NATIONAL LUNG CANCER ROUNDTABLE

American Cancer Society®

Project ECHO®

Addressing Lung Cancer Biomarker Testing Through Project ECHO: 2022-2023 Expansion

Session 7: "ASCO updates"

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ACS/NLCRT Lung Cancer Biomarker Testing Project ECHO

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Today's Agenda

Agenda Preview & Introductions (5 min)

Didactic Presentation: ***ASCO Updates*** (15 min)
Dr. Renato Martins, MD, MPH
Virginia Commonwealth University Massey Cancer Center

Case Presentation: Dr. Rick Hall (10 min)
University of Virginia

Case Presentation Recommendations/Discussion (15 min)

Post-Session Poll & Wrap Up (5 min)

This ACS/NLCRT Lung Cancer Biomarker Testing ECHO series is made possible by funding provided by:

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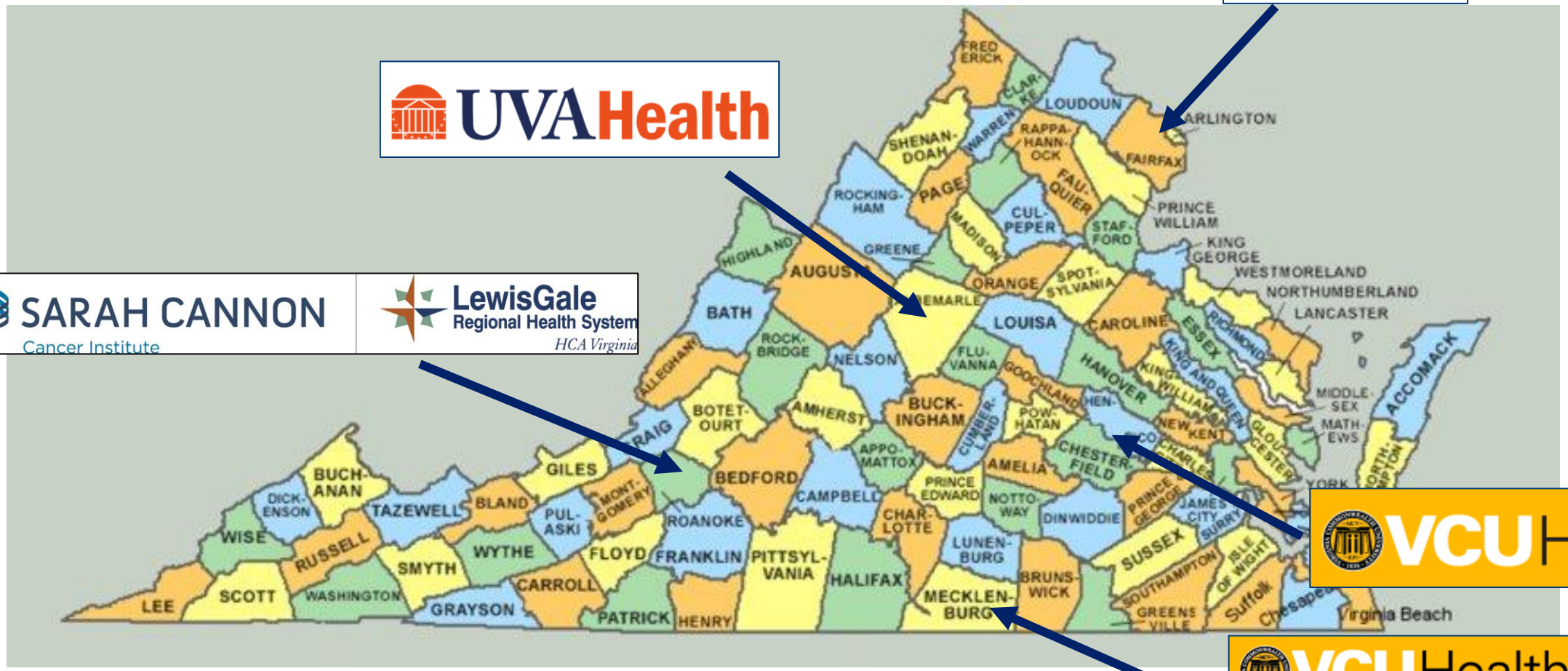

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DIDACTIC PRESENTATION

ASCO Updates

Renato Martins, M.D., M.P.H.
Division Chair of Hematology, Oncology, & Palliative Care
Virginia Commonwealth University
Massey Cancer Center

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2023 ASCO ANNUAL MEETING

Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC)

Roy S. Herbst[1], Masahiro Tsuboi[2], Thomas John[3], Terufumi Kato[4], Margarita Majem[5], Christian Grohé[6], Jie Wang[7], Jonathan Goldman[8], Shun Lu[9], Wu-Chou Su[10], Filippo de Marinis[11], Frances A. Shepherd[12], Ki Hyeong Lee[13], Nhieu Thi Le[14], Arunee Dechaphunkul[15], Dariusz Kowalski[16], Lynne Poole[17], Marta Stachowiak[18], Yuri Rukazenkov[19], Yi-Long Wu[20]

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PRESENTED BY: Roy S. Herbst

ADAURA Phase III study design

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
≥18 years (Japan / Taiwan: ≥20)
WHO performance status 0 / 1
Confirmed primary non-squamous NSCLC Ex19del / L858R‡
Brain imaging, if not completed pre-operatively
Complete resection with negative margins§
Maximum interval between surgery and randomization:
- 10 weeks without adjuvant chemotherapy
- 26 weeks with adjuvant chemotherapy

Stratification by:
Stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
Race (Asian vs non-Asian)

Randomization 1:1 (N=682)

Osimertinib 80 mg, once daily

Placebo, once daily

Planned treatment duration: 3 years

Treatment continued until:
- Disease recurrence
- Treatment completion
- Discontinuation criterion met

Follow-up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

Endpoints
- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

*At the time of recruitment, staging was determined by the AJCC / UICC Staging Manual 7th edition. Patients with stage IB disease were not eligible in Japan. †Pre-operative, post-operative, or planned radiotherapy was not allowed. ‡Centrally confirmed in tissue. §Patients received a CT scan after resection and within 28 days prior to treatment.

AJCC, American Joint Committee on Cancer; CT, computerized tomography; DFS, disease-free survival; EGFRm, epidermal growth factor receptor-mutated; Ex19del, exon 19 deletion; NSCLC, non-small cell lung cancer; OS, overall survival; UICC, Union for International Cancer Control; WHO, World Health Organization

Adjuvant osimertinib has significantly improved CNS DFS

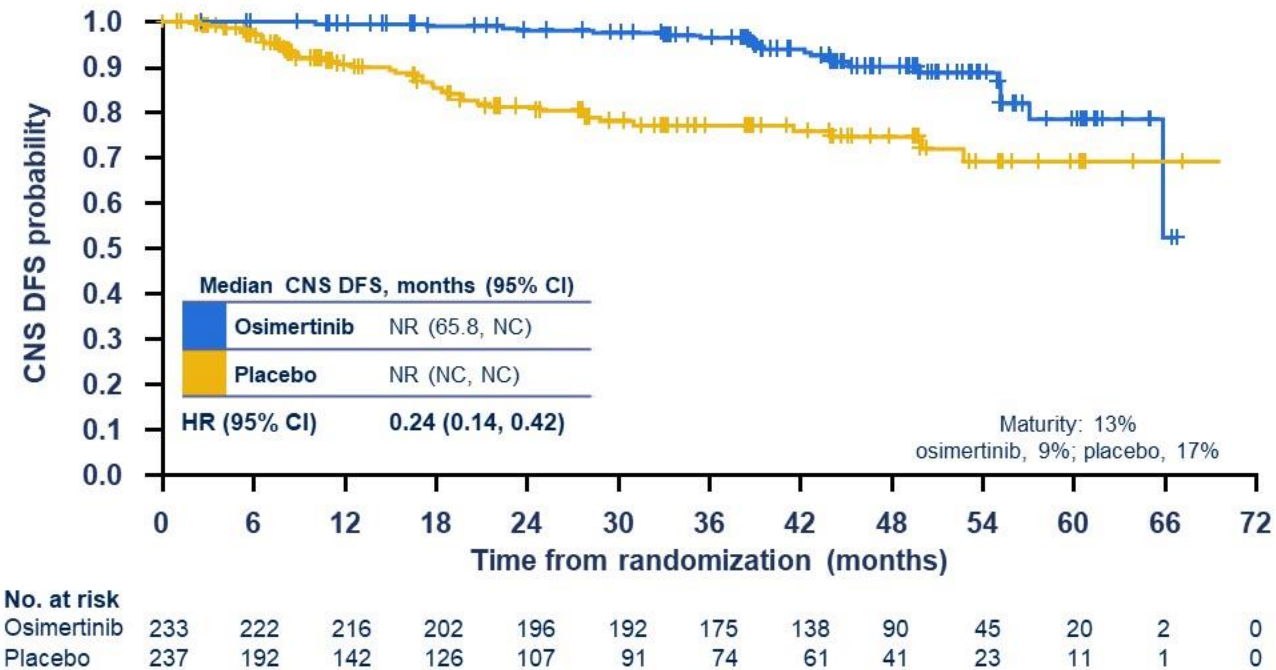
- CNS metastases are a poor prognostic factor among patients with NSCLC, and are associated with deterioration in quality of life[1]

Improved CNS efficacy with osimertinib treatment

- Osimertinib has shown greater penetration of the blood-brain barrier and higher exposure in the brain compared with other EGFR-TKIs[2–4]
- Adjuvant osimertinib demonstrated CNS DFS* benefit vs placebo in both the stage II–IIIA and IB–IIIA populations[5,6]

ADAURA updated CNS DFS analysis[5,6] (stage II–IIIA)

JCO January 2023



No. at risk													
Osimertinib	233	222	216	202	196	192	175	138	90	45	20	2	0
Placebo	237	192	142	126	107	91	74	61	41	23	11	1	0

Data cut-off: April 11, 2022.

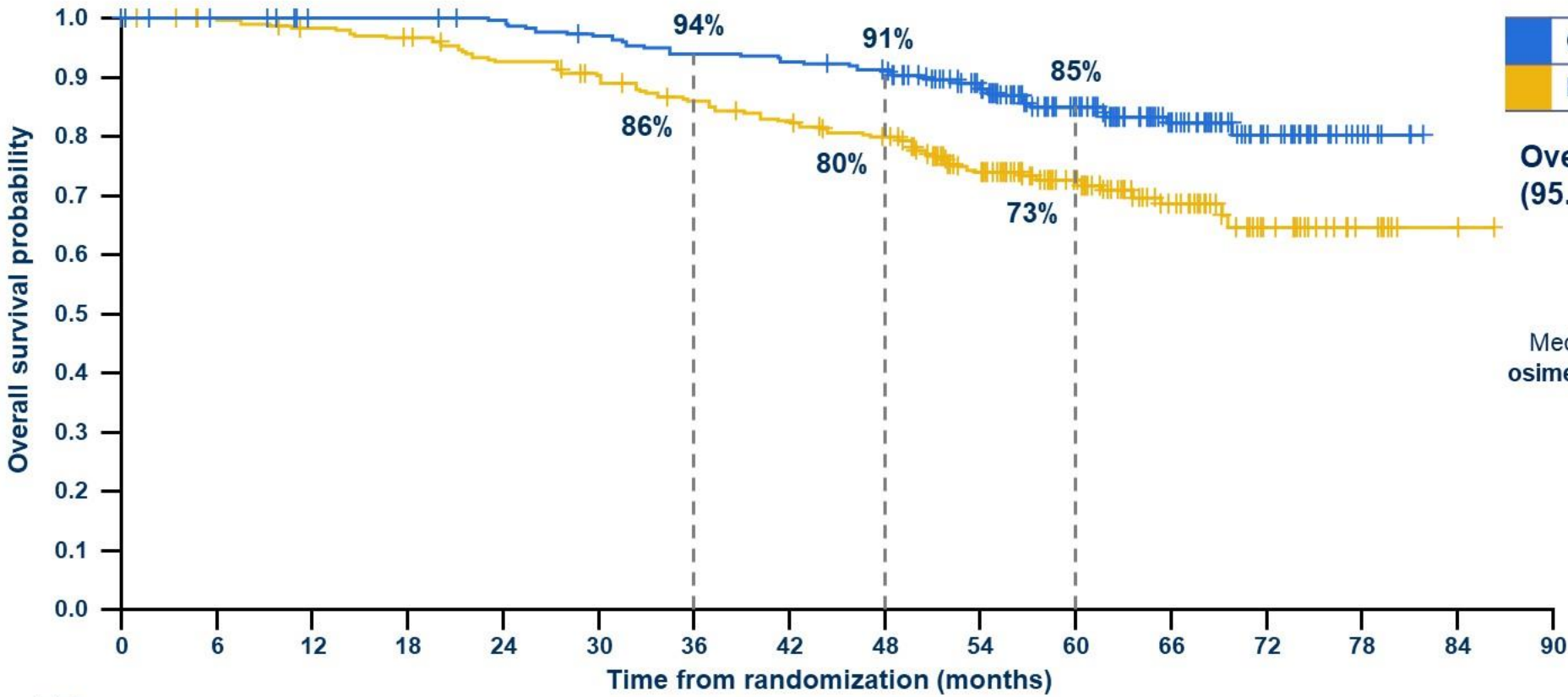
*CNS DFS events were defined as CNS disease recurrence or death by any cause.

1. Peters et al. Cancer Treat Rev 2016;45:139–162; 2. Colclough et al. Eur J Cancer 2016;69:S28; 3. Ballard et al. Clin Cancer Res 2016;22:5130–5140; 4. Vishwanathan et al. Cancer Res 2018; 78:CT013; 5. Herbst et al. J Clin Oncol 2023;41:1830–1840; 6. Tsuboi et al. Ann Oncol 2022;33(Suppl 7): abstract / oral LBA47.

CI, confidence interval; CNS, central nervous system; DFS, disease-free survival; EGFR, epidermal growth factor receptor; EGFRm, EGFR-mutated; EGFR-TKI, EGFR-tyrosine kinase inhibitor; HR, hazard ratio; NC, not calculable; NR, not reached; NSCLC, non-small cell lung cancer

Overall survival: patients with stage II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the primary population of stage II–IIIA disease



No. at risk																
Osimertinib	233	229	224	224	221	214	208	205	200	170	115	69	33	9	0	-
Placebo	237	232	226	221	210	202	190	182	171	138	94	53	25	8	2	0

5-year OS rate, % (95% CI)	
Osimertinib (n=233)	85 (79, 89)
Placebo (n=237)	73 (66, 78)

Overall OS HR (95.03% CI) **0.49 (0.33, 0.73); p=0.0004**

Maturity: 21%
osimertinib 15%, placebo 27%

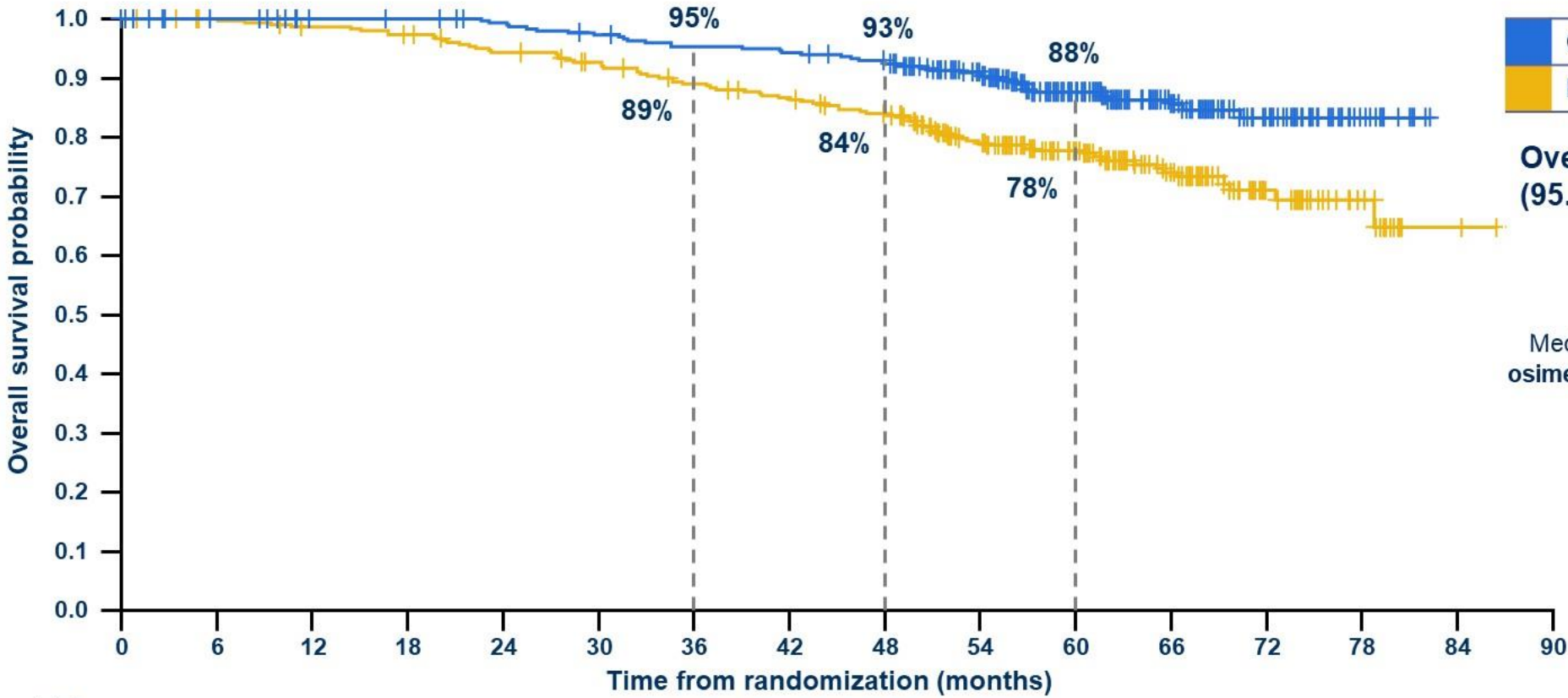
Median follow-up for OS* (censored patients):
osimertinib 61.7 months, placebo 60.4 months

Data cut-off: January 27, 2023.
Tick marks indicate censored data. Alpha allocation of 0.0497. *Median follow-up for OS (all patients): osimertinib 59.9 months, placebo 56.2 months.

CI, confidence interval; HR, hazard ratio; OS, overall survival

Overall survival: patients with stage IB / II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the overall population of stage IB–IIIA disease



5-year OS rate, % (95% CI)	
Osimertinib (n=339)	88 (83, 91)
Placebo (n=343)	78 (73, 82)

Overall OS HR (95.03% CI) **0.49 (0.34, 0.70); p<0.0001**

Maturity: 18%
osimertinib 12%, placebo 24%

Median follow-up for OS* (censored patients):
osimertinib 61.5 months, placebo 61.5 months

No. at risk

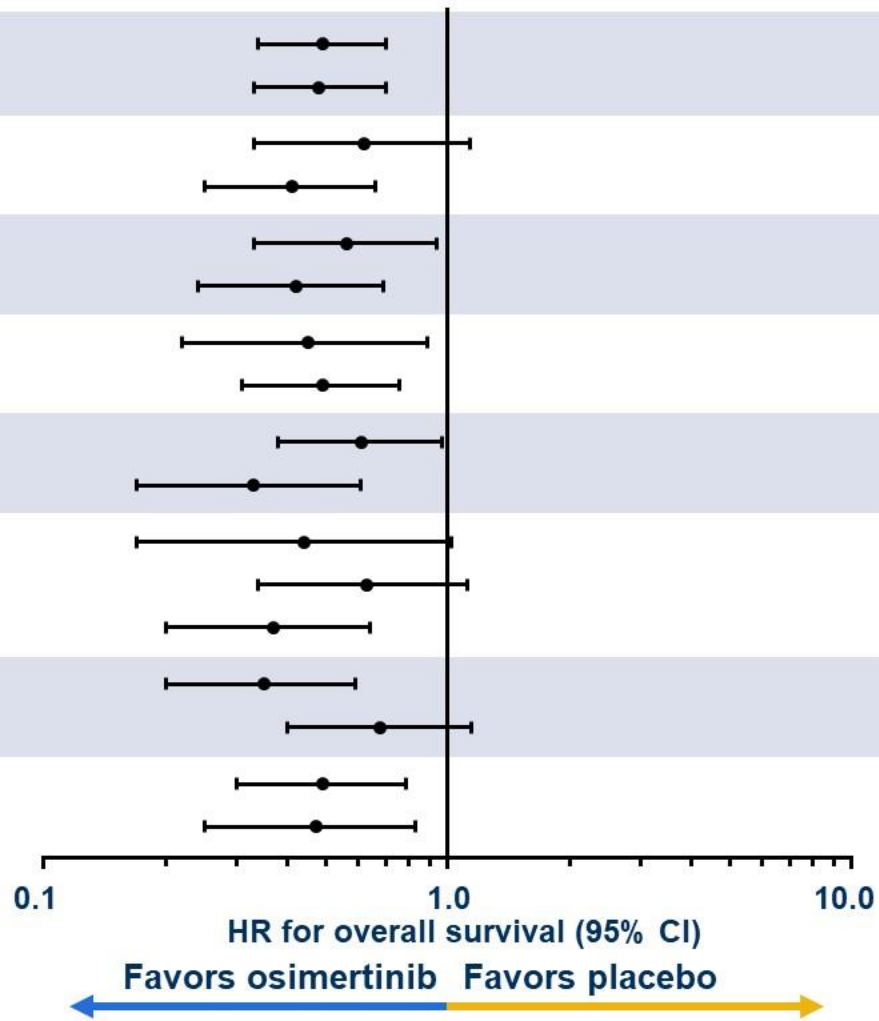
Osimertinib	339	332	325	324	319	311	304	301	294	252	176	108	50	15	0	-
Placebo	343	338	332	326	314	304	290	281	267	223	164	97	44	17	3	0

Data cut-off: January 27, 2023.
Tick marks indicate censored data. Alpha allocation of 0.0497. *Median follow-up for OS (all patients): osimertinib 60.4 months, placebo 59.4 months.

CI, confidence interval; HR, hazard ratio; OS, overall survival

OS across subgroups: patients with stage IB / II / IIIA disease

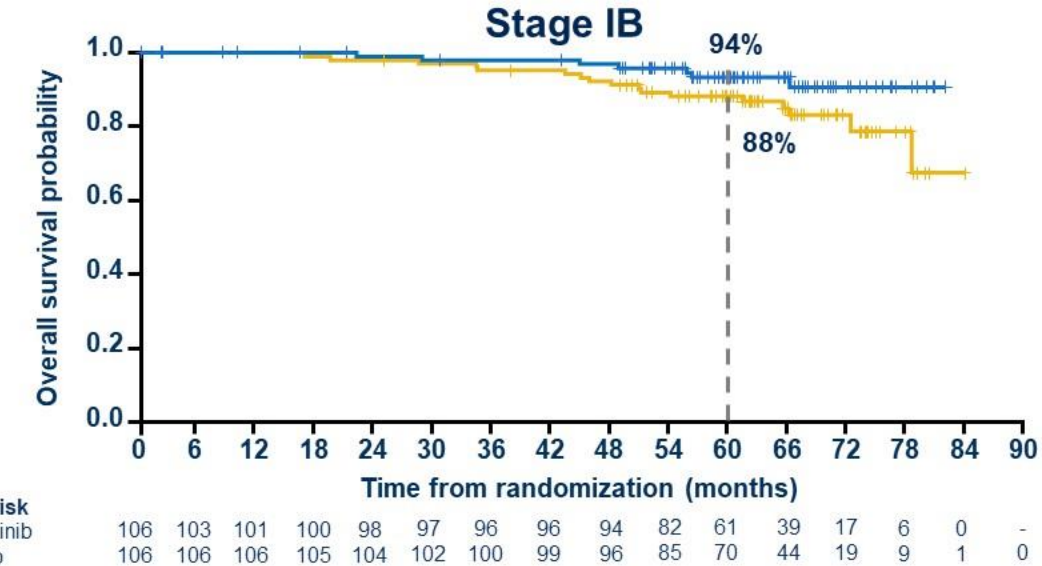
Subgroup		No. of events / patients	HR	95% CI
Overall (N=682)	Stratified log-rank	124 / 682	0.49	0.34, 0.70
	Unadjusted Cox PH	124 / 682	0.48	0.33, 0.70
Sex	Male	42 / 204	0.62	0.33, 1.13
	Female	82 / 478	0.41	0.25, 0.66
Age	<65 years	60 / 380	0.56	0.33, 0.94
	≥65 years	64 / 302	0.42	0.24, 0.69
Smoking history	Yes	34 / 194	0.45	0.22, 0.89
	No	90 / 488	0.49	0.31, 0.76
Race	Asian	73 / 434	0.61	0.38, 0.97
	Non-Asian	51 / 248	0.33	0.17, 0.61
Stage*	IB	24 / 212	0.44	0.17, 1.02
	II	46 / 236	0.63	0.34, 1.12
	IIIA	54 / 234	0.37	0.20, 0.64
EGFR mutation	Ex19del	65 / 378	0.35	0.20, 0.59
	L858R	59 / 304	0.68	0.40, 1.14
Adjuvant chemotherapy	Yes	74 / 410	0.49	0.30, 0.79
	No	50 / 272	0.47	0.25, 0.83



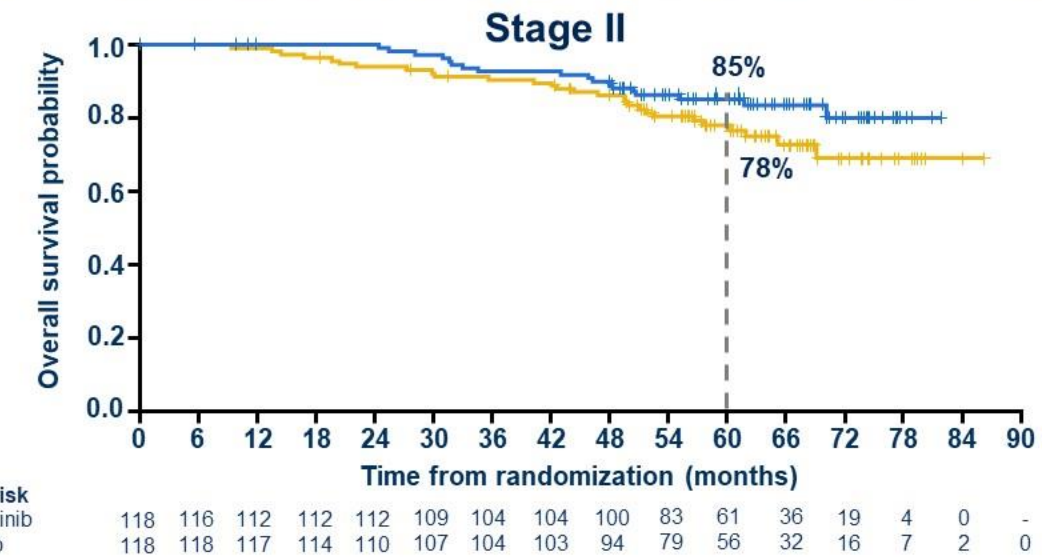
Data cut-off: January 27, 2023.
*AJCC / UICC 7th edition.

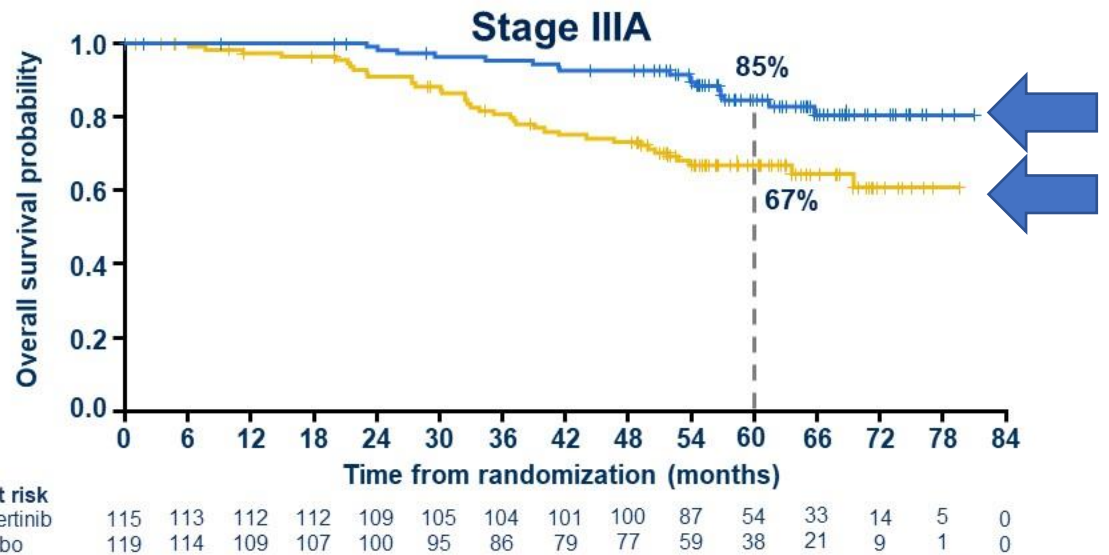
AJCC, American Joint Committee on Cancer; CI, confidence interval; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; HR, hazard ratio; OS, overall survival; PH, proportional-hazards model; UICC, Union for International Cancer Control

Overall survival by disease stage



	Stage IB	Stage II	Stage IIIA
5 year OS rate, % (95% CI)			
Osimertinib	94 (86, 97)	85 (77, 91)	85 (76, 91)
Placebo	88 (80, 93)	78 (69, 85)	67 (57, 75)
Overall HR (95% CI)	**0.44 (0.17, 1.02)**	**0.63 (0.34, 1.12)**	**0.37 (0.20, 0.64)**





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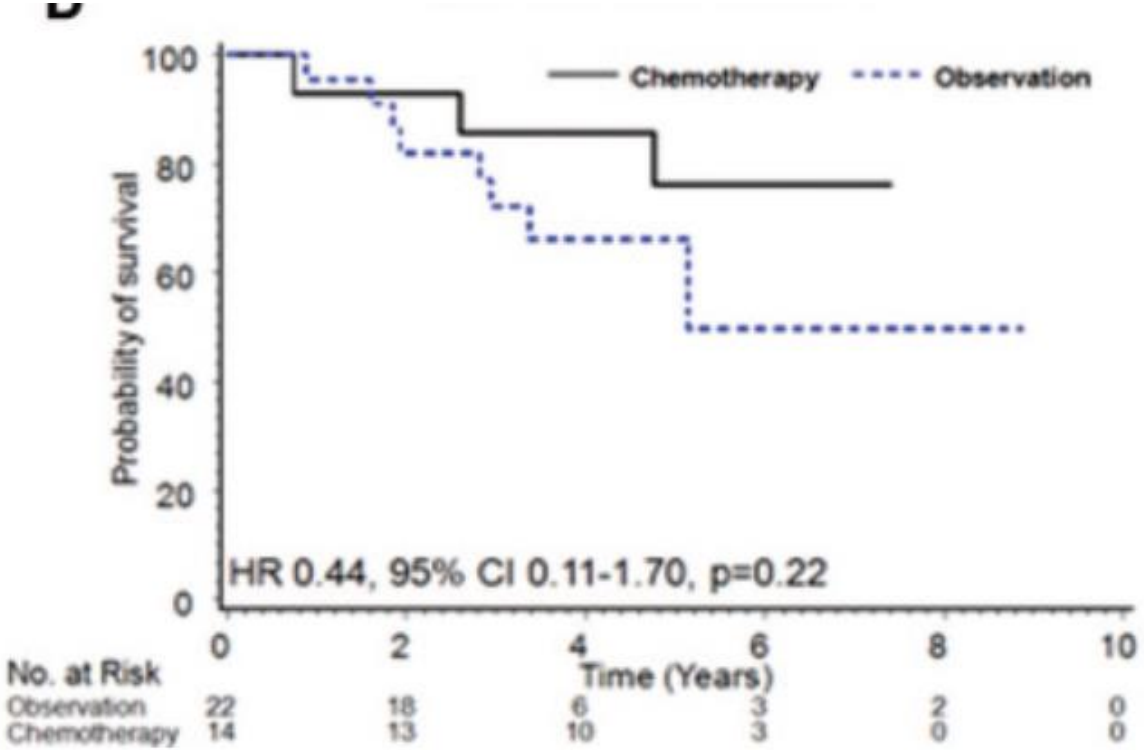
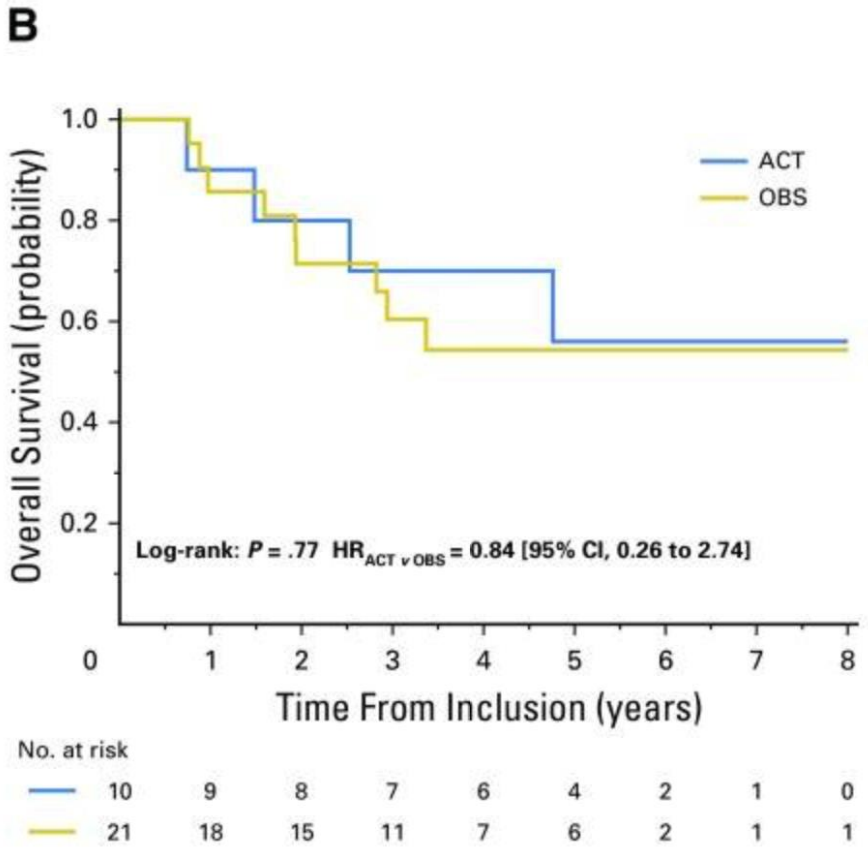
Data cut-off: January 27, 2023. Tick marks indicate censored data.
CI, confidence interval; HR, hazard ratio; OS, overall survival

What do we know about this question?



J Thorac Oncol 2011;6: 139-47



J Clin Oncol. 2017 Jun 20; 35(18): 2018–2027.

Summary

- Every patient with completely resected non-squamous NSCLC and stage II-III (8th edition) MUST be tested for the presence of EGFR mutation
- Osimertinib provides remarkable improvement in the overall survival of resected EGFR mutated NSCLC
- Osimertinib is the standard of care for these patients

Questions

- Is chemotherapy necessary ?
- Should one delay for 9-12 weeks the highly effective therapy to administer a marginally effective one ?
- Is there other combined genetic data that will help us make that decision ?

2023 ASCO ANNUAL MEETING

KEYNOTE-671: Randomized, Double-Blind, Phase 3 Study of Pembrolizumab or Placebo plus Platinum-Based Chemotherapy Followed by Resection and Pembrolizumab or Placebo for Early-Stage NSCLC

Heather Wakelee,[1] Moishe Liberman,[2] Terufumi Kato,[3] Masahiro Tsuboi,[4] Se-Hoon Lee,[5] Jie He,[6] Shugeng Gao,[6] Ke-Neng Chen,[7] Christophe Dooms,[8] Margarita Majem,[9] Ekkehard Eigendorff,[10] Gastón L Martinengo,[11] Olivier Bylicki,[12] Delvys Rodríguez-Abreu,[13] Jamie Chaft,[14] Silvia Novello,[15] Jing Yang,[16] Steven M Keller,[16] Ayman Samkari,[16] Jonathan D Spicer,[17] on behalf the KEYNOTE-671 Investigators

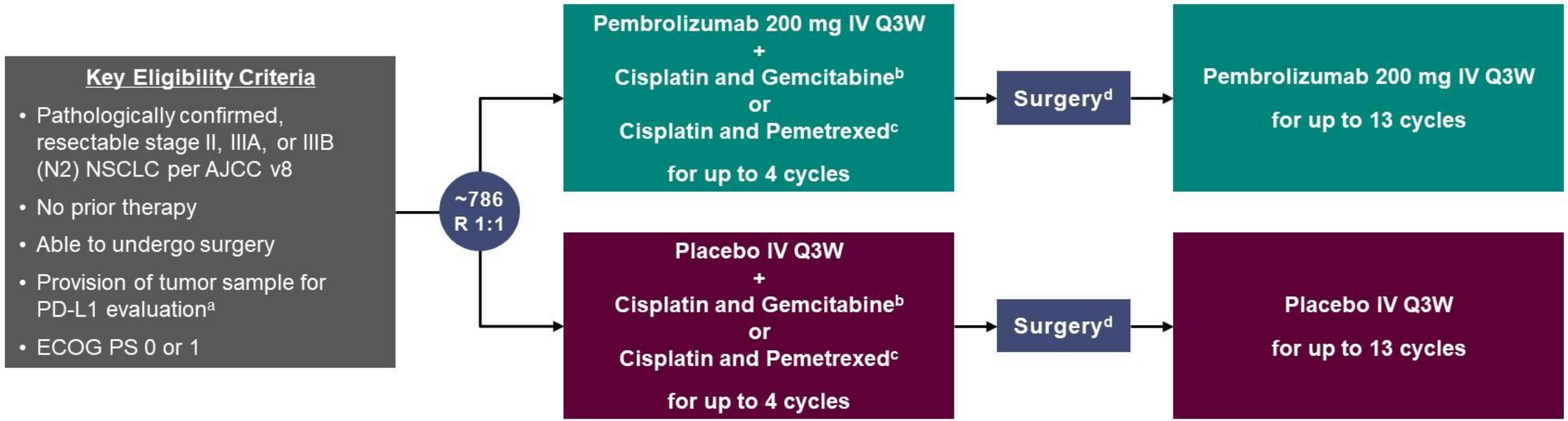
[1]Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA; [2]Centre Hospitalier de Universite to Montréal (CHUM), Montréal, QC, Canada; [3]Kanagawa Cancer Center, Yokohama, Japan; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [6]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [7]Beijing Cancer Hospital, Peking University, Beijing, China; [8]University Hospitals Leuven, Leuven, Belgium; [9]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [10]Zentralklinik Bad Berka, Bad Berka, Germany; [11]Sanatorio Parque, Córdoba, Argentina; [12]HIA Sainte-Anne, Toulon, France; [13]Hospital Universitario Insular de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain; [14]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA; [15]Department of Oncology, University of Turin, A.O.U. San Luigi Gonzaga di Orbassano, Turin, Italy; [16]Merck & Co. Inc., Rahway, NJ, USA; [17]McGill University Health Centre, Montréal, QC, Canada

Background

- PD-1 and PD-L1 inhibitors are a standard-of-care treatment for advanced and metastatic NSCLC
- Although recent phase 3 trials have shown a benefit for PD-(L)1 inhibitors given before[1] or after[2,3] resection of early-stage NSCLC, many patients still experience recurrence
- A perioperative approach that includes both neoadjuvant and adjuvant PD-(L)1 inhibition may provide benefit beyond either approach alone
- The recently reported phase 3 AEGEAN[4] and NEOTORCH[5] studies have shown significant improvement in EFS for neoadjuvant PD-(L)1 inhibition + platinum-based chemotherapy followed by surgery and adjuvant PD-(L)1 inhibition compared with neoadjuvant platinum-based chemotherapy and surgery alone for resectable NSCLC

[1]Forde PM et al. *N Engl J Med* 2022;386:1973-85. [2]Felip E et al. *Lancet* 2021;398:1344-57. [3]O'Brien M et al. *Lancet Oncol* 2022;23:1274-86.
[4]Heymach JV et al. AACR Annual Meeting 2023; Abstr CT005. [5]Lu S et al. ASCO Monthly Plenary Session, April 2023; Abstr 425126.

KEYNOTE-671 Study Design
Randomized, Double-Blind, Phase 3 Trial



Stratification Factors
- Disease stage (II vs III)
- PD-L1 TPS[a] (<50% vs ≥50%)
- Histology (squamous vs nonsquamous)
- Geographic region (east Asia vs not east Asia)

Dual primary end points: EFS per investigator review and OS

Key secondary end points: mPR and pCR per blinded, independent pathology review, and safety

[a] Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx. [b] Cisplatin 75 mg/m^2 IV Q3W + gemcitabine 1000 mg/m^2 IV on days 1 and 8 Q3W was permitted for squamous histology only. [c] Cisplatin 75 mg/m^2 IV Q3W + pemetrexed 500 mg/m^2 IV Q3W was permitted for nonsquamous histology only. [d] Radiotherapy was to be administered to participants with microscopic positive margins, gross residual disease, or extracapsular nodal extension following surgery and to participants who did not undergo planned surgery for any reason other than local progression or metastatic disease. ClinicalTrials.gov identifier: NCT03425643.

Treatment Disposition

Median Follow-Up[a]: 25.2 months (range, 7.5-50.6)

		Pembro Arm	Placebo Arm
Screening	Patients screened between April 2018 and December 2021	1364	
	Randomized (ITT population)	397	400
Neoadjuvant Treatment	Received ≥1 dose of neoadjuvant treatment (safety population)	396	399
	Completed 4 cycles of pembrolizumab or placebo	295 (74.5%)	297 (74.4%)
	Completed ≥3 cycles of pembrolizumab or placebo	346 (87.4%)	348 (87.2%)
	Continued to surgery and/or radiotherapy	342 (86.4%)	335 (84.0%)
	Discontinued all study therapy permanently	54 (13.6%)	64 (16.0%)
In-Study Surgery and/or In-Study Radiotherapy[b]	Underwent in-study surgery	325 (82.1%)	317 (79.4%)
	Underwent in-study radiotherapy	35 (8.8%)	53 (13.3%)
	Discontinued all study therapy permanently following surgery	45 (11.4%)	60 (15.0%)
	Discontinued all study therapy permanently following radiotherapy	7 (1.8%)	8 (2.0%)
Adjuvant Treatment	Received ≥1 dose of adjuvant treatment	290 (73.2%)	267 (66.9%)
	Completed adjuvant treatment	160 (40.4%)	141 (35.3%)
	Discontinued adjuvant treatment	88 (22.2%)	81 (20.3%)
	Adjuvant treatment ongoing	42 (10.6%)	45 (11.3%)

[a] Defined as time from randomization to data cutoff date. [b] In the pembro arm, 307 participants underwent in-study surgery alone, 18 underwent in-study surgery and in-study radiotherapy, and 17 underwent in-study radiotherapy alone. In the placebo arm, 282 participants underwent in-study surgery alone, 35 underwent in-study surgery and in-study radiotherapy, and 18 underwent in-study radiotherapy alone.
All percentages are based on the number of participants who received ≥1 dose of neoadjuvant treatment. Data cutoff date for IA1: July 29, 2022.

Baseline Characteristics

	Pembro Arm (N = 397)	Placebo Arm (N = 400)
Median age (range), years	63 (26-83)	64 (35-81)
Male	279 (70.3%)	284 (71.0%)
Race		
American Indian or Alaska Native	1 (0.3%)	0
Asian	124 (31.2%)	125 (31.3%)
Black or African American	6 (1.5%)	10 (2.5%)
Multiple	3 (0.8%)	10 (2.5%)
White	250 (63.0%)	239 (59.8%)
Missing data	13 (3.3%)	16 (4.0%)
Geographic region		
East Asia	123 (31.0%)	121 (30.3%)
Not east Asia	274 (69.0%)	279 (69.8%)
ECOG PS		
0	253 (63.7%)	246 (61.5%)
1	144 (36.3%)	154 (38.5%)
Histology		
Nonsquamous	226 (56.9%)	227 (56.8%)
Squamous	171 (43.1%)	173 (43.3%)

	Pembro Arm (N = 397)	Placebo Arm (N = 400)
Smoking status		
Current	96 (24.2%)	103 (25.8%)
Former	247 (62.2%)	250 (62.5%)
Never	54 (13.6%)	47 (11.8%)
Disease stage at baseline (per AJCC v8)		
II	118 (29.7%)	121 (30.3%)
IIIA	217 (54.7%)	225 (56.3%)
IIIB	62 (15.6%)	54 (13.5%)
pN status		
N0	148 (37.3%)	142 (35.5%)
N1	81 (20.4%)	71 (17.8%)
N2	168 (42.3%)	187 (46.8%)
PD-L1 TPS		
≥50%	132 (33.2%)	134 (33.5%)
1-49%	127 (32.0%)	115 (28.8%)
<1%	138 (34.8%)	151 (37.8%)
Known *EGFR* mutation[a]	14 (3.5%)	19 (4.8%)
Known *ALK* translocation[a]	12 (3.0%)	9 (2.3%)

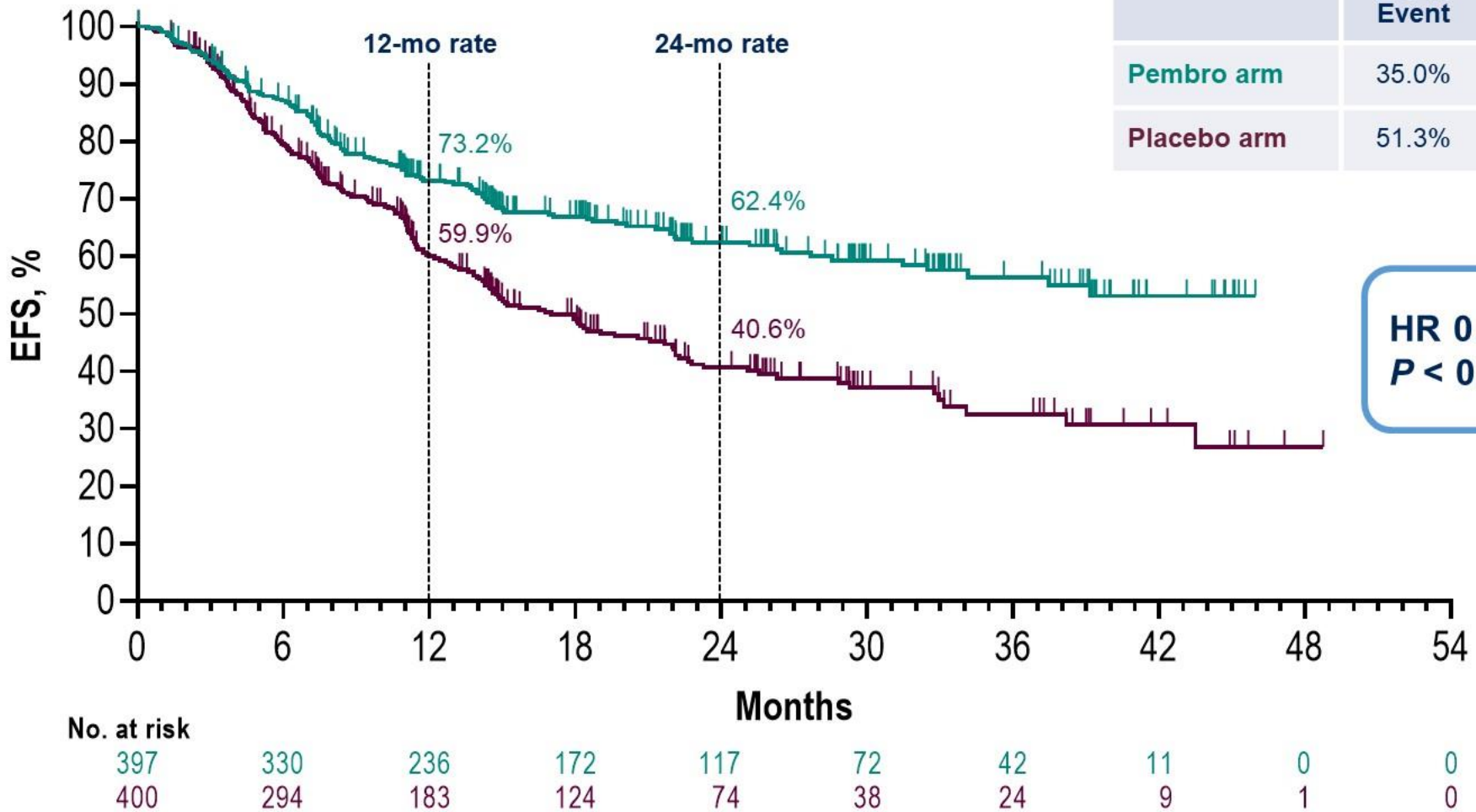
[a] *EGFR* mutation and *ALK* translocation status were tested locally per investigator discretion. *EGFR* status was unknown in 272 (68.5%) participants in the pembro arm and 254 (63.5%) in the placebo arm; *ALK* status was unknown in 281 (70.8%) and 258 (64.5%), respectively. Data cutoff date for IA1: July 29, 2022.

Surgical Details

	Pembro Arm N = 325	Placebo Arm N = 317
In-Study Surgery[a]		
Resected	320 (98.5%)	302 (95.3%)
Complete - R0	299 (92.0%)	267 (84.2%)
Incomplete - R1	17 (5.2%)	31 (9.8%)
Incomplete - R2	4 (1.2%)	4 (1.3%)
Unresected	5 (1.5%)	15 (4.7%)
Surgical procedure		
Lobectomy	256 (78.8%)	238 (75.1%)
Pneumonectomy	37 (11.4%)	39 (12.3%)
Bilobectomy	26 (8.0%)	26 (8.2%)
Exploratory thoracotomy	4 (1.2%)	13 (4.1%)
Other	2 (0.6%)[b]	1 (0.3%)[c]
30-day all-cause mortality	6 (1.8%)[d]	2 (0.6%)[e]

[a] An additional 8 participants in the pembro arm and 7 participants in the placebo arm underwent off-study surgery. [b] Lung segmentectomy (n=1), lung wedge resection (n=1). [c] Lymph node dissection only (planned surgery was lung lobectomy; need for more extensive surgery discovered during surgery, but consent was not granted). [d] Pulmonary embolism (n=2), pulmonary hemorrhage due to arterial injury during surgery (n=1), pulmonary sepsis (n=1), respiratory failure (n=1), and septic shock (n=1). [e] Respiratory failure (n = 1) and pneumonia (n = 1) Data cutoff date for IA1: July 29, 2022.

Event-Free Survival



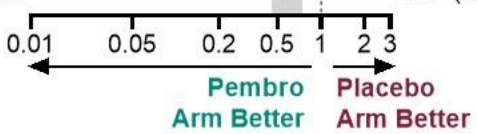
	Pts w/ Event	Median (95% CI), mo
Pembro arm	35.0%	NR (34.1-NR)
Placebo arm	51.3%	17.0 (14.3-22.0)

HR 0.58 (95% CI, 0.46-0.72)
***P* < 0.00001**

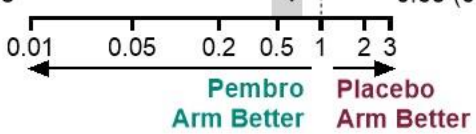
EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause.
Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).

Event-Free Survival in Subgroups

Subgroup	Events/participants Pembro Arm	Events/participants Placebo Arm	Hazard ratio (95% CI)
Overall	139/397	205/400	0.58 (0.46-0.72)
Age			
<65 y	74/221	113/214	0.53 (0.39-0.71)
≥65 y	65/176	92/186	0.64 (0.46-0.88)
Sex			
Female	31/118	55/116	0.44 (0.28-0.68)
Male	108/279	150/284	0.63 (0.49-0.80)
Race			
White	85/250	123/239	0.54 (0.41-0.72)
All others	46/134	70/145	0.62 (0.42-0.89)
Geographic region			
East Asia	43/123	57/121	0.66 (0.45-0.99)
Not east Asia	96/274	148/279	0.54 (0.41-0.69)
Smoking status			
Current	37/96	57/103	0.52 (0.34-0.78)
Former	84/247	128/250	0.57 (0.43-0.75)
Never	18/54	20/47	0.68 (0.36-1.30)
Histology			
Nonsquamous	73/226	107/227	0.58 (0.43-0.78)
Squamous	66/171	98/173	0.57 (0.41-0.77)

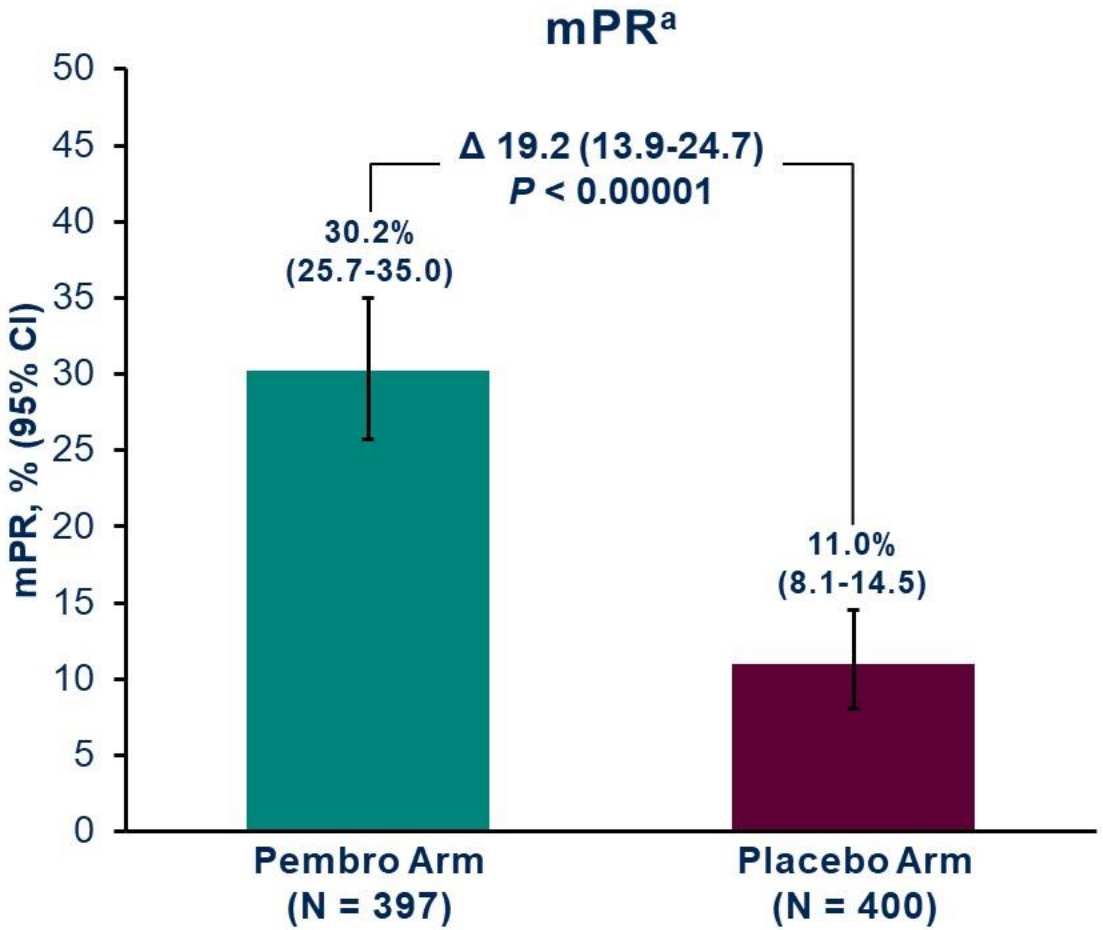


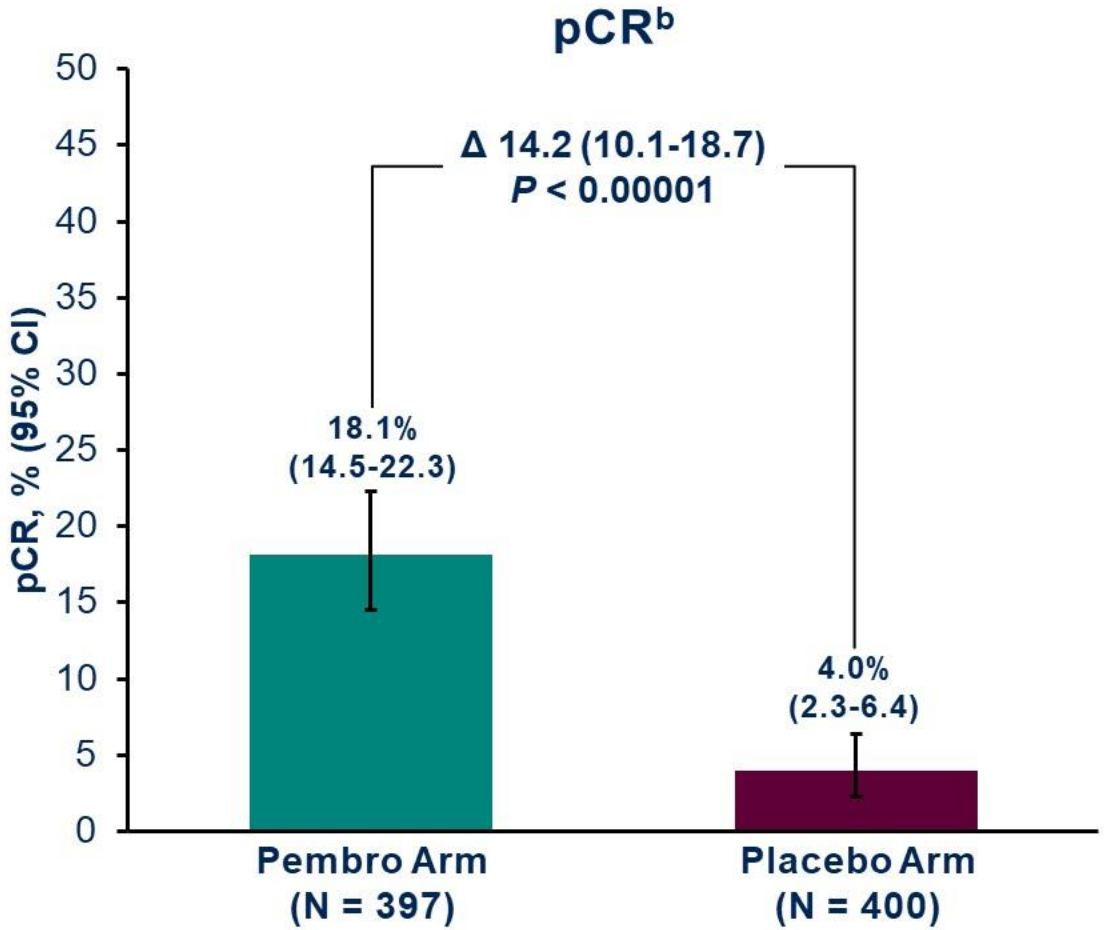
Subgroup	Events/participants Pembro Arm	Events/participants Placebo Arm	Hazard ratio (95% CI)
Overall	139/397	205/400	0.58 (0.46-0.72)
Pathologic stage			
II	34/118	48/121	0.65 (0.42-1.01)
IIIA	80/217	124/225	0.54 (0.41-0.72)
IIIB	25/62	33/54	0.52 (0.31-0.88)
pN status			
pN0	51/148	70/142	0.57 (0.40-0.82)
pN1	25/81	33/71	0.60 (0.36-1.01)
pN2	63/168	102/187	0.57 (0.42-0.78)
PD-L1 TPS			
<1%	63/138	80/151	0.77 (0.55-1.07)
1-49%	44/127	62/115	0.51 (0.34-0.75)
≥50%	32/132	63/134	0.42 (0.28-0.65)
***EGFR* mutation**			
No	31/111	64/127	0.48 (0.31-0.74)
Yes	1/14	10/19	0.09 (0.01-0.74)
Unknown	107/272	131/254	0.64 (0.49-0.83)
***ALK* translocation**			
No	29/104	76/133	0.41 (0.26-0.62)
Unknown	106/281	128/258	0.63 (0.49-0.82)



EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause. Per the prespecified analysis plan, subgroups with <30 participants are excluded from the forest plot. Subgroups for stage IIIA and IIIB and pN status were post hoc; all other subgroups were prespecified. Data cutoff date for IA1: July 29, 2022.

Pathologic Response
Assessed per Blinded, Independent Pathologist Review

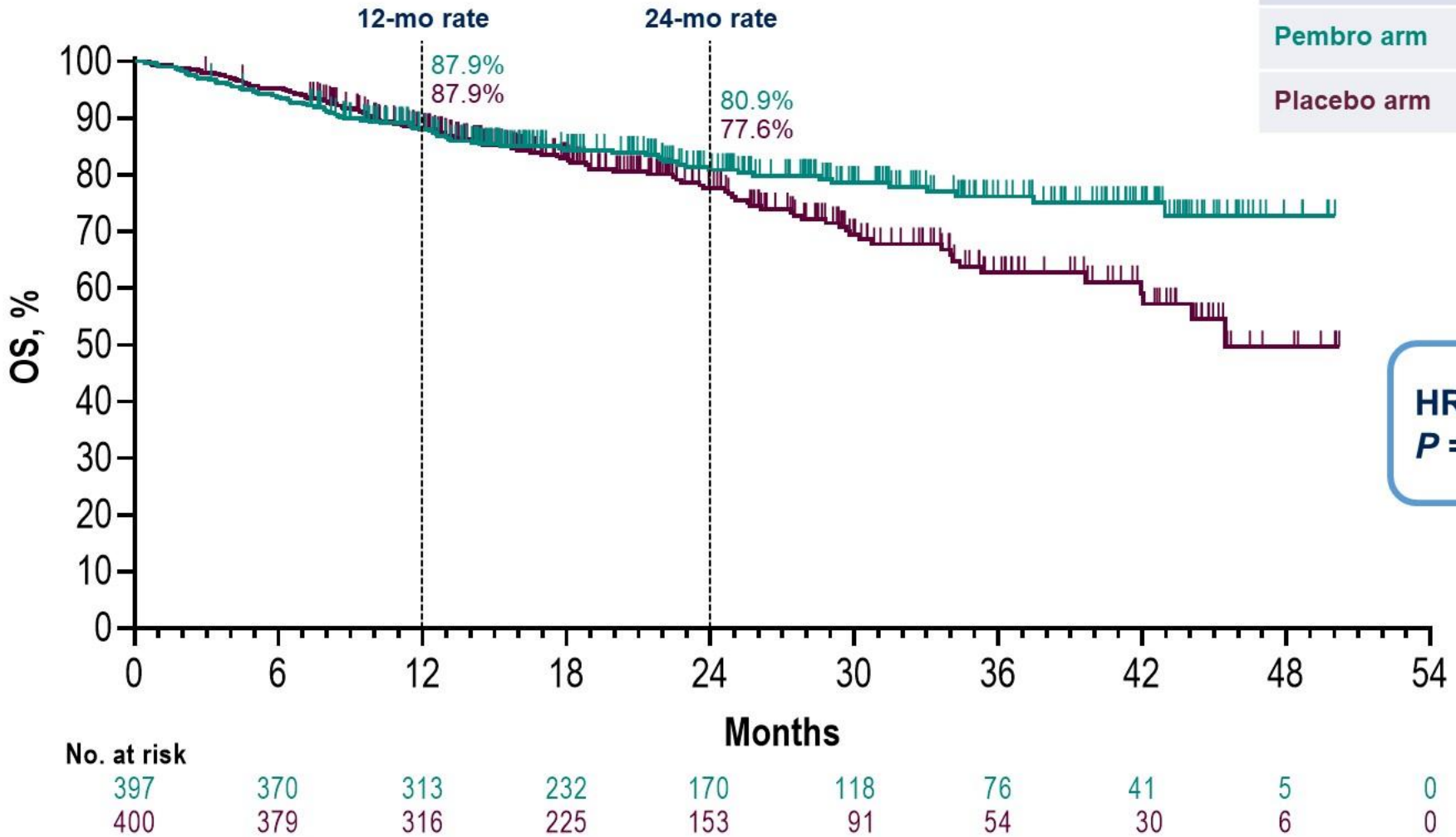




[a] Defined as ≤10% viable tumor cells in resected primary tumor and lymph nodes. [b] Defined as absence of residual invasive cancer in resected primary tumor and lymph nodes (ypT0/Tis ypN0). Data cutoff date for IA1: July 29, 2022.

Overall Survival

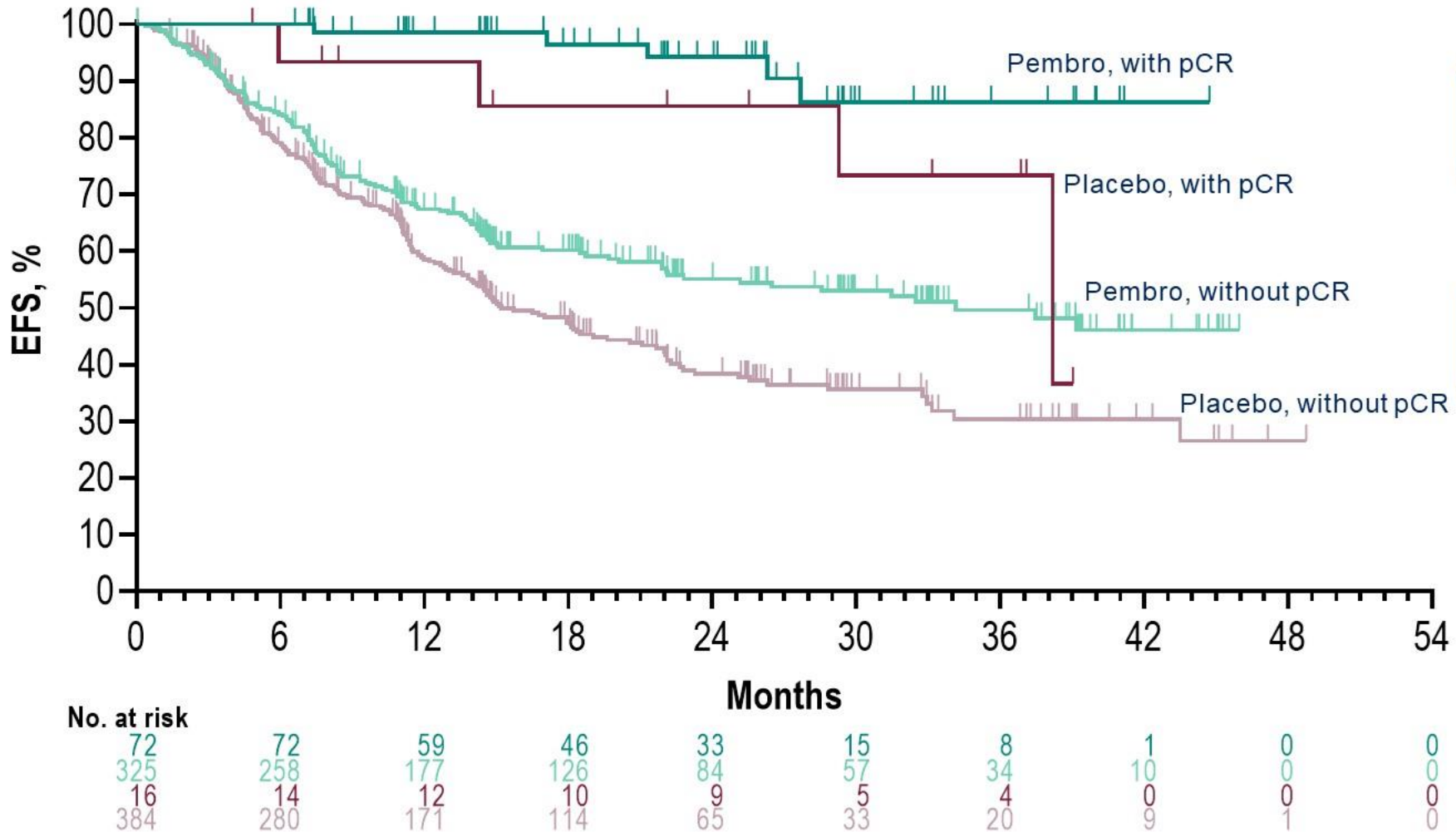
	Pts w/ Event	Median (95% CI), mo
Pembro arm	19.1%	NR (NR-NR)
Placebo arm	25.3%	45.5 (42.0-NR)



HR 0.73 (95% CI, 0.54-0.99)
***P* = 0.02124[a]**

OS defined as time from randomization to death from any cause. [a] Significance boundary not met at IA1; OS will continue to be tested according to the analysis plan. Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).

Exploratory Analysis of EFS by pCR Status

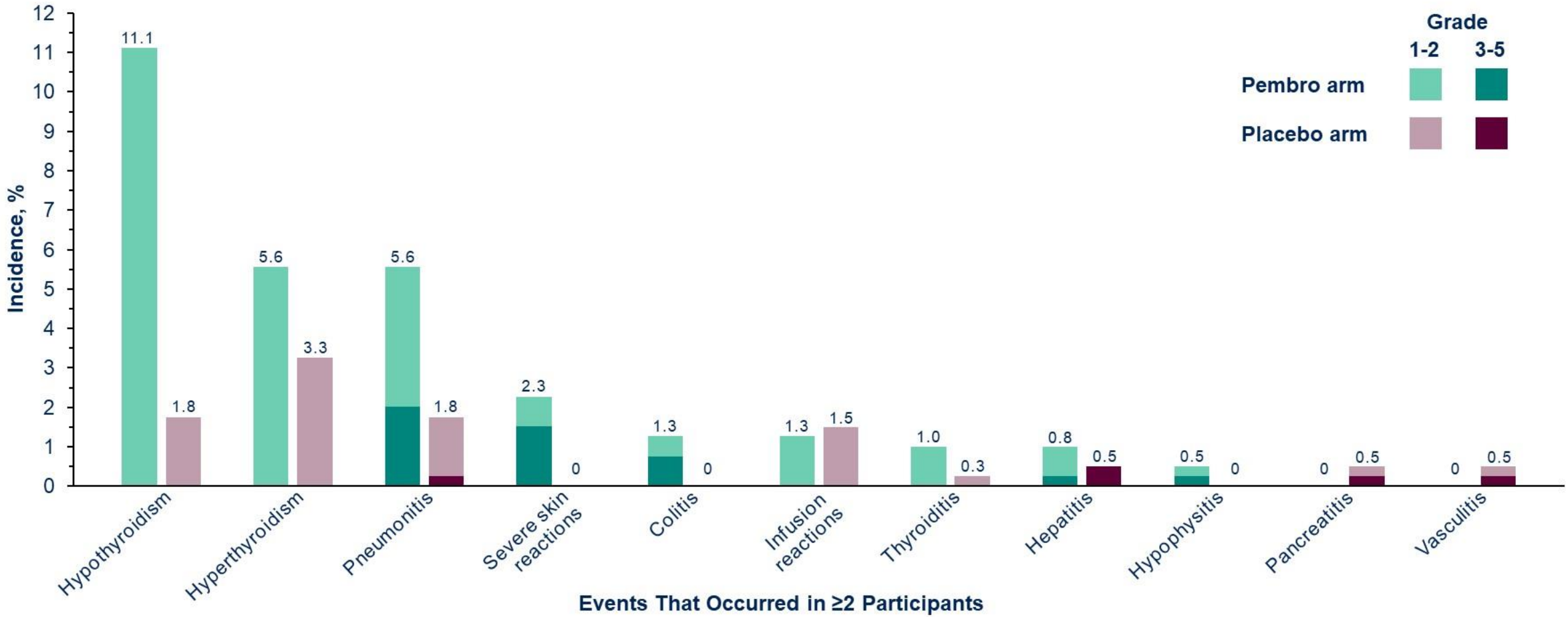


With pCR
HR 0.33 (95% CI, 0.09-1.22)

Without pCR
HR 0.69 (95% CI, 0.55-0.85)

pCR defined as absence of residual invasive cancer in resected primary tumor and lymph nodes (ypT0/Tis ypN0). EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause. Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).

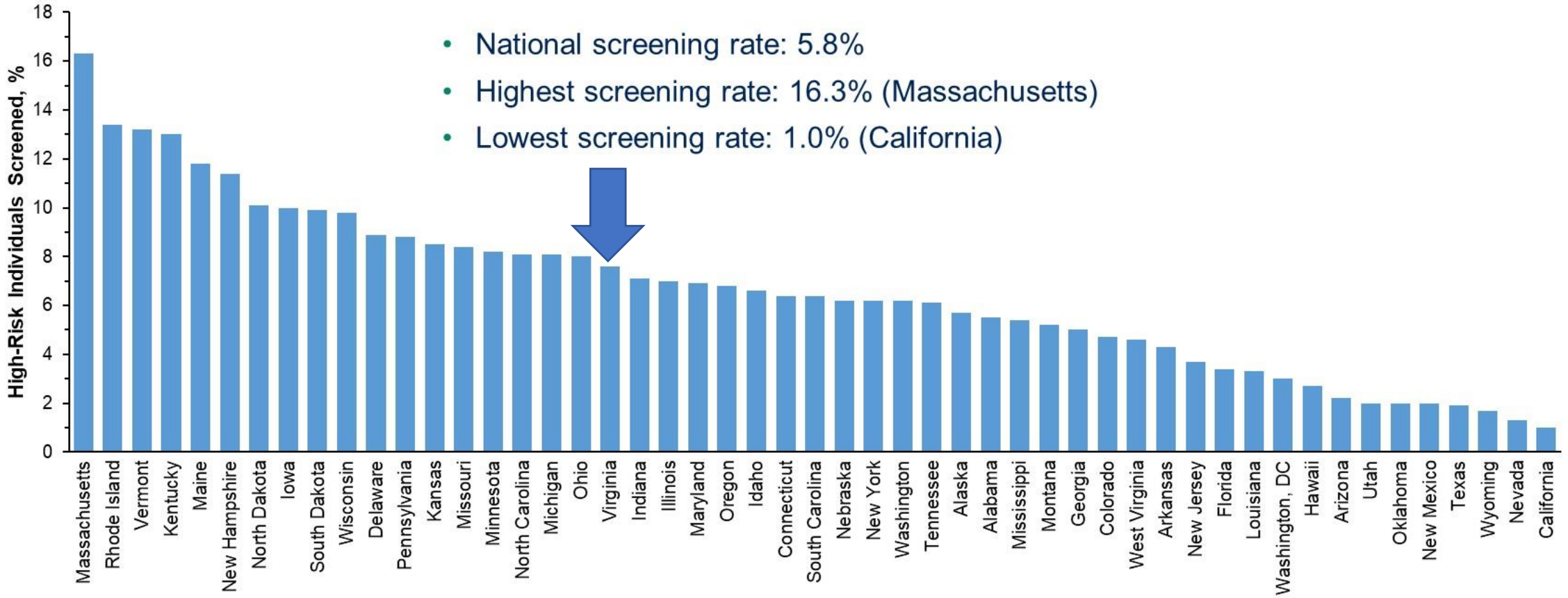
Immune-Mediated Adverse Events and Infusion Reactions Across Treatment Phases



Immune-mediated AEs and infusion reactions were based on a list of preferred terms prepared by the sponsor and considered regardless of attribution to study treatment by the investigator. Data cutoff date for IA1: July 29, 2022.

Adherence to USPSTF Lung Cancer Screening Guidelines for High-Risk Individuals by State[1]

- National screening rate: 5.8%
- Highest screening rate: 16.3% (Massachusetts)
- Lowest screening rate: 1.0% (California)



USPTF, United States Preventive Services Task Force. [1]American Lung Association™. State of Lung Cancer 2022. Available at https://www.lung.org/research/state-of-lung-cancer.

Summary

- Adding pembrolizumab to chemotherapy led to an improvement of overall survival which was superior to that observed with the addition of chemotherapy
- Almost 20% had a complete pathological response
- This trial, among others, does propose a new standard of care that address the issue of 3 cycles per op vs one year of adjuvant ICI
- For patient with stage II and III (about 70%) a DFS at 3 years around 60% represents a major improvement over the last 20 years as we added chemotherapy and now immunotherapy

Questions

- What is the necessary exposure to ICI?
- Combining this data with Checkmate 816[1] approximately 20% of patients have a complete pathological response. Do these patients need surgery ?
- How can we identify these patients prior to surgery ?
- Can one extrapolate these results to carboplatin treated patients?

1. N Engl J Med 2022; 386:1973-1985

Overall Conclusions

- The combination of these two trials show how much we (pharma, investigators and patients participating in trials) have improved the outcome of curable lung cancer
- Based on the DFS and OS seeing in these studies looks like every patient treated to surgery has a higher chance of prolonged DFS (cure?) rather than a recurrence
- Combining screening with better therapies the teaching before 2000 that “one third of lung cancer patients can have surgery and, of those, one third is cured” is now obsolete

CASE PRESENTATION

Richard D. Hall, MD, MS
University of Virginia
Associate Professor of Medicine
Hematology/Oncology Fellowship Program Director

American Cancer Society | Project ECHO

UVAHealth

CASE PRESENTATION:
GENOMIC CONUNDRUM IN THE PERIOPERATIVE SETTING

RICHARD HALL MD, MS

ASSOCIATE PROFESSOR OF MEDICINE, DIVISION OF HEMATOLOGY/ONCOLOGY

UNIVERSITY OF VIRGINIA

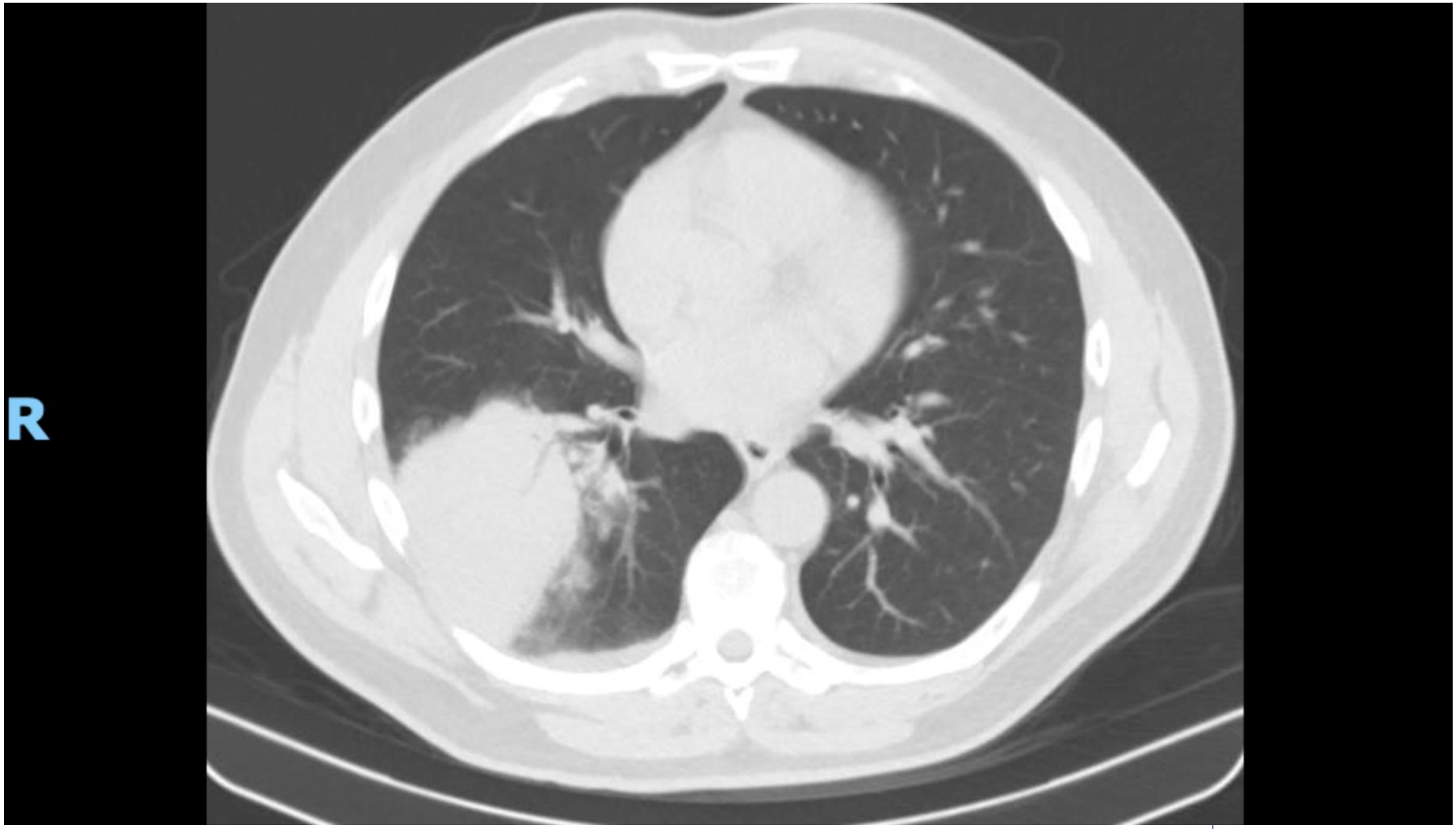
ACS PROJECT ECHO

JUNE 12, 2023

University of Virginia Health System

CASE OVERVIEW

- 59 yo patient with history of essential HTN and glucose intolerance
- Never smoker
- Presented to local ED in early 2023 with dyspnea, scant hemoptysis
- CT imaging revealed a RLL infiltrate, concerning for PNA
- Treated with abx, repeat imaging 6 weeks later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CASE OVERVIEW

- Referred to surgical oncology at another institution
- Underwent CT guided biopsy of the RLL notable for lung adenocarcinoma
- Referred to UVA surgical oncology and medical oncology
- EBUS/Bronchoscopy revealed a positive level VII LN for adenocarcinoma
- MRI brain negative for metastatic disease
- PET/CT with FDG uptake only in the RLL mass
- Clinically staged as cT4N2, stage IIIB

CASE OVERVIEW

- Given never smoker status, underwent ctDNA to determine if EGFR positive.

Guardant 360 ctDNA 3/21/23:

DETECTED ALTERATION(S) / BIOMARKER(S)	% CFDNA OR AMPLIFICATION	ASSOCIATED FDA-APPROVED THERAPIES	CLINICAL TRIAL AVAILABILITY
PDGFRA G898S	0.1%	None (VUS)§	No (VUS)§

- Patient otherwise fit, and surgical colleague believes he is a good candidate for resection.

CASE OVERVIEW

- Given no known EGFR mutation on ctDNA, he was evaluated for and opted to screen into a clinical trial for stage III disease
  - Study of neoadjuvant CTX + IO, surgery, then IO for up to 1 year post op for only stage III disease
- Tissue genomics were requested but not yet available
- Patient with significant, symptomatic cough
- Enrolled in study
- Received 1st cycle of CTX (cis / pem) + IO therapy
- Then…

CASE OVERVIEW

- **Tissue based genomics 10 days later revealed:**

Variants with Evidence of Clinical Significance in NSCLC

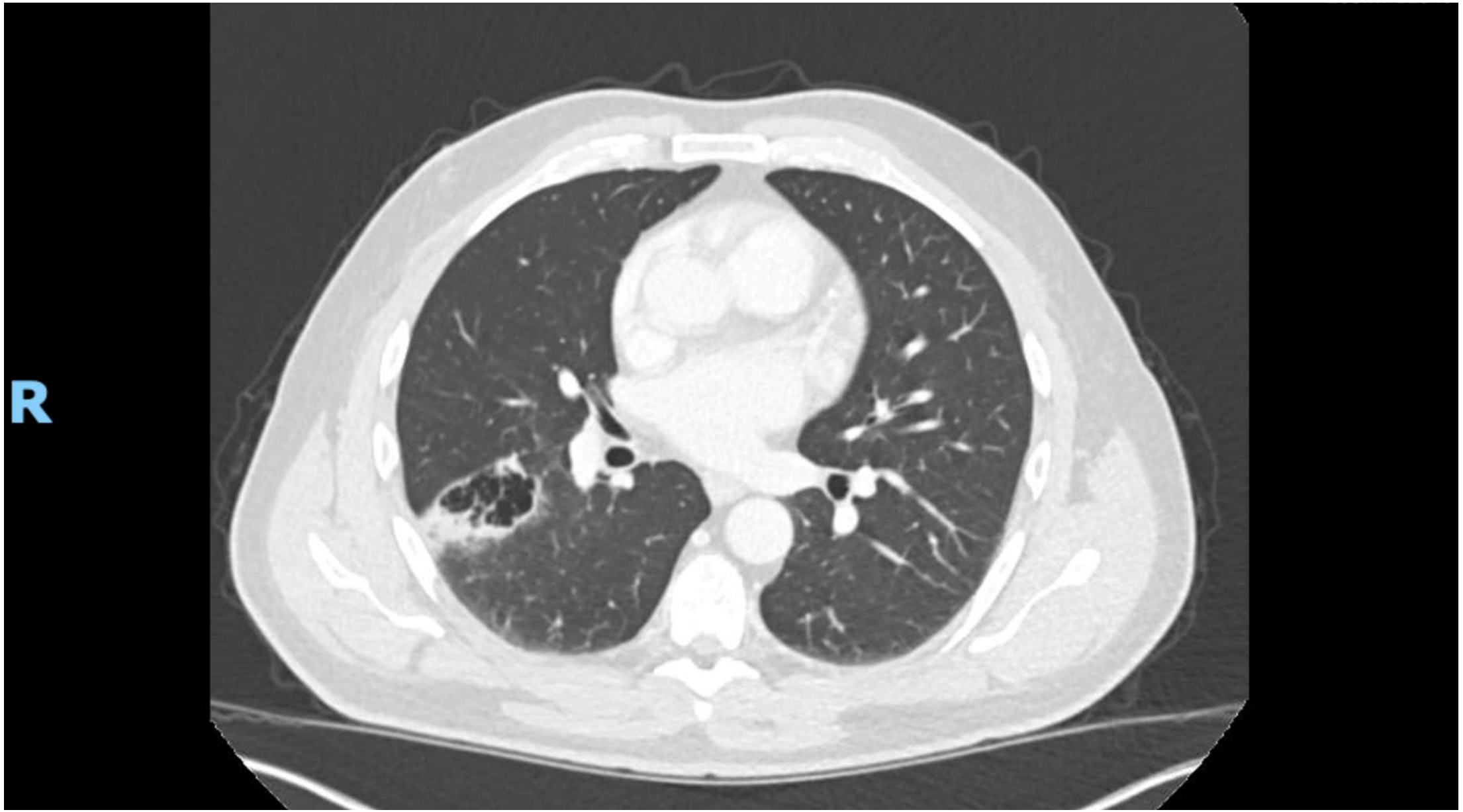
Gene	Alteration	Consequence	VAF (%)
EGFR	L858R	Missense	49.1

Variants with Potential Clinical Significance in NSCLC

Gene	Alteration	Consequence	VAF (%)
DDR1	R892W	Missense	17.8
GRIN2A	P985H	Missense	18.3
NFKBIA	R314H	Missense	14.9
PDPK1	L20del	In-frame Deletion	40.5
RBM10	E686*	Nonsense	63.1
RUNX1T1	E40*	Nonsense	28
TP53	n/a	Splice Site Acceptor	34.8

CASE OVERVIEW

- Given new EGFR L858R mutation result via tissue, study therapy was discontinued
- Continued on CTX neoadjuvantly (cisplatin and pemetrexed)
- Imaging after 2 cycles of therapy showed…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CASE DISCUSSION

- How often do you see discordance between blood and tissue based testing?
- How do we incorporate blood and tissue genomics in the peri-operative setting?
- What would the optimal approach be for this patient if we had all the genomics initially?

  - Neoadjuvant CTX then surgery followed by osimertinib?
  - Surgical resection then adjuvant CTX then osimertinib?
  - Concurrent CTX + RT, no surgery, durvalumab?

Wrap-Up & Next Steps

Reminder: Post-ECHO Series Assessment Survey

We need your help to continue improving this ECHO series and appreciate your feedback.

Please check your email inbox and spam folders for an email from redcap@vumc.org with a Post-ECHO Survey link.

You will receive a Six-Month Follow-Up Survey in late November/early December.

Materials and Resources will be made available via the ACS ECHO Website

Questions: Contact Korey.Hofmann@cancer.org or Annika.Dean@cancer.org

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THANK YOU!

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NATIONAL LUNG CANCER ROUNDTABLE