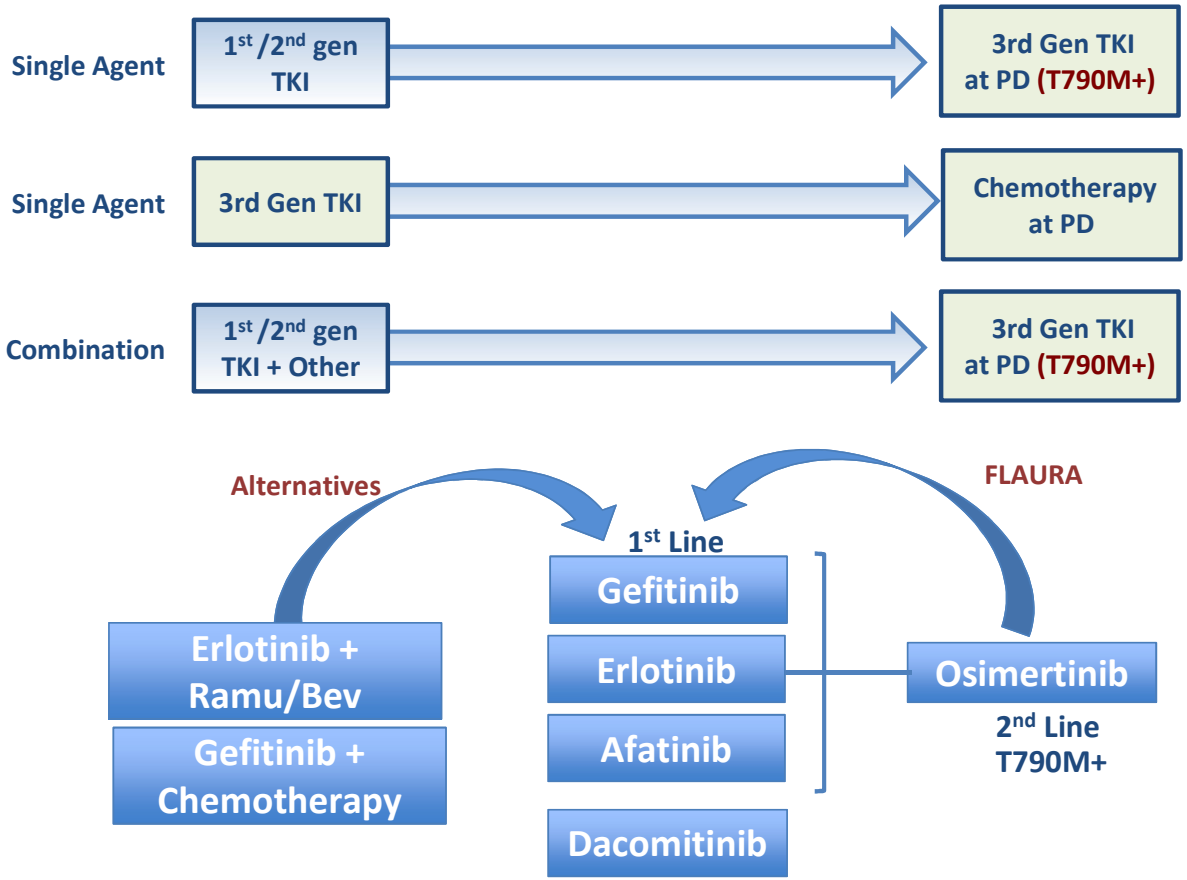
EGFR exon20 mutated NSCLC: New Therapeutic Approaches

- Comparative clinical outcomes for patients with *EGFR* exon20ins vs the common sensitizing *EGFR* mutations *(Girard)*
- Amivantamab in post-platinum *EGFR* exon20ins NSCLC: CHRYSALIS trial *(Sabari)*
- Mobocertinib in NSCLC with *EGFR* exon20ins: EXCLAIM trial *(Zhou)*

EGFR mutated NSCLC: Mechanisms of Resistance to EGFR TKIs & New Approaches

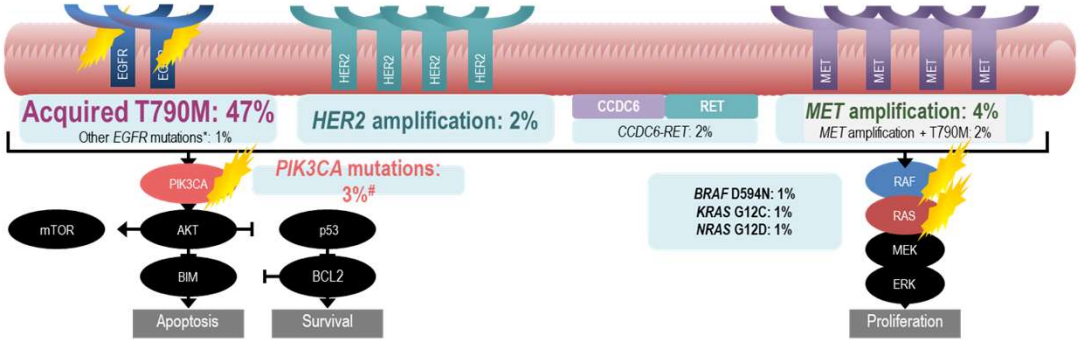
- Osimertinib + savolitinib in *EGFR*m *MET*-amplified/ overexpressed NSCLC: TATTON final analysis *(Han)*
- Efficacy and Safety of a HER3-Directed Antibody Drug Conjugate Patritumab Deruxtecan (HER3-DXd; U3-1402) in *EGFR*-Mutated NSCLC *(Yu)*

Strategies for Optimizing 1st-line Therapy for EGFR-mutated NSCLC: Options for 1st line Therapy



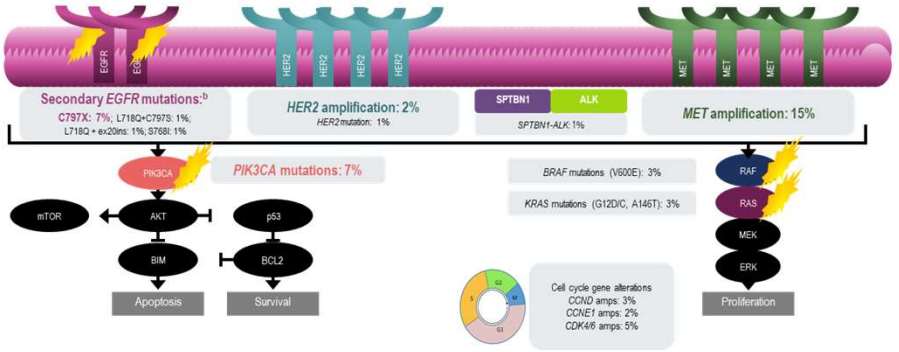
FLAURA: Acquired Resistance Mechanisms in Comparator EGFR TKIs (Gefitinib or Erlotinib)

Most common acquired resistance mechanisms were T790M (47%), *MET* amplification, PIK3CA mutations & *HER2* amplification



FLAURA: Acquired Resistance Mechanisms after Osimertinib 1st-line therapy

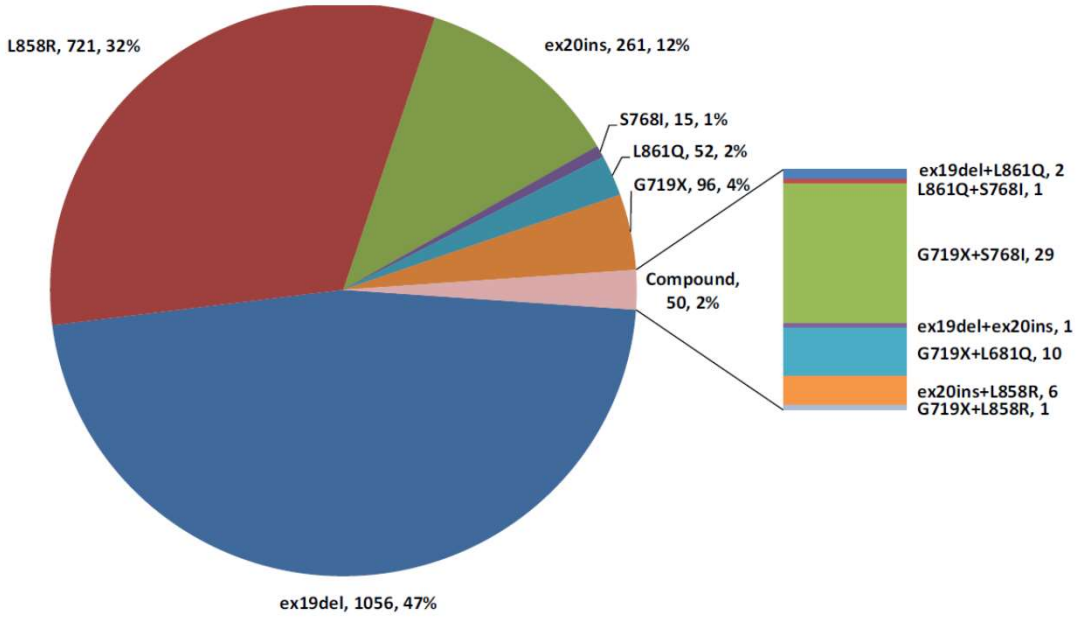
- **No cases of acquired *EGFR* T790M**
- **Most common mechanisms were *MET* amplification (15%) and *EGFR* C797X mutation (10%)**
  - **Other mechanisms included HER2 amplification/mutation (3%), *PIK3CA(7%), RAS/RAF* mutations and ALK transformation**



Ramalingam et al: ESMO 2019

EGFR Ex20ins-mutated NSCLC

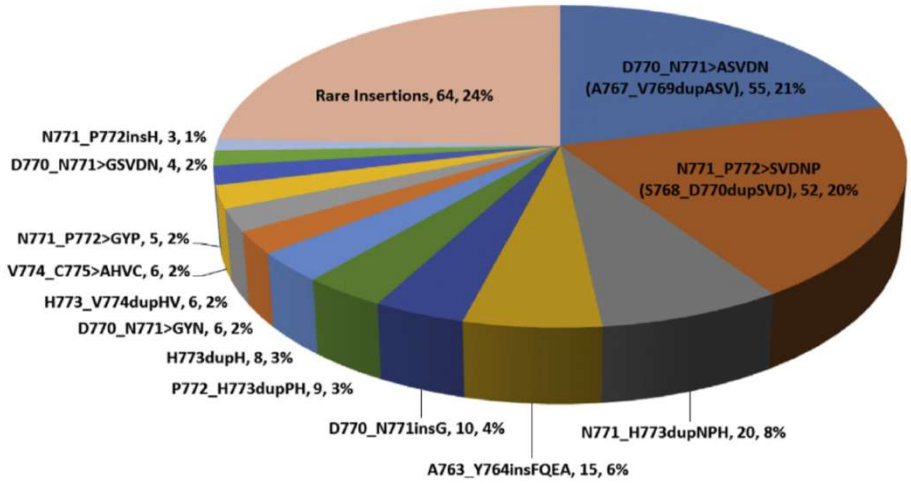
EGFR Mutation Subtypes (N=2,251)



Riess, Gandara et al. JTO 2018

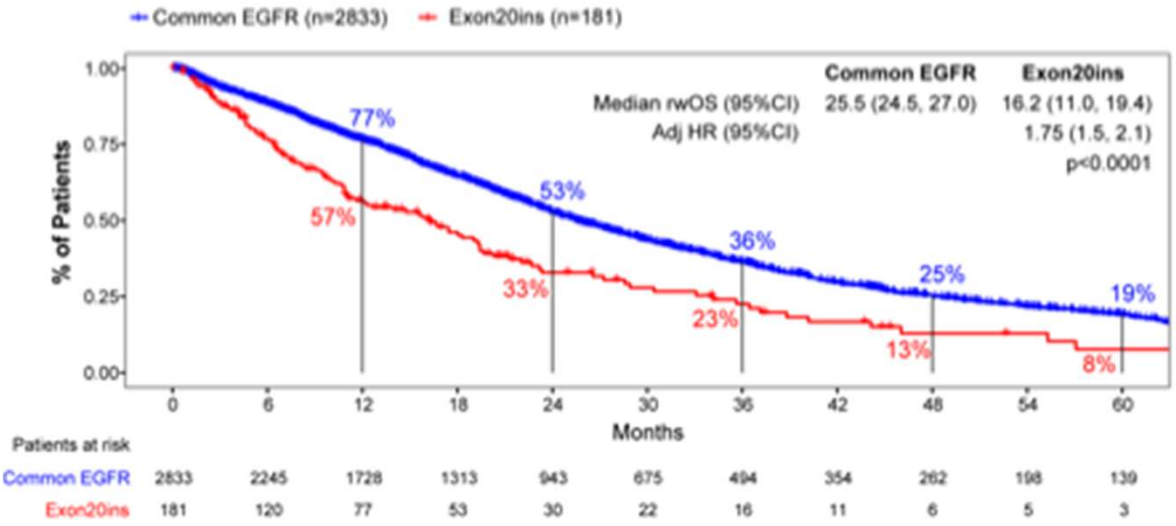
- **EGFR Ex20ins mutations (~2% of NSCLC)**
- **~12% of all EGFR mutations (3rd most common)**
- **Typically resistant to 1st Gen EGFR TKIs**

Distribution of EGFR Ex20ins mutations (N=263)



Comparative clinical outcomes for patients with NSCLC with *EGFR* exon20ins versus common *EGFR* mutations (Ex19del, L858R)

- Advanced NSCLC diagnosis between January 2011 to May 2020 in the Flatiron database (real-world evidence)
- *EGFR* L858R, exon19del, or exon20ins
- Predictive value analysis: any TKI treatment



Prognostic value of exon20ins compared with common *EGFR* mutations (N=3014)

Primary endpoint: rwOS

- Common *EGFRm* n=2833
- Exon20ins n=181

Predictive value of exon20ins for TKI treatment (N=2825)

Primary Endpoint: rwPFS

- Common *EGFRm* n=2749
- Exon20ins n=76

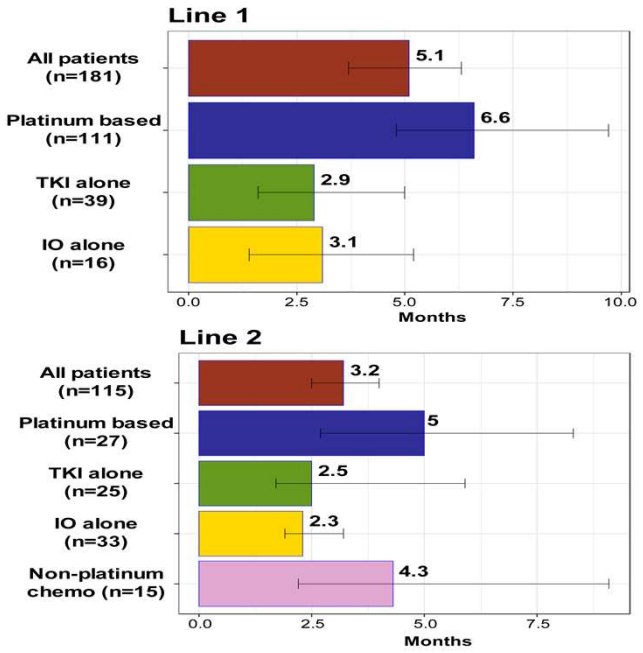
	Real-world data on PFS	
	Common *EGFRm*	**Exon20ins**
Median rwPFS (95% CI)	10.5 months (10.1, 10.9)	2.9 months (2.1, 3.9)
Adjusted HR (95% CI)		2.69 (2.1, 3.6) *P*<0.0001

Girard N et al. WCLC 2020. Abstract MA04.07.

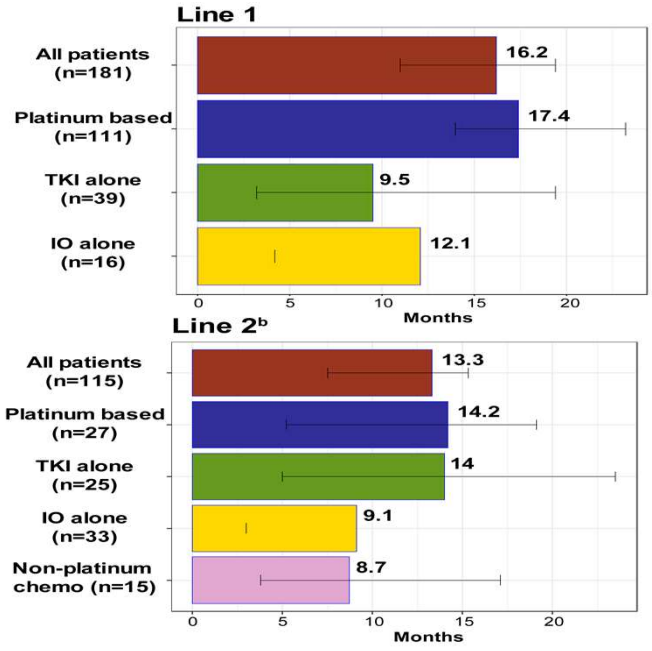
Presented by D. Gandara: BEST of WCLC 2020. March 27.2021

Clinical outcomes for patients with NSCLC with *EGFR* exon20ins mutations

Median (95% CI) rwPFS by Therapy



Median (95% CI) rwOS by Therapy



- Poorer prognosis compared with patients with common *EGFRm*
- Less benefit from EGFR TKIs compared with patients with common *EGFR*m
- Platinum-based therapies were the most common first-line treatment, no clear standard in second line
- 6.6 months can be considered median duration of response to first-line platinum-based chemotherapy for comparison studies of novel agents in patients with *EGFR* exon20ins

*EGFR*m, *EGFR* mutations;
rwOS, real-world overall survival;
rwPFS, real-world progression-free survival.
Girard N et al. WCLC 2020. Abstract MA04.07.

Current treatment landscape for EGFR Ex20 NSCLC

Drug	Class	*N*	ORR (%)
Chemotherapy[1]	Platinum-based	105 first line	19.2%
Gefitinib/ Erlotinib[2]	1G EGFR TKI	9 first line 16 pre-treated	8
Erlotinib[3]	1G EGFR TKI	11 pre-treated	25
Dacomitinib[4]	2G EGFR TKI	6 pre-treated	16
Afatinib[5]	2G EGFR TKI	21 TKI pre-treated 70 TKI naive	14.3 24.3
Osimertinib[6,7]	3G EGFR TKI	20 pre-treated, 80 mg OD 21 pre-treated, 160 mg OD	5 25
Poziotinib[8]	Pan-HER TKI	115 pre-treated	14.8
CLN-081[9]	EGFR TKI	22 pre-treated	35
Mobocertinib	EGFR TKI	114 pre-treated	23
Amivantamab	EGFR-MET bispecific Ab	81 pre-treated	40

[1]Yang G et al, Lung Cancer 2020; [2]Beau-Faller M et al, Ann Oncol 2014; [3]Naidoo J et al, Cancer 2015; [4]Janne PA et al, CCR 2011; [5]Yang JC et al, JTO 2020; [6]Veggel B et al, Ann Oncol 2018; [7]Piotrowska Z et al, ESMO 2020; [8]Le X et al, AACR 2020; [9]Piotrowska Z et al, ESMO 2020

Amivantamab in post-platinum *EGFR* exon20ins-mutant NSCLC[1]

- Amivantamab: Fully human *EGFR-MET* bispecific antibody[2,3]
- Targets activating and resistance *EGFR* mutations and *MET* mutations and amplifications[4,5]
- Demonstrated monotherapy activity in patients with diverse *EGFRm* disease including *EGFR* exon19del, L858R, T790M, C797S, exon20ins, and *MET* amplifications[4,5]
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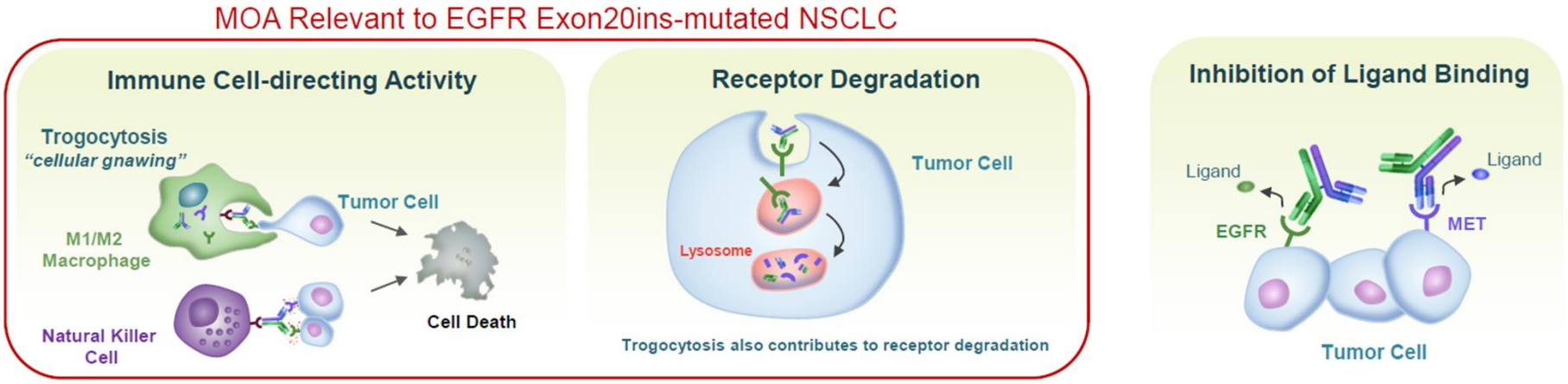
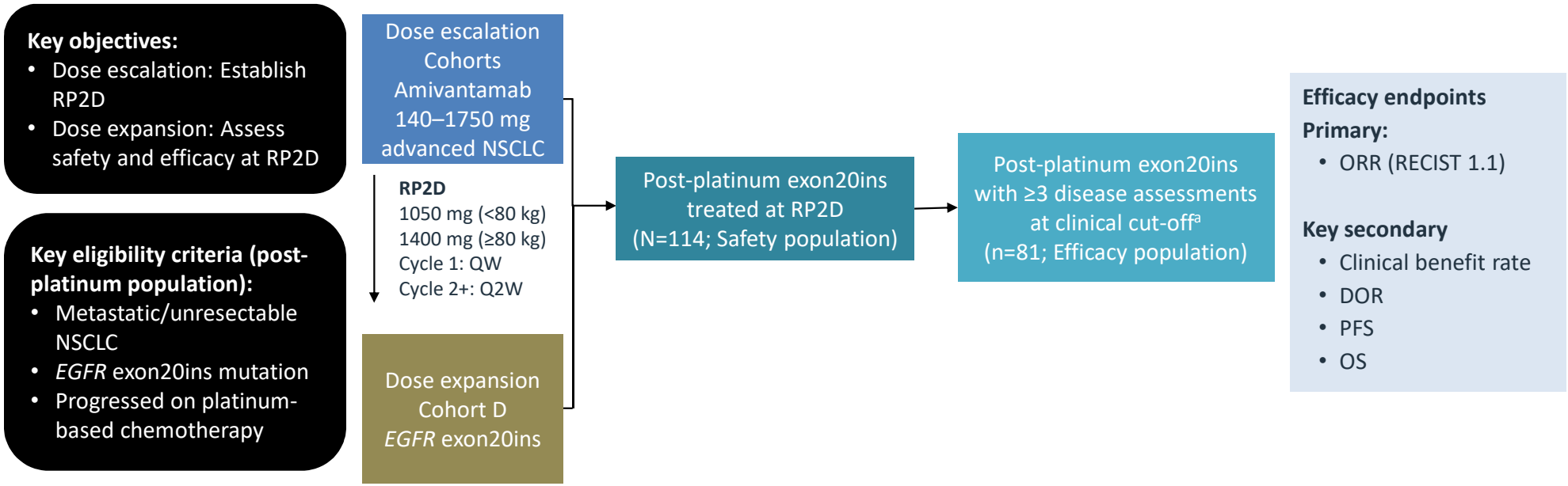


MOA, mechanism of action.

1. Sabari JK et al. WCLC 2020. Abstract OA04.04. 2. Vijayaraghavan S et al. *Mol Cancer Ther* 2020;19:2044–56. 3. Yun J et al. *Cancer Discov* 2020;10:1194–209.
4. Haura EB et al. *J Clin Oncol* 2019;37(15_suppl):9009. 5. Park K et al. *J Clin Oncol* 2020;38(15_suppl):9512.

CHRYSALIS study design: Post-platinum exon20ins population



NCT02609776.

[a]Postplatinum patients treated at the RP2D and had ≥3 scheduled disease assessments or discontinued, progressed, or died prior to the 3rd postbaseline assessment at the time of clinical cut-off (June 8, 2020). By October 8, 2020, all responders in the efficacy population had ≥6 months of follow-up from their first disease assessment.

DOR, duration of response; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; QW, weekly; Q2W, twice weekly; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended phase 2 dose.

Sabari JK et al. WCLC 2020. Abstract OA04.04.

Amivantamab: Demographics and Baseline Characteristics

Characteristic, n (%)	Efficacy Population (n=81)
Median age, years (range)	62 (42–84)
Male / Female	33 (41) / 48 (59)
Race	
Asian	40 (49)
White	30 (37)
Black	2 (3)
Not reported/multiple	9 (11)
Smoking history	
Non-smoker	43 (53)
Smoker	38 (47)
Median time from initial diagnosis, months (range)	17 (1–130)

Characteristic, n (%)	Efficacy Population (n=81)
History of brain metastases	18 (22)
Median number of prior lines (range)	2 (1–7)
Prior systemic therapy	81 (100)
Platinum-based doublet chemotherapy	81 (100)
Immuno-oncology therapy	37 (46)
EGFR TKI	20 (25)
1st-gen TKI	7 (9)
2nd-gen TKI	6 (7)
3rd-gen TKI	6 (7)
Poziotinib	1 (1)

CHRYSALIS: Amivantamab adverse events

AE (≥15% of treatment-emergent AEs), n (%)	Safety population (N=114)			
	Treatment-emergent AE		Treatment-related AE	
	Total	Grade ≥3	Total	Grade ≥3
EGFR-related				
Rash[a]	98 (86)	4 (4)	98 (86)	4 (4)
Paronychia	51 (45)	1 (1)	48 (42)	1 (1)
Stomatitis	24 (21)	0	21 (18)	0
Pruritus	19 (17)	0	19 (17	0
MET-related				
Hypoalbuminemia	31 (27)	3 (3)	17 (15)	2 (2)
Peripheral edema	21 (18)	0	11 (10)	0
Other				
Infusion-related reaction	78 (66)	3 (3)	75 (66)	3 (3)
Constipation	27 (24)	0	7 (6)	0
Nausea	22 (19)	0	13 (11)	0
Dyspnea	22 (19)	2 (2)	6 (5)	0
Fatigue	21 (18)	2 (2)	14 (12)	1 (1)
Increased ATL	17 (15)	1 (1)	14 (12)	1 (1)

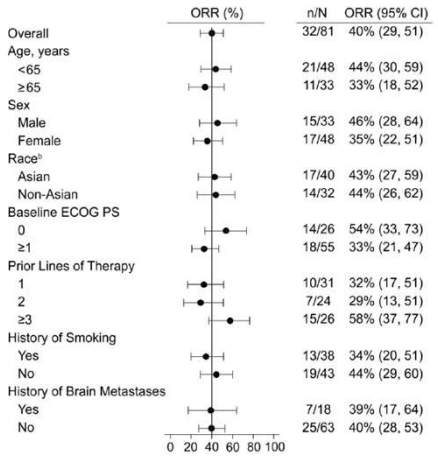
- Safety profile consistent with inhibition of EGFR and MET pathways
- 2% discontinued due to rash
- 12% had diarrhea (10% treatment-related)
  - 8.5% grade 1–2
  - 3.5% grade 3
- 94% of IRRs occurred with the first infusion and rarely impacted ability to continue with subsequent treatments

[a]Includes all rash-related AE.
AE, adverse event; ALT, alanine transaminase; IRR, infusion-related reaction.
Sabari JK et al. WCLC 2020. Abstract OA04.04.

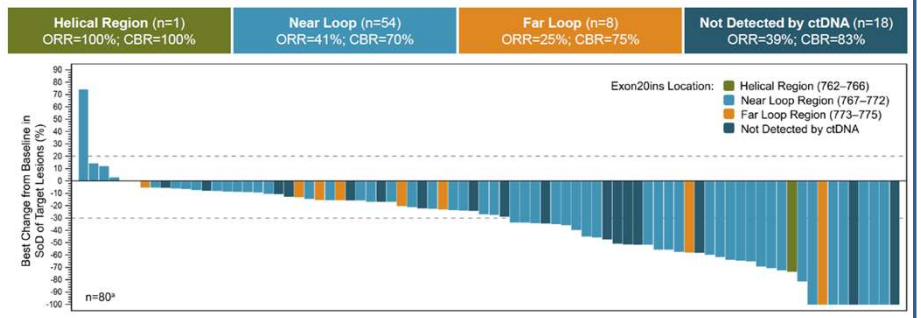
CHRYSALIS: Amivantamab efficacy

Efficacy by BICR

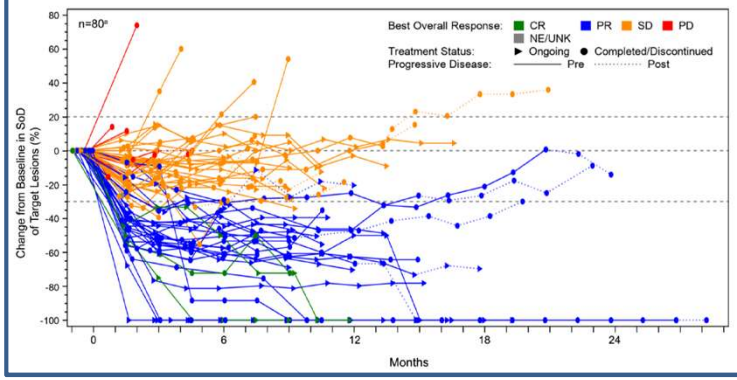
BICR-assessed response	Efficacy population (n=81)
ORR, % (95% CI)	**40%** (29, 51)
Median DOR (95% CI)	**11.1 months** (6.9, NR)
Best response, n (%)	
Complete response	3 (4)
Partial response	29 (36)
Stable disease	39 (48)
Progressive disease	8 (10)
Not evaluable	1 (1)
Clinical benefit rate[a] (95% CI)	74% (63, 83)



Best ORR by insertion region of exon20[a]



Response over time



- 15/32 (47%) patients remain on treatment at time of data cut-off
- 20/32 (63%) patients had responses ≥6 months
- mPFS: 8.3 months (95% CI: 6.5, 10.9)
- mOS: 22.8 months (95% CI, 14.6, NR)

- This update confirms safety and efficacy of amivantamab in *EGFR* ex20ins+ NSCLC
- These data compare favorably to other options in this *EGFR*-mutated subset
- FDA breakthrough designation (March 10, 2020)
- Randomized trials of combinations are being pursued in *EGFR* ex20ins+ and first-line *EGFR*-mutated NSCLC

[a]Detected by ctDNA; 25 distinct exon20ins identified by NGS of ctDNA (Guardant360®) from 63 evaluable patient samples.
BICR, blinded independent central review; CBR, clinical benefit rate; CR complete response; ctDNA, circulating tumor DNA; ECOG PS, Eastern Cooperative Oncology Group performance status; mOS, median overall survival; mPFS, median progression-free survival; NE, not reached; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of diameter; UNK, unknown.
Sabari JK et al. WCLC 2020. Abstract OA04.04.

Mobocertinib in NSCLC with *EGFR* exon20ins: Results from EXCLAIM and pooled platinum-pretreated patient populations

Patient demographics and baseline characteristics were similar between cohorts

Characteristic		PPP cohort (N=114)	EXCLAIM cohort (N=96)
Median age, years (range)		60 (27–84)	59 (27–80)
Female, %		66	65
Race, %	Asian White Black	60 37 3	69 29 2
ECOG PS, %	0 1	25 75	29 71
History of smoking, %	Never Current Former	71 2 27	73 2 25
Median no. of prior systemic anticancer regimes (range)		2 (1–7)	1 (1–4)
Prior systemic anticancer regimens, %	1 2 ≥3	41 32 27	51 31 18
Prior platinum therapy, %		100	90
Prior TKI therapy, %		25	31
Prior immunotherapy, %		43	34

Data cut-off May 29, 2020

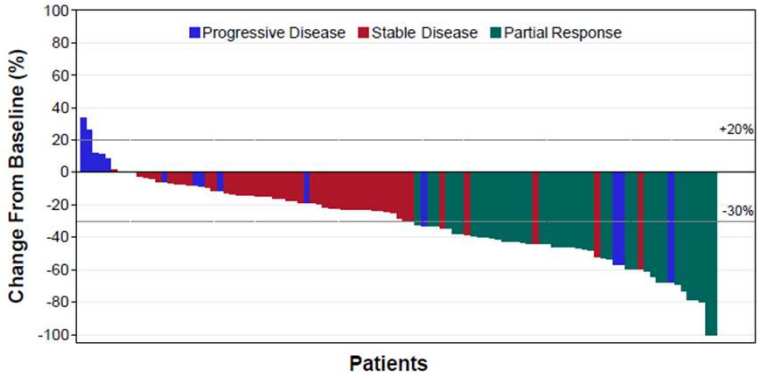
ECOG PS, Eastern Cooperative Oncology Group performance status; PPP, platinum pretreated patients.

Zhou C et al. WCLC 2020. Abstract OA04.03.

Mobocertinib in NSCLC with *EGFR* exon20ins: Efficacy results

Parameter	PPP cohort (N=114)	EXCLAIM cohort (N=96)
Median time on treatment, months (range)	7.0 (0–31)	6.5 (0–14)
Confirmed ORR per IRC, n (%) [95% CI]	30 (26) [19, 35]	22 (23) [15, 33]
Confirmed ORR per investigator, n (%) [95% CI]	40 (35) [26, 45]	31 (32) [23, 43]

PPP cohort: Change from baseline in sum of target lesions diameter[a]

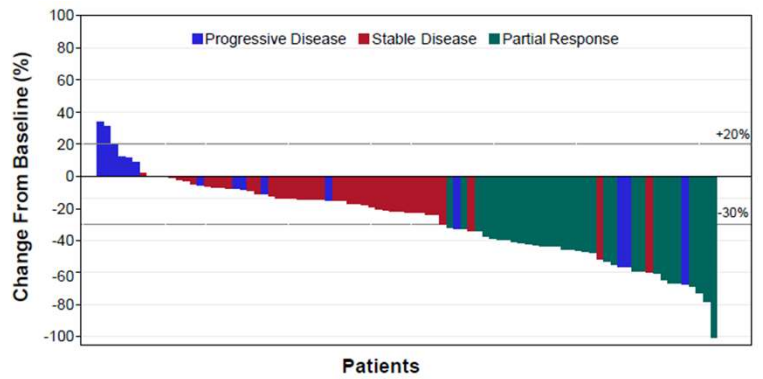


- 94 patients 82% had a reduction from baseline in the sum of target lesion diameter

Median DOR
>12 months

Median PFS
7.3 months

EXCLAIM cohort: Change from baseline in sum of target lesions diameter[a]



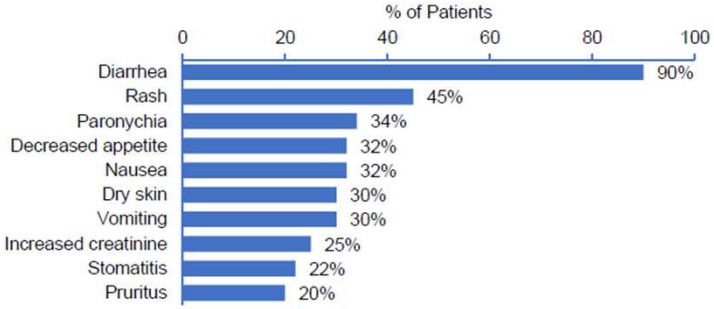
- 77 patients 80% had a reduction from baseline in the sum of target lesion diameter

[a]Per investigator assessment.
DOR, duration of response; IRC, independent review committee; ORR, objective response rate; PFS, progression-free survival; PPP, platinum pretreated patients.
Zhou C et al. WCLC 2020. Abstract OA04.03.

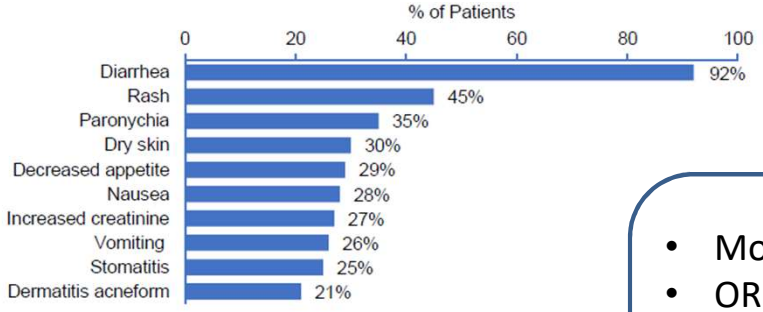
Mobocertinib safety profile was consistent between the PPP and EXCLAIM cohorts

n (%)	PPP cohort (N=114)	EXCLAIM cohort (N=96)
Any treatment-related AE	113 (99)	95 (99)
Grade ≥3 treatment-related AE	53 (46)	39 (41)
Serious treatment-emergent AEs	52 (46)	39 (41)
AEs leading to dosage reduction	28 (25)	20 (21)
AEs leading to treatment discontinuation	19 (17)	10 (10)
Treatment-related AEs leading to death	1 (1)	1 (1)

PPP cohort (N=114)



EXCLAIM cohort (N=96)



Grade 3/4 TRAEs in ≥5% of patients, n (%)	PPP cohort (N=114)	EXCLAIM cohort (N=96)
Diarrhea	24 (21)	15 (16)

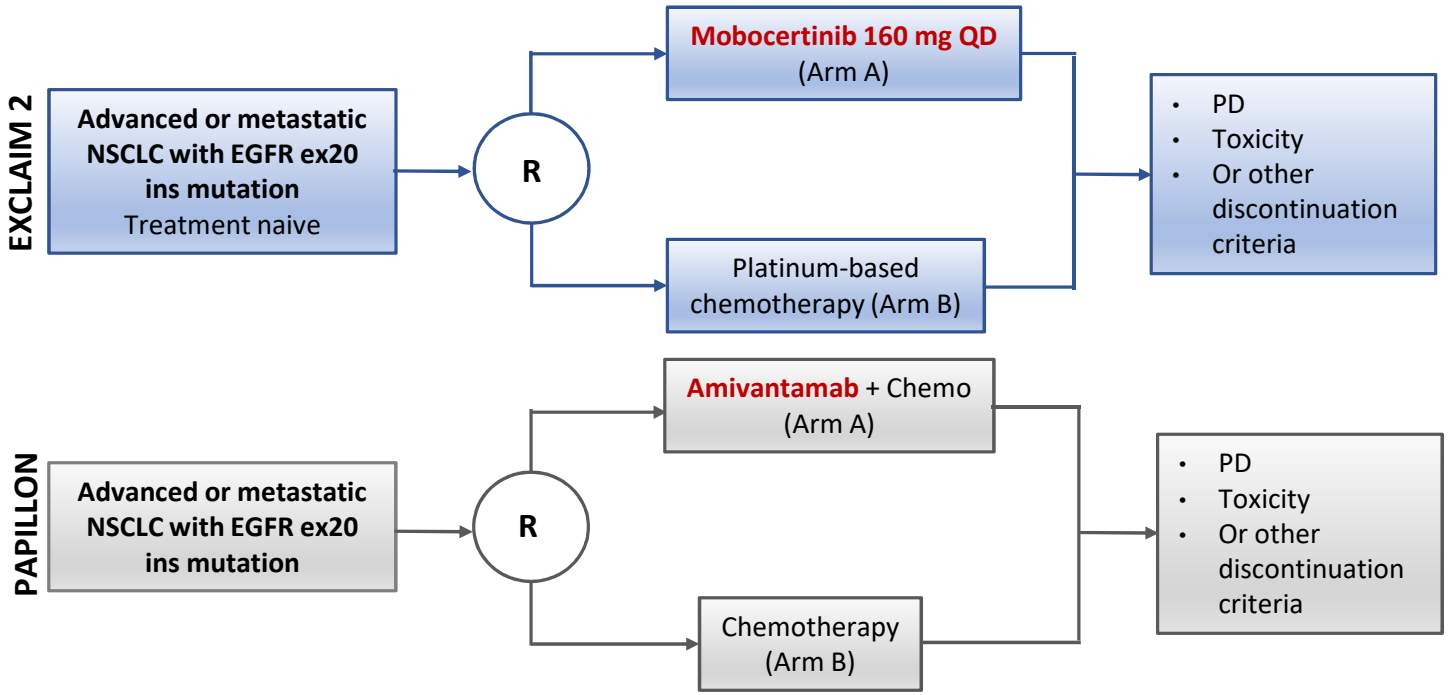
- Mobocertinib in Ex20ins
- ORR ~30% in both cohorts (~25%–35%)
- Promising efficacy but GI toxicity (diarrhea) is challenging

AE, adverse event; DOR, duration of response; GI, gastrointestinal; ORR, objective response rate; PFS, progression-free survival; PPP, platinum pretreated patients; TRAE, treatment-related adverse event.

Zhou C et al. WCLC 2020. Abstract OA04.03.

Ongoing studies in EGFR Ex20ins NSCLC

PHASE 3

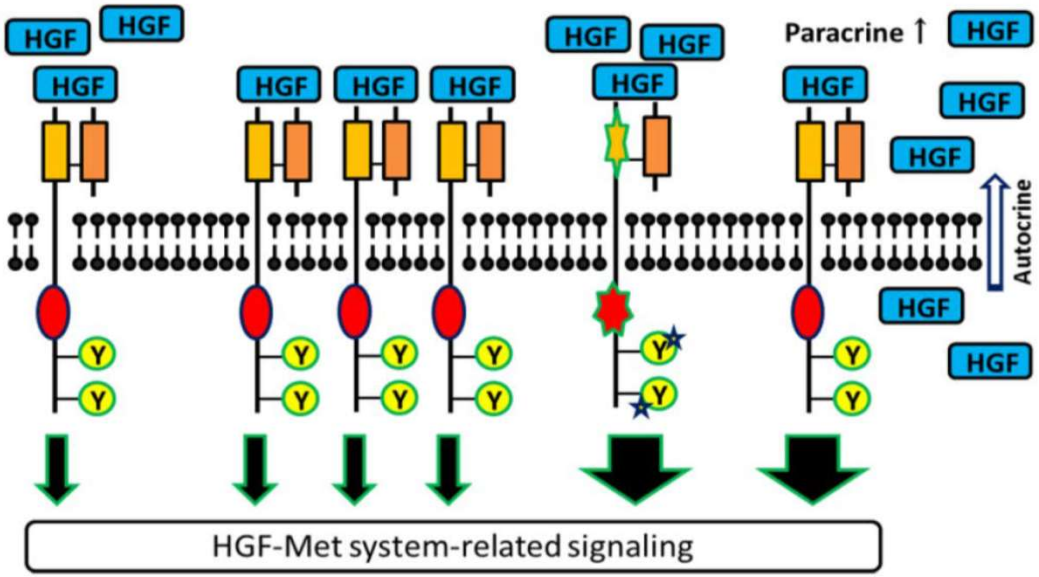


Gillianne G.Y. Lai: Discussant –WCLC Singapore, Jan 2021

MET as a Mechanism of Resistance in EGFR-mutated NSCLC

Measuring MET pathway Activation in Cancer

Normal | **MET over-expression Protein- IHC Amplification** | **MET Mutation Ex14 skipping** | **Up-regulation of HGF**



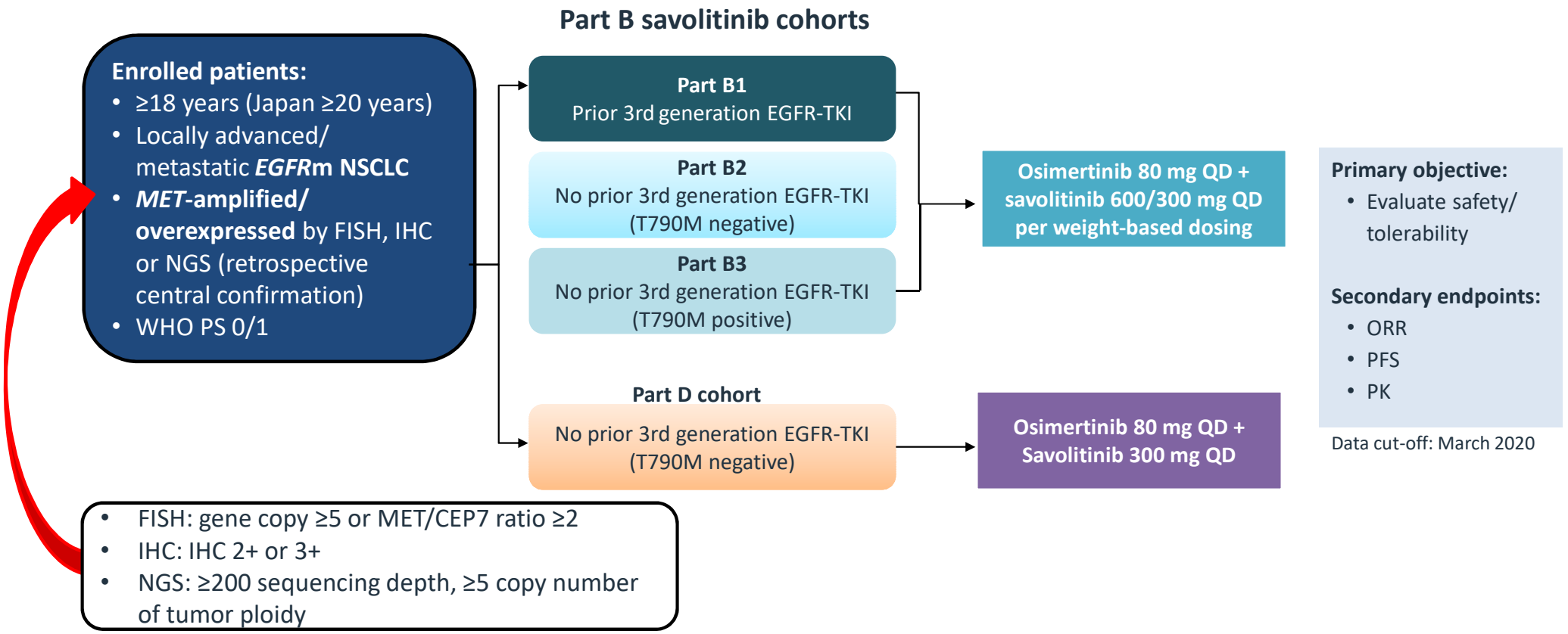
MET TKIs: Efficacy in *MET* ex14 NSCLC

Agent	*MET* testing	n	ORR, % (95% CI)	DOR (months)	PFS (months)
Capmatinib[1]	Tissue RT-PCR	97 1L: 28 2/3L: 69	1L: 68 (47.6–84.1) 2L/3L: 41 (28.9–53.1)	1L: 11.1 (5.55–NE 2L: 9.7 (5.55–12.98)	1L: 9.7 (5.5–13.86) 2L/3L: 5.4 (4.2–6.97)
Tepotinib[2]	Liquid (DNA-based NGS) Tissue (RNA-based NGS)	73 Liquid: 48 Tissue: 51	Liquid: 50 (35.2–64.8) 1L: 59 (32.0–81.6) 2L: 53 (26.6–78.7) ≥3L: 37.5 (15.2–64.6) Tissue: 45 (31.1–59.7) 1L: 44 (21.5–69.2) 2L: 50 (26–74) ≥3L: 40 (16.3–67.7)	Liquid: 12.4 (5.8–NE) Tissue: 15.7 (9.0–NE)	Liquid: 9.5 (6.7–NE) Tissue: 10.8 (6.9–NE)
Crizotinib[3]	Tissue-local Prospective central tissue & liquid ctDNA	65	32 (21–45)	9.1 (6.4–12.7)	7.3 (5.4–9.1)
Savolitinib[4]	Tissue	29	55	na	na

1. Wolf J, et al. ASCO 2019. Abstract 9004. 2. Paik, PK et al. ASCO 2019; Abstract 9005. 3. Drilon A, et al. WCLC 2018. 4. Lu S, et al. AACR 2019.

Courtesy of K Reckamp

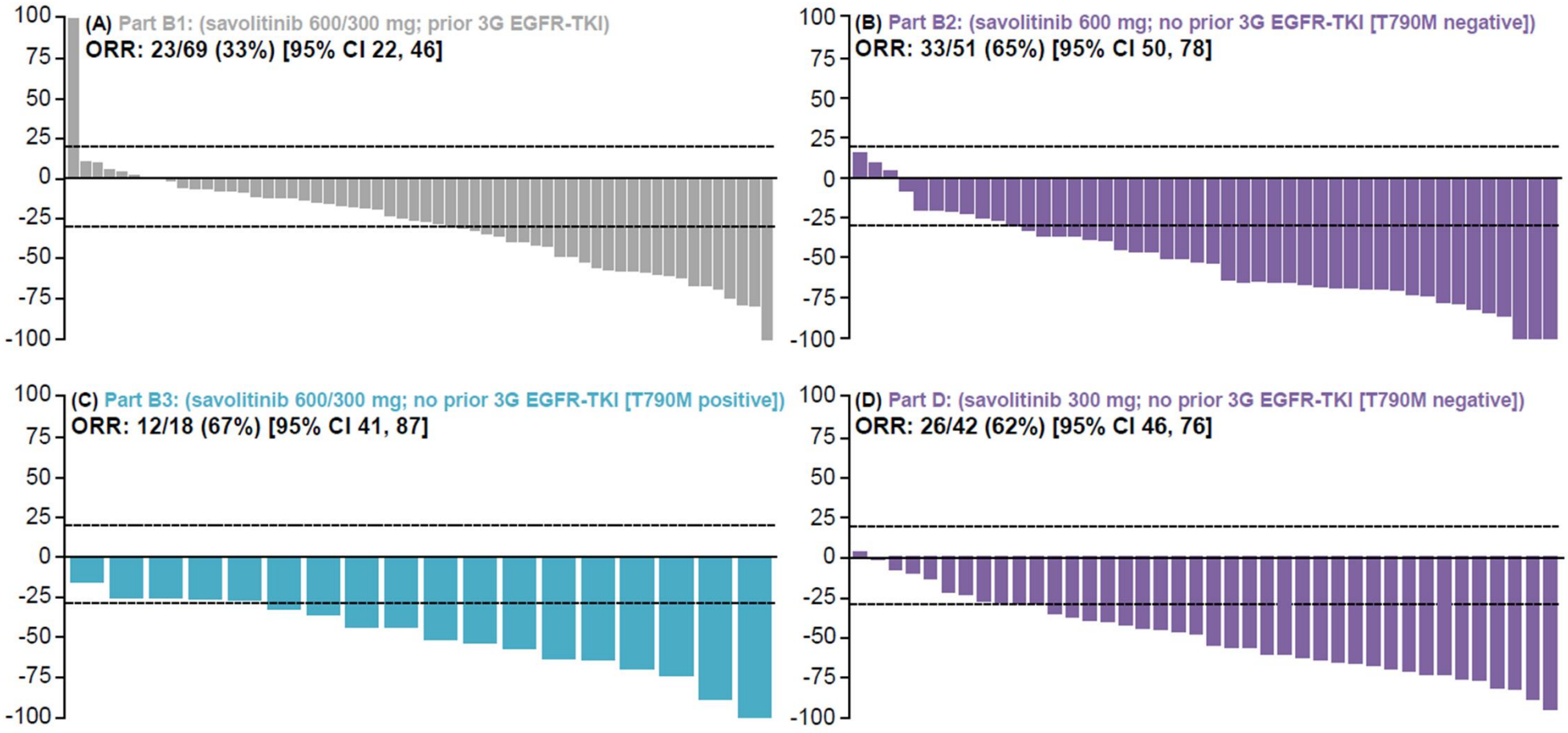
TATTON: Phase Ib multi-cohort study of osimertinib-based combinations



IHC, immunohistochemistry; FISH, fluorescence in situ hybridization; NGS, next-generation sequencing; ORR, objective response rate; PFS, progression-free survival; PK, pharmacokinetics; PS, performance status; QD once daily; WHO, World Health Organization.

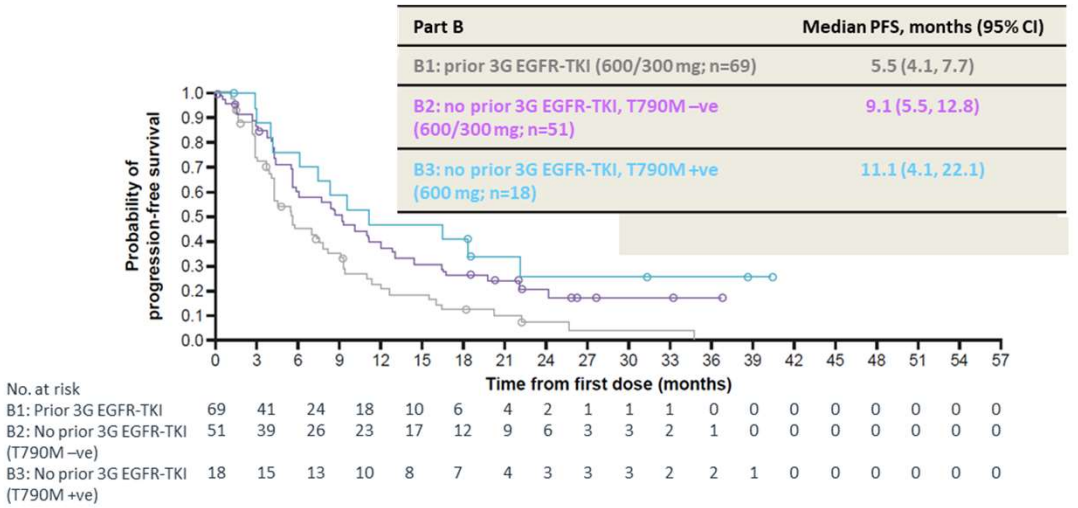
Han J et al. WCLC 2020. Abstract FP14.03.

Response rate to Savolitinib + Osimertinib in various cohorts



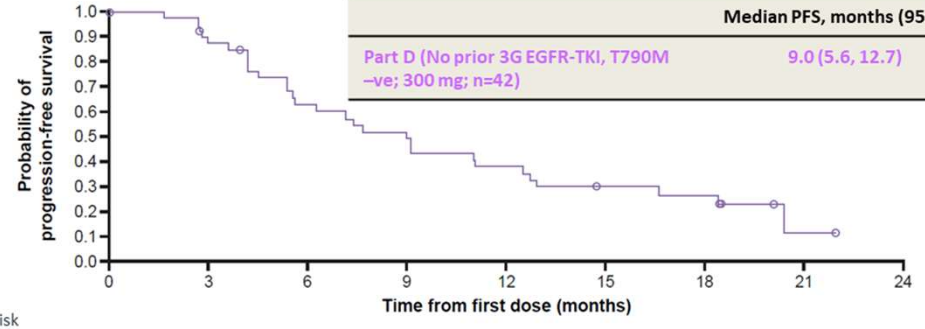
3G, 3rd generation; IHC, immunohistochemistry; FISH, fluorescence in situ hybridization; NGS, next-generation sequencing; ORR, objective response rate.
Han J et al. WCLC 2020. Abstract FP14.03.

PFS with Savolitinib + Osimertinib in various cohorts



Part B	Median PFS, months (95% CI)
B1: prior 3G EGFR-TKI (600/300 mg; n=69)	5.5 (4.1, 7.7)
B2: no prior 3G EGFR-TKI, T790M –ve (600/300 mg; n=51)	9.1 (5.5, 12.8)
B3: no prior 3G EGFR-TKI, T790M +ve (600 mg; n=18)	11.1 (4.1, 22.1)

No. at risk																			
B1: Prior 3G EGFR-TKI	69	41	24	18	10	6	4	2	1	1	1	0	0	0	0	0	0	0	0
B2: No prior 3G EGFR-TKI (T790M –ve)	51	39	26	23	17	12	9	6	3	3	2	1	0	0	0	0	0	0	0
B3: No prior 3G EGFR-TKI (T790M +ve)	18	15	13	10	8	7	4	3	3	3	2	2	1	0	0	0	0	0	0



	Median PFS, months (95% CI)
Part D (No prior 3G EGFR-TKI, T790M –ve; 300 mg; n=42)	9.0 (5.6, 12.7)

No. at risk									
D: No prior 3G EGFR-TKI (T790M –ve)	42	33	23	19	14	9	8	1	0

Han J et al. WCLC 2020. Abstract FP14.03.

Toxicity of the Savolitinib-Osimertinib Combination

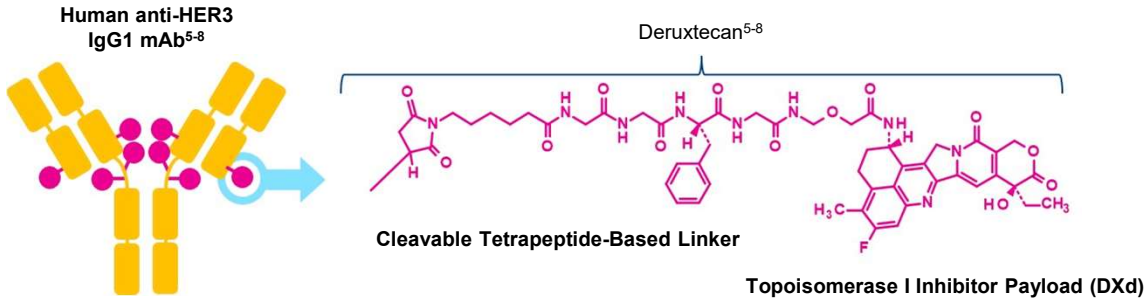
AE, n (%)	Part B (n=138)		Part D (n=42)	
	AE causally related to savolitinib	AE causally related to osimertinib	AE causally related to savolitinib	AE causally related to osimertinib
ALT increased	7 (5)	6 (4)	0	0
Anaphylactic reaction	5 (4)	1 (1)	1 (2)	0
AST increased	8 (6)	6 (4)	0	0
Diarrhea	3 (2)	2 (1)	2 (5)	2 (5)
Drug hypersensitivity	5 (4)	2 (1)	3 (7)	2 (5)
Fatigue	4 (3)	0	0	0
Generalised edema	0	0	2 (5)	0
Myalgia	3 (2)	0	2 (5)	2 (5)
Nausea	4 (3)	4 (3)	0	0
Neutropenia	4 (3)	3 (2)	0	0
Neutrophil count decreased	9 (7)	8 (6)	1 (2)	1 (2)
Edema peripheral	4 (3)	2 (1)	1 (2)	0
Rash	4 (3)	2 (1)	1 (2)	0
Vomiting	6 (4)	4 (3)	0	0
WBC count decreased	4 (3)	4 (3)	0	0

- Combination is reasonably well tolerated
- The osimertinib/savolitinib combination is promising in *MET* +ve EGFR TKI-resistant NSCLC
- Need to define the MET biomarker more clearly (IHC vs FISH vs NGS)
- Uncertain if savolitinib 300 mg or 600 mg is optimal for the combination

AE, adverse event;
ALT alanine aminotransferase;
AST, aspartate aminotransferase;
WBC, white blood count.
Han J et al. WCLC 2020. Abstract FP14.03.

Efficacy and Safety of a HER3-Directed Antibody Drug Conjugate Patritumab Deruxtecan (HER3-DXd; U3-1402) in *EGFR*-Mutated NSCLC

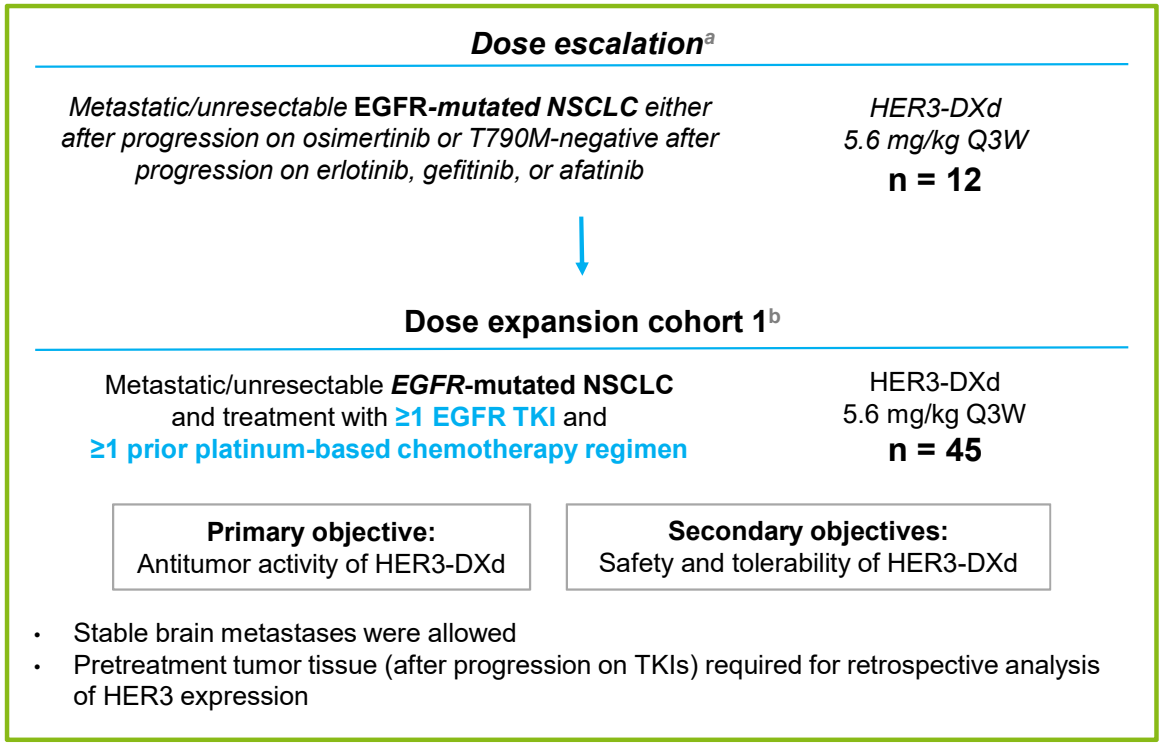
- Patients with advanced *EGFR*-mutated NSCLC have few treatment options after failure of EGFR TKIs and platinum-based chemotherapy[1,2]
- **HER3 is expressed in most lung cancers**, including in >80% of *EGFR*-mutated NSCLC, and overexpression has been associated with worse clinical outcomes[1,3-4]
  - HER3 therefore represents a promising therapeutic target; however, no HER3 directed therapies are currently approved[3,4]
- **Patritumab deruxtecan (HER3-DXd**; U3-1402) is a novel, investigational HER3-directed ADC comprising a fully human anti-HER3 IgG1 mAb (patritumab) covalently linked to a topoisomerase I inhibitor payload, an exatecan derivative, via a tetrapeptide-based cleavable linker[5-8]



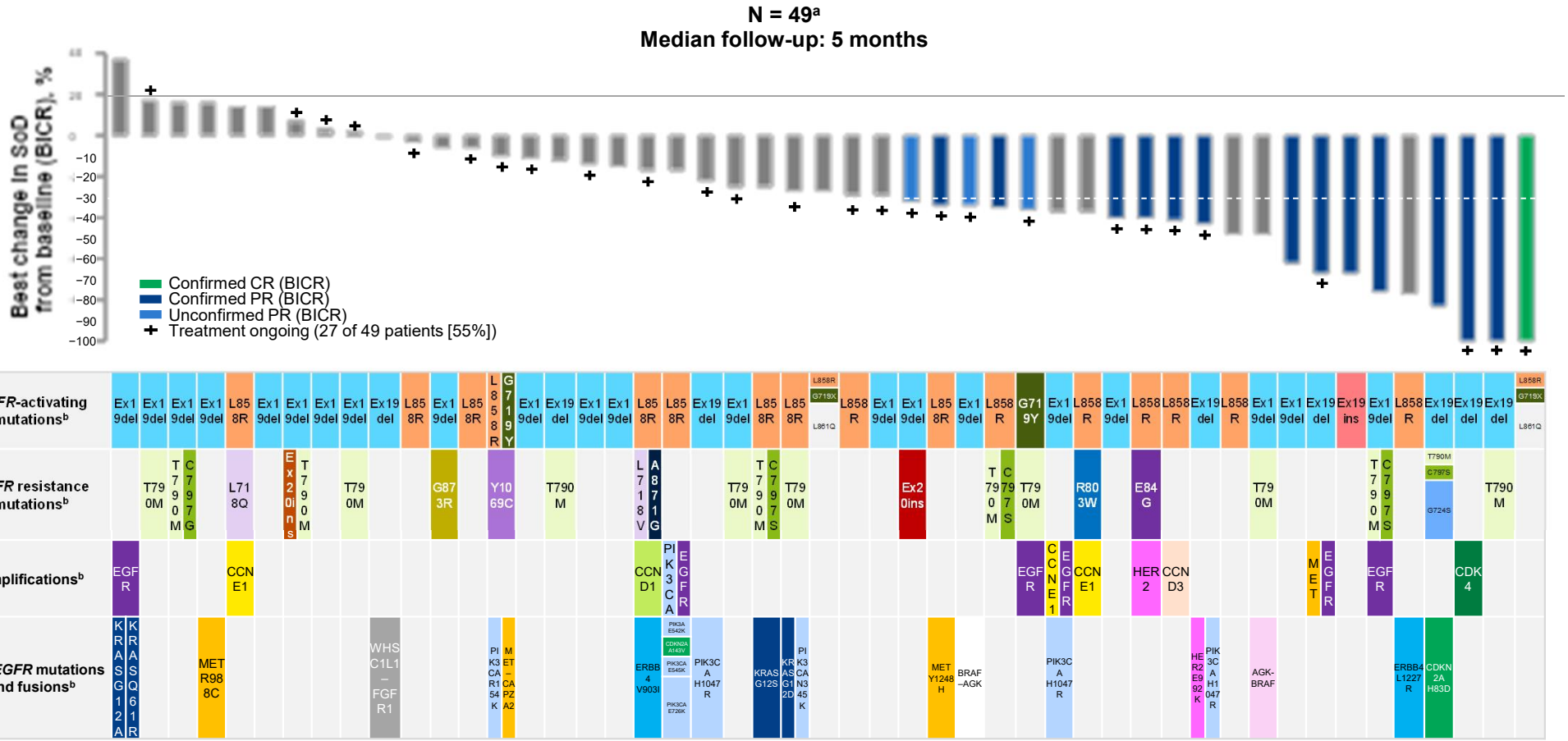
1. Tan CS, et al. *Mol Cancer.* 2018;17:29. 2. Lee CK, et al. *J Thorac Oncol.* 2017;12:403-407. 3. Scharpenseel H, et al. *Sci Rep*. 2019:9:7406. 4. Yi ES, et al. *Mod Pathol.* 1997:142-148. 5. Hashimoto Y, et al. *Clin Cancer Res*. 2019;25:7151-7161. 6. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185. 7. Ogitani Y, et al. *Clin Cancer Res.* 2016;22(20):5097-5108. 8. Koganemaru S, et al. *Mol Cancer Ther.* 2019;18:2043-2050.

Phase 1 Study of HER3-DXd in *EGFR*-Mutated NSCLC

- HER3-DXd is being evaluated in a global, multicenter, open-label phase 1 study in patients with metastatic/unresectable NSCLC, including patients harboring an *EGFR*-activating mutation (NCT03260491)
- In the dose escalation portion of the study[1,a]:
  - RDE was determined to be 5.6 mg/kg IV Q3W
  - Safety was manageable
  - Antitumor activity was observed in patients across multiple resistance mechanisms



HER3-DXd 5.6 mg/kg Demonstrated Antitumor Activity in *EGFR*-Mutated NSCLC With Diverse TKI Resistance Mechanisms



HER3-DXd 5.6 mg/kg Continues to Demonstrate a Manageable Safety Profile

- The most common grade ≥3 TEAEs were thrombocytopenia (16 patients [28%]) and neutropenia (11 patients [19%])
- TEAEs associated with discontinuation (9%) included fatigue (n = 2), decreased appetite (n = 1), interstitial lung disease (n = 1), pneumonitis (n = 1), and URI (n = 1)
  - No discontinuations were due to thrombocytopenia or neutropenia
- Three (5.3%) interstitial lung disease events were adjudicated by an independent central review committee as being related to treatment
- There were no treatment-related TEAEs associated with death

TEAEs (regardless of causality), n (%)	N = 57
TEAEs	57 (100)
Grade ≥3	38 (67)
Associated with discontinuation	5 (9)
Associated with dose reduction	10 (18)
Associated with dose interruption	17 (30)
Associated with death	3 (5)
Treatment-emergent SAEs	21 (37)
Grade ≥3	18 (32)
Treatment related	11 (19)

TEAEs in ≥20% of patients, n (%)	N = 57	
	All grades	Grade ≥3
Fatigue	33 (58)	5 (9)
Nausea	31 (54)	2 (4)
Thrombocytopenia[a]	30 (53)	16 (28)
Decreased appetite	20 (35)	1 (2)
Neutropenia[b]	19 (33)	11 (19)
Vomiting	17 (30)	1 (2)
Alopecia	17 (30)	NA
Anemia[c]	15 (26)	5 (9)
Constipation	14 (25)	0