What is Next After Osimertinib Progression?

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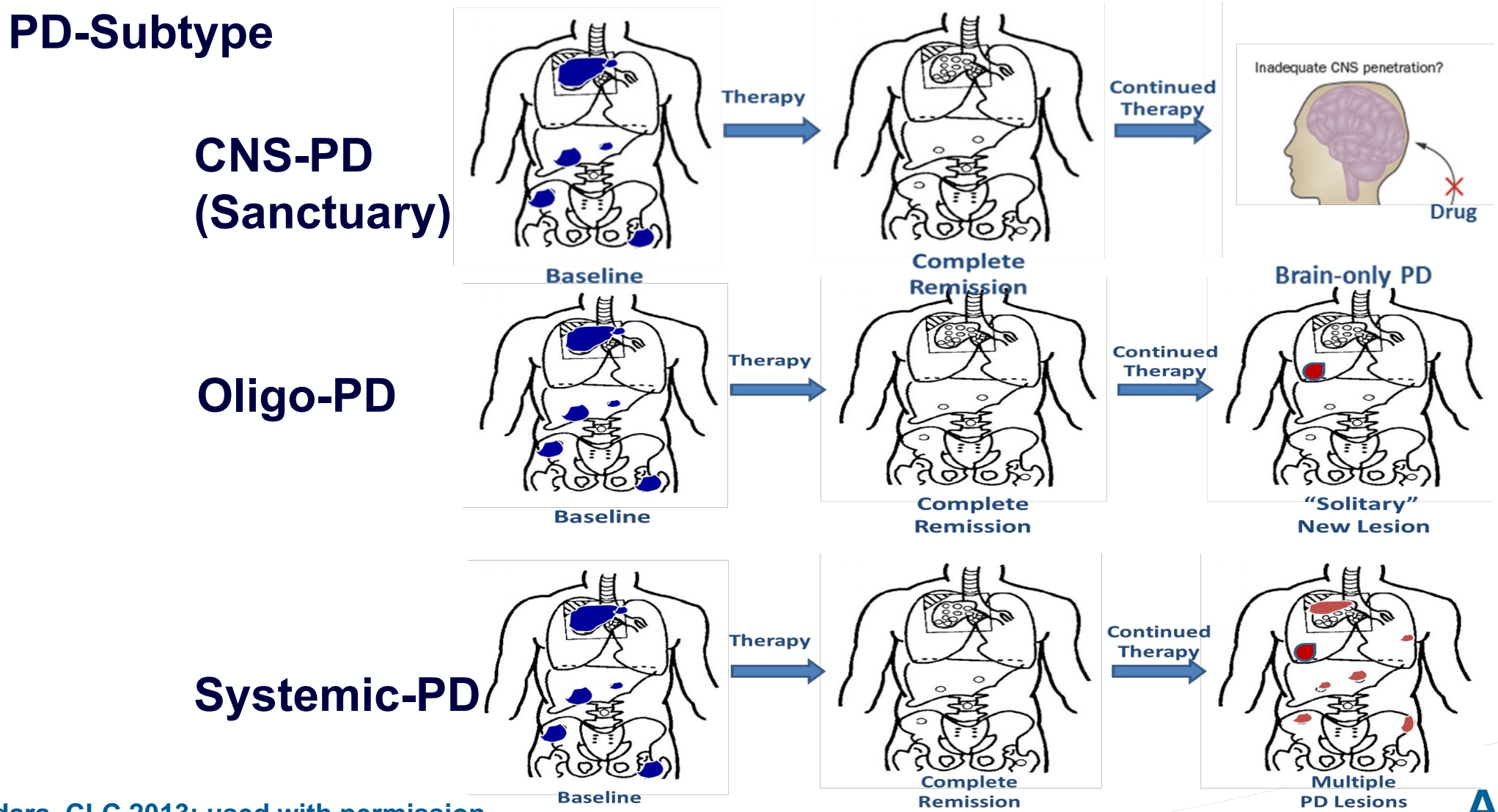
Considerations

- Pace and sites of progression
- Is there a role for loco-regional therapies (oligo-progression)
- Should tissue biopsy be done (histologic transformation)
- Presence of co-mutations
- Plasma testing results (should be routine first move)
- Acquired resistance mechanism identified?
- Is continuation of a TKI necessary?

At Least 3 Clinical Subtypes of Acquired Resistance to Targeted TKIs



Gandara, CLC 2013; used with permission

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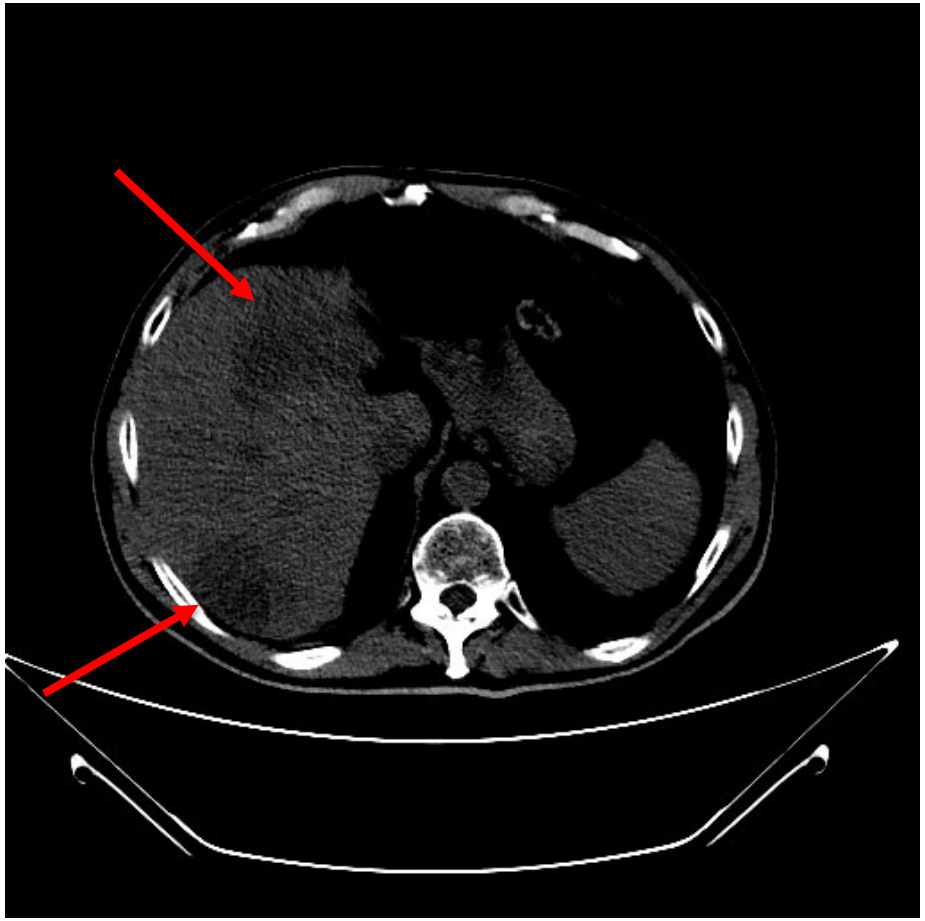
66 yo male diagnosed with stage IV adenocarcinoma, EGFR L858R mutation positive in October 2019 initially treated with osimertinib. Developed progressive weakness, abdominal pain. CT demonstrated new liver mets and RP adenopathy in December 2023

March 27, 2024



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Re-biopsy of liver metastasis was performed. Path showed adenocarcinoma, 95% PD-L1 +. Molecular testing showed native EGFR mutation as well as met amplication

Result:

Solid Tumor Profiling assay (50 genes) by Next Generation Sequencing and ALK1 rearrangement by immunohistochemical stain.
Results:
Specimen Adequacy:
Adequate: Estimated tumor cellularity (area used for testing) is 40%.
The following mutation(s) is/are identified:
Gene Name pVariant Variant Allele Fraction
EGFR exon 21 L858R 0.133
TP53 P151S 0.223

MET amplification with copy number of 8.2

Clinical significance:
Per clinical note, the patient was on osimertinib treatment and now is have disease progression. The MET amplification identified suggests that the resistance to osimertinib treatment may be associated MET amplification. The copy number of MET by NGS is slightly less than 10 copies, a cut-off usually defining MET amplification in tissue specimen. However, given this particular specimen shows low tumor cell content (40%), the MET copy number in cancer cells is likely more than 10 copies. If further evaluation of MET copy number is needed, please contact lab at 407-303-9427 to request the test to be performed at a reference lab. Please correlate clinically.

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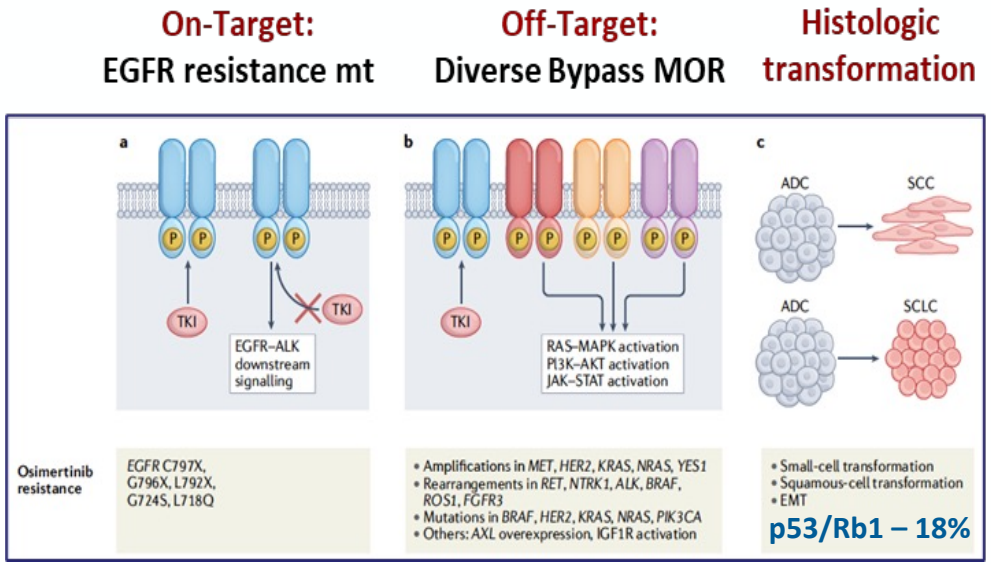
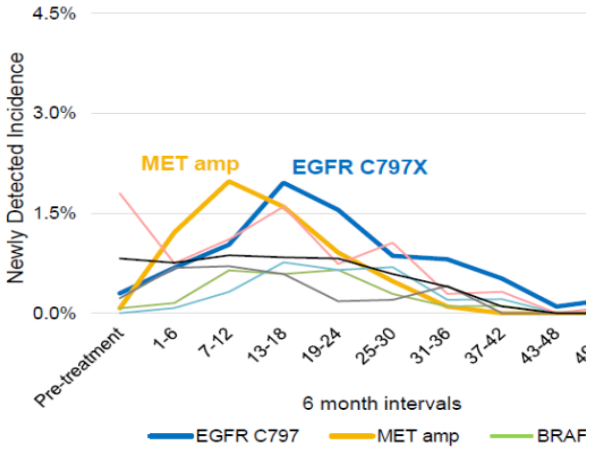
Broad Mechanisms of Resistance to EGFR-TKI and Temporal Occurrence

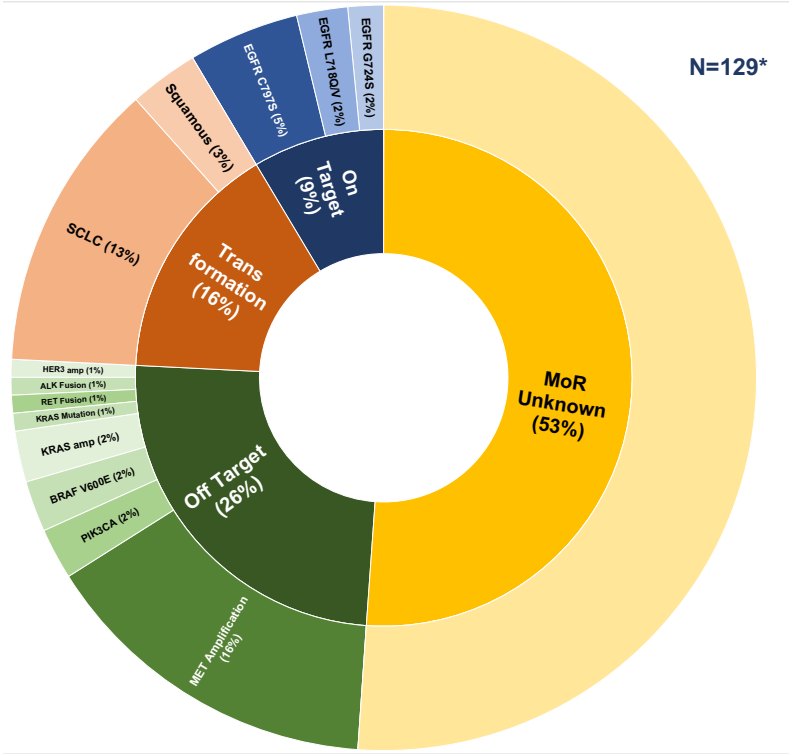


Cooper AS, et al, Nat Rev Clin Oncol 2022



Presented by S. Ramalingam WCLC 2022

Osimertinib Resistance Mechanisms (Real World Tissue)



- **Pre-Existing Comutations Mediating Resistance (Impact for locally advanced/early stage treatment)**
- **Resistance to Immunotherapy**

Z. Piotrowska et al. ASCO 2023

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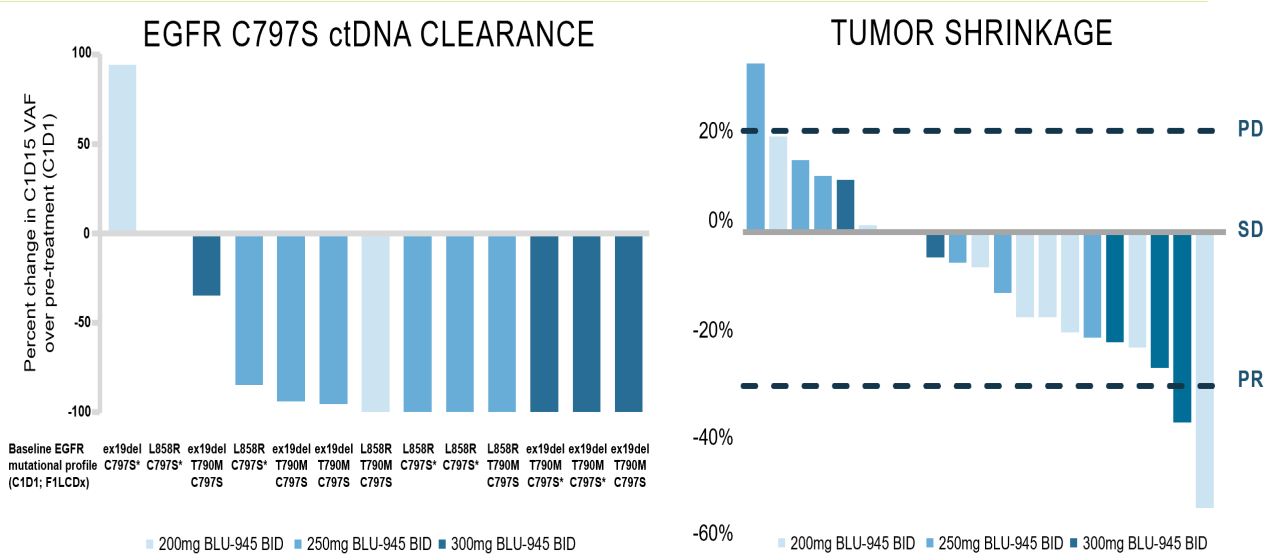
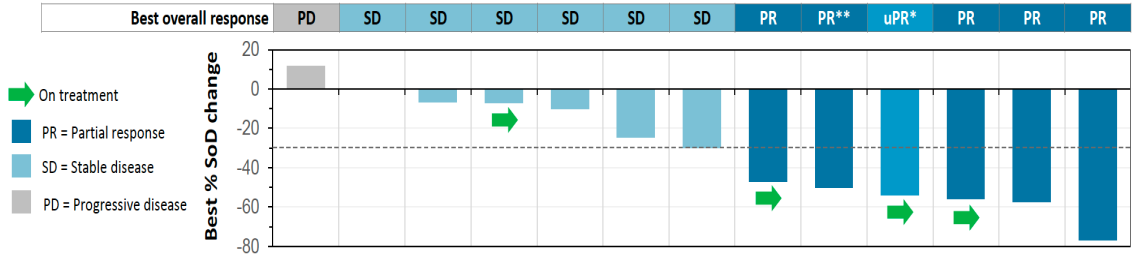
On-Target - 4th Generation C797S EGFR TKIs in the Clinic

BLU-945: Preliminary Efficacy Data Monotherapy Cohorts, Top Dose Levels



Adapted from: Mar, B. Presented to EGFR Exon 20 Research Consortium

BDTX-1535 in Efficacy Evaluable Population



Assigned dose level, mg QD		300	400	200	200	200	200	400	400	300	200	200	300	100
EGFR mutation (retrospective central testing)	Classical	L858R		Ex19del	L858R#	Ex19del	Ex19del		Ex19del	Ex19del	L858R		L858R	L858R
	Non-classical	L833V	G719A		E709V#		G724S	S768I			E709V	L747P		L718Q
	Acquired	C797S		C797S		C797S	C797S		C797S	C797S			C797S	C797S
Prior lines of therapy	1st line	Osi	Osi	Osi	Gefi	Osi	Osi	Erlo	CPI	Osi	Osi	Osi	C	Osi
	2nd line	Daco, Osi	C		C	CPI, C		C	Osi	Osi+Gefi	C	CPI/C	Osi	
	>2 line	CPI, C	Afa						C	BLU-701		C	C	

Osi = Osimertinib; Afa = Afatinib; Gefi = Gefitinib; Daco = Dacomitinib; Erlo = Erlotinib; CPI = Checkpoint inhibitor, C = Chemotherapy; # - mutations were absent on confirmatory test; * uPR=unconfirmed partial response-patient had a PR on a post-baseline scan, but a radiologist was unable to confirm a response on a subsequent scan; this patient remains on study treatment without evidence of PD. **%SoD was updated to -50% from prior data release
24July2023 BDTX-1535-101 clinical data extract
Data from Poster at EORTC/AACR/NCI International Conference on Molecular Targets and Cancer Therapeutics October 2023

Efficacy-Evaluable Patients
5 cPR, 1 uPR of 13 by RECIST

Post-Osimertinib Patients
5 cPR, 1 uPR of 11 by RECIST

Adapted from Poster at EORTC/AACR/NCI Triple Meeting October 2023

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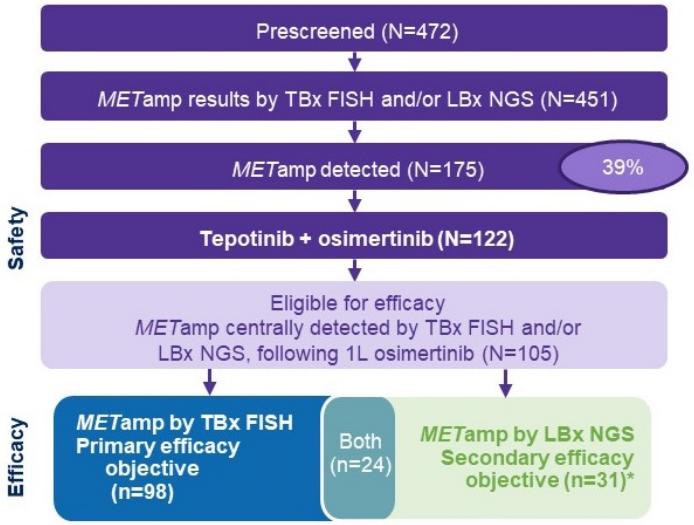
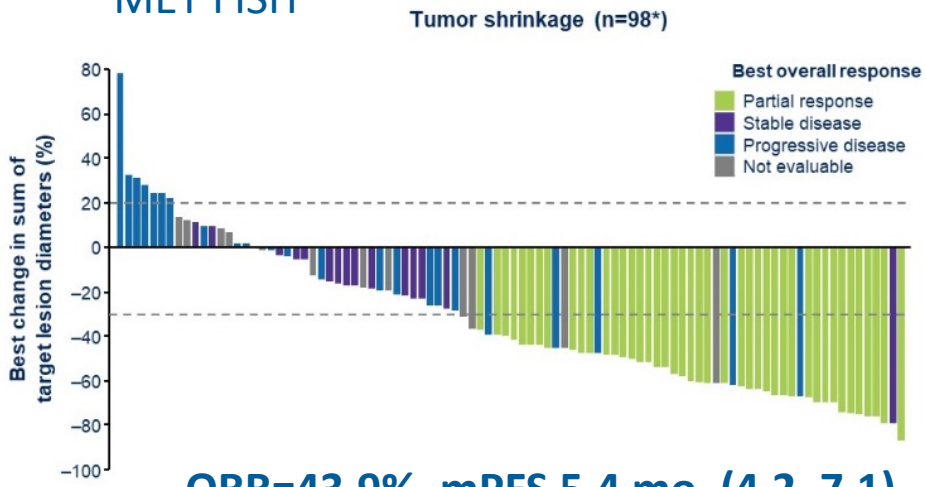
MET Inhibition - INSIGHT 2: Osimertinib + Tepotinib for MET-amplified EGFRm NSCLC

- ***MET*amp detected** by: **TBx FISH** (*MET* GCN ≥5 and/or *MET*/*CEP7* ≥2) and/or by **LBx NGS** (*MET* GCN ≥2.3; Archer®)
- Comprehensive analysis of prescreening *MET*amp by **TBx FISH** & **LBx NGS** is reported by Yu et al. (**Poster 9074, ASCO 2023**)
- **Primary endpoint:** objective response by IRC for patients with centrally detected *MET*amp by **TBx FISH**



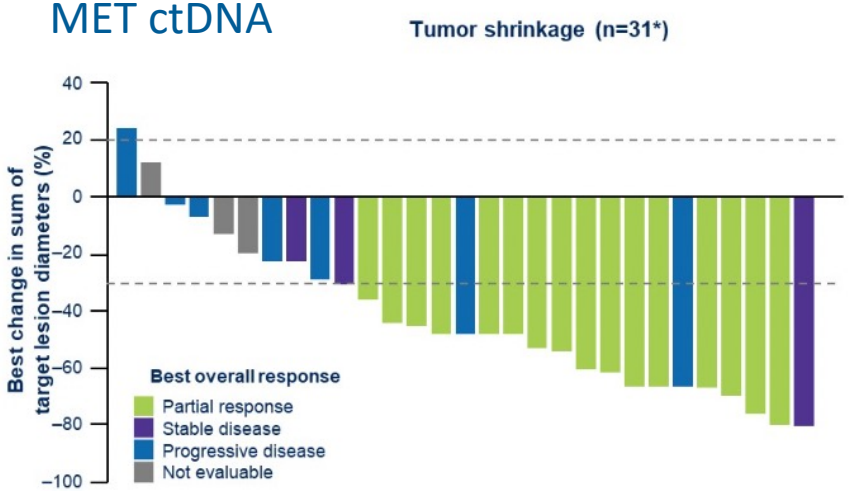
- At data cut-off (September 26, 2022), efficacy population had ≥3 months' follow-up
- Primary analysis will be conducted at ≥9 months' follow-up

MET FISH



ORR=43.9%, mPFS 5.4 mo. (4.2, 7.1)

MET ctDNA



ORR=51.6%, mPFS 4.6 mo. (2.7, 6.9)

D. Tan et al. ASCO 2023.

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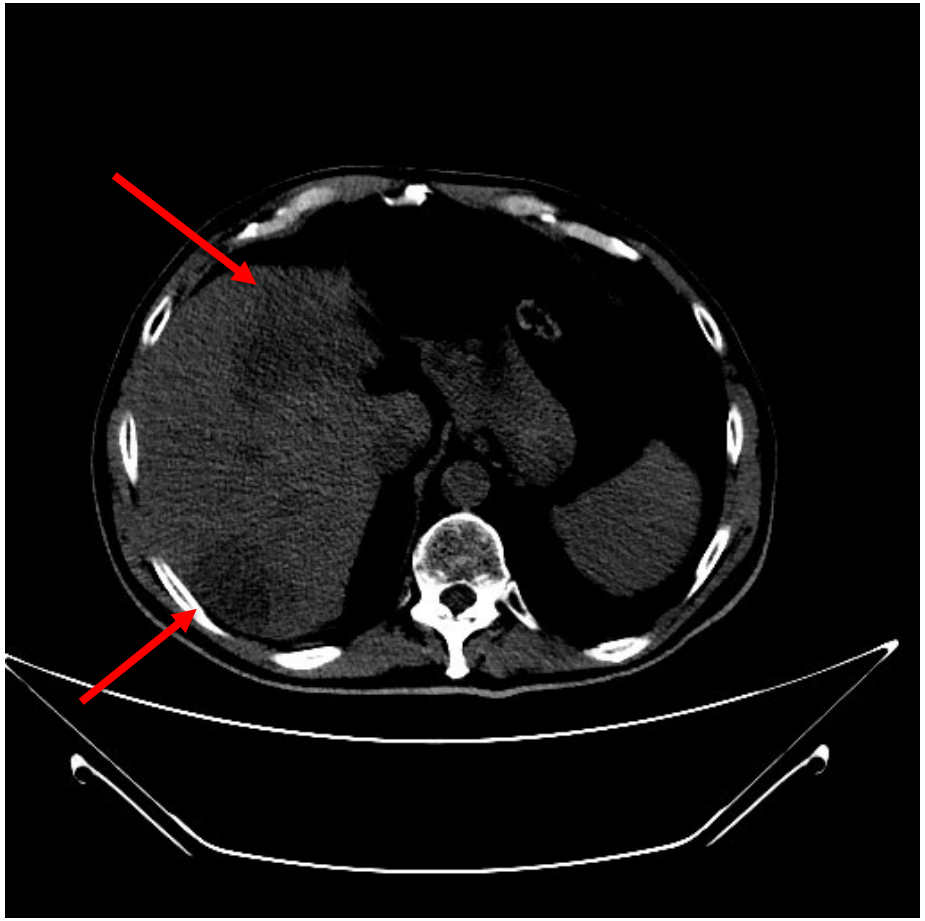
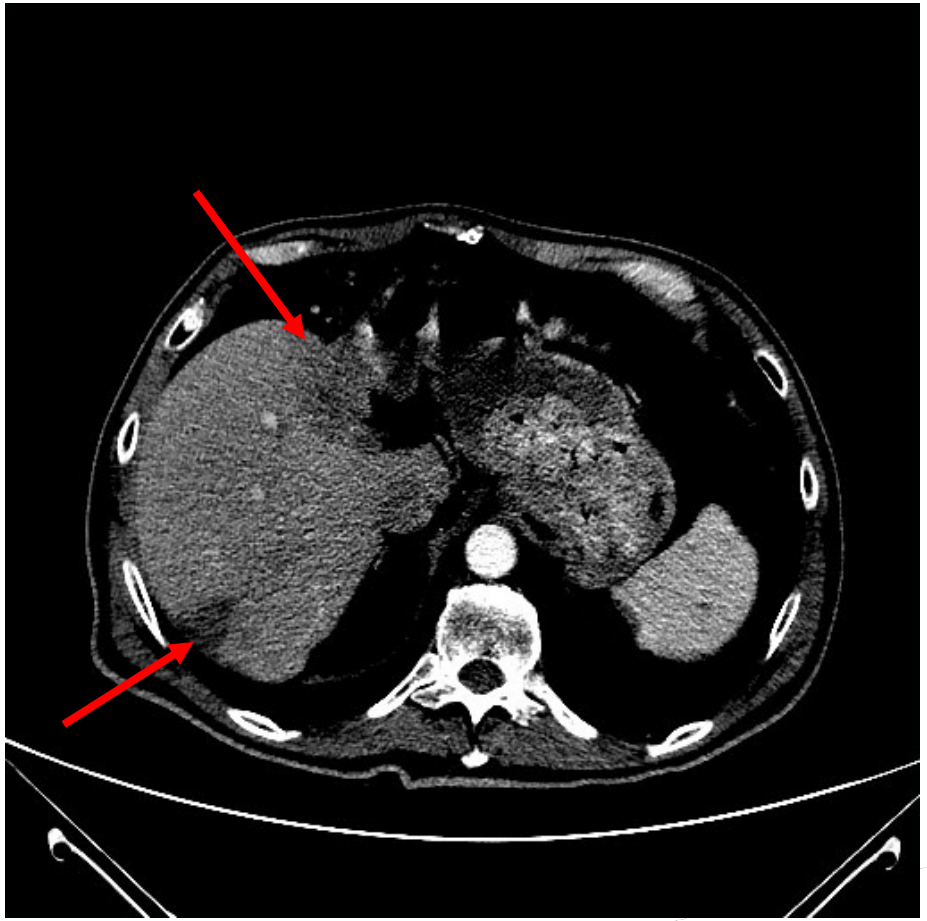
Tepotinib added to osimertinib. Abdominal pain resolved in 2-3 days, PS improved

March 27, 2024



May 10, 2024



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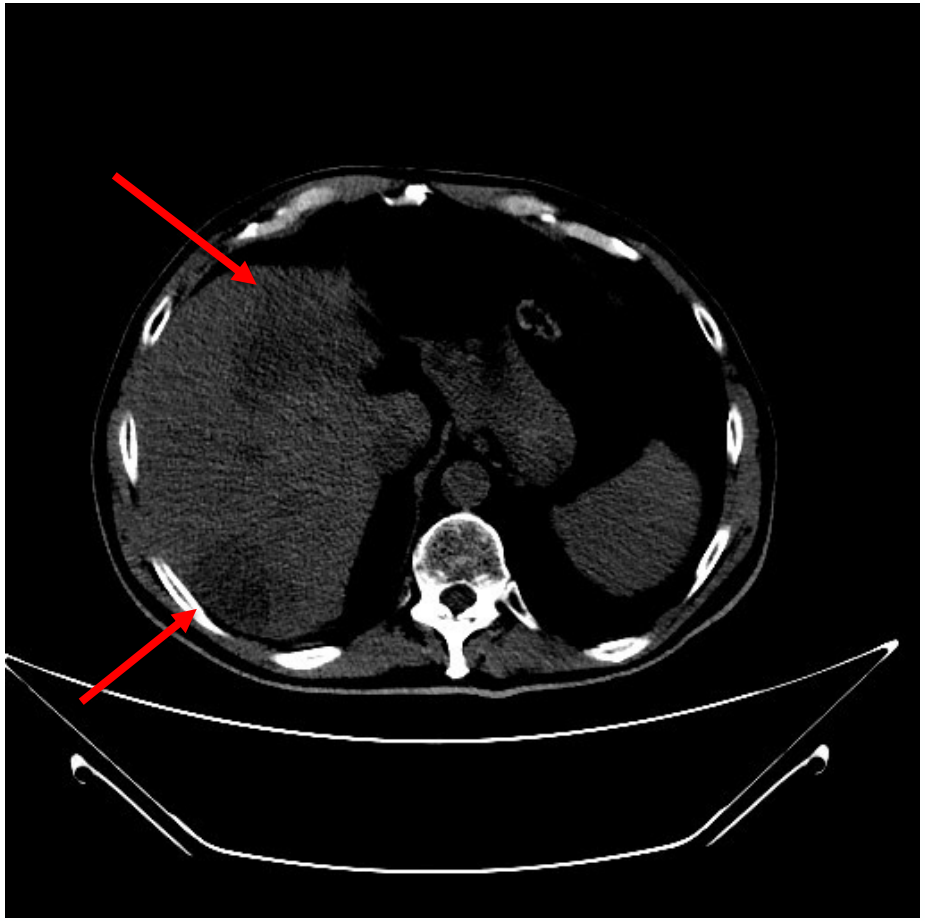
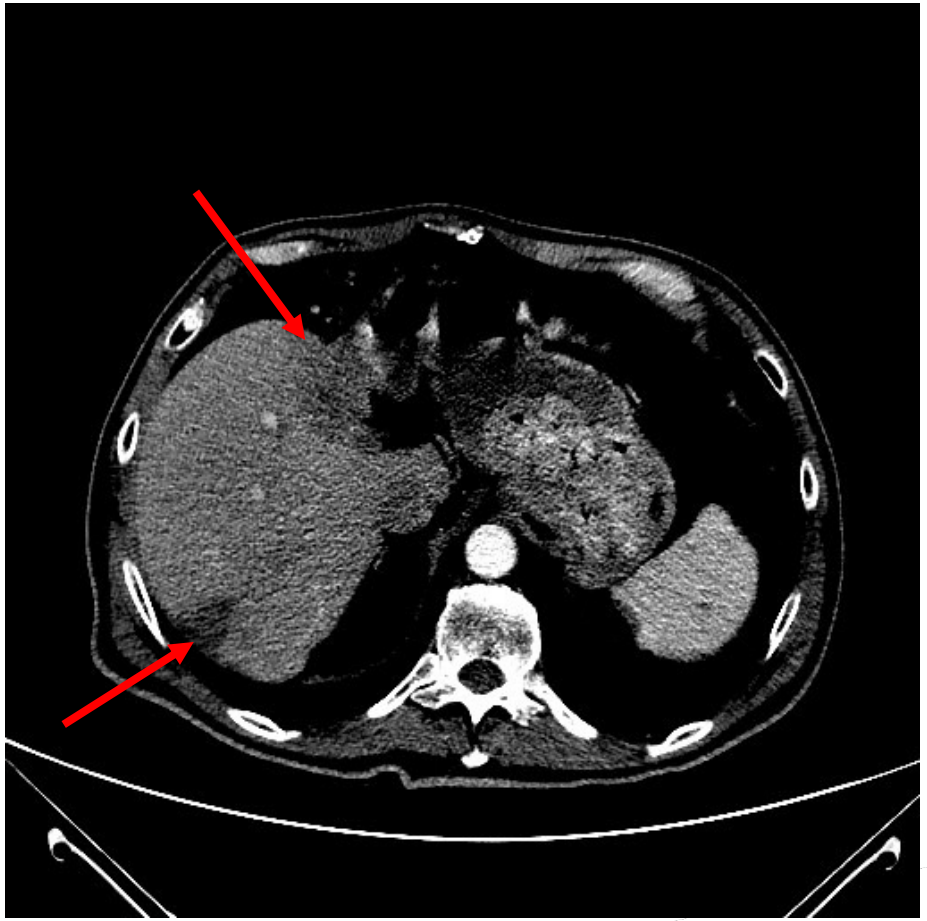


Target lesions

48 mm → 37 mm
21 mm → 9 mm
28 mm → 16 mm
30 mm → 14 mm
69 mm → 27 mm

May 10, 2024



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Other Bypass Tracts That Are Potentially Actionable

ALK Fusions

Osimertinib + Alectinib
6 months DoR
Case Reports

BRAF Fusions

Osimertinib + Trametinib
Response, D/c at 5 mo (Tox)
Case Report

BRAF V600E

Osimertinib + Dabrafenib/Trametinib
7-8 months DoR

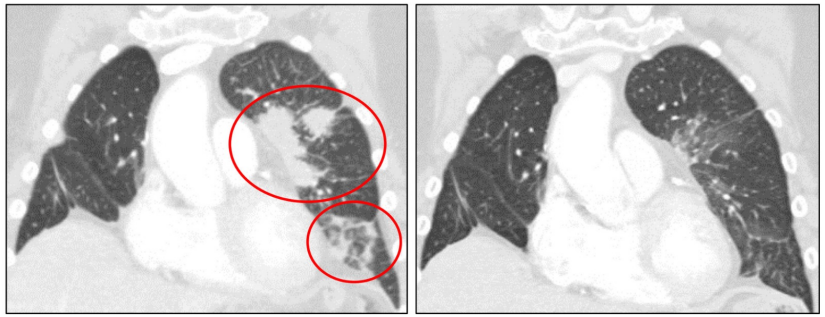
Osimertinib+Vemurafenib
7+ months DoR
Case Reports

Jebbink et al. MA02.07. WCLC 2021; Schrock JTO 2018; Offin et al JCP Precis Oncol. 2018;
Ribero et al, npj precision oncology 2021; Huang et al JTO 2019; Sun et al Thorac Cancer 2022; Dagogo-Jack et al. JTO. 2019
J. Rotow et al. WCLC 2021
Z. Piotrowska et al. Cancer Discovery 2018.

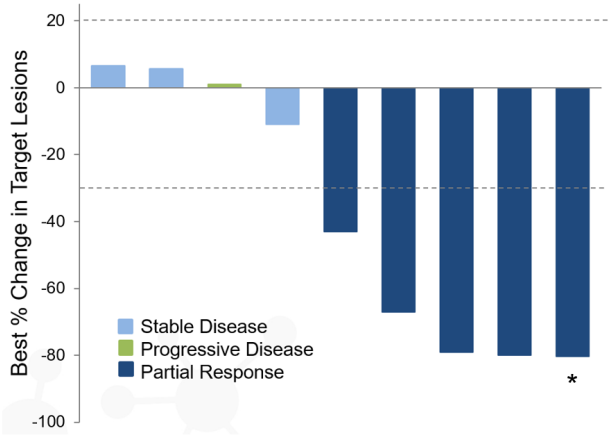
Osimertinib + RET TKI in Acquired Resistance Mediated by RET Fusion

Pralsetinib

B



Selpercatinib



Best Response (n=10)	
Objective Response n (%)	**5 (50%)**
Partial Response*	5 (50%)
Stable Disease	3 (30%)
Progressive Disease	2 (20%)
Disease Control Rate n (%)	**8 (80%)**
Median Depth of Response (%)	**-43%**

*One partial response unconfirmed

One patient with clinical progression without radiographic evaluation not shown

Z. Piotrowska et al. Cancer Discovery 2022

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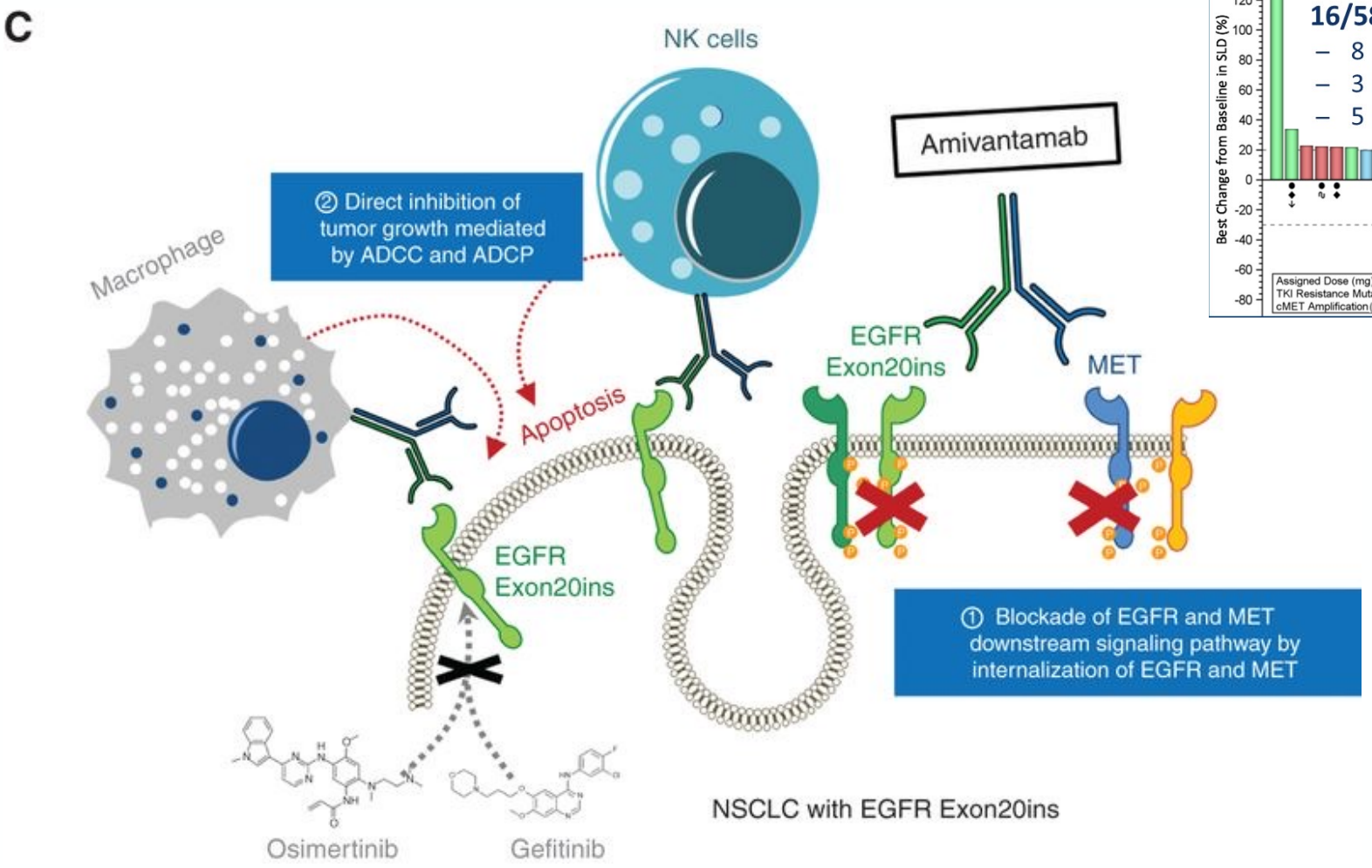
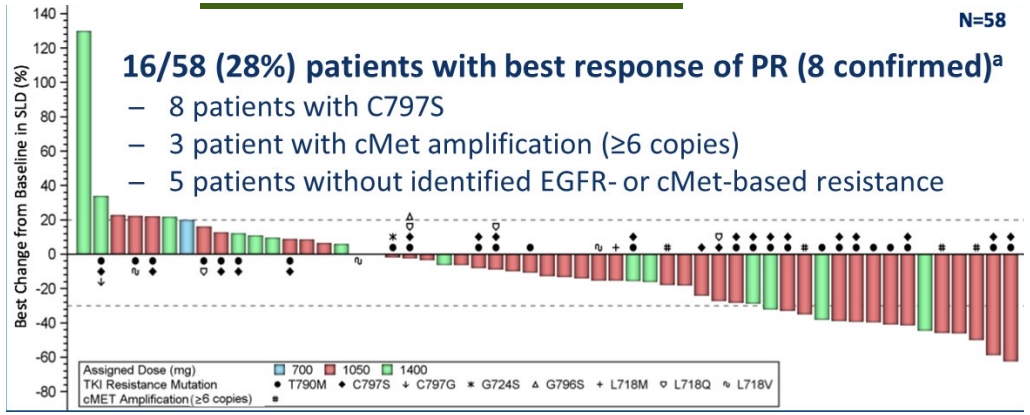
Amivantamab



Jiyeon Yun et al. Cancer Discov 2020;10:1194-1209

CHRYSALIS trial



Haura et al 2019 ASCO Annual Meeting

- Amivantamab has single agent activity after osimertinib
- Activity is independent MET amplification or 2nd site *EGFR* mutation/amplification.

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MARIPOSA-2: Phase 3 Study Design

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Documented *EGFR* Ex19del or L858R
- *Progressed on or after osimertinib monotherapy (as most recent line)*
- ECOG PS 0 or 1
- Stable brain metastases were allowed; radiation/definitive therapy was not required (untreated)

Stratification Factors

- Osimertinib line of therapy (1st vs 2nd)
- Asian race (yes or no)
- History of brain metastases (yes or no)

2:2:1 Randomization (N=657)

Serial brain MRIs were required for all patients[a]

Amivantamab-Lazertinib-Chemotherapy (n=263)

Chemotherapy (n=263)

Amivantamab-Chemotherapy (n=131)

Dosing (in 21-day cycles)

Amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) every 3 weeks starting at Cycle 3 (week 7)

Lazertinib: 240 mg daily starting after completion of carboplatin[b]

Chemotherapy administered at the beginning of every cycle:

- **Carboplatin:** AUC5 for the first 4 cycles
- **Pemetrexed:** 500 mg/m² until disease progression

Dual primary endpoint of PFS[c] by BICR per RECIST v1.1:

- **Amivantamab-Lazertinib-Chemotherapy** vs **Chemotherapy**
- **Amivantamab-Chemotherapy** vs **Chemotherapy**

Secondary endpoints:

- Objective response rate (ORR)[c]
- Duration of response (DoR)
- Overall survival (OS)[c]
- Intracranial PFS
- Time to subsequent therapy[d]
- PFS after first subsequent therapy (PFS2)[d]
- Symptomatic PFS[d]
- Safety

MARIPOSA-2 (ClinicalTrials.gov Identifier: NCT04988295) enrollment period: December 2021 to April 2023; data cut-off: 10-Jul-2023

[a]Patients who could not have MRI were allowed to have CT scans.
[b]All patients randomized before 7Nov2022 initiated lazertinib on the first day of Cycle 1 (see next slide).
[c]Key statistical assumptions: 600 patients with 350 events across all 3 arms would provide approximately 83% and 93% power for amivantamab-chemotherapy and amivantamab-lazertinib-chemotherapy, respectively, vs chemotherapy to detect a HR of 0.65 using a log-rank test, with an overall two-sided alpha of 0.05 (median PFS of 8.5 months for amivantamab-containing arms vs 5.5 for chemotherapy). Statistical hypothesis testing included PFS, ORR, and then OS.
[d]These secondary endpoints (time to subsequent therapy, PFS2, and symptomatic PFS) will be presented at a future congress.

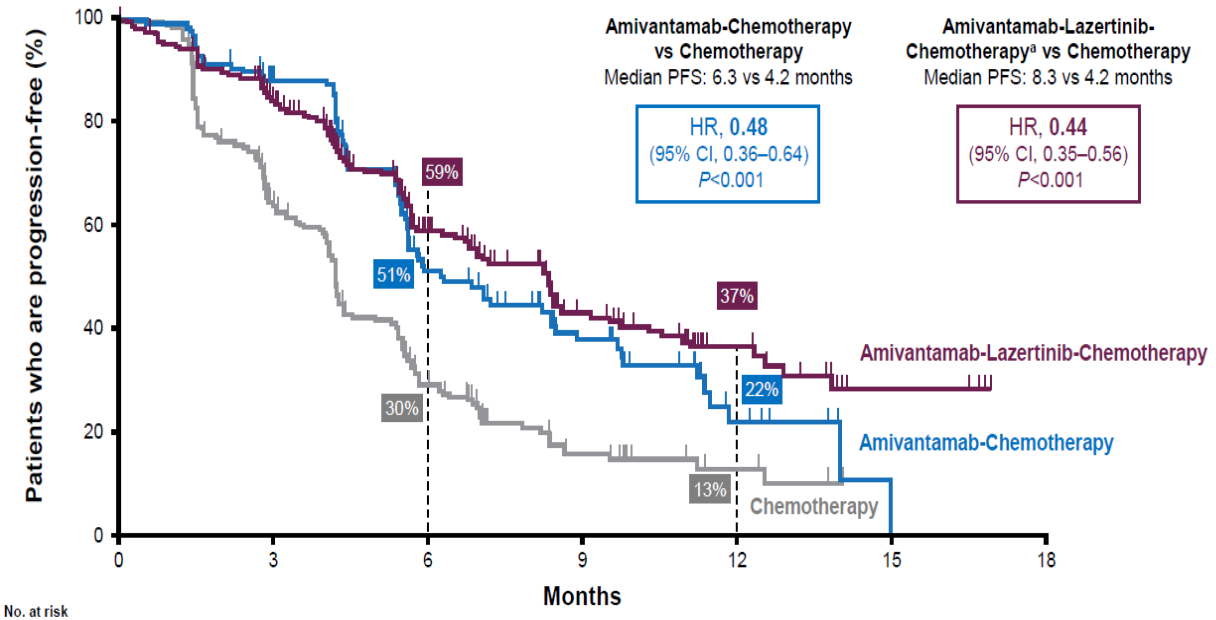
AUC, area under the curve; BICR, blinded independent central review; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, Exon 19 deletions; HR, hazard ratio; IDMC, independent data monitoring committee; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

MADRID 2023 ESMO congress

Passaro et al. ESMO 2023 and Ann Oncol. 2023 Oct 23:S0923-7534(23)04281-3

Primary Endpoint: Progression-free Survival by BICR

At a median follow-up of 8.7 months, amivantamab-chemotherapy and amivantamab-lazertinib-chemotherapy reduced the risk of progression or death by 52% and 56%, respectively



Consistent PFS benefit by investigator: HR, 0.41 (8.2 vs 4.2 mo; *P*<0.001[b]) & HR, 0.38 (8.3 vs 4.2 mo; *P*<0.001[b])

[a]Amivantamab-lazertinib-chemotherapy arm includes all patients regardless of the dosing regimen received. [b]Nominal *P*-value; endpoint not part of hierarchical hypothesis testing.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

MADRID 2023 ESMO congress

No Crossover to Ami or Ami + Laz

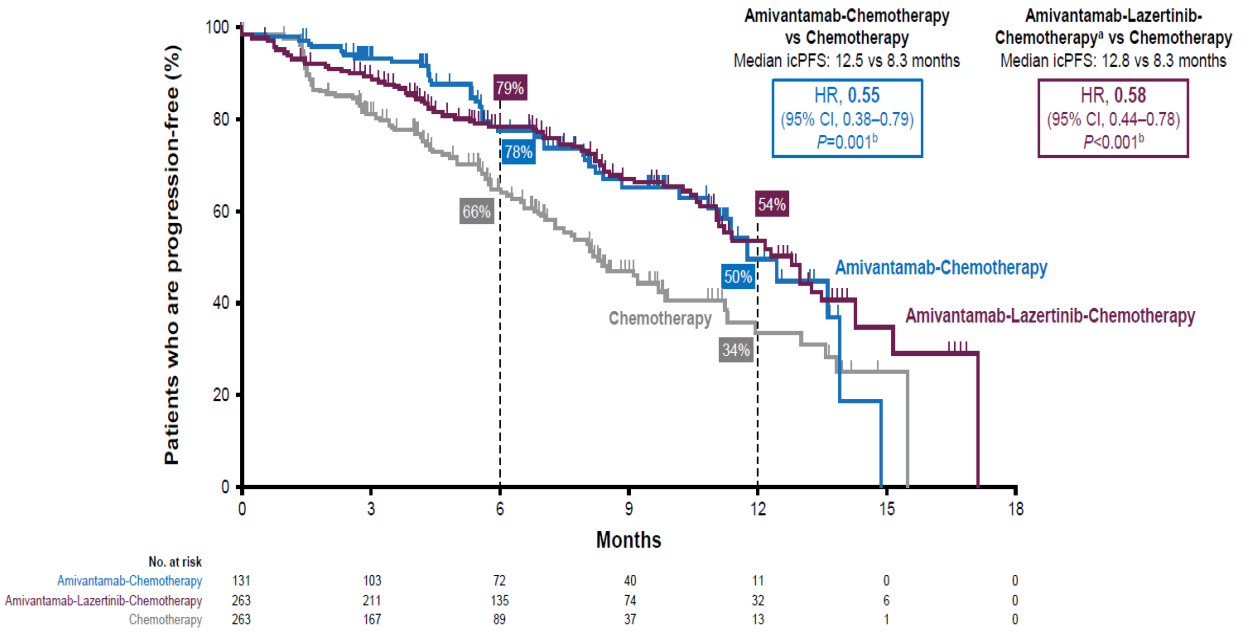
Passaro et al. ESMO 2023 and Ann Oncol. 2023 Oct 23:S0923-7534(23)04281-3

- Benefits across all subgroups (Race, Sex, *EGFR* mutation type)
- ORR:
  - 36 % chemo
  - 64% chemo + Ami
  - 63% chemo + Ami +Laz
- mDOR 5.6 vs. 6.9 vs. 9.4 months
- Overall Survival data immature
- Higher Toxicity with Lazartinib:
  DVT/PE (prophylaxis required),
  Grade TEAEs ≥ G3 48%, 72% and 92%
  Discontinuations of all agents due to treatment- related AEs was 2%, 8%, and 10%

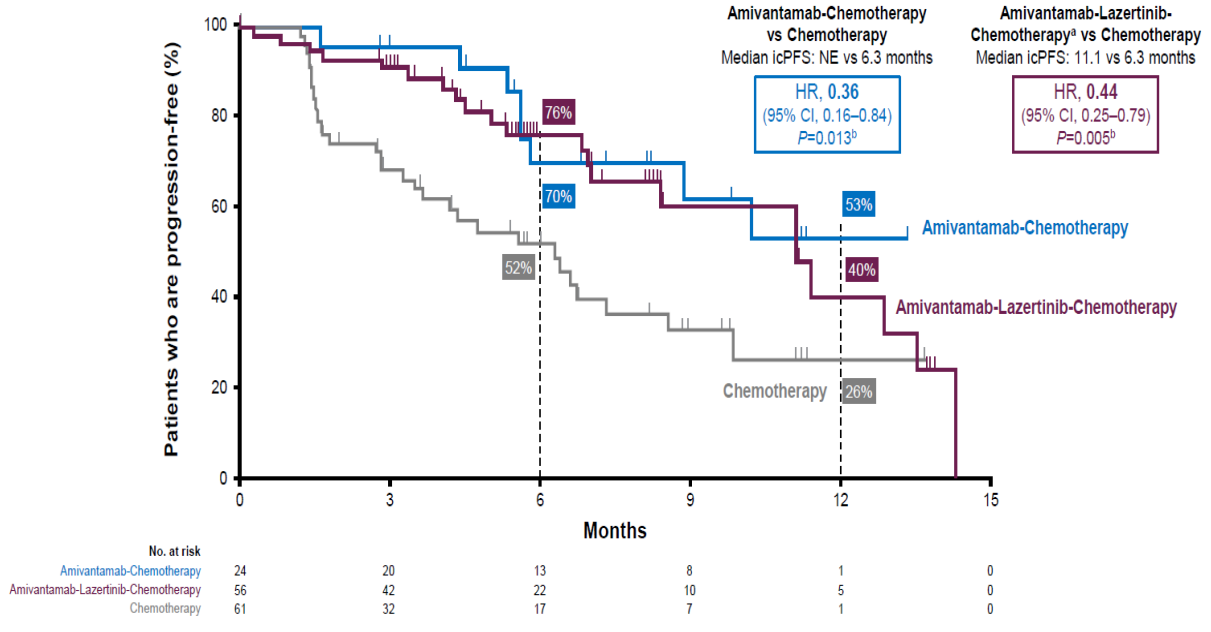
What about CNS disease control in the absence of a TKI?

Intracranial Progression-free Survival by BICR

Amivantamab-chemotherapy and amivantamab-lazertinib-chemotherapy reduced the risk of intracranial progression or death by 45% and 42%, respectively



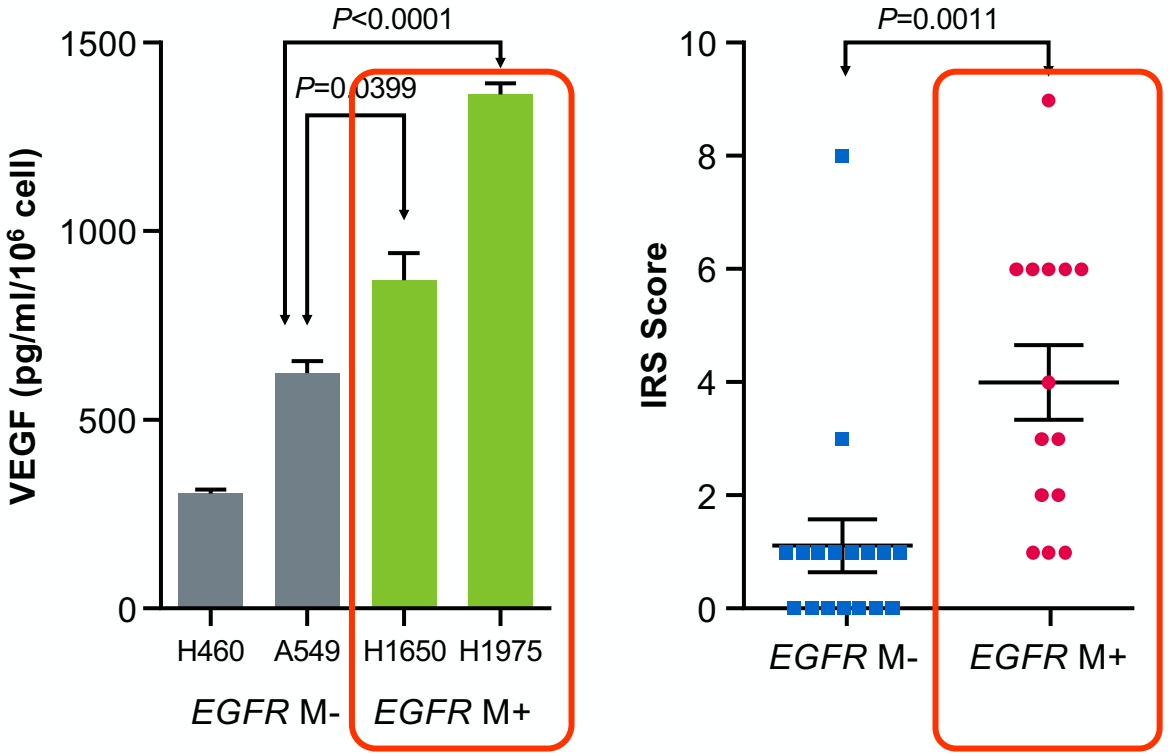
Intracranial Progression-free Survival by BICR Among Patients With a History of Brain Metastases and No Prior Brain Radiotherapy



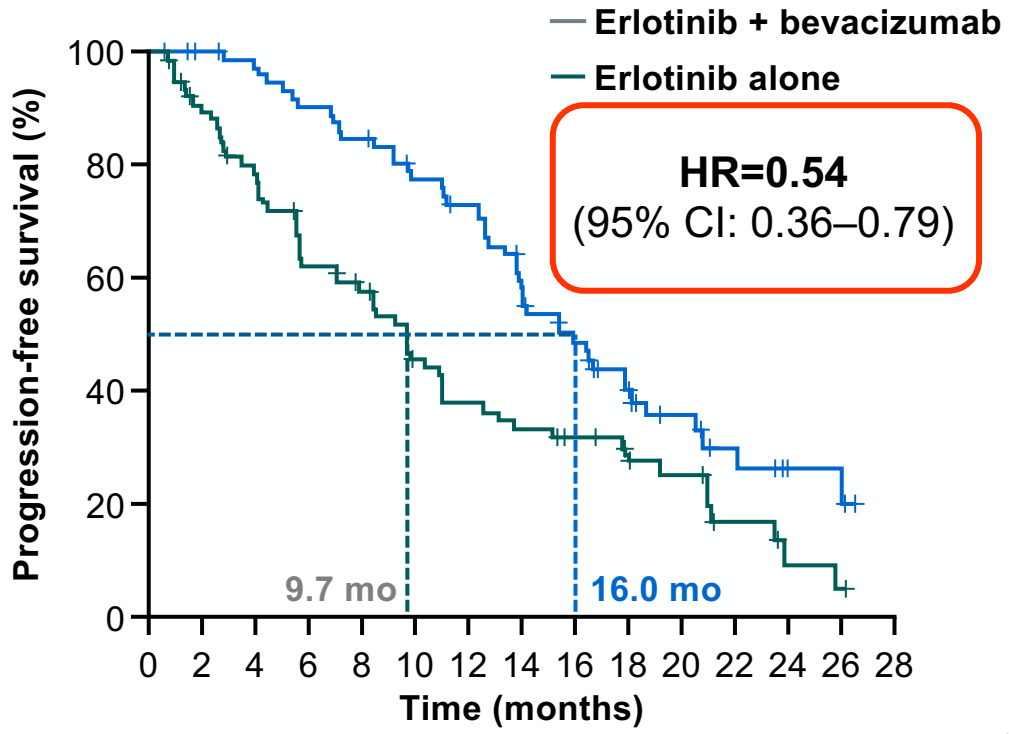
Passaro et al. ESMO 2023 and Ann Oncol. 2023 Oct 23:S0923-7534(23)04281-3

What is the role of VEGF in patients with *EGFR*+ NSCLC?

EGFR signal activation increases VEGF production



JO25567: *EGFR*+ NSCLC patients have increased sensitivity to bevacizumab



Hung, et al. Oncol Lett 2016; Seto, et al. Lancet Oncol 2014

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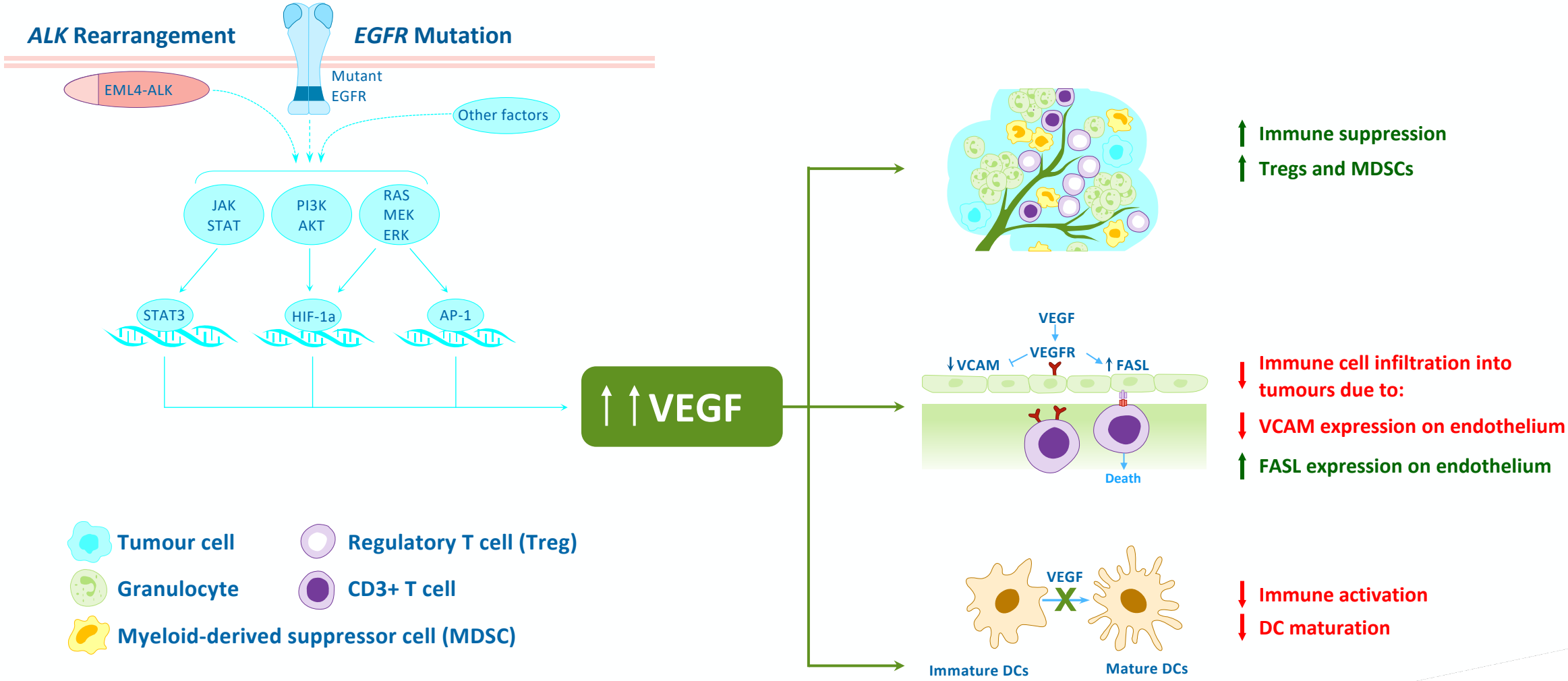
VEGF-mediated immunoregulation may be stimulated by EGFR/ALK signalling



Chen & Hurwitz. Cancer J 2018; Cao, et al. BMC Cancer 2009; Seo, et al. Cancer 2000; Jośko, et al. Med Sci Monit 2004; Niu, et al. Oncogene 2002; Concha-Benavente, et al. Front Pharmacol. 2017; Stockhausen, et al. Neuro Oncol 2010; Semenza, et al. Nat Rev Cancer 2003; Bancroft, et al. Int J Cancer 2002; Chong, et al. Nat Med 2013

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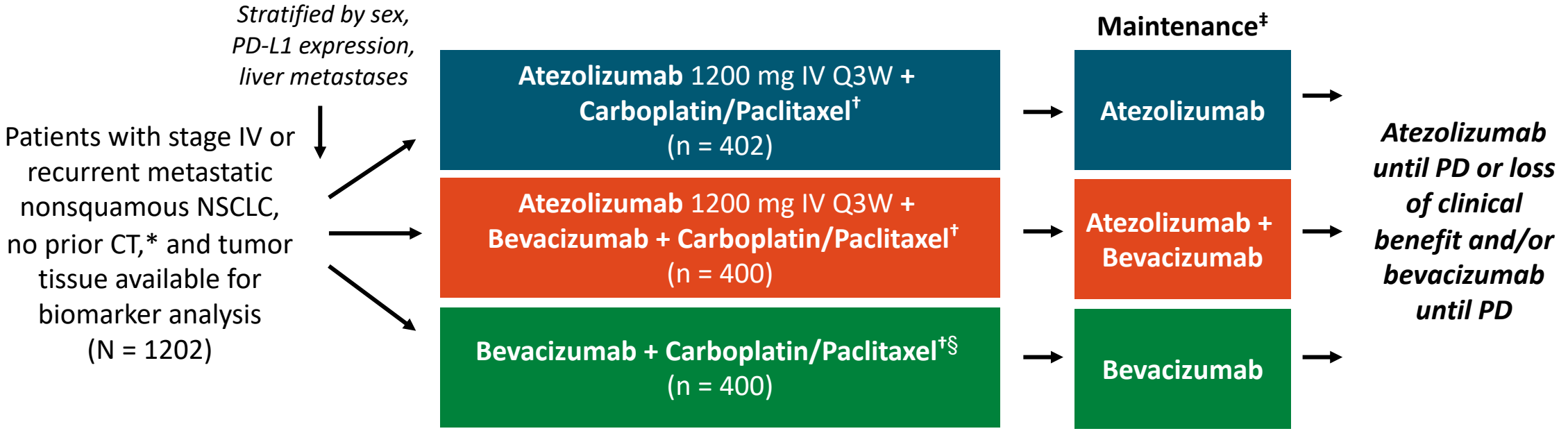
IMpower150: Addition of Atezolizumab and/or Bevacizumab to CT in Metastatic NSCLC

- Multicenter, open-label, randomized phase III trial (data cutoff: January 22, 2018)



*If sensitizing *EGFR* mutation or *ALK* translocation present, must have PD on or intolerance to ≥ 1 approved targeted therapy. †Bevacizumab 15 mg/kg; carboplatin AUC 6; paclitaxel 200 mg/m^2; all given IV Q3W for 4 or 6 cycles. ‡No crossover permitted. §Control arm.

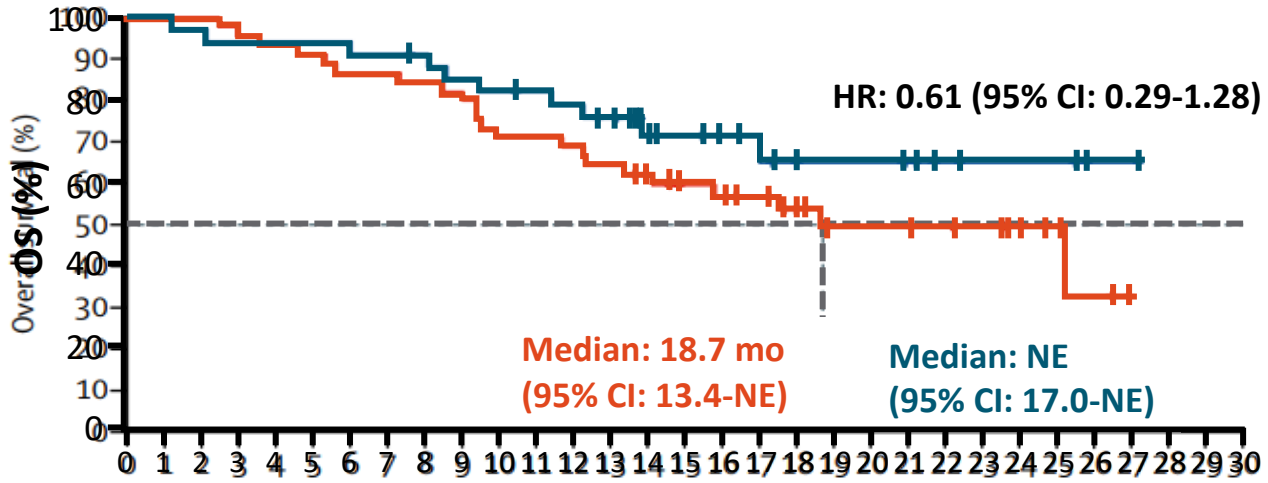
- Coprimary endpoints: investigator-assessed PFS in ITT WT, Teff-high WT; OS in ITT WT
- Secondary endpoints: investigator-assessed PFS, OS in ITT; investigator-assessed PFS in PD-L1 subgroups; IRF-assessed PFS; ORR, DoR per RECIST v1.1; safety in ITT

Socinski. NEJM. 2018;378:2288. Reck. Lancet Respir Med. 2019;7:387. Socinski. J Thorac Oncol. 2021;16:1909.

IMpower150: Survival in Patients with *EGFR* Mutations

OS With Atezo + Carbo/Pac + BEV vs Carbo/Pac + BEV in Advanced *EGFR*+ NSCLC Post EGFR TKI (n = 124)[1]

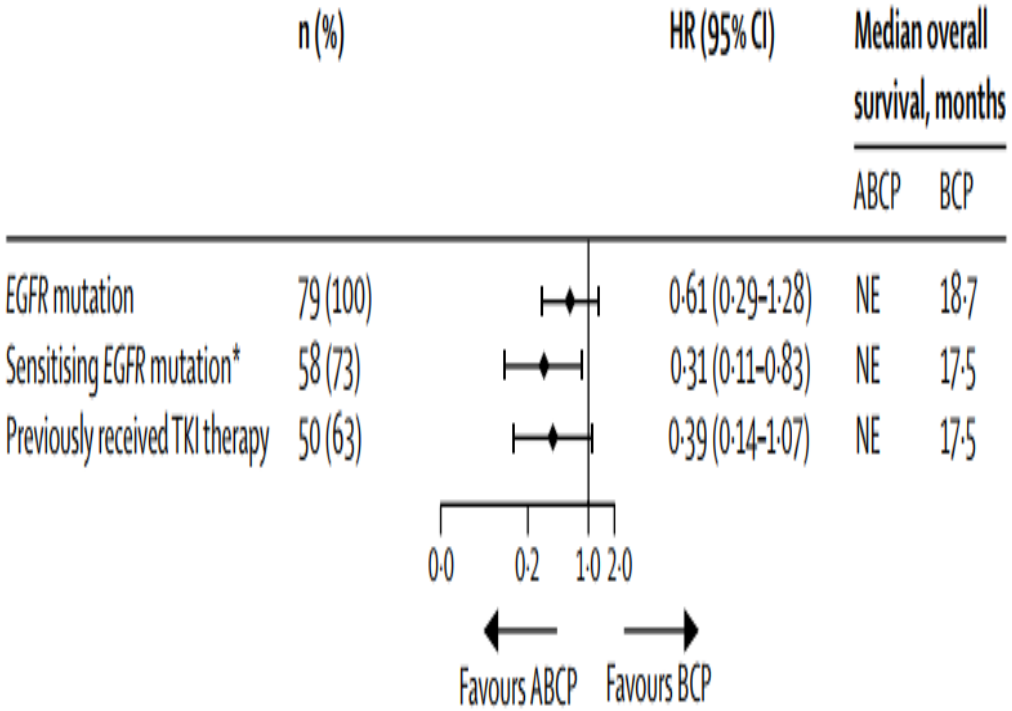
	Landmark OS, % (95% CI)		
	12 Mo	18 Mo	24 Mo
ABCP	78.9 (65.0-92.8)	65.0 (46.1-84.0)	65.0 (46.1-84.0)
BCP	68.9 (55.4-82.4)	53.9 (38.7-69.0)	49.7 (33.7-65.7)



Mo Since Randomization

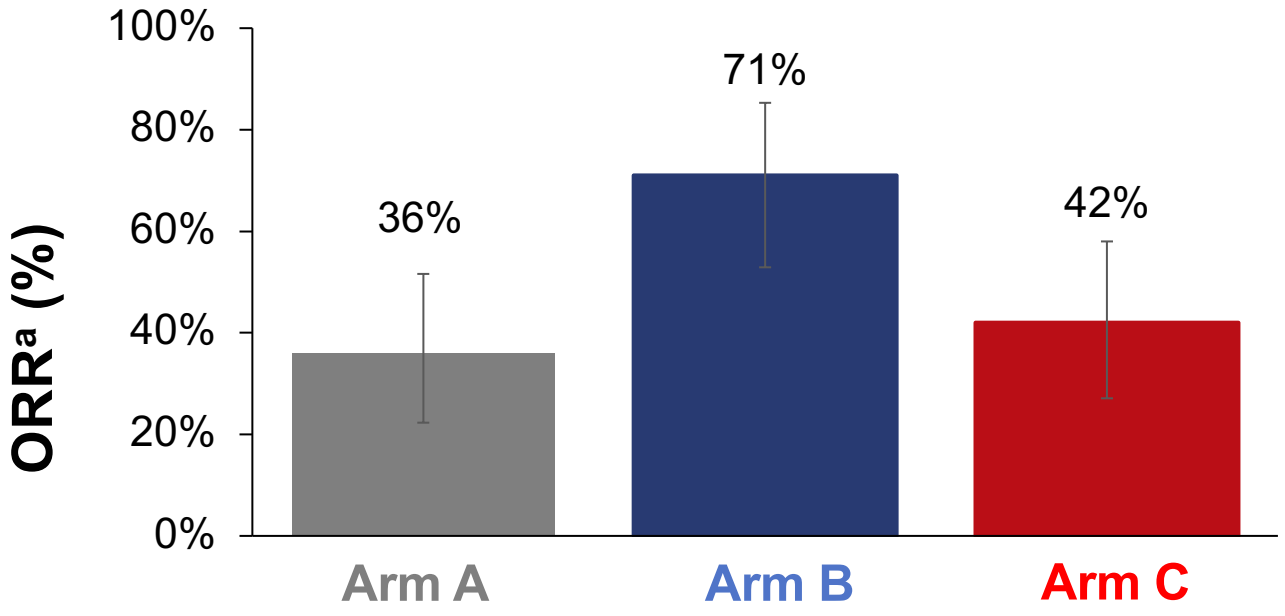
Number at risk

ABCP	34	34	33	32	32	32	32	31	30	28	27	26	25	23	17	15	12	11	9	8	8	6	4	3	3	3	1	1	..	..	..
BCP	45	45	45	43	42	41	39	39	38	37	32	32	31	29	25	22	21	19	14	11	11	11	10	8	6	4	2	..	..	..	..



Reck. Lancet Respir Med. 2019;7:387.

ORR and DOR in *EGFR*-mt patients



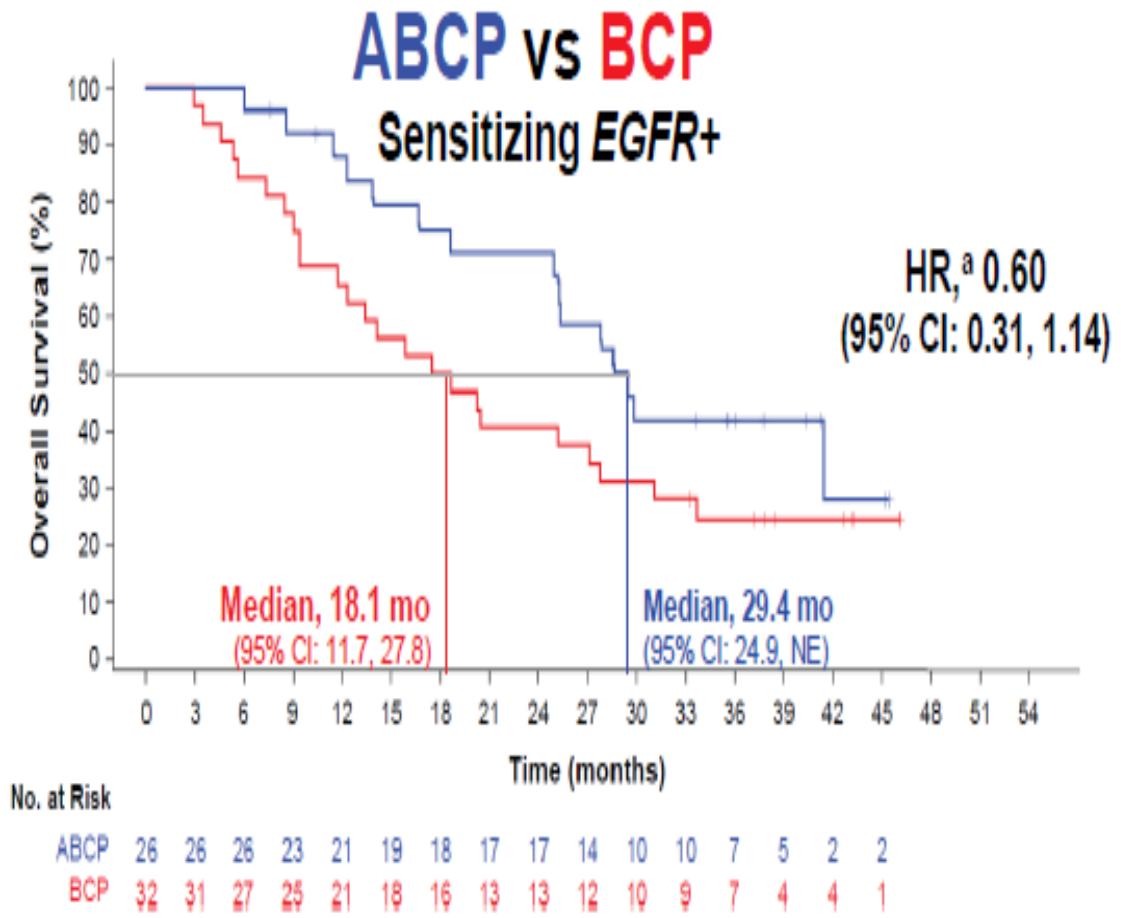
	Atezo + CP	Atezo + bev + CP	Bev + CP
Median DOR (range), mo	5.6 (2.6–15.2)	11.1 (2.8–18.0)	4.7 (2.6–13.5)

- The addition of bevacizumab to atezolizumab and chemotherapy almost doubled the overall response rate and duration of response in *EGFR*-mt patients

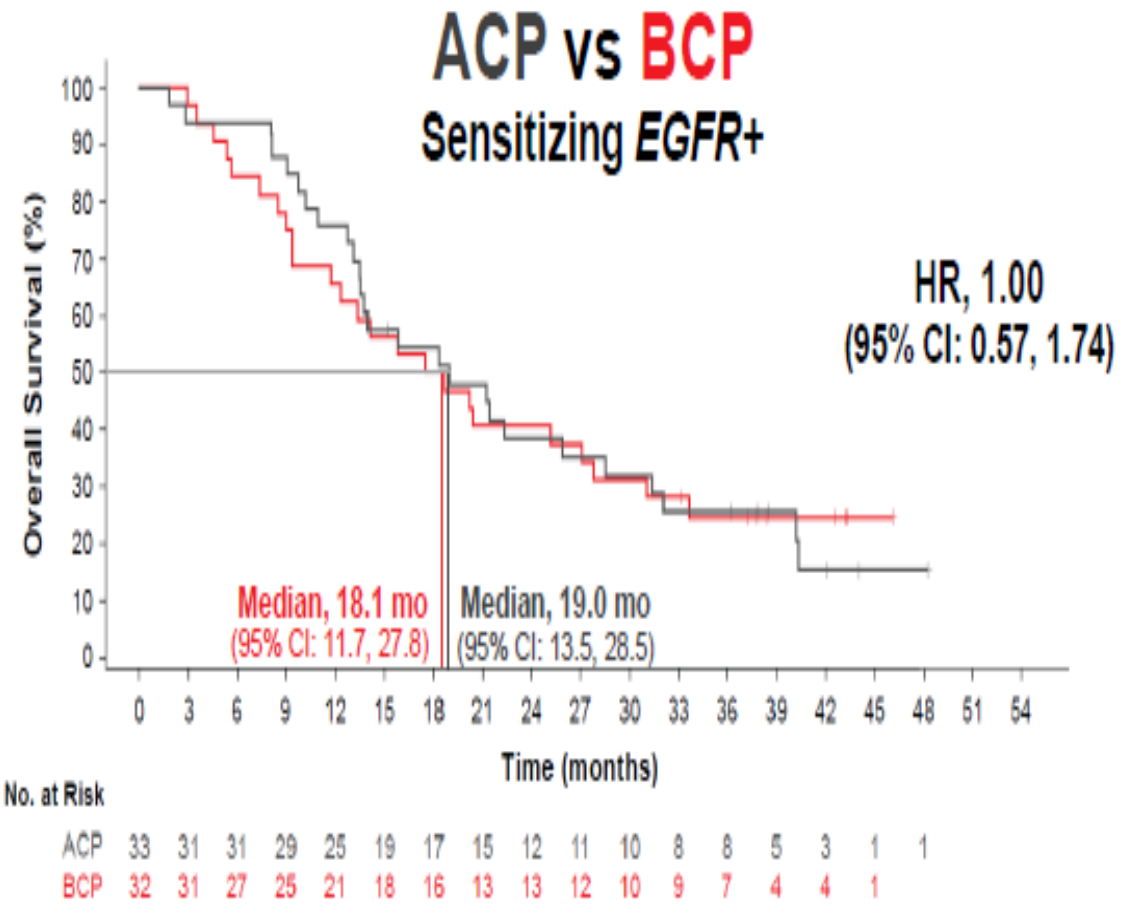
[a] Responses are confirmed.
Data cutoff Jan 22, 2018.

Mok et al. IMpower150 in *EGFR*-mt pts

Final OS analysis

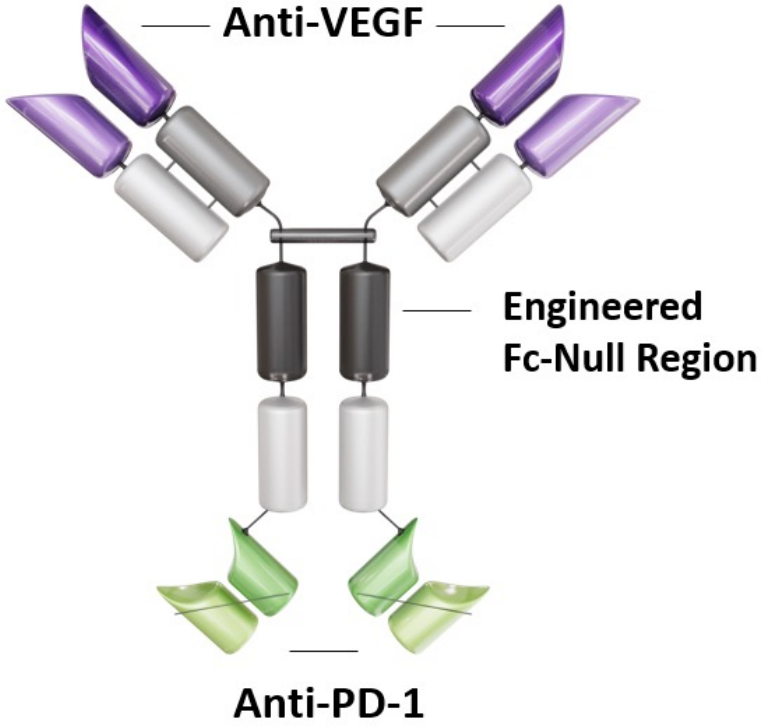


Arm B vs Arm C



Arm A vs Arm C

Ivonescimab - Background



- For patients with EGFR-mutant NSCLC, upfront treatment with tyrosine kinase inhibitors is standard. However, drug resistance remains a challenge, and an effective therapy after progression is needed.
- Ivonescimab (AK112/SMT112) is an anti-PD-1/VEGF bispecific antibody displaying cooperative binding characteristics.
- Phase II clinical studies have shown potential efficacy of Ivonescimab plus chemotherapy in NSCLC patients with EGFR mutations who progressed on prior EGFR-TKIs therapies[1-2].

1. L Zhang et al: ASCO 2023; 2. YY Zhao et al: eClinicalMedicine 2023;62: 102106.

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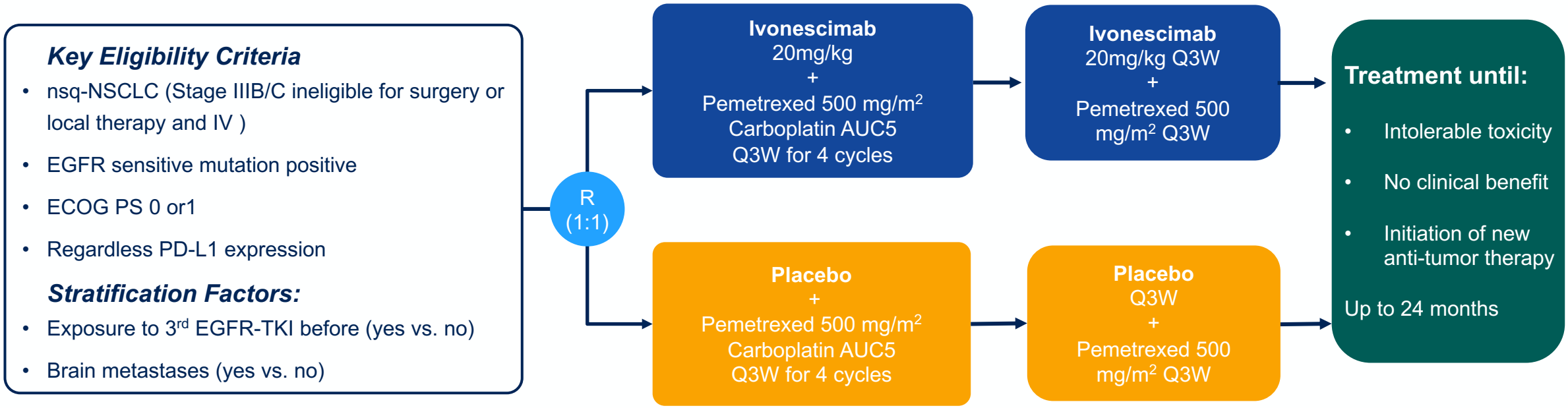
HARMONi-A Study Design



Endpoints

- Primary: Progression-free survival by independent radiologic review committee (IRRC)
- Secondary: Overall survival, Response rate, Duration of response, Time to response and Safety

ClinicalTrials.gov, NCT05184712; NSCLC, non-small cell lung carcinoma; EGFR, epidermal growth factor receptor; ECOG, eastern copperative oncology group; TKI, tyrosine-kinase inhibitor; Q3W, every 3 weeks.

ASCO 2024, Abstract 8508

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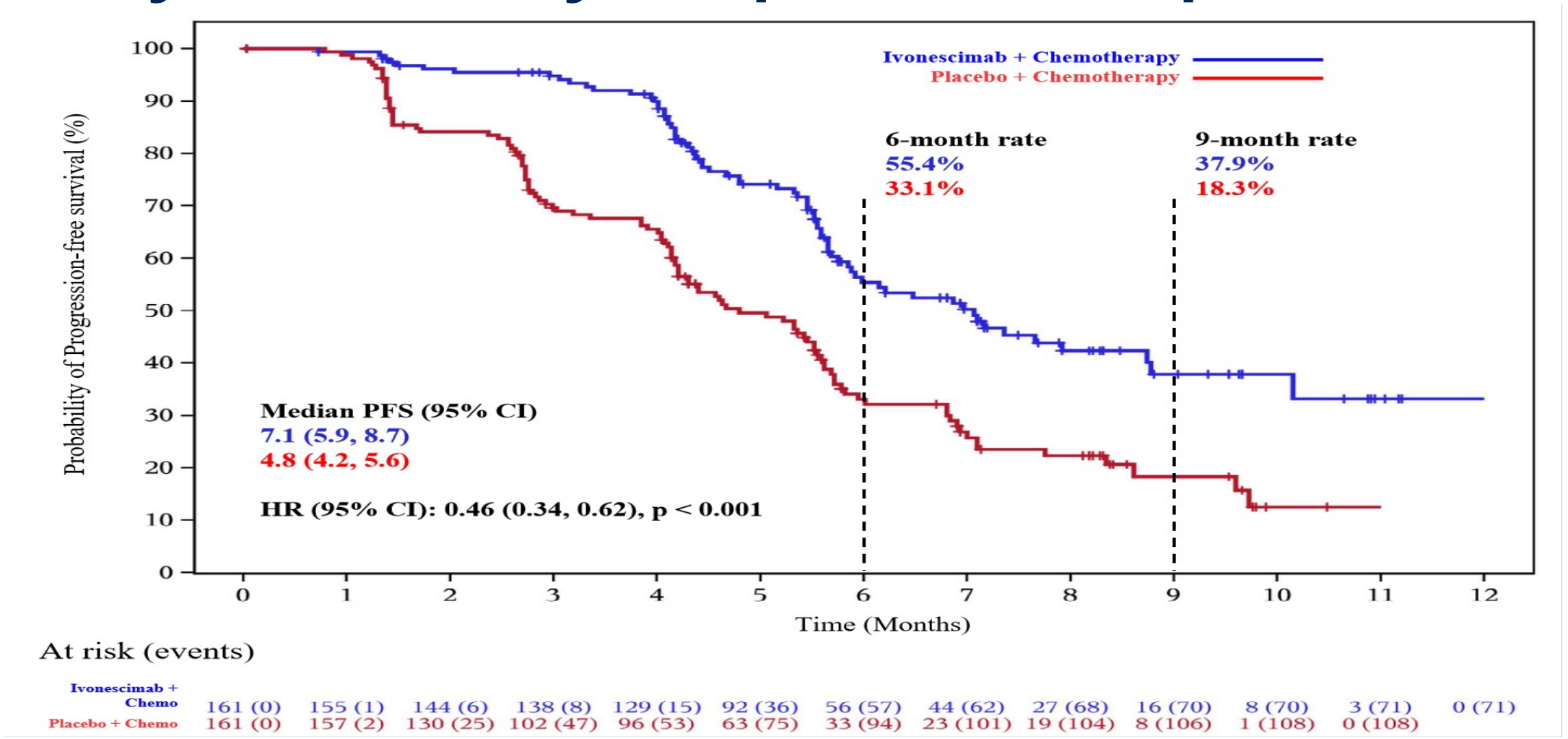
Study Met Primary Endpoint of PFS per IRRC



HR and P-value were stratified by previous 3rd Gen EGFR-TKI ues (yes vs. no) and presence of brain metastases (yes vs. no), and were calculated with stratified Cox model and log rank test. The two-sided P-value boundary is 0.024 as calculated using Lan-Demets spending function with O'Brien-Fleming approximation.
HR, hazard ratio; CI, confidence interval; IRRC, independent radiology review committee.

ASCO 2024, abstract 8508

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Conclusions

- Ivonescimab plus chemotherapy significantly improved PFS in patients who progressed on prior EGFR-TKIs treatments: **PFS HR 0.46 (95% CI: 0.34, 0.62), P<0.001**
- The prespecified subgroup analysis showed PFS benefit favoring patients receiving ivonescimab over those receiving the placebo across all subgroups.
- OS analyses show a favorable trend for prolonged OS for ivonescimab-chemotherapy
- The safety profile was generally manageable, without any unexpected adverse events and a low rate of treatment discontinuation.
- This study is being expanded globally, HARMONi (NCT06396065), to include patients from North America and Europe.

With the recent approval in China, ivonescimab plus chemotherapy is a new standard treatment option for NSCLC patients who progress after EGFR-TKI treatment

ASCO 2024, abstract 8508

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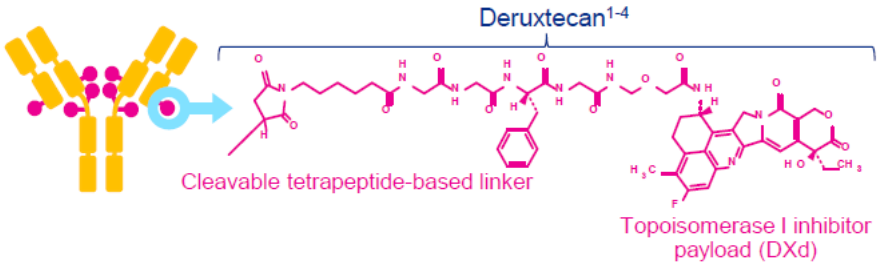
Anti-HER3 ADC: Patritumab Deruxtecan(HER3-DXd)

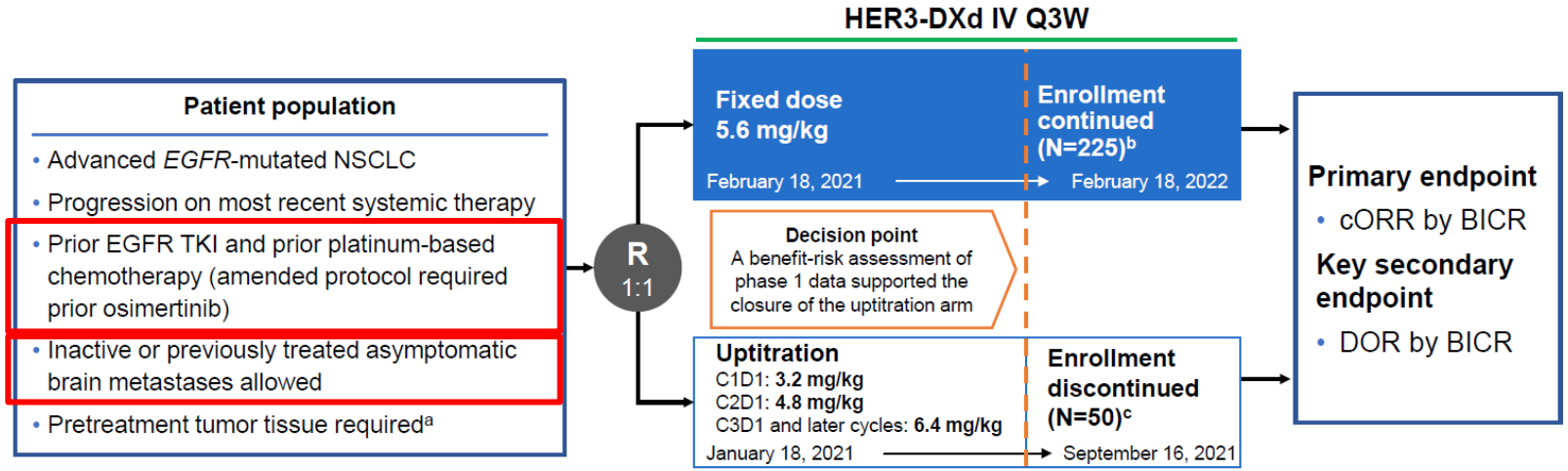
HER3-DXd is an ADC composed of 3 parts[1-4]:

- A fully human anti-HER3 IgG1 mAb (patritumab)
- A topoisomerase I inhibitor payload (DXd)
- A tetrapeptide-based cleavable linker that covalently bonds the other 2 components



Payload mechanism of action: topoisomerase I inhibitor[1-4,a]
High potency of payload[1-4,a]
High drug to antibody ratio ≈8[1,2,a]
Payload with short systemic half-life[2,3,a,b]
Stable linker-payload[2-4,a]
Tumor-selective cleavable linker[1-5,a]
Bystander antitumor effect[2,6,a]

HERTHENA-Lung01 Study Design[1]



- 51% prior brain metastases (32 % at baseline)
- Median lines of therapy: 3 (93% 3rd generation TKI, 40% prior IO)

Yu et al. WCLC 2023; Yu et al. JCO 2023;

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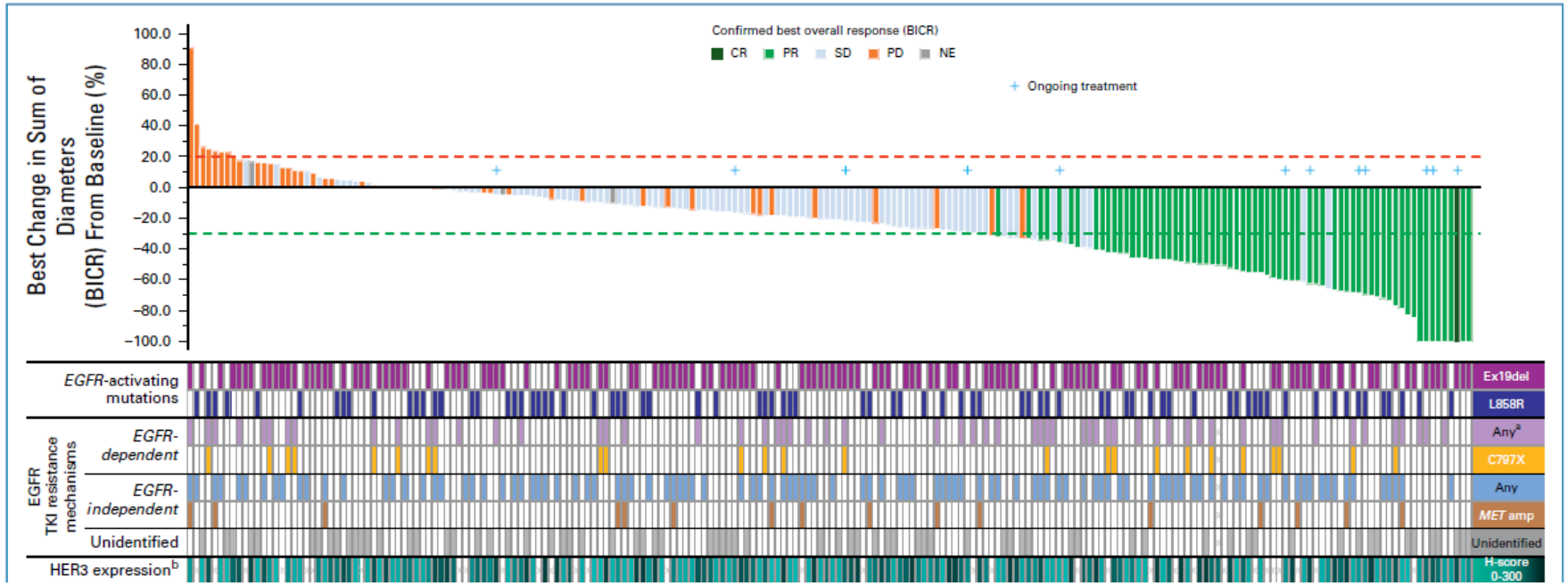
Anti-HER3 ADC: Patritumab Deruxtecan(HER3-DXd)



	Type of EGFR TKI resistance mechanism			
	EGFR-dependent, only (n=34)	*EGFR*-independent, only (n=81)	Both *EGFR*-dependent and -independent (n=32)	None identified (n=77)
Confirmed ORR (95% CI), %	32.4 (17.4-50.5)	27.2 (17.9-38.2)	37.5 (21.1-56.3)	27.3 (17.7-38.6)

Snapshot data cutoff, 18 May 2023.
Median study follow-up, 18.9 (range, 14.9-27.5) months.

- Benefits across all subgroups.
- Benefit across EGFR TKI resistance mechanisms.
- Benefit seen regardless of HER3 IHC expression.

mPFS 5.5 months (5.1-5.9)
mDOR 6.4 months (4.9-7.8)
mOS 11.9 months (11.2-13.1)

Yu et al. WCLC 2023; Yu et al. JCO 2023;

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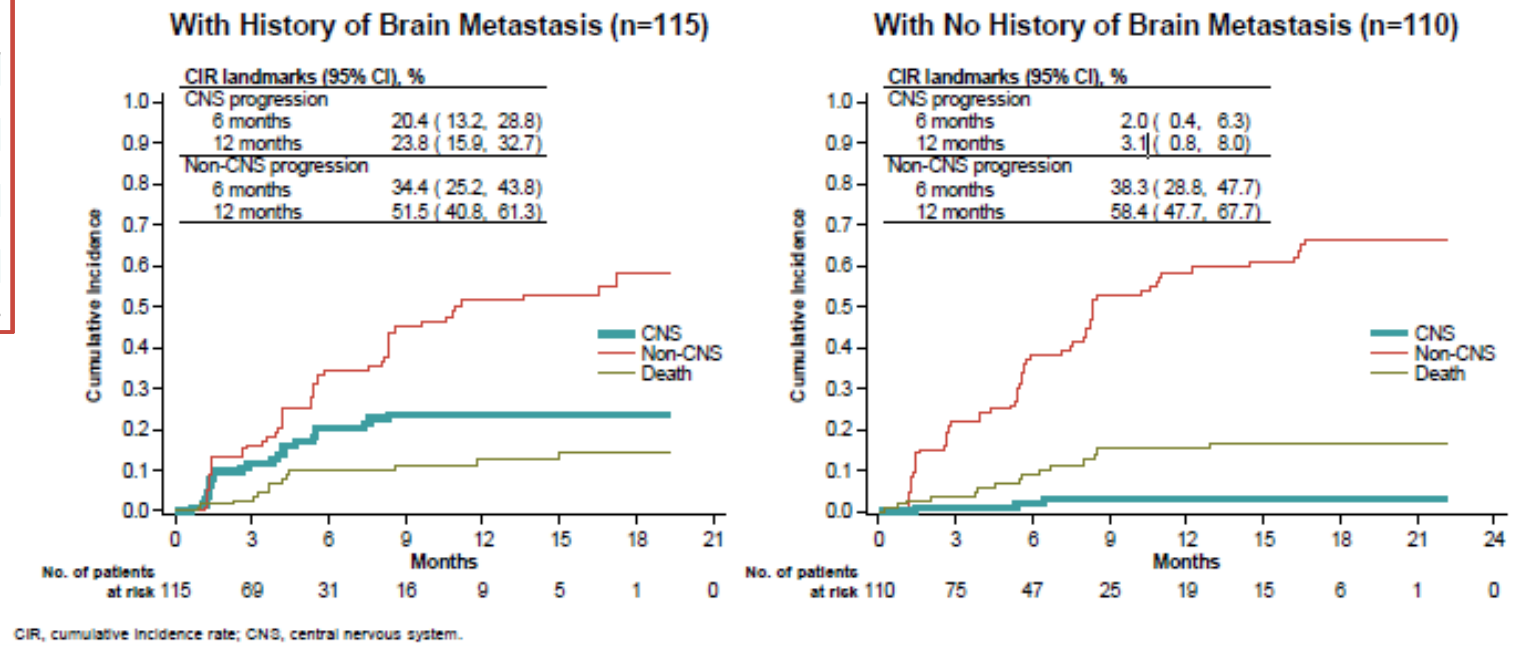
What about CNS disease control in the absence of a TKI?

Responses by CNS BICR[a]	All patients with baseline BM by CNS BICR (n=95)	Patients whose baseline BM had not been irradiated (n=30)[b]
CNS cORR, n (%) [95% CI]	19 (20.0) [12.5, 29.5]	10 (33.3) [17.3-52.8]
CR, n (%)	15 (15.8)	9 (30.0)[c]
PR, n (%)	4 (4.2)	1 (3.3)
SD/non-CR/non-PD, n (%)	57 (60.0)	13 (43.3)
PD, n (%)	13 (13.7)	4 (13.3)
NE, n (%)	6 (6.3)	3 (10.0)
CNS DCR (95% CI), %	80.0 (70.5, 87.5)	76.7 (57.7-90.1)
CNS DOR, median (95% CI), mo	9.2 (8.1-11.1)	8.4 (5.8-9.2)

Snapshot data cutoff, 18 May 2023.
Median study follow-up, 18.9 (range, 14.9-27.5) months.



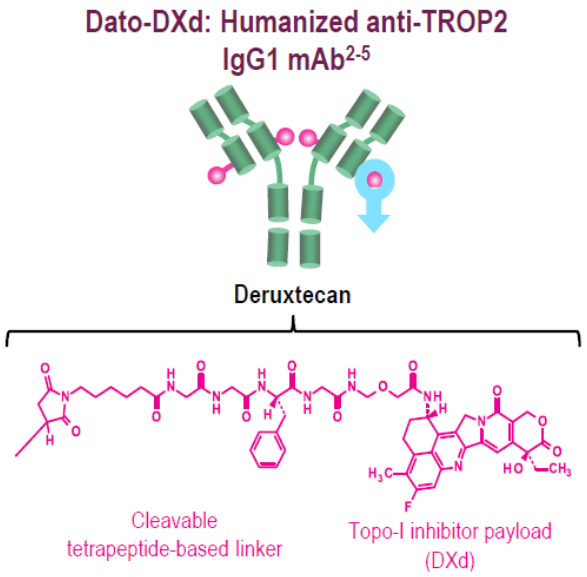
CIR, cumulative incidence rate; CNS, central nervous system.

Site of first PD:

- 21% of patient with h/o BM
- 3% of patients without h/o BM

Johnson et al. ESMO 2023; Yu et al. WCLC 2023; Yu et al. JCO 2023

Trop2-ADCs: Datopotamab deruxtecan (Dato-DXd)



TROPION-Lung05(NCT04484142)

Screening

Key inclusion criteria

- Stage IIIB, IIIC, or IV NSCLC
- Presence of ≥1 actionable genomic alteration (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
- ECOG PS of 0 or 1
- ≥1 line of targeted therapy
- 1 or 2 prior cytotoxic agent–containing therapies including platinum-based therapy in the metastatic setting
- Radiographic disease progression after targeted therapy

Treatment

Dato-DXd 6 mg/kg Q3W

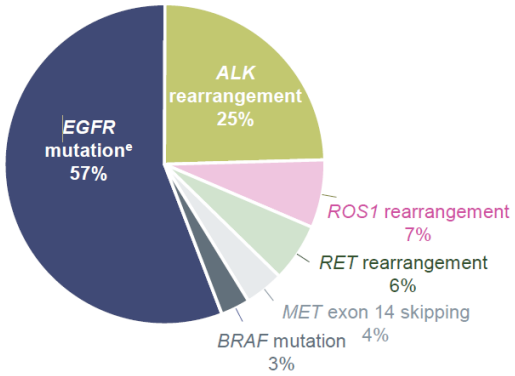
Endpoints[a]

Primary: ORR by BICR

Secondary:

- By BICR and investigator: DOR, DCR, CBR, PFS, TTR
- By investigator: ORR
- OS, safety, PK, immunogenicity

Relative Frequency of Genomic Alterations[b-d]



Disposition	At the time of data cutoff (December 14, 2022):
	• Median (range) treatment duration was 4 (1-21) months
	• 60 participants (44%) were ongoing in study
	• 20 participants (15%) were ongoing on study treatment

Heavily pretreated patient cohort:

- 72 % ≥ 3 lines of therapy (60% ≥ 2 prior TKIs)
- 51% patients with BM
- 3% of patients without h/o BM

Paz-Ares et al. ESMO 2023, Ahn et al. ESMO 2023.

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Datopotamab deruxtecan (Dato-DXd)

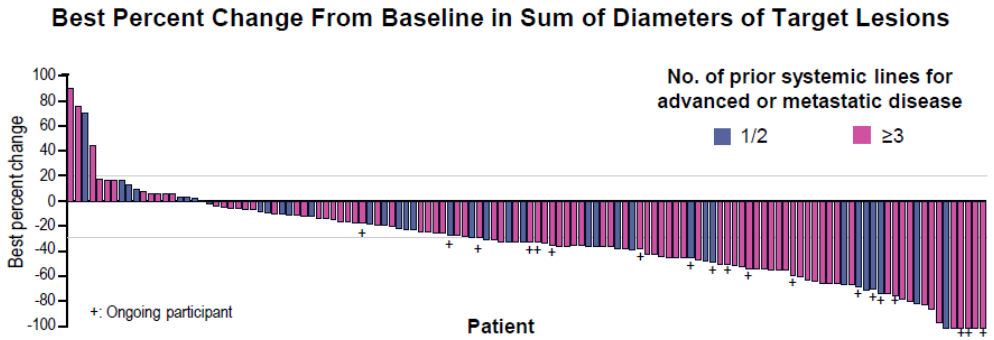
TROPION-Lung05(NCT04484142)

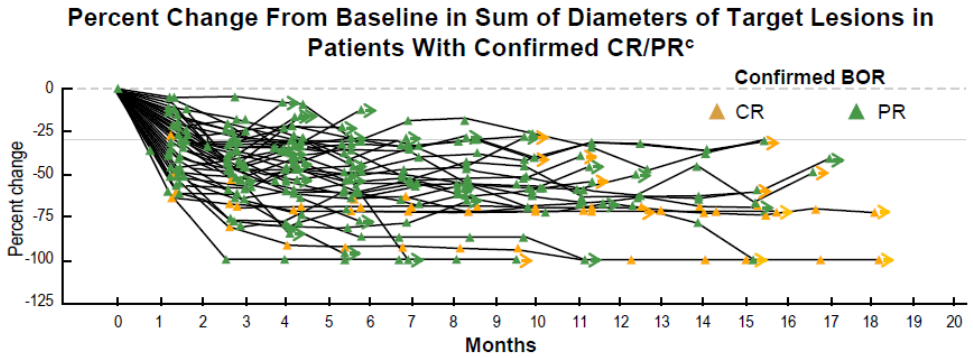
Efficacy Summary

Response per BICR	All treated patients (N=137)	Patients with *EGFR* mutations (N=78)	Patients with *ALK* rearrangement (N=34)
ORR confirmed, n (%) [95% CI][a]	49 (35.8) [27.8-44.4]	34 (43.6) [32.4-55.3]	8 (23.5) [10.7-41.2]
Median DOR (95% CI), months	7.0 (4.2-9.8)	7.0 (4.2-10.2)	7.0 (2.8-8.4)
DCR confirmed, n (%) [95% CI][a]	108 (78.8) [71.0-85.3]	64 (82.1) [71.7-89.8]	25 (73.5) [55.6-87.1]
Median PFS, (95% CI), months[b]	5.4 (4.7-7.0)	5.8 (5.4-8.3)	4.3 (2.6-6.9)

BOR: In the overall population (N=137), 4 patients (3%) achieved a CR and 45 (33%) achieved a PR

***EGFR* subset:** Among patients with sensitizing or T790M mutations (N=68), the ORR was 49.1% in those previously treated with osimertinib





BICR, blinded independent central review; BOR, best overall response; CR, complete response; DCR, disease control rate; DOR, duration of response; ORR, objective response rate; PFS, progression-free survival; PR, partial response.
[a]The 2-sided 95% CIs are based on the Clopper-Pearson exact binomial method. [b]Median PFS and PFS probabilities are based on the Kaplan-Meier method. [c]Per BICR.

- Most toxicities were Grade 1-2 (nausea, stomatitis, fatigue, vomiting.
- grade ≥ 3 (stomatitis, ocular, rare ILD) TRAE 29% grade ≥ 3
- Phase 3 Tropion-Lung 01 PFS HR 0.38 Dato-DXd vs. docetaxel in the alteration positive population.
- Other Trop2-ADCs are being explored (sacituzumab govitecan, SKB264)

Paz-Ares et al. ESMO 2023, Ahn et al. ESMO 2023.

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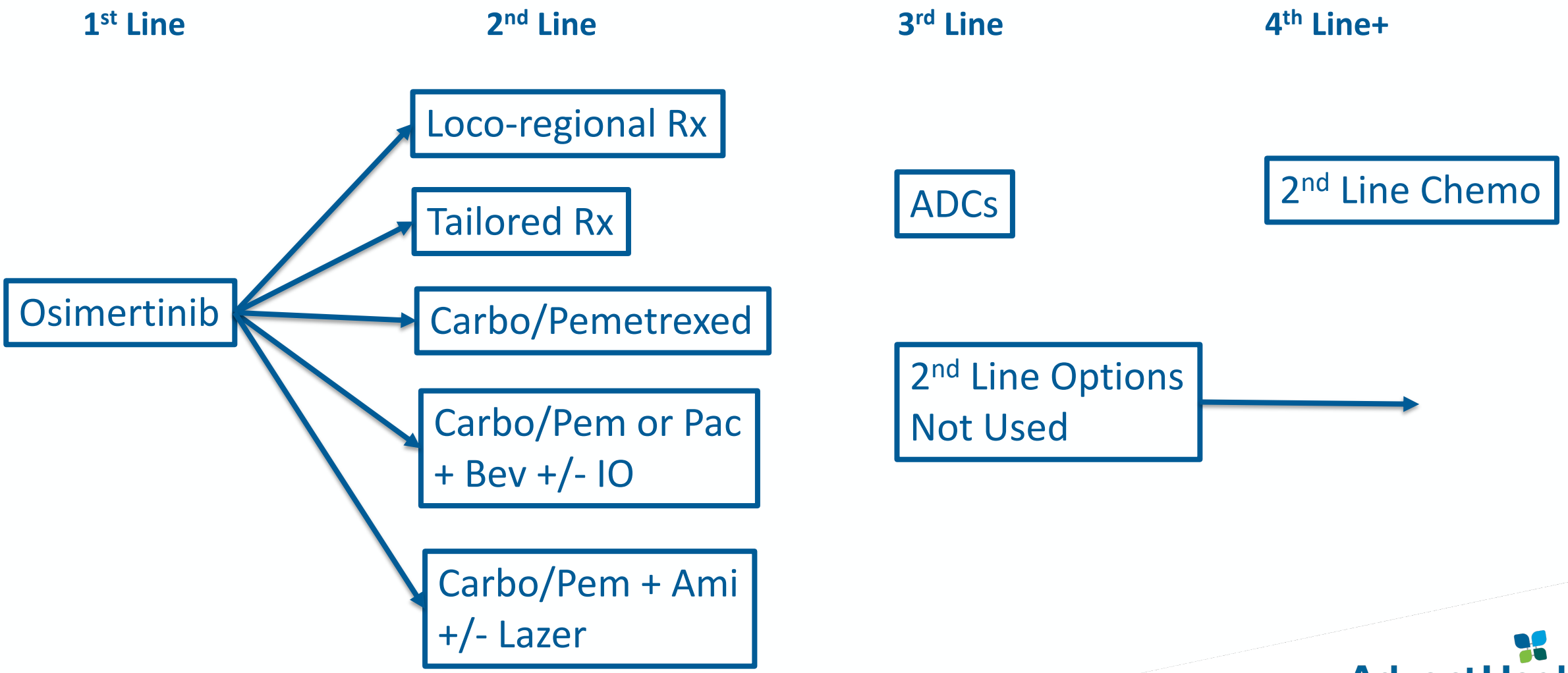
What is Next After Osimertinib Progression?



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