25th Multidisciplinary Management of Cancers: A Case-based Approach

MMC Thoracic Tumor Board 2025
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Disclosures

Faculty Name	Role	Type of Financial Relationship	Company
Jonathan Riess	**Chair**		
Aneeqa Zafar	**Fellow**	Advisory Board or Panel	Advisory Board with honoraria paid to individual - BMS, Janssen, Genentech, Regeneron, Merus NV, Catalyst, Amgen, Oncohost, Merck, Pfizer, GSK, Daichi Sankyo, and Replimune
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		Grants/Research Support	Research funding paid to institution - Pfizer, Boehringer Ingelheim, Revolution Medicines, ArriVent, Nuvalent, Kinnate, IO Biotech, AstraZeneca, Merck, Novartis, and Summit
Leah Backhus	Panelist	Advisory Board or Panel	Johnson & Johnson, AstraZeneca, and Genentech
		Grants/Research Support	Department of Veterans Affairs and NIH
Deepti Behl	Panelist	Advisory Board or Panel	BMS, Boehringer, Janssen and Janssen, and Caris
Colin Blakely	Panelist	Advisory Board or Panel	Gilead, Bayer, BMS, Takeda, Pfizer, Janssen, and Taiho
		Grants/Research Support	AstraZeneca, Genentech, Mirati, Puma, and Novartis
David Cooke	Panelist	Speaker's Bureau	Bristol Myers Squibb - Speaker Honoraria
		Grants/Research Support	Intuitive Surgical - In kind education support
		Other Financial or Material Support (royalties, patents, etc.)	Oxford University Press - Royalties

ANCO and i3 Health have mitigated all relevant financial relationships.

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Disclosures

David Gandara	Panelist	Advisory Board or Panel	Mirati Therapeutics and Regeneron
		Consultant	AstraZeneca, Exact Sciences, Genentech,Guardant Health, Henlius USA, and Foundation Medicine
		Grants/Research Support	Astex Pharma, Amgen Inc., and Genentech
Johannes Kratz	Panelist	Advisory Board or Panel	Intuitive Surgical ION Medical Advisory Board
		Speaker's Bureau	Razor Genomics; Consultant: Razor Genomics and Intuitive Surgical
Ana Velazquez Manana	Panelist	Advisory Board or Panel	AbbVie, AstraZeneca Pharmaceuticals, Janssen, Merus NV, Novocure, and Regeneron
		Other Financial or Material Support (royalties, patents, etc.)	Merck and Pfizer
Meera Ragavan	Panelist	Consultant	Trial Library, Inc.
		Grants/Research Support	Community Benefit Program and The Permanente Medical Group
Lucas Vitzthum	Panelist	Disclosed no relevant financial relationships.	

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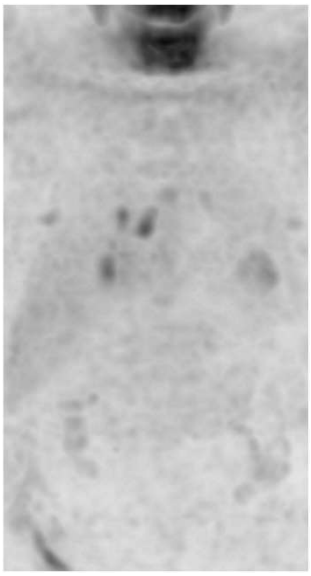
Case 1



71 year-old man, never smoker, presented with cough

- **CXR**: RLL mass
- **PET-CT:** FDG avid RLL lung mass (2 cm SUV=6), with FDG avid hilar (1.5 cm mSUV 5.1) & subcarinal LN(4 cm, SUV6)
- **MR brain:** negative.
- **CT guided biopsy of RLL:** NSCLC, adenocarcinoma
- (TTF1+)

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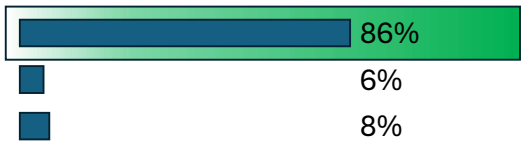
The patient has suspected N1 and N2 disease on PET CT with FDG avid subcarinal and hilar LN.

Question 1A:
Do you stage the mediastinum prior to determining treatment options?



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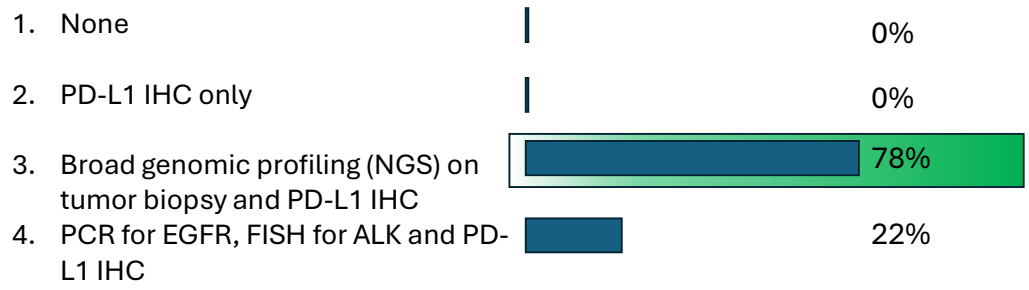
The patient has EBUS with TBNA of station 4R, 7 and 11R. All are positive for NSCLC-adenocarcinoma

Question 1B:

In this 71 year old never smoker with Stage IIIA NSCLC-adenocarcinoma (pT1bpN2Mx) (bulky multi station N2 disease), what molecular testing on tumor tissue would you order?



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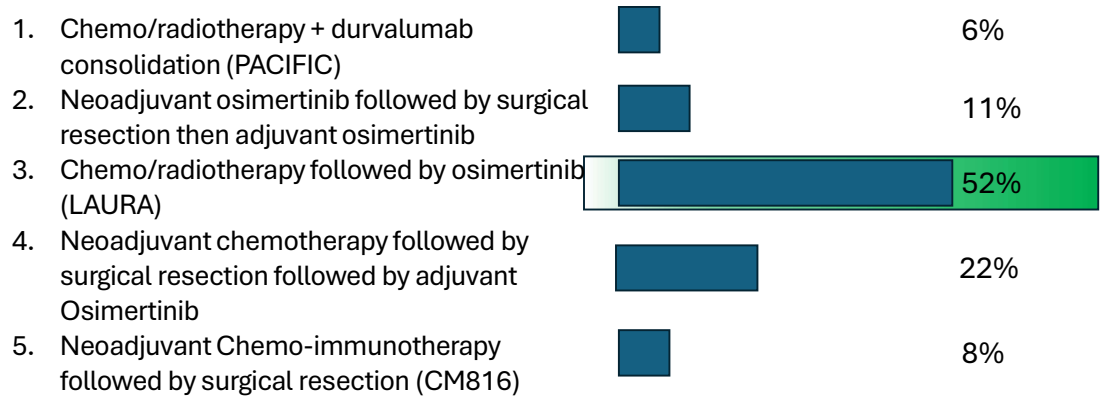
Tissue NGS: ***EGFR Exon19del+***, PD-L1 TPS 70%, *ALK/ROS* negative

Question 1C: What general treatment approach would you take with this never smoker 71-year-old patient with stage IIIA (pT1bpN2Mx) (multistation N2 disease-bulky), NSCLC-adenocarcinoma *EGFR E19del+* on molecular testing and high PD-L1 IHC?



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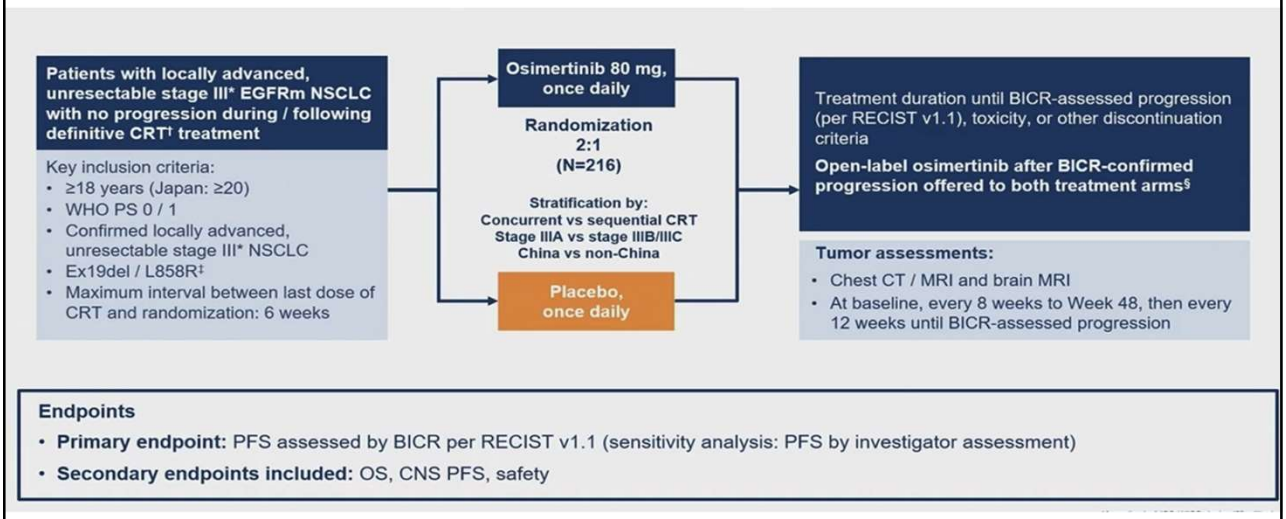
LAURA – *Improved PFS with adjuvant Osimertinib after Chemoradiotherapy in Stage III EGFR-Mutated NSCLC*



Shun Lu et al. N Engl J Med 2024;391:585-597

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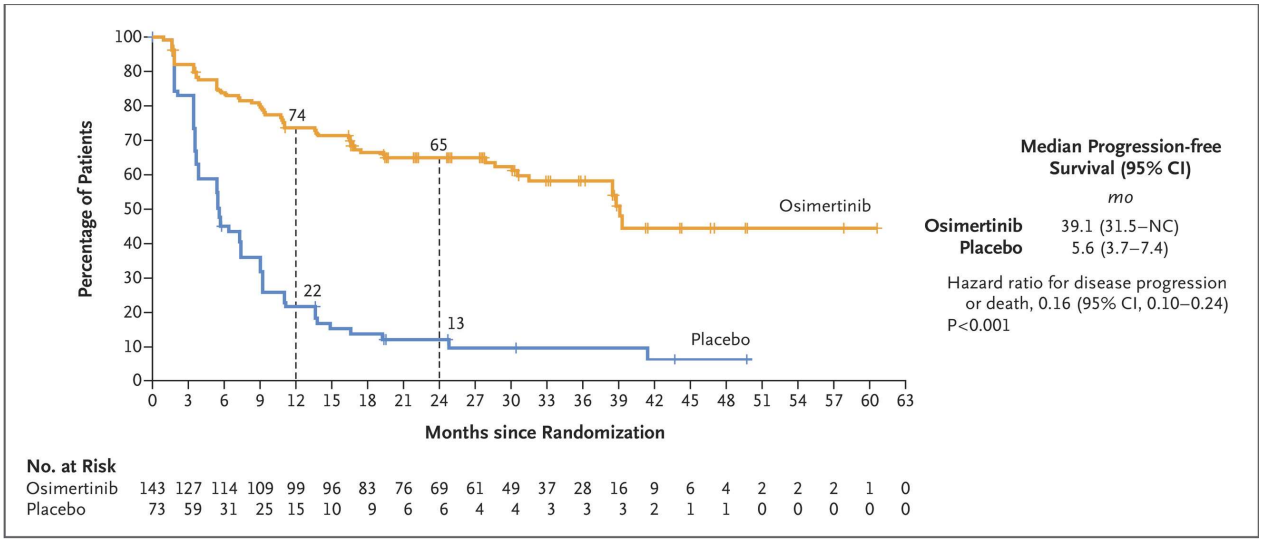

Shun Lu et al. N Engl J Med 2024;391:585-597 14

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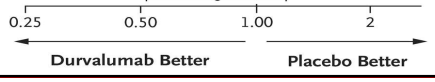
PACIFIC: *Progression-Free Survival after Chemoradiotherapy with or without Durvalumab in EGFR-mut NSCLC*

Subgroup	Durvalumab	Placebo	Unstratified Hazard Ratio for Disease Progression or Death (95% CI)
	no. of patients		
All patients	476	237	0.55 (0.45–0.68)
Sex			
Male	334	166	0.56 (0.44–0.71)
Female	142	71	0.54 (0.37–0.79)
Age at randomization			
<65 yr	261	130	0.43 (0.32–0.57)
≥65 yr	215	107	0.74 (0.54–1.01)
Smoking status			
Smoker	433	216	0.59 (0.47–0.73)
Nonsmoker	43	21	0.29 (0.15–0.57)
NSCLC disease stage			
IIIA	252	125	0.53 (0.40–0.71)
IIIB	212	107	0.59 (0.44–0.80)
Tumor histologic type			
Squamous	224	102	0.68 (0.50–0.92)
Nonsquamous	252	135	0.45 (0.33–0.59)
Best response			
Complete response	9	7	—
Partial response	232	111	0.55 (0.41–0.75)
Stable disease	222	114	0.55 (0.41–0.74)
PD-L1 status			
≥25%	115	44	0.41 (0.26–0.65)
<25%	187	105	0.59 (0.43–0.82)
Unknown	174	88	0.59 (0.42–0.83)
EGFR mutation			
Positive	29	14	0.76 (0.35–1.64)
Negative	315	165	0.47 (0.36–0.60)
Unknown	132	58	0.79 (0.52–1.20)



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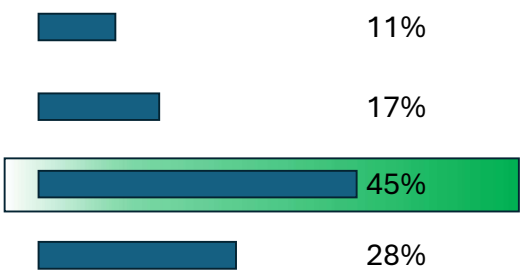
EGFR Exon19del+, PD-L1 TPS 70%, *ALK/ROS* negative

The patient is treated with concurrent weekly carboplatin+paclitaxel and radiation, followed by consolidation osimertinib. About 8 months after initiating osimertinib he develops shortness of breath. CT Chest reveals large R pleural effusion and bilateral pulmonary nodules. Thoracentesis improves symptoms and cytology on cell block shows lung adenocarcinoma (TTF1+). NGS off the cell block shows the EGFR E19del and no clear mechanism of resistance.

Question 1D: What would you treat the patient with as next line of treatment?

1. Add carboplatin/pemetrexed to Osimertinib
2. Stop osimertinib, start carboplatin/pemetrexed +/- bevacizumab
3. Stop osimertinib, start carboplatin/pemetrexed and amivantamab.
4. Stop osimertinib, start amivantamab and Lazertinib



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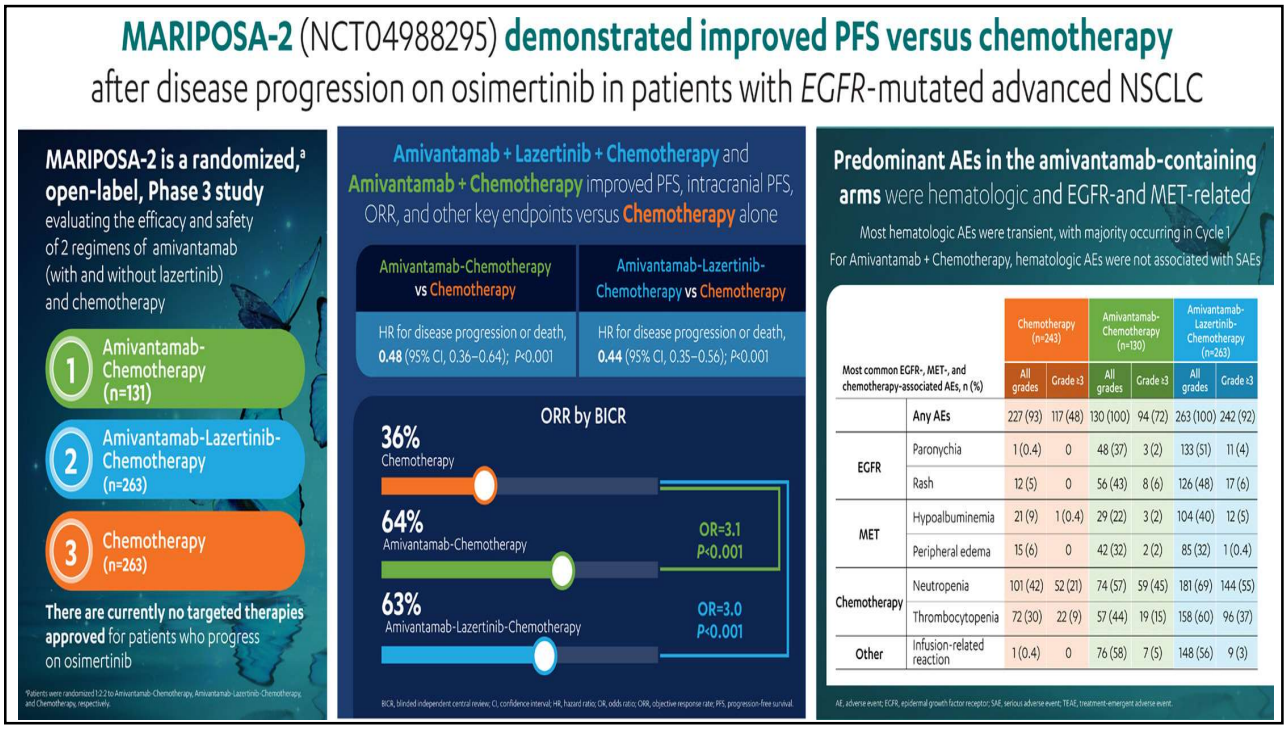

Most common EGFR-, MET-, and chemotherapy-associated AEs, n (%)		Chemotherapy (n=243)		Amivantamab-Chemotherapy (n=130)		Amivantamab-Lazertinib-Chemotherapy (n=263)	
		All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
	Any AEs	227 (93)	117 (48)	130 (100)	94 (72)	263 (100)	242 (92)
EGFR	Paronychia	1 (0.4)	0	48 (37)	3 (2)	133 (51)	11 (4)
	Rash	12 (5)	0	56 (43)	8 (6)	126 (48)	17 (6)
MET	Hypoalbuminemia	21 (9)	1 (0.4)	29 (22)	3 (2)	104 (40)	12 (5)
	Peripheral edema	15 (6)	0	42 (32)	2 (2)	85 (32)	1 (0.4)
Chemotherapy	Neutropenia	101 (42)	52 (21)	74 (57)	59 (45)	181 (69)	144 (55)
	Thrombocytopenia	72 (30)	22 (9)	57 (44)	19 (15)	158 (60)	96 (37)
Other	Infusion-related reaction	1 (0.4)	0	76 (58)	7 (5)	148 (56)	9 (3)

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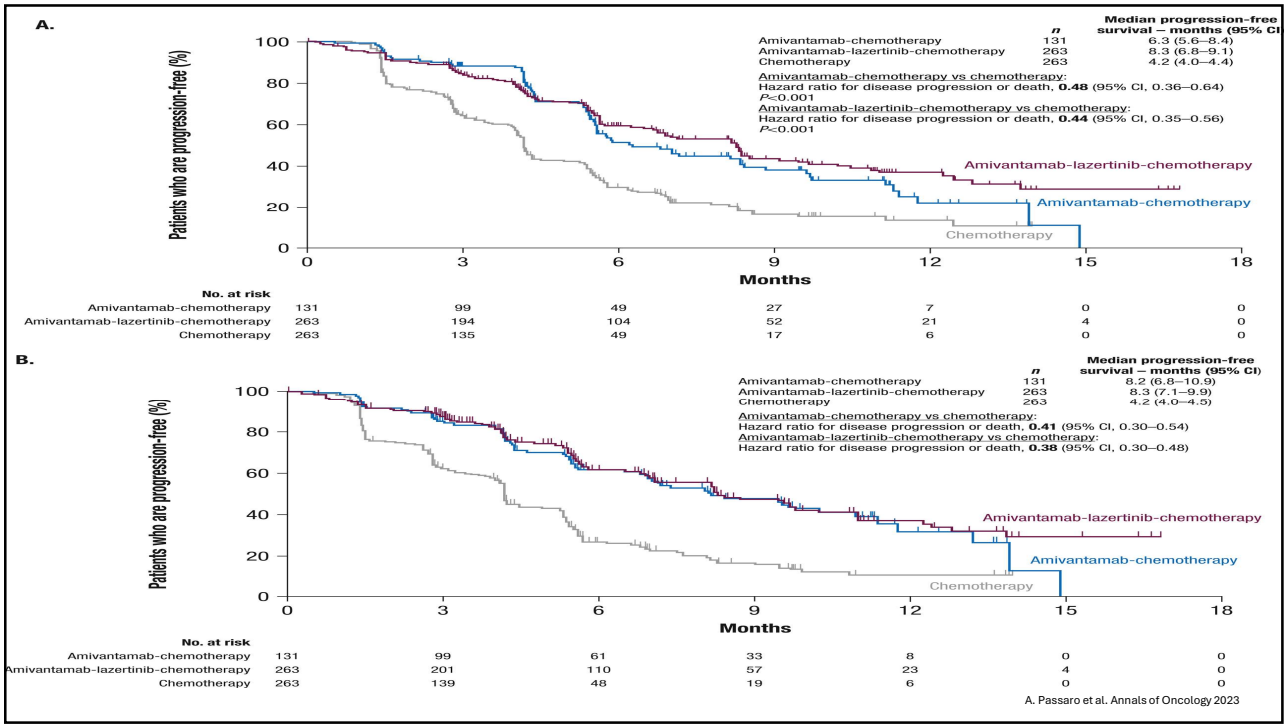

A. Passaro et al. Annals of Oncology 2023

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Case 1 – Take Home Messages

- **LAURA:** Adding Osimertinib after concurrent chemoradiation resulted in significantly longer progression-free survival than placebo in patients with unresectable stage III *EGFR*-mutated NSCLC
- **PACIFIC:** No benefit from adding consolidation durvalumab after definitive CRT in EGFR mutated, stage III NSCLC patients and higher frequency of irAEs
- **MARIPOSA-2:** amivantamab + carbo + pemetrexed for EGFR-mutated NSCLC after progression on osimertinib improves PFS vs carbo + pemetrexed alone. Overall survival data immature, but trend towards OS.

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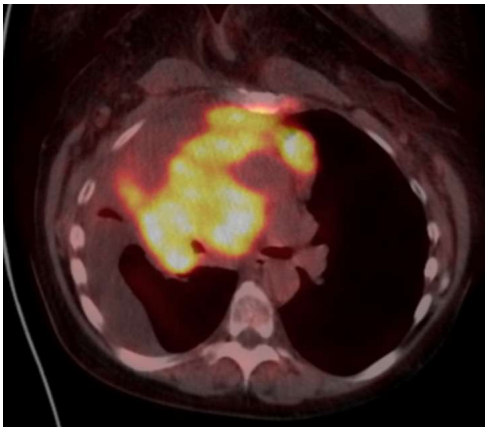
Case 2

53 yo F, 25 ppd smoker, presented with SOB,

Cough & chest pain

- **CXR:** RUL lung mass.
- **PET CT:** FDG avid RUL lung mass, mediastinal LAD, R hilar LN and R SCL LN
- **MR brain:** negative
- **EBUS bx:** small cell lung cancer.

Drainage of R pleural effusion with neg cytology for malignancy.



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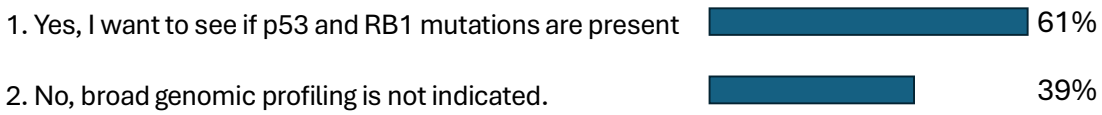
Question 2A: Would you order broad genomic profiling for this 53 year old woman with 25 pack-year smoking history and newly diagnosed limited stage SCLC?



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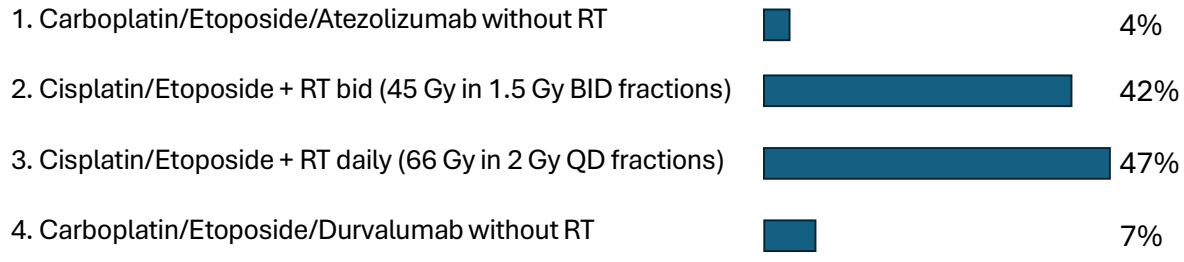
Molecular testing confirms p53 and RB1 co-mutations. You diagnose the patient with limited stage small cell lung cancer.

Question 2B: What treatment and radiation schedule would you offer?



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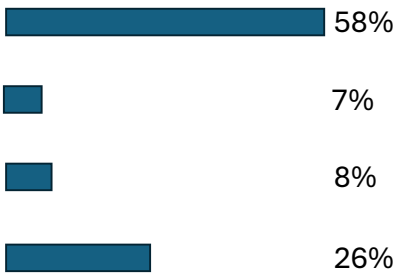
The patient completes Cisplatin/Etoposide/XRT given in once daily 2 Gy fractions with a response to treatment.

Question 2C: What would you offer next?



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ADRIATIC study design

Phase 3, randomized, double-blind, placebo-controlled, multicenter, international study (NCT03703297)

- Stage I–III LS-SCLC (stage I/II inoperable)
- WHO PS 0 or 1
- Had not progressed following cCRT*
- PCI* permitted before randomization

N=730

R‡

Durvalumab
1500 mg Q4W
N=264

Placebo
Q4W
N=266

Durvalumab + tremelimumab
D 1500 mg Q4W + T 75 mg Q4W for 4 doses, followed by D 1500 mg Q4W
N=200

cCRT components
- Four cycles of platinum and etoposide (three permitted†)
- RT: 60–66 Gy QD over 6 weeks or 45 Gy BID over 3 weeks
- RT must commence no later than end of cycle 2 of CT

Stratified by:
Disease stage (I/II vs III)
PCI (yes vs no)

Treatment until investigator-determined progression or intolerable toxicity, or for a **maximum of 24 months**

Dual primary endpoints:
- Durvalumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

Key secondary endpoints:
- Durvalumab + tremelimumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

Other secondary endpoints:
- OS/PFS landmarks
- Safety

*cCRT and PCI treatment, if received per local standard of care, must have been completed within 1–42 days prior to randomization.
†If disease control was achieved and no additional benefit was expected with an additional cycle of chemotherapy, in the opinion of the investigator.
‡The first 600 patients were randomized in a 1:1:1 ratio to the 3 treatment arms; subsequent patients were randomized 1:1 to either durvalumab or placebo.

BICR, blinded independent central review; BID, twice daily; CT, chemotherapy; D, durvalumab; PCI, prophylactic cranial irradiation; PS, performance status; Q4W, every 4 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; RT, radiotherapy; T, tremelimumab; WHO, World Health Organization.

2024 ASCO ANNUAL MEETING #ASCO24 PRESENTED BY: Dr David R. Spigel

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Spigel et al, JCO, ASCO 2024 meeting abstract

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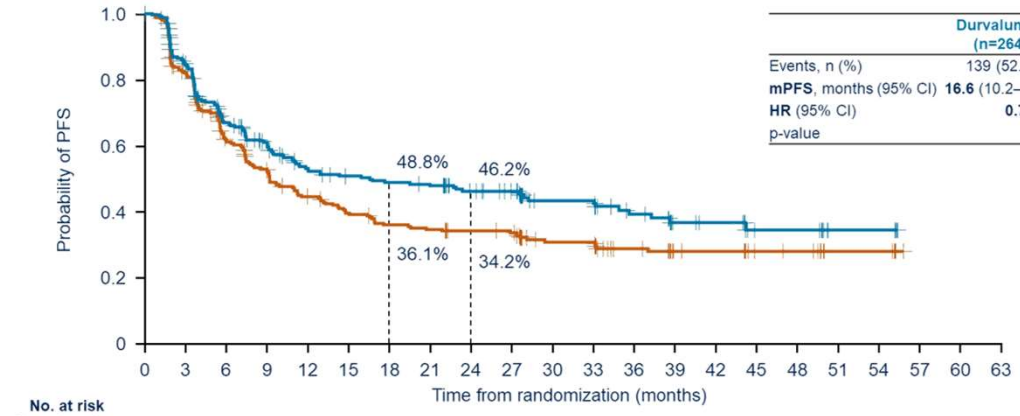
Progression-free survival* (dual primary endpoint)

- Median duration of follow up in censored patients: 27.6 months (range 0.0–55.8)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	139 (52.7)	169 (63.5)
mPFS, months (95% CI)	**16.6** (10.2–28.2)	**9.2** (7.4–12.9)
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

No. at risk																					
Durvalumab	264	212	161	135	113	105	101	98	84	78	51	51	33	21	19	10	10	4	4	0	0	0
Placebo	266	208	146	122	100	88	79	76	71	69	47	47	34	23	22	15	14	5	5	0	0	0

*By BICR per RECIST v1.1.

PFS was analyzed using a stratified log-rank test adjusted for disease stage (I/II vs III) and receipt of PCI (yes vs no). The significance level for testing PFS at this interim analysis was 0.00184 (2-sided) at the 0.5% level, and 0.02805 (2-sided) at the overall 5% level. Statistical significance for PFS was achieved through the recycling multiple testing procedure framework and testing at the 5% (2-sided) alpha level (adjusted for an interim and final analysis).

mPFS, median PFS.

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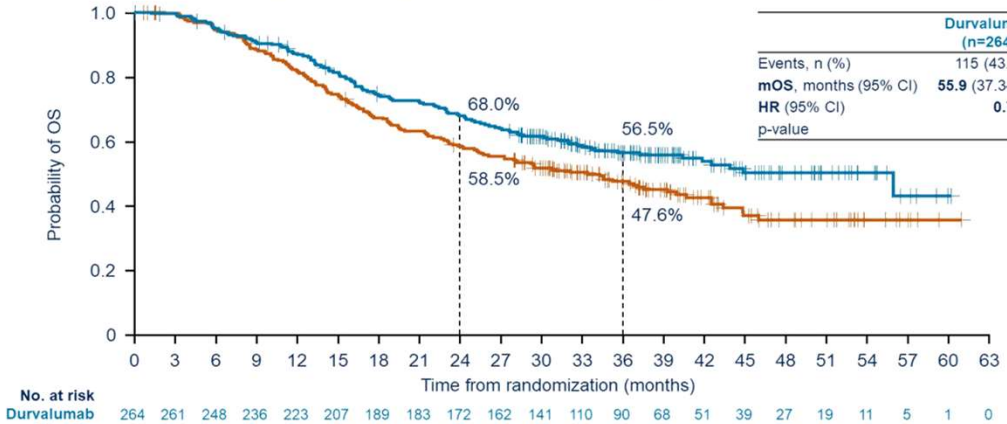
Overall survival (dual primary endpoint)

- Median duration of follow up in censored patients: 37.2 months (range 0.1–60.9)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

No. at risk																					
Durvalumab	264	261	248	236	223	207	189	183	172	162	141	110	90	68	51	39	27	19	11	5	1	0
Placebo	266	260	247	231	214	195	175	164	151	143	123	97	80	62	44	31	23	19	8	5	1	0

OS was analyzed using a stratified log-rank test adjusted for receipt of PCI (yes vs no). The significance level for testing OS at this interim analysis was 0.01679 (2-sided) at the overall 4.5% level, allowing for strong alpha control across interim and final analysis timepoints.

CI, confidence interval; mOS, median OS; NE, not estimable.

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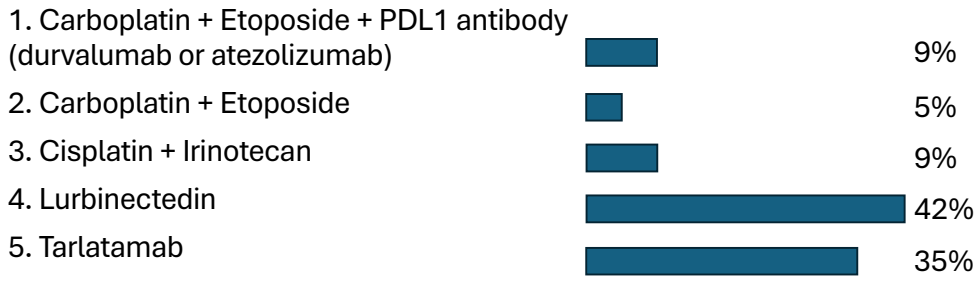
Three months after starting consolidation durvalumab, she develops metastasis to the adrenal gland, liver, lung and lymph nodes. Brain MRI is negative. She still has good performance status, ECOG 1

Question 2D: What second line therapy would you offer?



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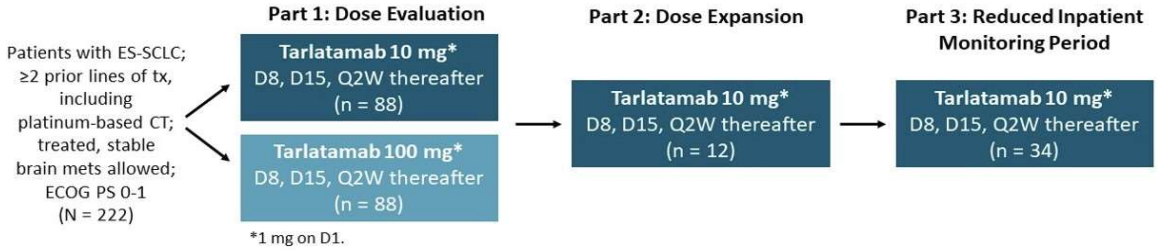
DeLLphi-301: *Tarlatamab improves ORR and DOS in previously treated SCLC*

- Open-label phase II study
  - Patients required to have received 1 platinum-based regimen and ≥1 other line of tx; median lines of tx: 2 (range: 1-8)



*1 mg on D1.

- **Primary endpoints:** ORR per RECIST v1.1 by BICR
- **Secondary endpoints:** DoR, DCR, PFS, OS, safety, drug serum concentration

Myung-Ju Ahn N Engl J Med 2023;389:2063-2075

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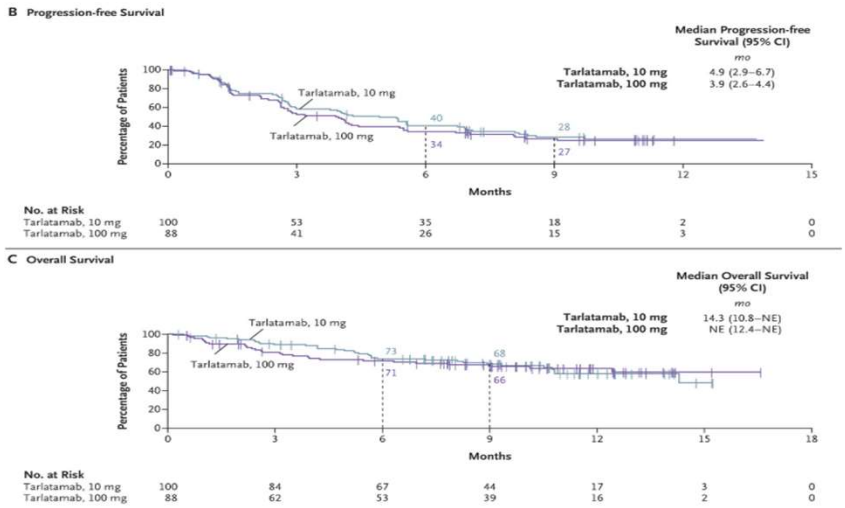
DeLLphi-301: *Tarlatamab improves ORR and DOS in previously treated SCLC*



Objective response in 10mg group: 40%

Objective response in 100mg group: 32%

Median duration of response was at least 6 months in 59% patients.

Myung-Ju Ahn N Engl J Med 2023;389:2063-2075

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Question 2F: Patient is started on Tarlatamab. 16 hours after the first dose is administered, and while monitored in an inpatient-like setting, the patient develops a new fever of 39.2C. She is hypotensive and oxygenation saturation is 88%. Infectious work up is sent but there is low suspicion for infection. Imaging is unrevealing.

What treatment would you offer next?

1. Start supplemental oxygen, draw blood cultures and treat empirically for pneumonia with antibiotics — 2%
2. Give supplemental oxygen, start IV steroids and tocilizumab — 97%
3. Continue symptomatic treatment — 2%

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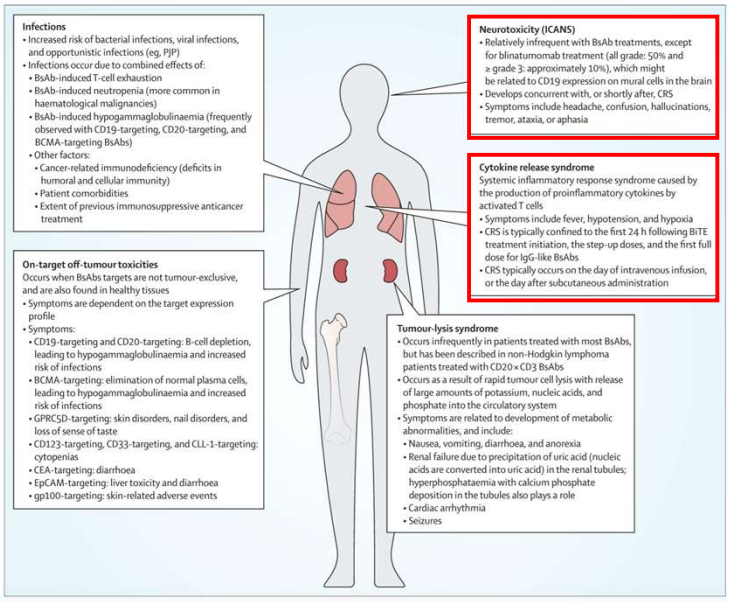
Key Toxicities with Bispecific Antibody Treatment



<u>Cytokine Release Syndrome</u>
CRS with tarlatamab
– G3 1% 10 mg, 6% 100 mg

IL-6 driven
-Glucocorticoids
- Tocilizumab (anti-IL-6R ab)

N. van de Donk, S. Zweegman Lancet 2023.

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DeLLphi-301: *Tarlatamab improves ORR and DOS in previously treated SCLC*

Incidence of CRS in 10-mg group: 51%
Incidence of CRS in 100-mg group: 61%

Grade 1 CRS: 30% vs 32%
Grade 2 CRS: 20% vs 23%
Grade 3 CRS: 1% vs 6%

Median onset of CRS: 13H
Median duration of CRS: 4 days

Grade 1-2 ICANS: 8% vs 28%
Grade 3 ICANS: None vs 5%

Median onset of ICANS: 5 days

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CRS Grade	Defining Symptoms	IMDELLTRA Dosage Modification	Management
Grade 1	Symptoms require symptomatic treatment only (e.g., fever ≥ 100.4°F without hypotension or hypoxia).	Withhold IMDELLTRA until event resolves, then resume IMDELLTRA at the next scheduled dose[b].	• Administer symptomatic treatment (e.g., acetaminophen) for fever.
Grade 2	Symptoms require and respond to moderate intervention. • Fever ≥ 100.4°F, • Hypotension responsive to fluids not requiring	Withhold IMDELLTRA until event resolves, then resume IMDELLTRA at the next scheduled dose[b].	• Recommend hospitalization for a minimum of 24 hours with cardiac telemetry and pulse oximetry. • Administer symptomatic treatment (e.g., acetaminophen) for fever. • Administer supplemental oxygen and intravenous fluids when indicated. • Consider dexamethasone[c] (or equivalent) 8 mg IV. • Consider tocilizumab (or equivalent).
Grade 3	Severe symptoms defined as temperature ≥ 38°C with: • Hemodynamic instability requiring a vasopressor (with or without vasopressin) or • Worsening hypoxia or respiratory distress requiring high flow nasal canula (> 6 L/min oxygen) or face mask.	Withhold IMDELLTRA until the event resolves, then resume IMDELLTRA at the next scheduled dose[b]. For recurrent Grade 3 events, permanently discontinue IMDELLTRA.	In addition to Grade 2 treatment: • Recommend intensive monitoring, e.g., ICU care. • Administer dexamethasone[c] (or equivalent) 8 mg IV every 8 hours up to 3 doses. • Vasopressor support as needed. • High flow oxygen support as needed. • Recommend tocilizumab (or equivalent) • Prior to the next dose, administer concomitant medications as recommended for Cycle 1 (see Table 3). When resuming treatment at the next planned dose, monitor patients from the start of the IMDELLTRA infusion for 22 to 24 hours in an appropriate healthcare setting.
Grade 4	Life-threatening symptoms defined as temperature ≥100.4°F with: • Hemodynamic instability requiring multiple vasopressors (excluding vasopressin). • Worsening hypoxia or respiratory distress despite oxygen administration requiring positive pressure.	Permanently discontinue IMDELLTRA.	• ICU care. • Per Grade 3 treatment. • Recommend tocilizumab (or equivalent).

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ICANS management

ICANS Grade[a]	Defining Symptoms	IMDELLTRA Dosage Modifications	Management
Grade 1[a]	ICE score 7-9[b] with no depressed level of consciousness.	• Withhold IMDELLTRA until ICANS resolves, then resume IMDELLTRA at the next scheduled dose[c].	• Supportive care.
Grade 2[a]	ICE score 3-6[b] and/or mild somnolence awaking to voice.	• Withhold IMDELLTRA until ICANS resolves, then resume IMDELLTRA at the next scheduled dose[c].	• Supportive care. • Dexamethasone[d] (or equivalent) 10 mg IV. Can repeat every 6 hours or methylprednisolone 1 mg/kg IV every 12 hours if symptoms worsen. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Monitor patients for 22 to 24 hours following the next dose of IMDELLTRA.
Grade 3[a]	ICE score 0-2[b] and/or depressed level of consciousness awakening only to tactile stimulus and/or any clinical seizure focal or generalized that resolves rapidly or nonconvulsive seizures on EEG that resolve with intervention and/or Focal or local edema on neuroimaging.	• Withhold IMDELLTRA until the ICANS resolves, then resume IMDELLTRA at the next scheduled dose[c]. • If there is no improvement to grade ≤ 1 within 7 days or grade 3 toxicity reoccurs within 7 days of reinitiation, permanently discontinue IMDELLTRA.	• Recommend intensive monitoring, e.g., ICU care. • Consider mechanical ventilation for airway protection. Dexamethasone[d] (or equivalent) 10 mg IV every 6 hours or methylprednisolone 1 mg/kg IV every 12 hours. • Consider repeat neuroimaging (CT or MRI) every 2-3 days if patient has persistent Grade ≥ 3 neurotoxicity. • Monitor patients for 22 to 24 hours following the next dose of IMDELLTRA.
Grade 4[a]	ICE score 0[b] (patient is unarousable and unable to perform ICE) and/or Stupor or coma and/or Life-threatening prolonged seizure (> 5 minutes) or repetitive clinical or electrical seizures without return to baseline in between and/or diffuse cerebral edema on neuroimaging, decerebrate or decorticate posturing or papilledema, cranial nerve VI palsy, or Cushing's triad.	• Permanently discontinue IMDELLTRA.	• ICU care. • Consider mechanical ventilation for airway protection. • High dose corticosteroids[d]. • Consider repeat neuroimaging (CT or MRI) every 2-3 days if patient has persistent Grade ≥ 3 neurotoxicity. • Treat convulsive status epilepticus per institutional guidelines.

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Case 2 – Take Home Messages

- **ADRIATIC:** Consolidation durvalumab improved both PFS and OS in patients with limited stage SCLC who did not progress after concurrent chemoradiation
- **DELPHI 301:** Tarlatamab, administered as a 10-mg dose every 2 weeks, showed antitumor activity with durable objective responses and promising survival outcomes in patients with previously treated SCLC.
- Most common adverse effects from Tarlatamab were grade 1 CRS, managed with supportive care. Consider IV steroids and/or tocilizumab for higher grade CRS.

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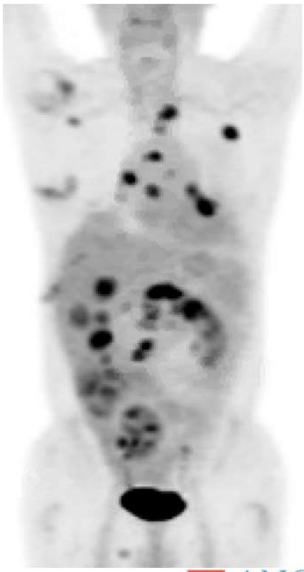
Case 3

58 yo M, 30 pack-year former smoker, presented with cough and dyspnea

- **PET-CT:** LLL primary with lymphadenopathy in the hilum and mediastinum. Diffuse bone and liver mets noted
- **MRI brain:** negative.
- **Biopsy:** NSCLC, squamous histology
- PD-L1 TPS = <1%
- **ECOG:** 1

Stage IVB (pT3N3M1C) squamous NSCLC



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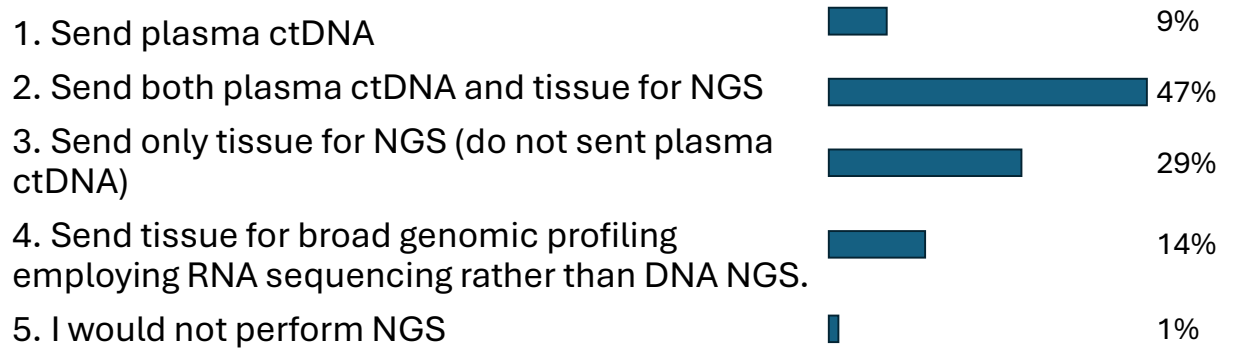
Question 3A: Do you perform NGS on a patient with a smoking history and Stage IV squamous cell lung cancer?



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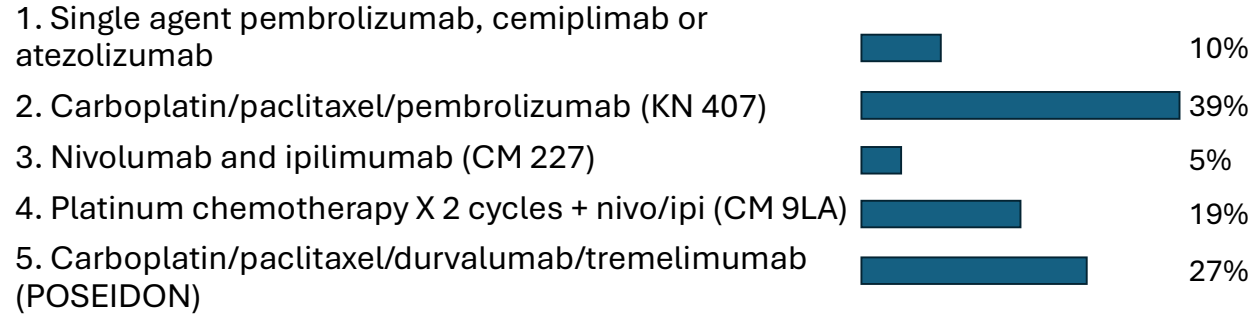
25th Multidisciplinary Management of Cancers: A Case-Based Approach

Tissue NGS is sent and shows a KEAP-1 mutation and TMB=15 mut/mb

Question 3B: What treatment would you offer for Stage IVB NSCLC-squamous histology PD-L1 <1% and KEAP-1 mutation



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	KEYNOTE 407 5 year survival outcomes (Novello et al, JCO 2023)	CHECKMATE 227-PART 1 5 year survival outcomes (Brahmer et al JCO 2022)	CHECKMATE 9LA 5 year survival outcomes (Paz-Ares et al, JTO 2023)	POSEIDON (Johnson et al JCO 2022)
COMPARISON	Carbo-Taxol + Pembro vs Carbo-Taxol-placebo x 4 cycles -> pembro vs placebo for 35 cycles	PD-L1 ≥ 1%: Nivo/Ipi, Nivo or chemo PD-L1<1%: Nivo/Ipi, Nivo/chemo, chemo alone	Nivo/Ipi + 2 cycles chemotherapy vs 4 cycles of chemotherapy.	Tremelimumab plus durvalumab and chemotherapy (T + D + CT) and D + CT vs CT alone 1L mNSCLC
PFS	10.8% vs 3.5 [5 year]	PD-L1>1% : 5.1 vs 4.2 vs 5.6 PD-L1<1%: 5.1 vs 5.6 vs 4.7	5 year PFS 55% vs 38%	D+ CT: 5.5 v 4.8 mo D+ CT + T: 6.2 v 4.8mo
OS based on PD-L1 status	PD-L1 > 50% 19.9 v 11.5% [5-yr] PD-L1 < 1% 15% v 11% [5 -yr]	5-year OS rate of 39% (combined PD-L1 populations). PD-L1>1%: 17mo vs 14.9 vs 15.7mo PD-L1<1%: 17.4mo vs 15.2 vs 12.2mo	PD-L1 ≥ 1%, 15.8 vs 10.9 mo PD-L1 < 1%, 17.7mo vs 9.8mo	D+CT: PD-L1 > 50% HR 0.63 [0.5-0.88] PD-L1 <1% HR 0.99 [0.7-1.30] D+CT+T PD-L1 > 50% HR 0.65 [0.47-0.89] PD-L1 <1% HR 0.77 [0.48-1]
OS based on histology:	Squamous: PD-L1 > 50% 19.9 v 11.5% [5-yr] PD-L1 < 1% 15% v 11% [5 -yr]	Non-squamous PD-L1 ≥ 1%: 0.82 [0.67 to 0.99]; PD-L1 < 1%: 0.70 [0.54 to 0.90] squamous PD-L1 ≥ 1%: 0.69 [0.52 to 0.91] PD-L1 < 1%: 0.52 [0.34 to 0.82]	squamous: 14.5 vs 9.1mo non squamous: 17.8 vs. 12mo	D+CT Squamous HR 0.84 [0.6-1.10] Non squamous HR 0.82[0.6-1.03] D+CT+T Squamous HR 0.88 [0.68-1.16] - NS Non squamous HR 0.70 [0.5-0.87]

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POSEIDON: *Exploratory analysis showed improved OS with D+CT+T regardless of KEAP-1 mutation*

Mutation-evaluable population	T+D+CT	D+CT	CT
***KRAS*m, n**	72	83	64
Median OS (95% CI), months	16.0 (9.7–27.8)	11.4 (8.1–14.8)	10.5 (7.6–12.6)
OS HR vs CT (95% CI)	0.63 (0.42–0.92)	0.83 (0.58–1.20)	–
24-month OS rate (95% CI), %	44.4 (32.8–55.4)	26.5 (17.6–36.3)	23.0 (13.4–34.2)
***KRAS*wt, n**	253	247	254
Median OS (95% CI), months	13.4 (11.5–15.8)	13.7 (11.5–15.8)	12.8 (10.6–15.2)
OS HR vs CT (95% CI)	0.84 (0.69–1.01)	0.86 (0.71–1.05)	–
24-month OS rate (95% CI), %	29.2 (23.7–34.9)	30.6 (24.9–36.4)	22.7 (17.7–28.0)
***STK11*m, n**	47	41	25
Median OS (95% CI), months	11.7 (8.9–18.7)	6.4 (3.9–11.4)	10.7 (6.0–14.9)
OS HR vs CT (95% CI)	0.80 (0.48–1.38)	1.19 (0.70–2.05)	–
24-month OS rate (95% CI), %	23.4 (12.6–36.2)	17.1 (7.5–29.9)	8.3 (1.4–23.3)
***STK11*wt, n**	278	289	293
Median OS (95% CI), months	14.6 (12.5–16.6)	14.0 (12.2–15.8)	12.2 (10.6–14.1)
OS HR vs CT (95% CI)	0.77 (0.64–0.92)	0.82 (0.68–0.98)	–
24-month OS rate (95% CI), %	34.2 (28.7–39.9)	31.3 (26.0–36.8)	24.0 (19.2–29.0)
***KEAP1*m, n**	22	23	6
Median OS (95% CI), months	13.7 (7.2–26.5)	8.1 (4.0–12.9)	8.7 (5.1–NE)
OS HR vs CT (95% CI)	0.43 (0.16–1.25)	0.77 (0.31–2.15)	–
24-month OS rate (95% CI), %	35.0 (16.1–54.7)	19.3 (6.2–37.9)	0.0 (0.0–0.0)
***KEAP1*wt, n**	303	307	312
Median OS (95% CI), months	14.0 (11.8–16.1)	13.5 (11.7–14.9)	12.2 (10.6–13.9)
OS HR vs CT (95% CI)	0.79 (0.66–0.94)	0.85 (0.71–1.01)	–
24-month OS rate (95% CI), %	32.5 (27.2–37.8)	30.3 (25.2–35.5)	23.2 (18.6–28.1)

Mutation-evaluable population	T+D+CT	D+CT	CT
Non-squamous histology*			
***KRAS*m, n**	60	69	53
Median OS (95% CI), months	25.7 (9.9–36.5)	12.6 (7.5–16.9)	10.4 (7.5–13.6)
OS HR vs CT (95% CI)	0.56 (0.36–0.88)	0.80 (0.53–1.21)	–
24-month OS rate (95% CI), %	51.7 (38.4–63.4)	30.4 (20.1–41.4)	25.6 (14.6–38.1)
***STK11*m, n**	31	34	22
Median OS (95% CI), months	15.0 (8.2–23.8)	6.9 (3.6–12.9)	10.7 (6.0–14.9)
OS HR vs CT (95% CI)	0.56 (0.30–1.03)	1.03 (0.59–1.84)	–
24-month OS rate (95% CI), %	32.3 (16.9–48.6)	20.6 (9.1–35.3)	4.5 (0.3–18.9)

Data cutoff: 12 March 2021. HRs calculated by unstratified analysis. Mutation categories are not mutually exclusive, with some patients having co-mutations. The mutation-evaluable population included patients with both squamous and non-squamous histology. CI, confidence interval; NE, not estimable. *The subgroup with *KEAP1*m non-squamous mNSCLC was not analysed due to insufficient patient numbers.

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Results of Phase III POSEIDON study. Johnson et al. *Journal of Thoracic Oncology*

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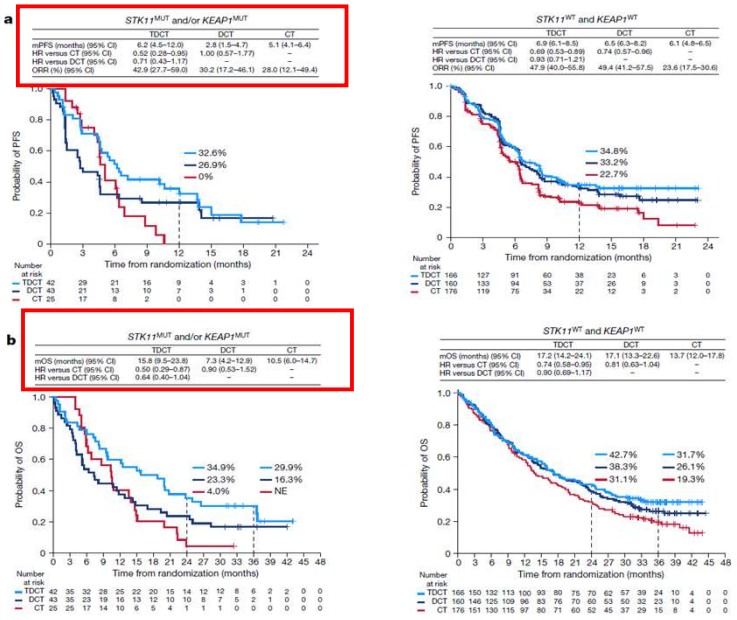
CTLA4 blockade abrogates *KEAP1/STK11*-related resistance to PD-(L)1 inhibitors



https://doi.org/10.1038/s41586-024-0794-7

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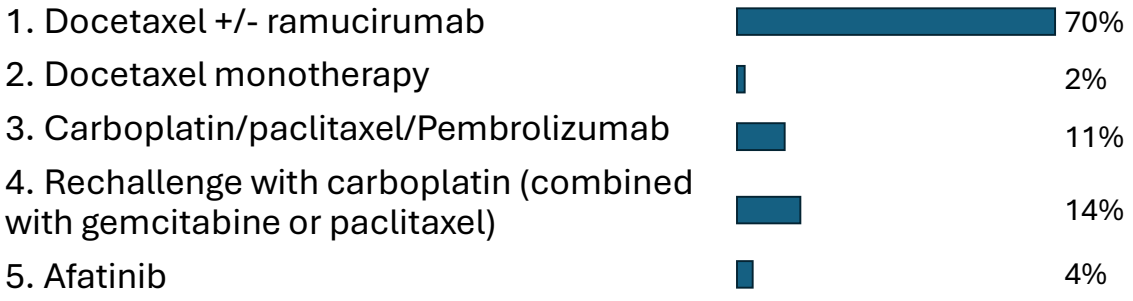
25th Multidisciplinary Management of Cancers: A Case-Based Approach

The patient is initiated on nivolumab+ ipilumumab + carboplatin/paclitaxel (9LA). The patient develops multiple new lung nodules and several bone sites after 8 months of stable disease. He still has excellent performance status (PS=1)and is interested in further treatment.

Question 3C: What would you treat with next?



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24th Multidisciplinary Management of Cancers: A Case-Based Approach

The patient was treated with docetaxel/ramucirumab

Case 3 – Take home messages

- **KEYNOTE 407:** Pembro combined with chemotherapy improves PFS and OS in previously untreated mNSCLC, squamous histology. Patients who completed 35 cycles of IO had ORR > 90%
- **CHECKMATE 9LA:** Dual ICI with Nivo/Ipi + chemo provided long-term, durable clinical benefit in metastatic NSCLC. Magnitude of benefit was higher in PD-L1 < 1% or squamous histology subgroups. Treatment discontinuation due to TRAEs had no negative impact on efficacy
- **POSEIDON:** 1L tremelimumab + durvalumab + chemotherapy (T+D+CT) demonstrated improved PFS & OS compared to chemotherapy alone.
- STK11/KEAP1 mutations, portend poor prognosis and worse response to ICIs. Exploratory analysis suggests that adding a CTLA4 inhibitor to PD-(L)1 inhibitor might improve outcomes. Prospective clinical trials are needed to validate these findings.

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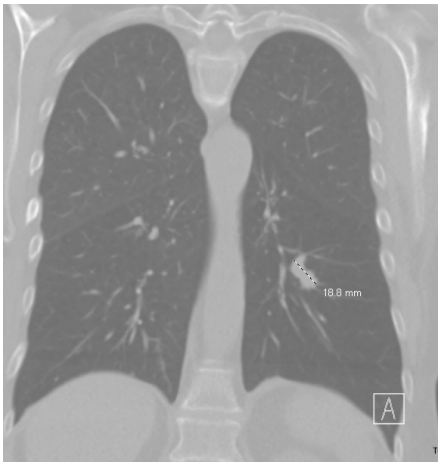
25th Multidisciplinary Management of Cancers: A Case-Based Approach

Case 4

67 yo F, heavy smoker, found to have 2cm LLL nodule on low dose CT chest screening.

- **PET CT:** 2 cm LLL nodule max SUV 9. No other sides of metastatic disease are noted
- **MR brain:** negative
- **Biopsy:** NSCLC, adenocarcinoma
- **EBUS:** negative. Mediastinal LN negative
- **NGS/IHC:** Positive for KRAS G12C mutation, TMB=15, PD-L1 40%



Staged as Stage IB NSCLC-adenocarcinoma (pT1bN0)

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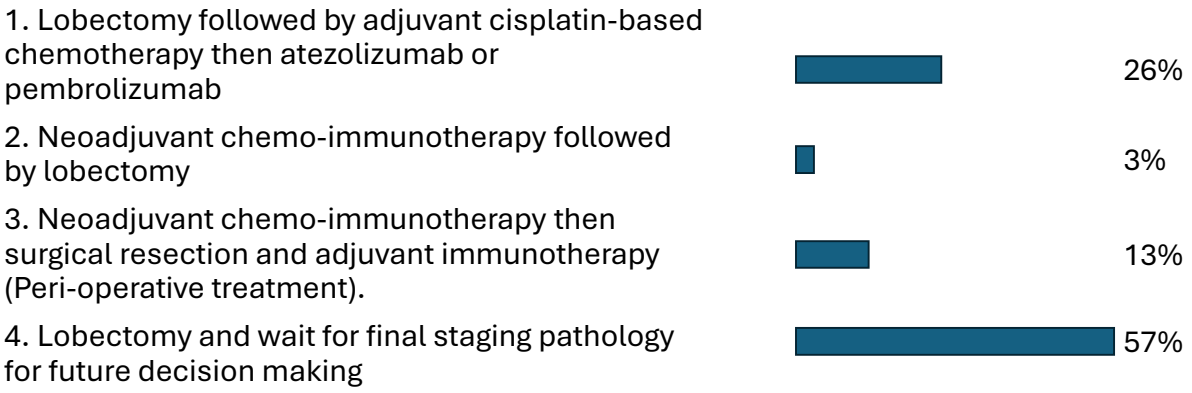
25th Multidisciplinary Management of Cancers: A Case-Based Approach

Questions 4A: What would be the optimal management for this patient with presumptive Stage IB NSCLC-adenocarcinoma (pT1bN0), PD-L1=40% and KRAS G12C mutation?



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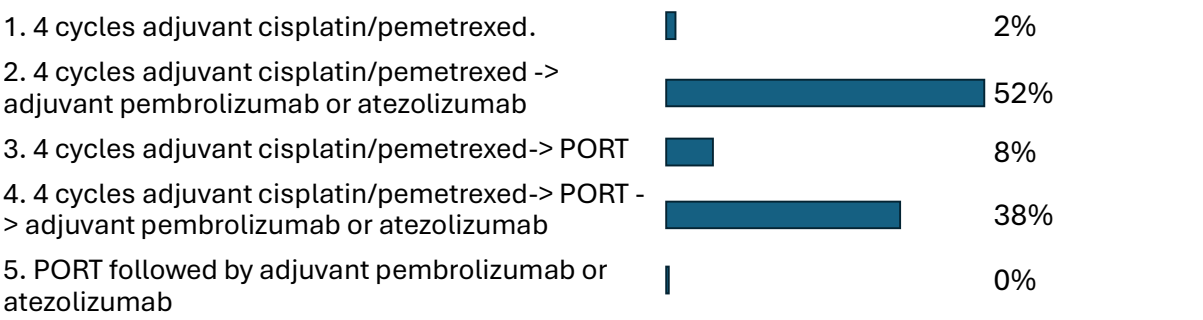
25th Multidisciplinary Management of Cancers: A Case-Based Approach

The patient has a LLL lobectomy. Margins are negative but there are multiple ipsilateral mediastinal and hilar LN positive (11/18). Final pathologic Stage IIIA (T1bN2M1x)

Question 4B: What would you do for adjuvant treatment for this patient with Stage IIIA NSCLC-adenocarcinoma. 50 pack-years smoking. PD-L1 IHC positive (40%), KRAS on NGS, TMB=15.



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25th Multidisciplinary Management of Cancers: A Case-Based Approach

The patient receives adjuvant cisplatin/pemetrexed followed by pembrolizumab (PEARLS/KN-091). 6 months after completing adjuvant treatment with chemotherapy and immunotherapy she develops widespread metastatic disease

Question 4C: What would you do for treatment for this patient with recurrent metastatic NSCLC-adenocarcinoma. 50 pack-years smoking. PD-L1 IHC positive (40%), KRAS G12C on NGS, TMB=15.

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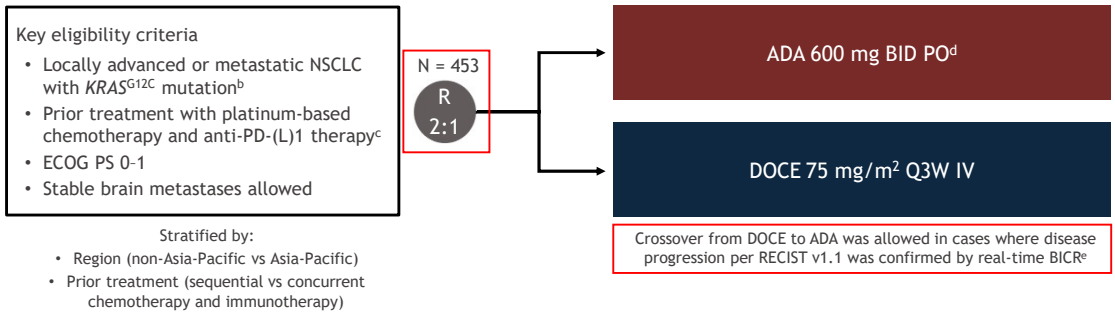
KRYSTAL-12: ADA in previously treated KRAS^{G12C} NSCLC

KRYSTAL-12 – *Improved PFS and ORR with Adagrasib vs Docetaxel in previously treated KRAS^{G12C}-mutated NSCLC*



Database lock: March 19, 2024. Data cut-off: December 31, 2023.
[a]NCT04685135. [b]Detected in tumor tissue using sponsor-approved local or central testing. [c]No washout period was required between prior therapy and study treatment. [d]Tablet formulation, except for four patients who initially received the capsule formulation. [e]Other crossover criteria: ECOG PS 0-2, recovery from DOCE-related AEs to grade 1 or baseline (except peripheral neuropathy and alopecia for which grade 2 is acceptable).

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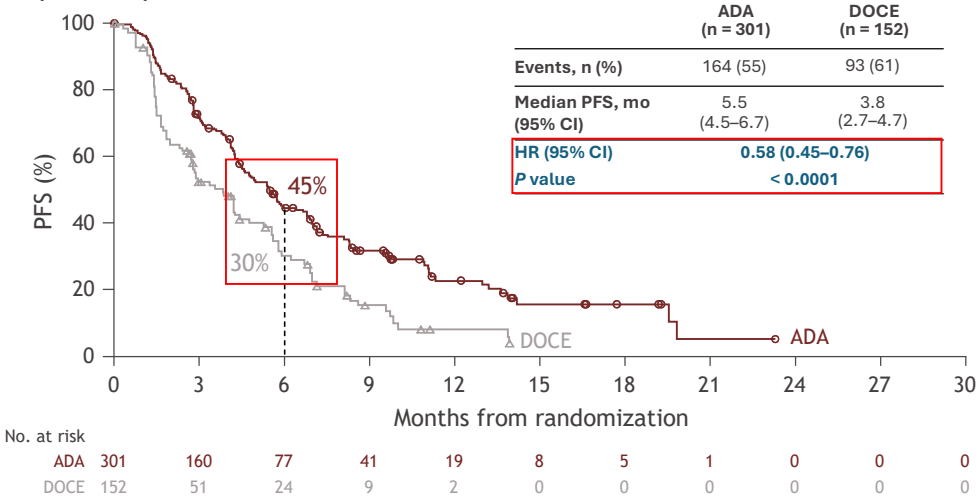
KRYSTAL-12 – *Improved PFS and ORR with Adagrasib vs Docetaxel in previously treated KRAS^{G12C}-mutated NSCLC*

Primary endpoint: PFS[a] per BICR



	ADA (n = 301)	DOCE (n = 152)
Events, n (%)	164 (55)	93 (61)
Median PFS, mo (95% CI)	5.5 (4.5–6.7)	3.8 (2.7–4.7)
HR (95% CI)	0.58 (0.45–0.76)	
P value	< 0.0001	

Median follow-up: 7.2 months.
[a]Time from randomization to the date of disease progression per BICR or death due to any cause, whichever occurs first. For patients who started a subsequent anticancer therapy prior to disease progression or death, PFS was censored at the date of the last tumor assessment prior to the start of the new therapy.

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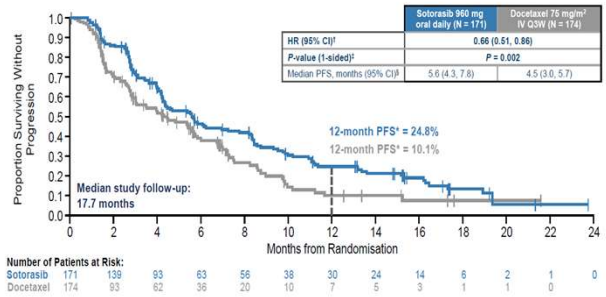
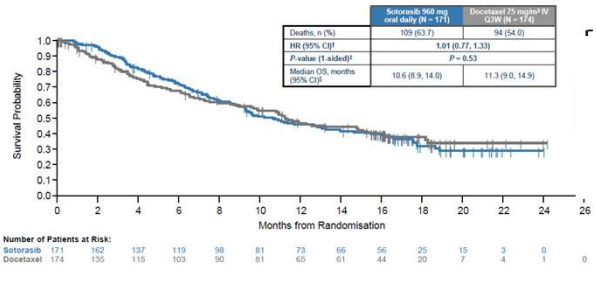
CodeBreaK 200: *Improved PFS with Sotorasib versus docetaxel for previously treated non-small-cell lung cancer with KRAS^{G12C} mutation*

Primary Endpoint: PFS by BICR



OS: Sotorasib vs Docetaxel‡



Johnson ML, et al. ESMO 2022. Abstract LBA10

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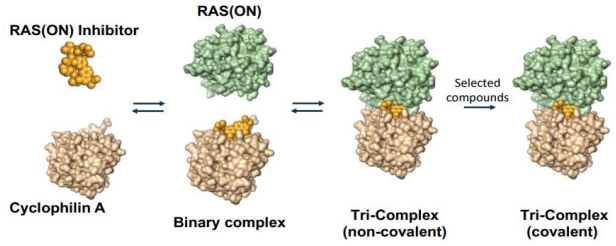
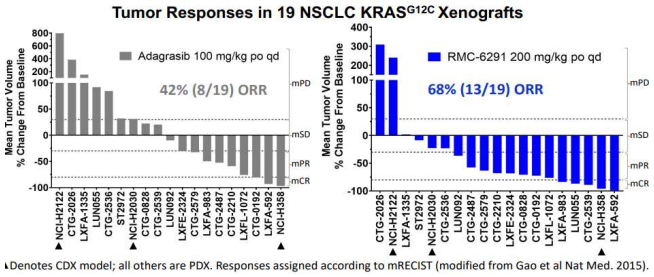
Next Generation RAS Inhibitors

- Less susceptible to adaptive resistance compared to GDP bound RAS
- RMC-6291 KRAS G12C (ON) inhibitor
- RMC-9805 KRAS G12D (ON) inhibitor
- RMC-6236-Pan RAS (ON)
- Divarasib – Single arm study
  ORR = 53.4% (95% CI, 39.9 to 66.7), and mPFS was 13.1 months (95% CI, 8.8 to, could not be estimated)





Denotes CDX model; all others are PDX. Responses assigned according to mRECIST (modified from Gao et al Nat Med. 2015).

Sacher et al N Engl J Med 2023;389:710-721.

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25th Multidisciplinary Management of Cancers: A Case-Based Approach

Case 4 - Take home messages

- 1st line therapy for advanced KRAS G12C-mutated NSCLC remains ICI +/- chemotherapy. KRAS G12C inhibitors reserved for 2nd line
- **KRYSTAL-12:** In patients with previously treated *KRAS*^{G12C}-mutated NSCLC, Adagrasib demonstrated a statistically significant improvement in PFS and ORR over docetaxel.
- **CodeBreaK 200**: Sotorasib significantly increased progression-free survival compared with docetaxel, in patients with previously treated advanced NSCLC with *KRAS*^{G12C} mutation
- Several new next generation KRAS inhibitors are being tested in clinical trials

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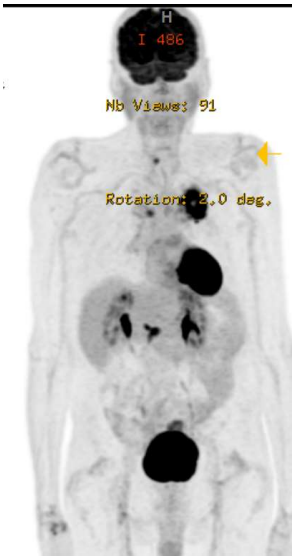
Case 5



- 60 yo M, never smoker presented with cough and low back pain
- **PET-CT:** LUL primary with hypermetabolic lymphadenopathy in the hilum & mediastinum. Diffuse bone mets also noted
- **MRI brain:** negative.
- **Biopsy:** NSCLC, adenocarcinoma
- **NGS/IHC:** PD-L1 TPS = 80%, **not enough tissue for NGS sampling**

Stage IVB (pT3N2M1C) NSCLC-adenocarcinoma

He completes palliative RT to sacral metastases for low back pain.

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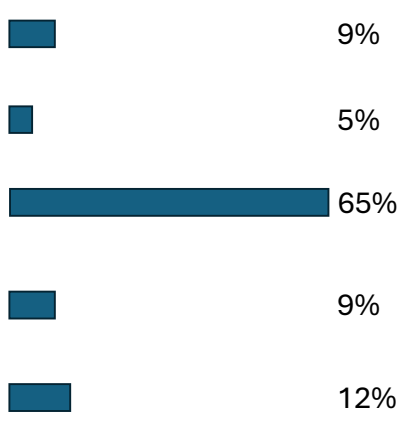
Question 5A: What would you do during the time the patient is receiving palliative radiation in this patient with Stage IV adenocarcinoma, high PD-L1 80%?



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- Plasma ctDNA is positive for *EML4-ALK fusion*

Question 5B: What would you initiate as 1L systemic treatment for Stage IV NSCLC-adenocarcinoma with *EML4-ALK fusion* and PD-L1 TPS of 80%.

1. Carboplatin/Pemetrexed/Pembrolizumab (KN 189) — 7%
2. Brigatinib — 2%
3. Lorlatinib — 46%
4. Alectinib — 46%
5. Ensartinib — 0%

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The patient is initiated on Lorlatinib. He develops oligo-progressive disease to the adrenal gland after 30 months on treatment

Question 5C: Would you repeat biopsy in this patient prior to instituting next line of treatment?

1. Yes, send plasma for NGS ctDNA only — 0%
2. Yes, send plasma ctDNA and tissue biopsy for histology and NGS — 0%
3. No, proceed to next line of treatment. — 0%

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Repeat tissue biopsy again shows ALK fusion with no explanation for TKI resistance

Question 5D: What would you initiate as 2L systemic treatment for Stage IV NSCLC-adenocarcinoma with EML4-ALK fusion mutation and PD-L1 TPS of 80% after PD on Lorlatinib?

1. Switch to carboplatin/pemetrexed/pembrolizumab — 0%
2. Continue Lorlatinib and consult Surgical Oncology for resection of adrenal met — 0%
3. Stop lorlatinib and switch to carboplatin/Pemetrexed — 0%
4. Continue Lorlatinib and consult Rad-Onc for XRT to adrenal gland — 0%

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How to Choose? FDA Approved Next Generation ALK inhibitors for 1L Therapy: Comparison of Efficacy and Toxicity

	Alectinib	Brigatinib	Lorlatinib	Ensartinib
ORR	79%	71%	76%	74%
Med PFS by ICR	25.7 mo	24 mo	NR (3yr follow-up)	
Med PFS by IR	34.8	30.8	NR (5-yr PFS=60%)	25.8mo
Med OS	>5 yr	NR	NR	NR
Toxicity	Fatigue, constipation, myalgia (CPK), edema, transaminitis (moderate) Weight gain	Nausea, diarrhea, fatigue, HA, HTN, pulmonary tox, transaminitis	Edema, neuropathy, cognitive changes (mood), lipids, weight gain	rash, musculoskeletal pain, constipation, cough, pruritis, nausea, edema, pyrexia, and fatigue

- 1L, first-line

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CROWN: *Significantly improved PFS with lorlatinib vs crizotinib in advanced NSCLC*

Current Post Hoc Analyses at 5 Years

Endpoint evaluation by BICR stopped after the 3-year analysis

Key eligibility criteria
- Stage IIIB/IV *ALK*+ NSCLC
- No prior systemic treatment for metastatic disease
- ECOG PS 0-2
- Asymptomatic treated or untreated CNS metastases were permitted
- ≥1 extracranial measurable target lesion (RECIST 1.1) with no prior radiation required

Randomized 1:1 N=296

Stratified by:
- Presence of brain metastases (yes vs no)
- Ethnicity (Asian vs non-Asian)

Lorlatinib 100 mg once daily n=149

Crizotinib 250 mg twice daily n=147

No crossover between treatment arms was permitted

Current analyses
Data cutoff: October 31, 2023
- **Investigator Assessed**
  - PFS[a]
  - ORR and IC ORR
  - DOR and IC DOR
  - IC TTP
- Safety
- Biomarker analyses

- The median duration of follow-up for PFS was 60.2 months (95% CI, 57.4-61.6) in the lorlatinib arm and 55.1 months (95% CI, 36.8-62.5) in the crizotinib arm

CNS, central nervous system; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; IC, intracranial; ORR, objective response rate; NSCLC, non-small cell lung cancer; PFS, progression-free survival; PS, performance status; RECIST, Response Evaluation Criteria in Solid Tumors; TTP, time to tumor progression.
[a] Defined as the time from randomization to RECIST-defined progression or death due to any cause.

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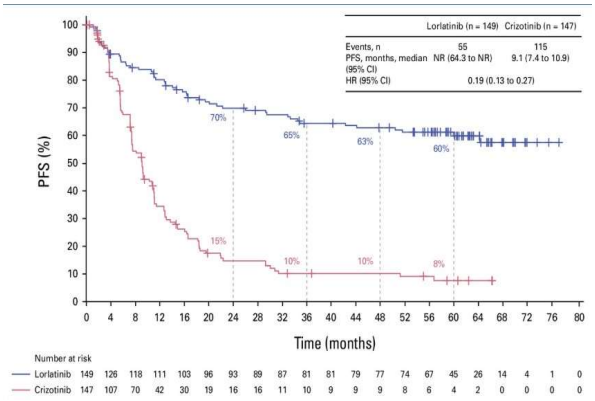
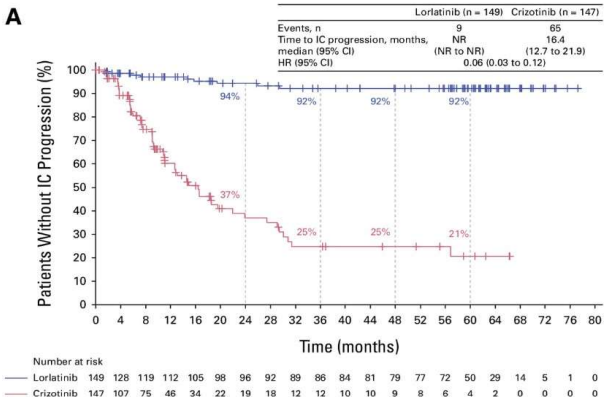
CROWN: *Significantly improved PFS with lorlatinib vs crizotinib in advanced NSCLC*





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CROWN: *Emerging New ALK Mutations Were Not Detected in ctDNA Collected at the End of Lorlatinib Treatment*

	Lorlatinib (n=31) n (%)	Crizotinib (n=89) n (%)
Resistance mechanisms		
New single ALK mutation	0	8 (9)
ALK compound mutation	0	2 (2)
Bypass mechanism	9 (29)	10 (11)
MAPK pathway aberration	3 (10)	1 (1)
PI3K/MTOR/PTEN pathway aberration	2 (6)	0
RTK pathway aberration	4 (13)	5 (6)
Cell cycle pathway aberration	2 (6)	5 (6)
Other gene aberration	11 (35)	19 (21)
Unknown	13 (42)	56 (63)

ctDNA from plasma collected at screening was analyzed with a validated, commercially available, 74-gene ctDNA next-generation sequencing assay (Guardant360 panel version 2.11; bioinformatics pipeline version 3.5.3; Guardant Health, Inc., Redwood City, CA).
ctDNA, circulating tumor DNA.

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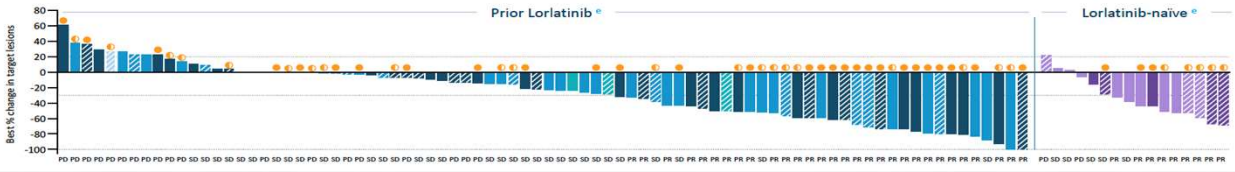
ALKOVE: NVL-655, *New Next Generation ALK-TKI*

Preliminary Activity: Radiographic Tumor Responses Across Previously Treated Patients with ALK+ NSCLC

RECIST 1.1 ORR, % (n/N) *All patients ± chemotherapy*	NSCLC Response-Evaluable (Any Prior ALK TKI, range 1 – 5)			Prior Lorlatinib (≥2 ALK TKIs)			Lorlatinib-naive (≥1 2G ± 1G)	
	All	Any ALK mutation [a]	G1202R [b]	All	Any ALK mutation	Compound ALK mutation [c]	All	Any ALK mutation
All Doses	38% (39/103)	52% (30/58)	69% (22/32) [d]	35% (30/85)	47% (23/49)	54% (15/28)	53% (9/17)	88% (7/8)
RP2D	38% (15/39)	55% (12/22)	71% (10/14)	35% (11/31)	50% (8/16)	64% (7/11)	57% (4/7)	80% (4/5)



Data cut-off: 15 June 2024. Response-evaluable patients with NSCLC. All responses were confirmed.
NSCLC, non-small cell lung cancer; **ORR**, objective response rate; **PD**, progressive disease; **PR**, partial response; **RECIST 1.1**, Response Evaluation Criteria in Solid Tumours version 1.1; **RP2D**, Recommended Phase 2 dose (150 mg QD); **SD**, stable disease; **TKI**, tyrosine kinase inhibitor.
[a] Includes all patients with ≥1 identified ALK resistance mutation as per local or central testing of blood (ctDNA) or tissue. Responses observed in patients with ALK I1171N/S, V1180L, L1196Q, L1198F, D1203N, or E1210K mutations, including where multiple mutations co-occur, in addition to those with G1202R.
[b] Includes patients with G1202R single and compound (≥2) mutations.
[c] Cis-allelic configuration has not been confirmed for all patients with compound (≥2) ALK resistance mutations.
[d] ORR = 67% (20/30) for G1202R patients with prior lorlatinib, and ORR= 100% (2/2) for lorlatinib-naïve G1202R patients.
[e] Five response-evaluable patients (4 with no known ALK mutations and 1 with single ALK mutation) not shown due to incomplete or missing post-baseline tumor assessments in the setting of PD or symptomatic deterioration.

KEY: PATIENT DETAILS

Lorlatinib Pre-treated:
- ≥ 3 prior ALK TKIs
- 2 prior, 2G + lorlatinib
- 2 prior, 1G + lorlatinib
- 1 prior (lorlatinib only)

Lorlatinib-naïve:
- ≥ 2 prior ALK TKIs
- 1 prior, alectinib
- Patient treated at RP2D

- ALK single resistance mutation
- ALK compound (≥2) resistance mutation

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Lorlatinib is continued and radiation oncology is consulted for radiation to adrenal gland.

Case 5 – Take home messages

- **CROWN:** 5 year survival analysis continues to show **s**ignificantly improved PFS of lorlatinib when compared to crizotinib in previously untreated ALK-EML4 positive NSCLC. Lorlatinib has better CNS activity.
- After 5 years of follow-up, median PFS has yet to be reached in the lorlatinib group, corresponding to the longest PFS ever reported with any single-agent molecular targeted treatment in advanced NSCLC and across all metastatic solid tumors.
- Emerging new ALK mutations were not detected in ctDNA collected at the end of Lorlatinib treatment
- **ALKOVE-1**: NVL-655 shows promising results in heavily pre-treated ALK-EML4 mutated NSCLC, including patients with CNS involvement.

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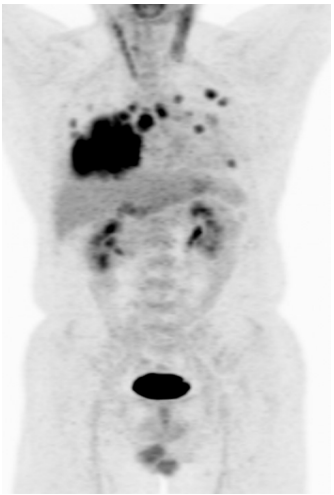
25th Multidisciplinary Management of Cancers: A Case-Based Approach

Case 6

58 yo M, never smoker, presented with cough and DOE

- **PET CT:** R sided lung mass, bilateral lung nodules and bilateral mediastinal LAD
- **Biopsy:** NSCLC, adenocarcinoma
- **NGS/IHC:** PD-L1 = 0%, HER2 Exon 20 insertion on NGS



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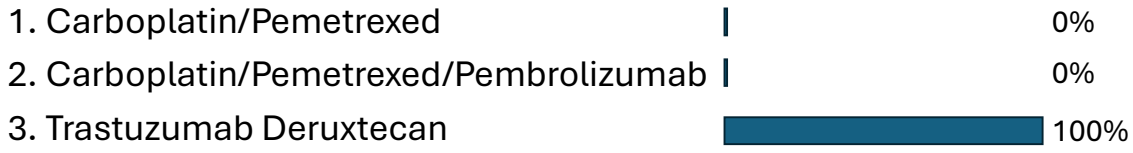
Question 6A: What would you offer as first line therapy?



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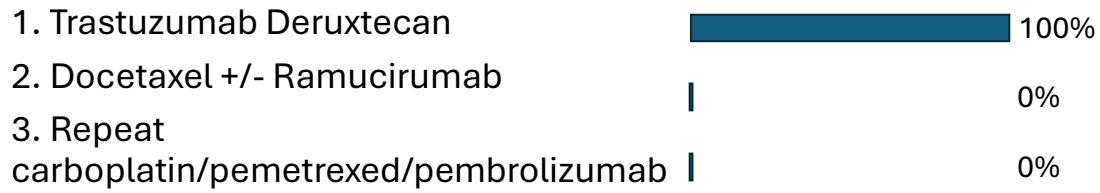
The patient receives carboplatin, pemetrexed and pembrolizumab with an initial response followed by progressive disease 5 months later with new liver metastases and growing lung lesions.

Question 6B: What would you offer as next line of treatment?



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The patient receives 2 cycles of 2L trastuzumab deruxtecan with partial response to treatment. He then develops worsening SOB. CT Chest shows bilateral interstitial opacities. You make the diagnosis of grade 2 pneumonitis from trastuzumab deruxtecan

Question 6C: What do you do next for grade 2 pneumonitis from trastuzumab deruxtecan?

1. Initiate corticosteroids. Consider restarting trastuzumab deruxtecan when off steroids and symptoms and radiologic findings resolve. — 0%
2. Initiate corticosteroids. Permanently discontinue trastuzumab deruxtecan. — 0%
3. Initiate corticosteroids. Consider restarting alternate HER2 directed therapy when off steroids and symptoms/ radiologic findings resolve (i.e. Trastuzumab with chemotherapy, afatinib or TDM-1). — 100%

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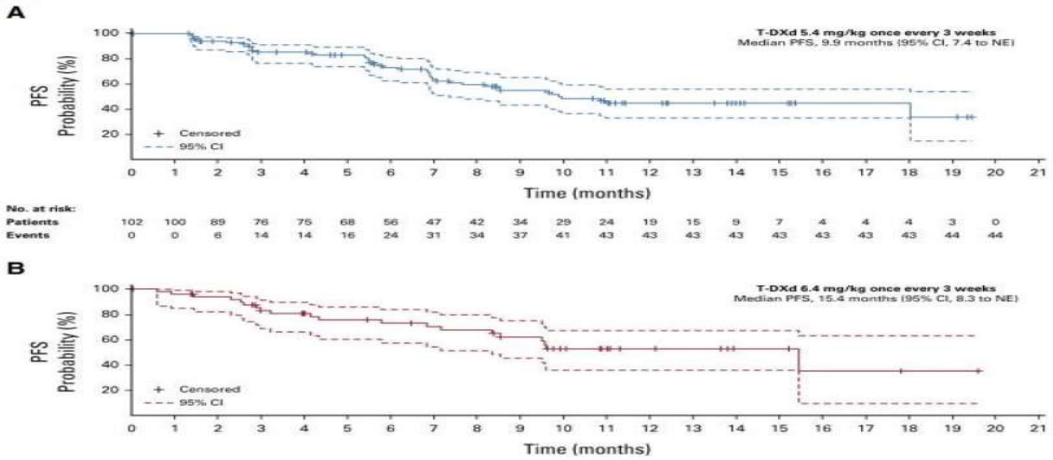
DESTINY-Lung02: *Durable response with T-DXd in previously treated metastatic HER-2 positive NSCLC*



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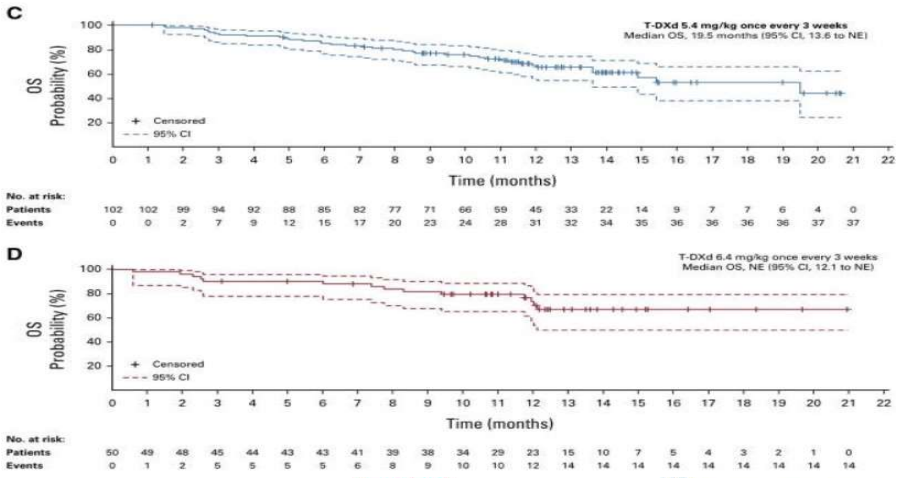
DESTINY-Lung02: *Durable response with T-DXd in previously treated metastatic HER-2 positive NSCLC*



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DESTINY-PanTumor02

DESTINY-PanTumor02: A Phase 2 Study of T-DXd for HER2-Expressing Solid Tumors

An open-label, multicenter study (NCT04482309)

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer guidelines[1])[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1

T-DXd 5.4 mg/kg q3w

n≈40 per cohort planned

(Cohorts with no objective responses in the first 15 patients were to be closed)

- Cervical cancer
- Endometrial cancer
- Ovarian cancer
- Biliary tract cancer
- Pancreatic cancer
- Bladder cancer
- Other tumors[b]

Primary endpoint

- Confirmed ORR (investigator)[c]

Secondary endpoints

- DOR[c]
- DCR[c]
- PFS[c]
- OS
- Safety

Data cut-off for analysis:

- Nov 16, 2022

[a]Patients were eligible for either test. All patients were centrally confirmed. [b]Patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer.
[c]Investigator-assessed per Response Evaluation Criteria in Solid Tumors version 1.1.
2L, second-line; ASCO, American Society of Clinical Oncology; DCR, disease control rate; CAP, College of American Pathologists; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization.

1. Hofmann M, et al. *Histopathology* 2008;52(7):797–805.

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PRESENTED BY: Funda Meric-Bernstam, MD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

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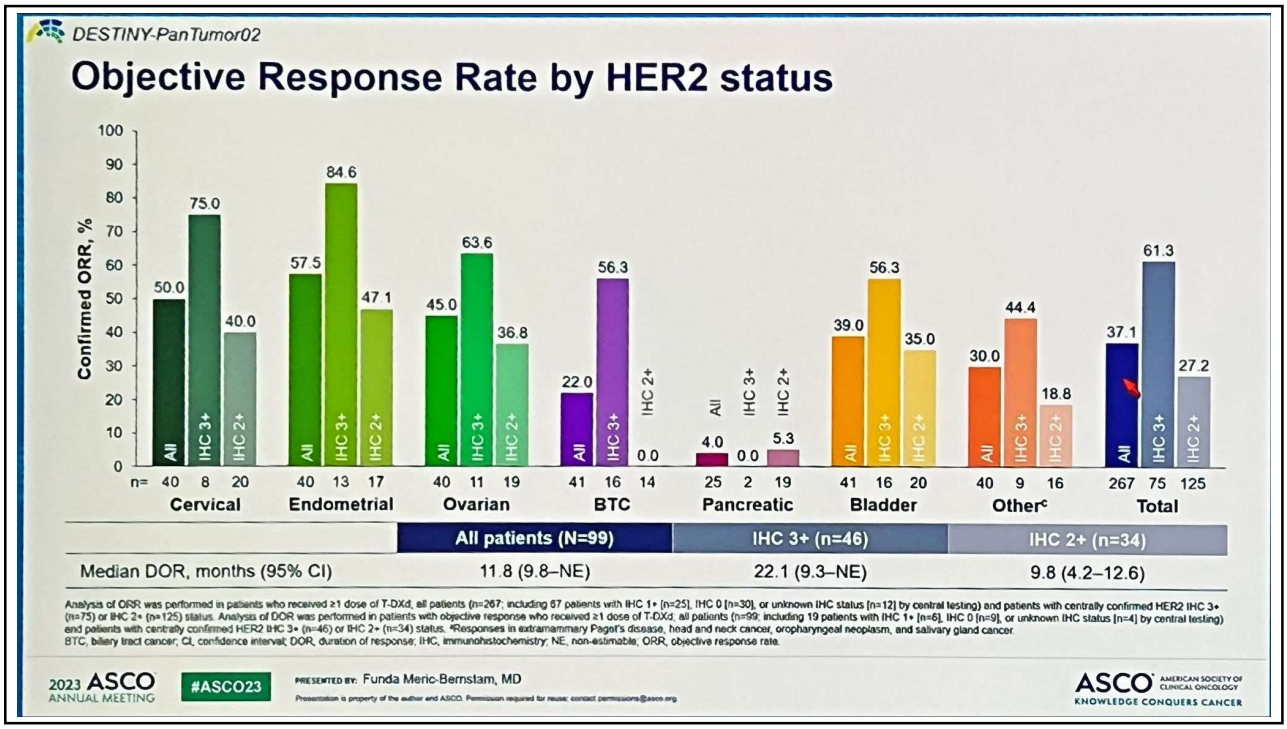

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25th Multidisciplinary Management of Cancers: A Case-Based Approach

Case 6 – Take home messages

- **DESTINY-Lung02:** T-DXd showed durable response rates, PFS and duration of response in previously treated (platinum based chemotherapy), HER2 Exon 20 ins NSCLC
- **DestinyPanTumor02:** T-DXd demonstrated clinically meaningful activity across a broad range of HER-2 expressing solid tumors with best outcomes at the higher HER2 expression level.
- New HER2 TKIs are in development (zongertinib, NVL-330, BAY-2927088)

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