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Cancer Center

Updates on management of Lung Cancer. Era of Hope.

FLASCO 12th Annual Puerto Rico Oncology Symposium

02/04/23

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- Consulting/Advisory Boards:

  AstraZeneca, Janssen, Alpha-2, Turning Point, Cardinal Health

Outline

- Epidemiology of lung cancer
- Updates on management of early-stage NSCLC
- Updates on management of stage IV NSCLC

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- Epidemiology of lung cancer
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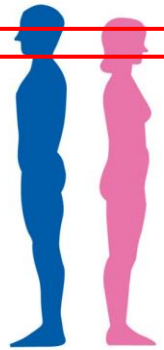
Epidemiology

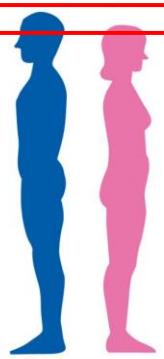
Estimated New Cases

Males			Females		
Prostate	288,300	29%	Breast	297,790	31%
Lung & bronchus	117,550	12%	Lung & bronchus	120,790	13%
Colon & rectum	81,860	8%	Colon & rectum	71,160	8%
Urinary bladder	62,420	6%	Uterine corpus	66,200	7%
Melanoma of the skin	58,120	6%	Melanoma of the skin	39,490	4%
Kidney & renal pelvis	52,360	5%	Non-Hodgkin lymphoma	35,670	4%
Non-Hodgkin lymphoma	44,880	4%	Thyroid	31,180	3%
Oral cavity & pharynx	39,290	4%	Pancreas	30,920	3%
Leukemia	35,670	4%	Kidney & renal pelvis	29,440	3%
Pancreas	33,130	3%	Leukemia	23,940	3%
All Sites	**1,010,310**	**100%**	**All Sites**	**948,000**	**100%**



Estimated Deaths

Males			Females		
Lung & bronchus	67,160	21%	Lung & bronchus	59,910	21%
Prostate	34,700	11%	Breast	43,170	15%
Colon & rectum	28,470	9%	Colon & rectum	24,080	8%
Pancreas	26,620	8%	Pancreas	23,930	8%
Liver & intrahepatic bile duct	19,000	6%	Ovary	13,270	5%
Leukemia	13,900	4%	Uterine corpus	13,030	5%
Esophagus	12,920	4%	Liver & intrahepatic bile duct	10,380	4%
Urinary bladder	12,160	4%	Leukemia	9,810	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,400	3%
Brain & other nervous system	11,020	3%	Brain & other nervous system	7,970	3%
All Sites	**322,080**	**100%**	**All Sites**	**287,740**	**100%**



Life time risk of lung cancer : 1 in 15

In the US (2023):

Incidence:

238 K/year

Deaths:

127 K/year

Worldwide (2020)

Incidence:

2.2 million/year

Deaths:

1.8 million/year

***World Cancer Research Fund International data*

Cancer Statistics 2023. Siegel R, et al CA: A Cancer Journal for Clinicians 2023

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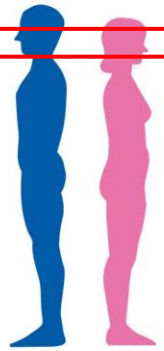

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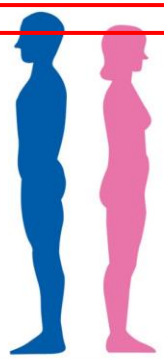

In Puerto Rico (2015-2019):

Incidence rate per 100,000:
F: 337
M: 411

Mortality rate per 100,000:
F: 86
M: 132

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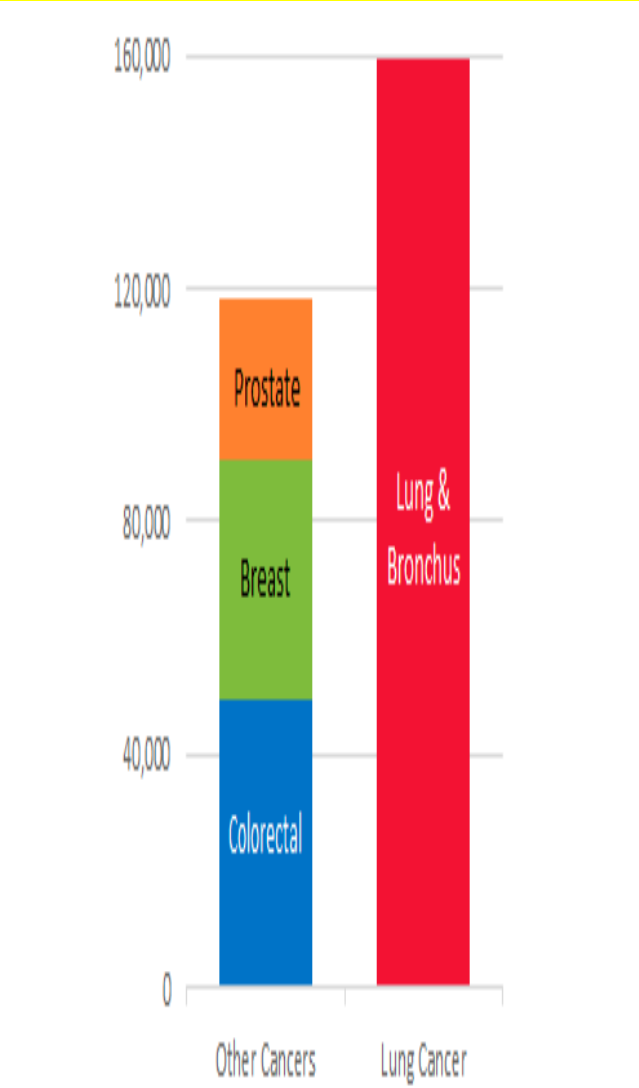
Cancer Statistics 2023. Siegel R, et al CA: A Cancer Journal for Clinicians 2023

Epidemiology



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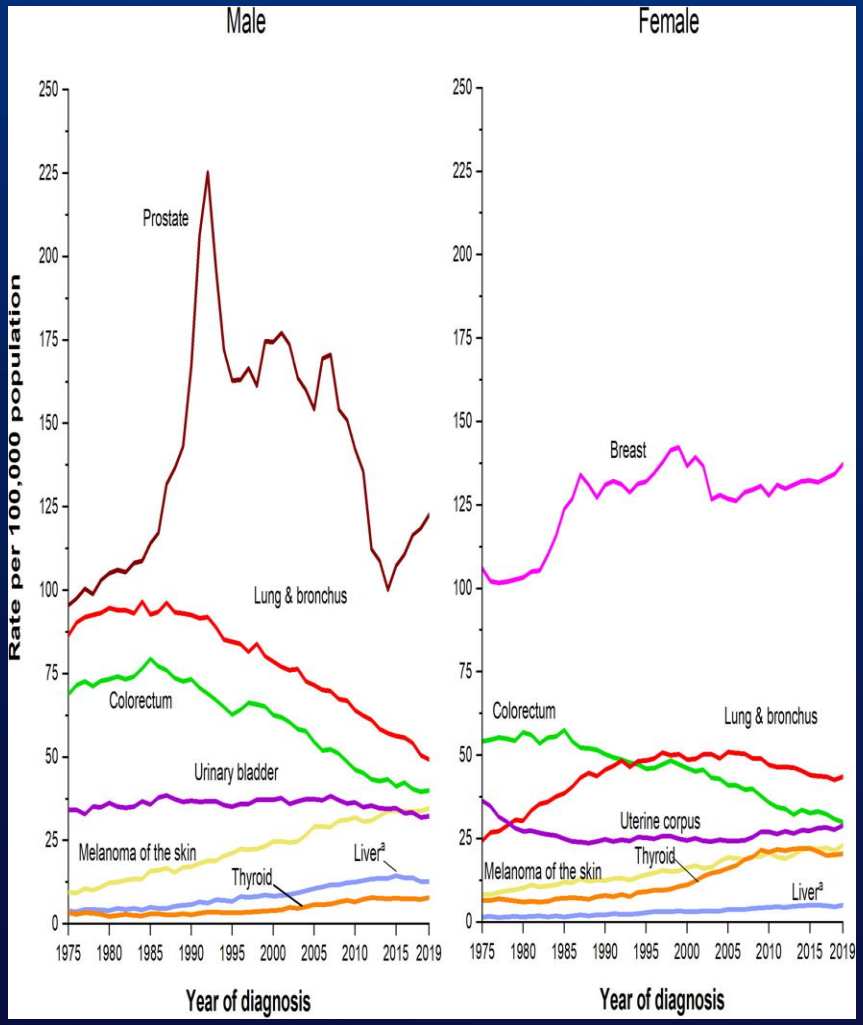
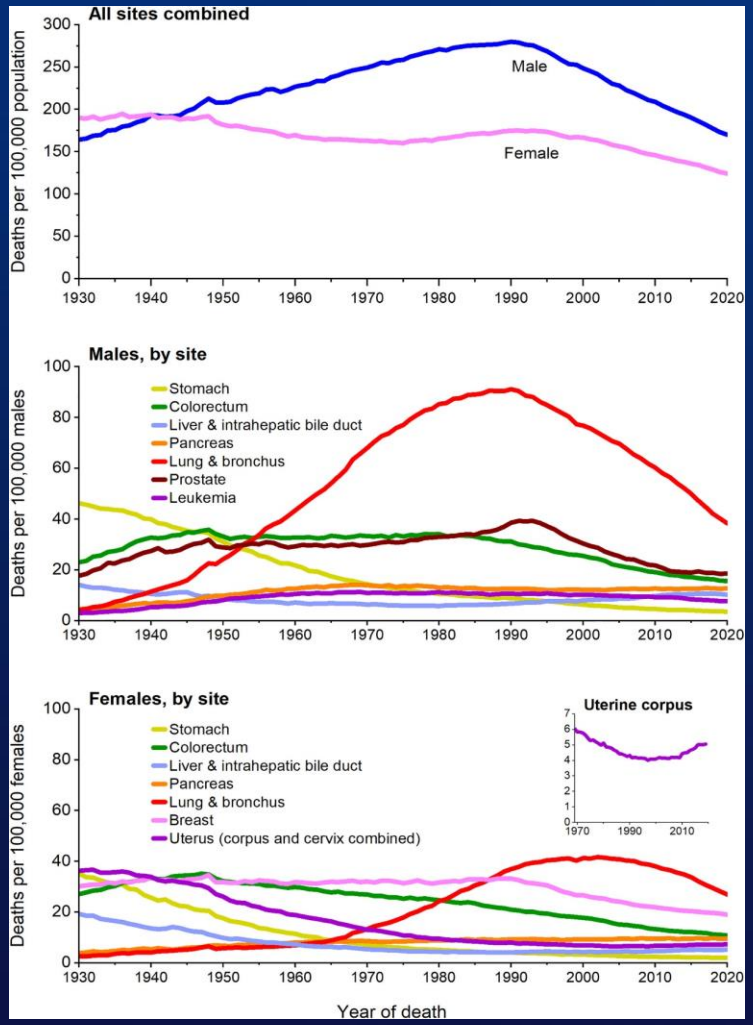
Epidemiology





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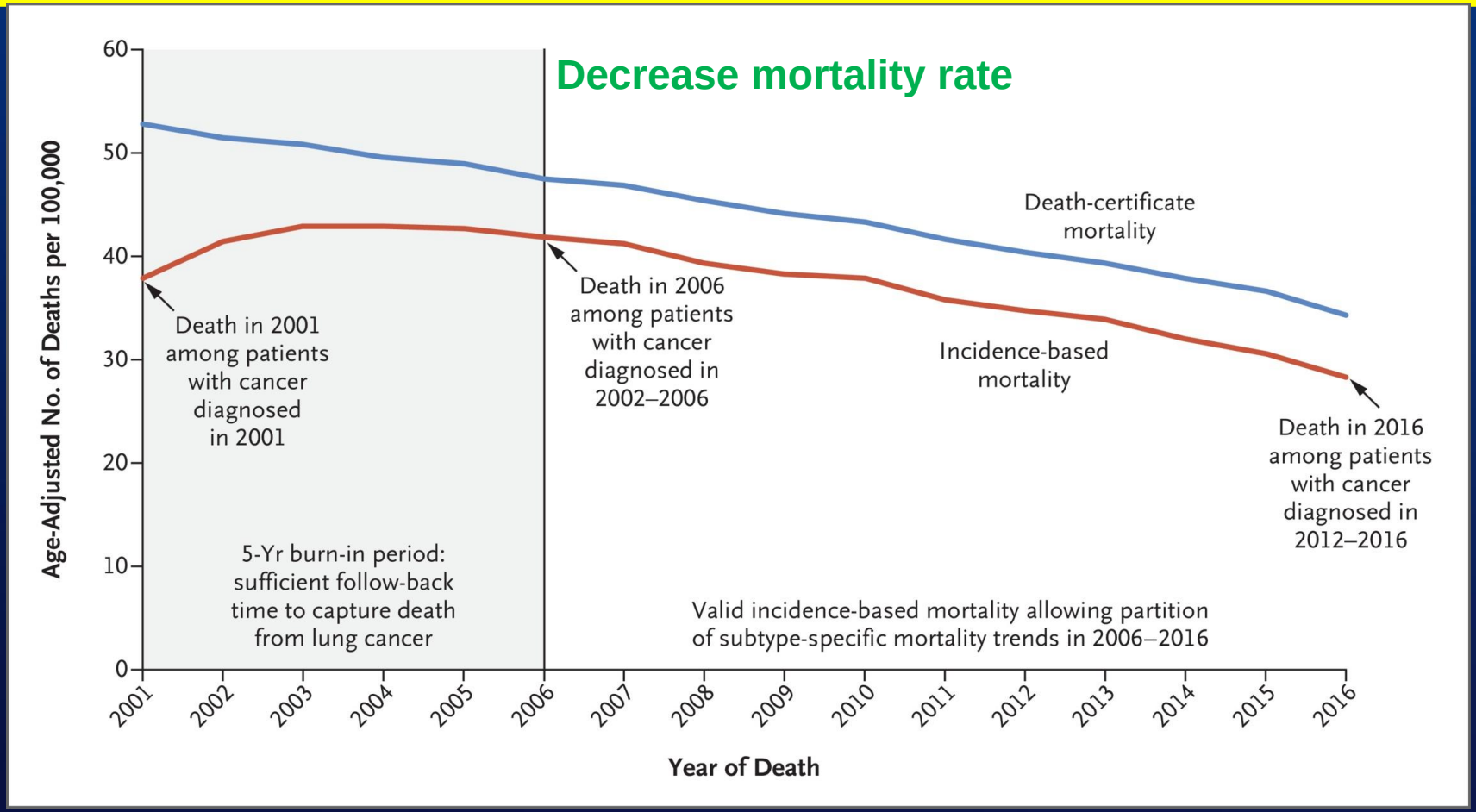
Cancer Statistics 2023. Siegel R, et al CA: A Cancer Journal for Clinicians 2023

WHY KEEPING THE HOPE



SEER database study. Howlader N et al. N Engl J Med Aug 2020

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Lung Cancer Screening Saves Lives

New Lung Cancer Screening Guidelines

50–80 Years Old

Have a 20 pack-year history, such as one pack per day for 20 years; or two packs per day for 10 years., etc.

Currently smoke or quit smoking in the last 15 years.

American Lung Association.

Lung Cancer Screening Saves Lives

- Lung Cancer screening results in a favorable shift to:
  - Increase in stage I
  - Decline in stage IV
  - NO increase in overall incidence of lung cancer

  Vacchani et al. JTO Sep 2022

- Lung Cancer screening is associated with lower risk of brain mets

  Su et al, JTI June 2021

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- Epidemiology of lung cancer
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Treatment options for early-stage NSCLC

Stage IA

-Surgery

-If not surgical candidate: XRT (conventional or SBRT)

-No adjuvant therapy

Stage IB-IIIA

-Surgery: Especially for IB-IIIA (non-N2 disease)

Post surgery:

Adjuvant chemo for stage II and above

Adjuvant IO (Atezolizumab *IMPower 010*, or Pembrolizumab *Keynote091*)

Adjuvant Osimertinib if EGFR (exon 19 or 21)+ *ADAURA*

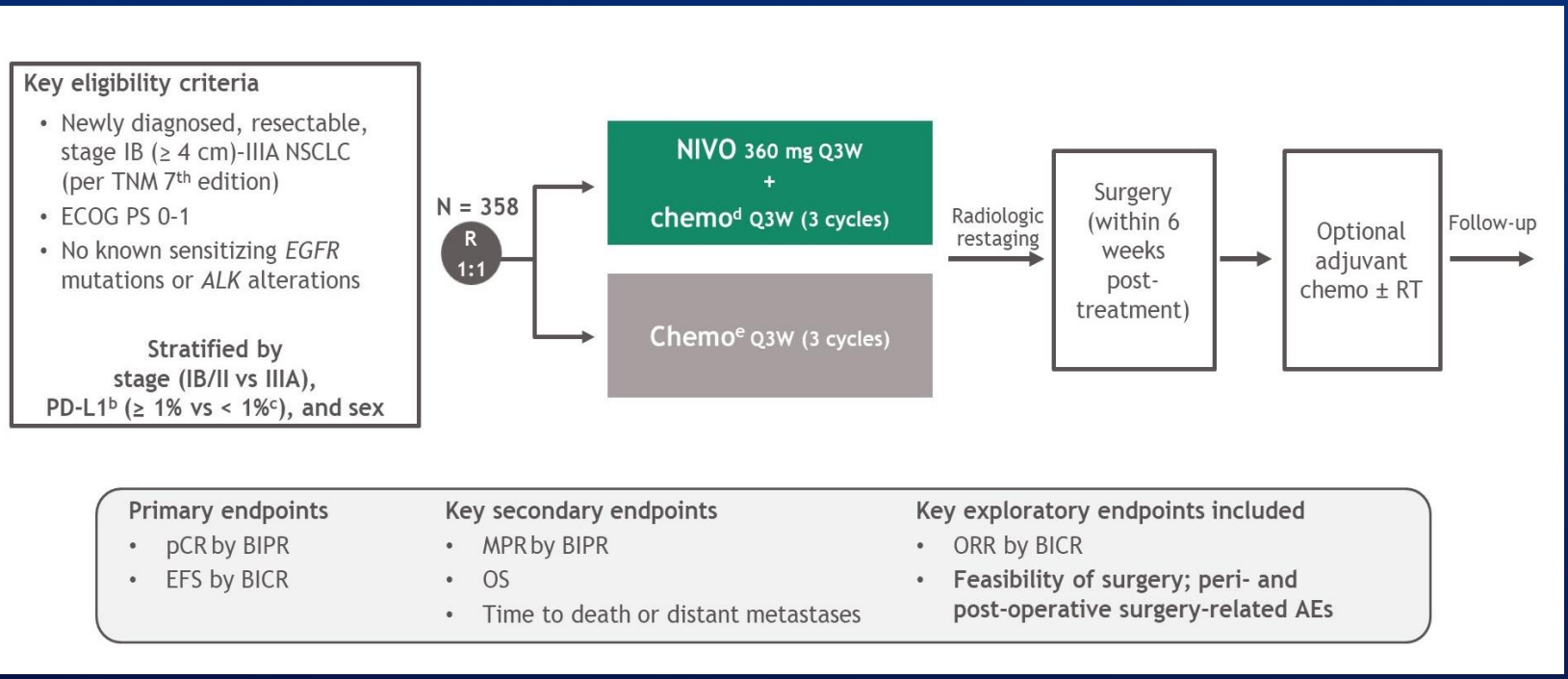
-Neoadjuvant chemoimmuno (chemo + nivo) followed by surgery *(checkmate 816)*

Unresectable Stage IIIA or IIIB/C

Definitive concurrent chemoradiation followed by consolidation durvalumab *(Pacific)*

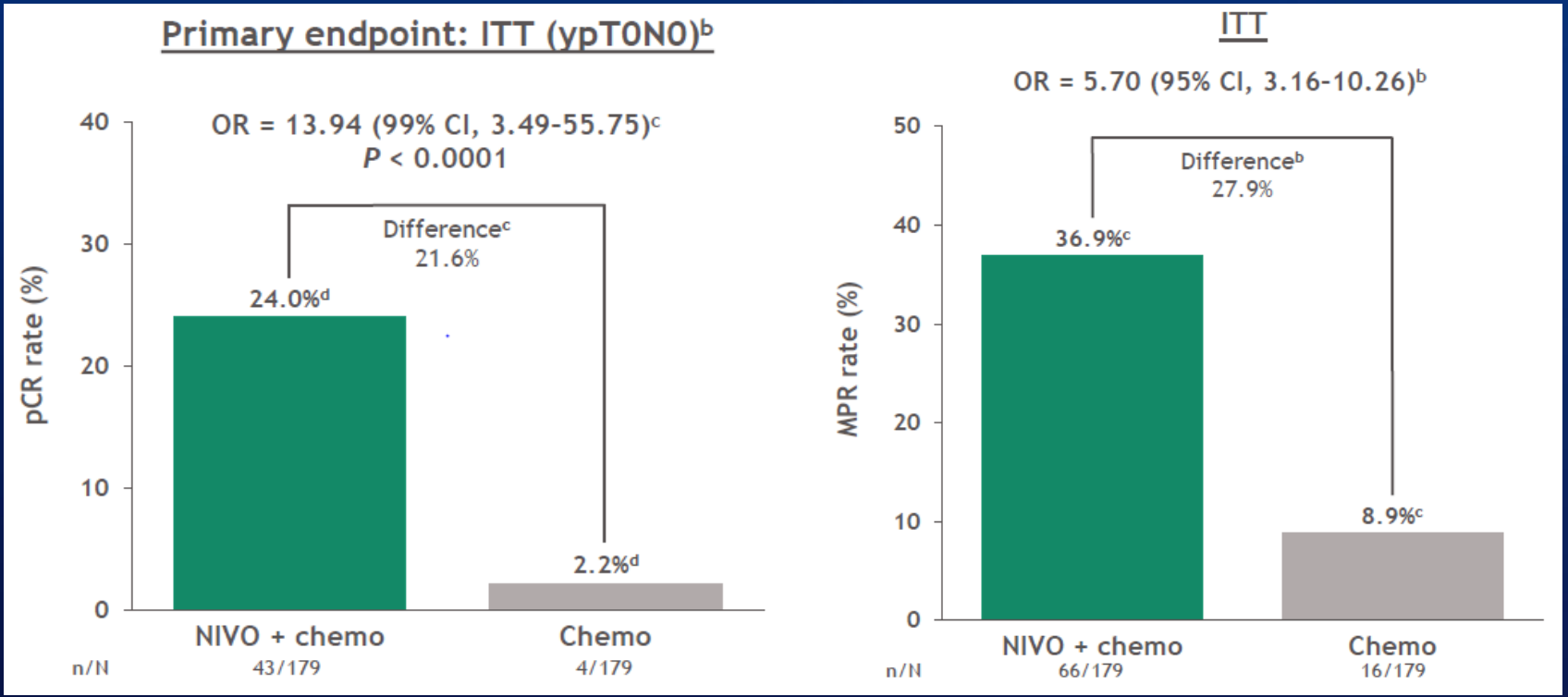
Neoadjuvant Therapy

CHECKMATE-816



Forde AACR 2021; Forde NEJM 2022

CHECKMATE-816: Pathological response



Forde AACR 2021; Forde NEJM 2022

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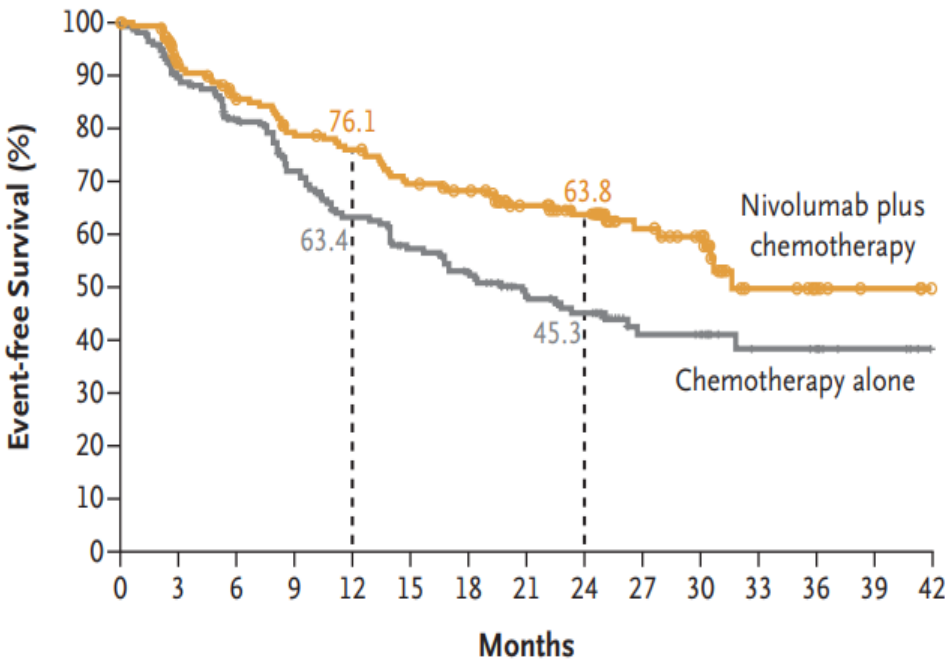
CHECKMATE-816: Event-free survival



	No. of Patients	Median Event-free Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	31.6 (30.2–NR)
Chemotherapy Alone	179	20.8 (14.0–26.7)

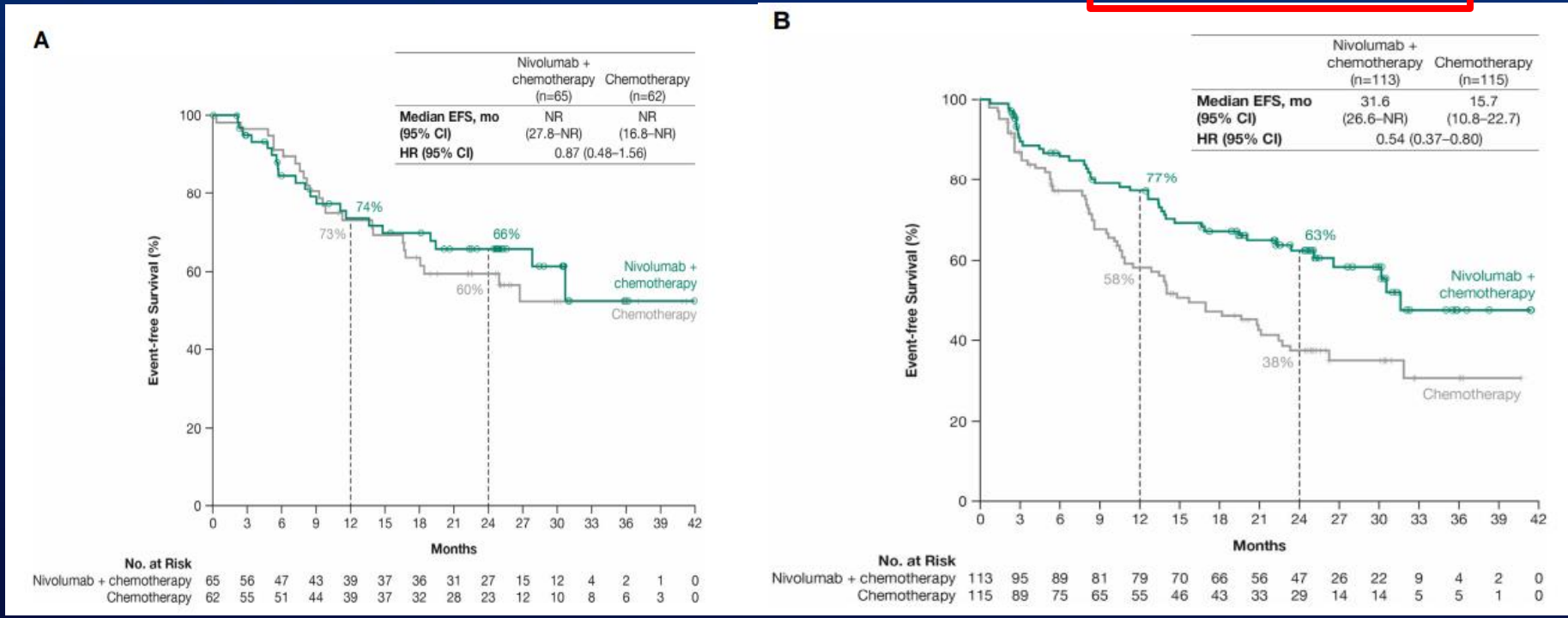
Hazard ratio for disease progression, disease recurrence, or death, 0.63 (97.38% CI, 0.43–0.91)
P=0.005

Forde AACR 2021; Forde NEJM 2022

CHECKMATE-816: EFS by stage

Stage IB-II

Stage IIIA (63%)



Forde AACR 2021; Forde NEJM 2022

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CHECKMATE-816: Subgroup analysis

	pCR[a] rate, %		Unweighted pCR difference, % (95% CI)	Unweighted pCR difference, %
	NIVO + chemo (n = 179)	Chemo (n = 179)		
Overall (N = 358)	24	2		22
< 65 years (n = 176)	27	0		27
≥ 65 years (n = 182)	21	4		17
Male (n = 255)	23	2		20
Female (n = 103)	28	2		26
North America (n = 91)	22	2		20
Europe (n = 66)	24	0		24
Asia (n = 177)	28	3		25
Stage IB-II (n = 128)	26	5		21
Stage IIIA (n = 228)	23	1		22
Squamous (n = 182)	25	4		21
Non-squamous (n = 176)	23	0		23
Current/former smoker (n = 318)	26	2		23
Never smoker (n = 39)	10	0		10
PD-L1 < 1% (n = 155)	17	3		14
PD-L1 ≥ 1% (n = 178)	33	2		30
PD-L1 1-49% (n = 98)	24	0		24
PD-L1 ≥ 50% (n = 80)	45	5		40
TMB < 12.3 mut/Mb (n = 102)	22	2		21
TMB ≥ 12.3 mut/Mb (n = 76)	31	3		28
Cisplatin (n = 258)	22	2		20
Carboplatin (n = 72)	31	0		31

[a]Per BIPR in ITT.

Forde AACR 2021; Forde NEJM 2022

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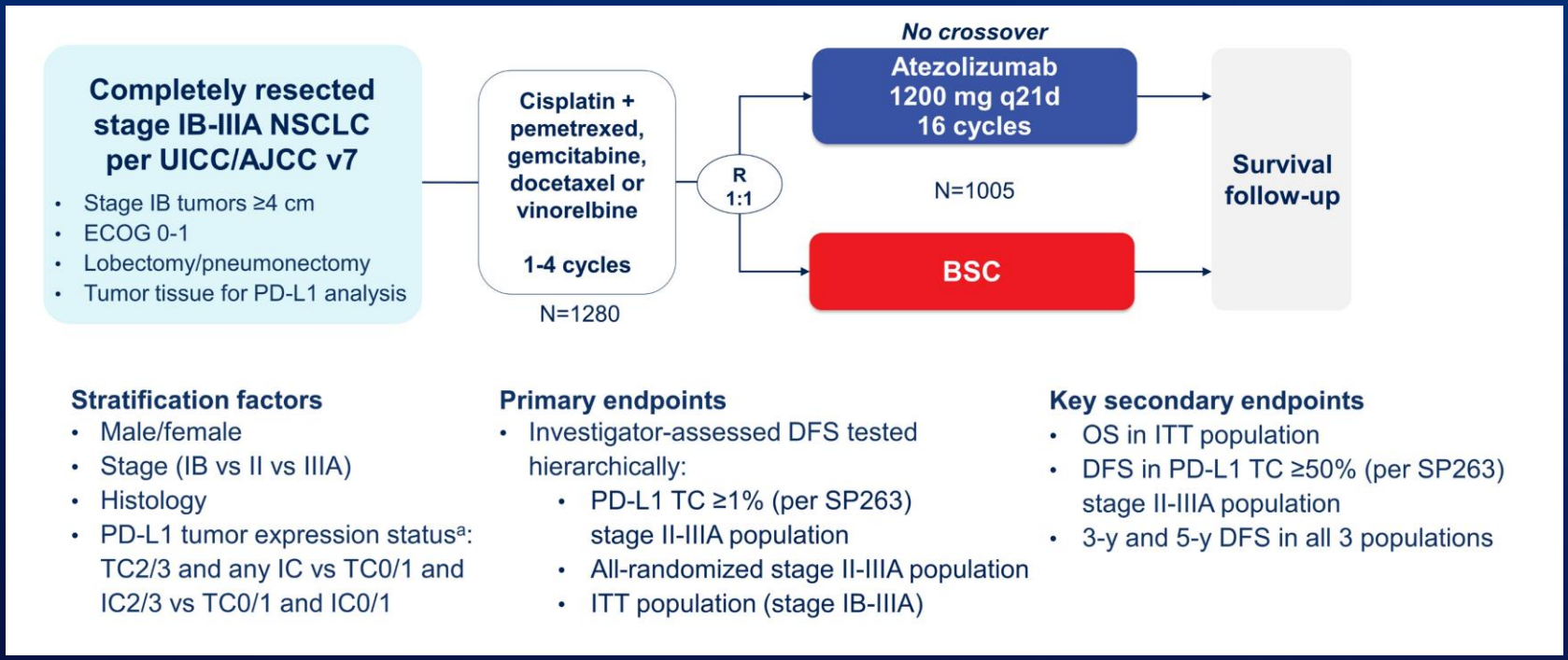
Adjuvant Therapy

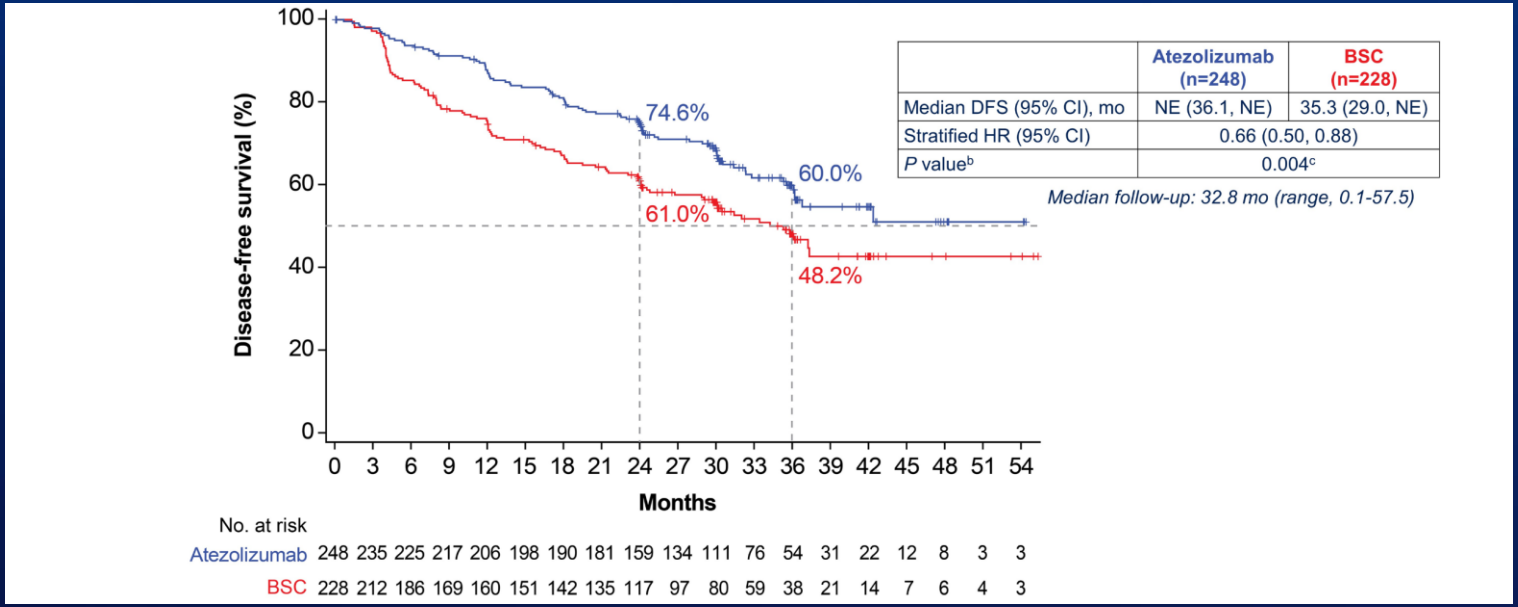
Impower-010: Adjuvant Atezolizumab

Phase III Randomized Trial



Wakelee, ASCO Meeting 2021; Felip, Lancet 2021

Impower-010 Disease-free survival



	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	

Median follow-up: 32.8 mo (range, 0.1-57.5)

Wakelee, ASCO Meeting 2021; Felip, Lancet 2021

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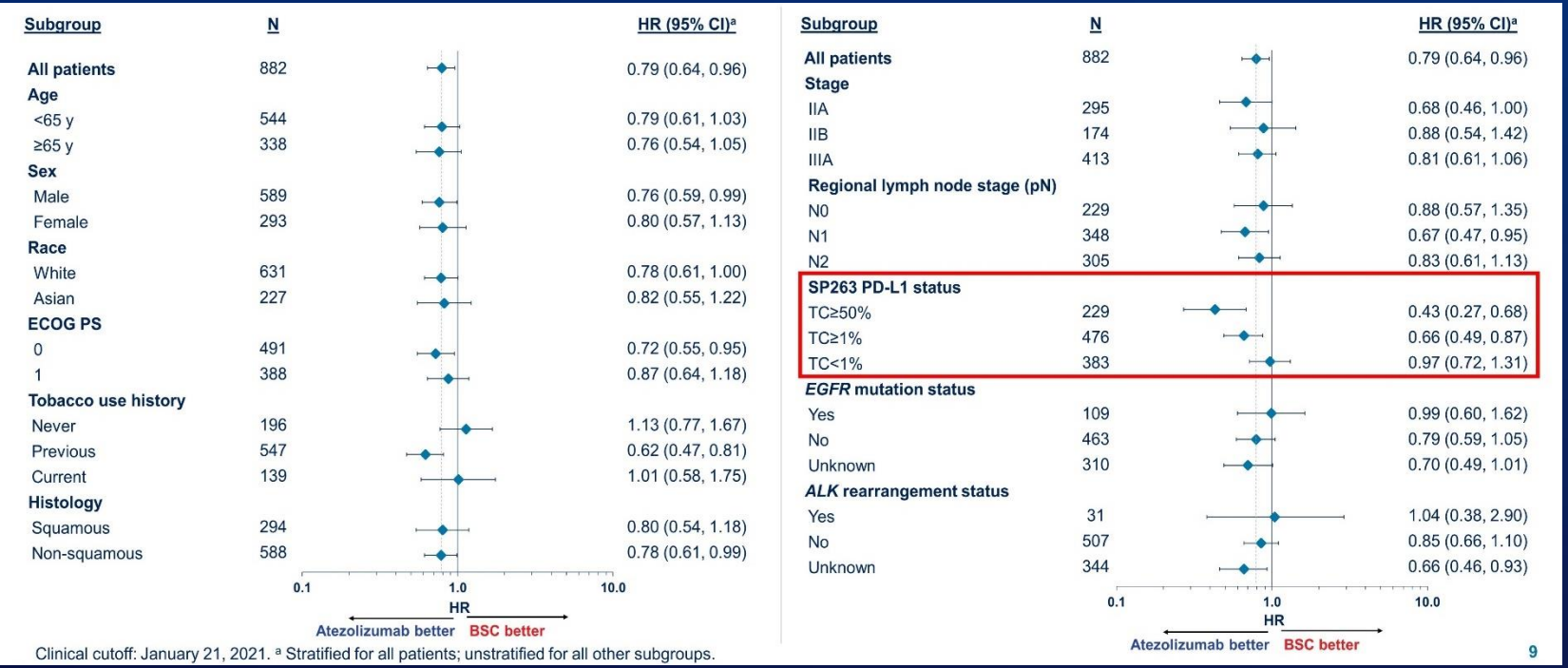
Impower-010 Key subgroups



Wakelee, ASCO Meeting 2021; Felip, Lancet 2021

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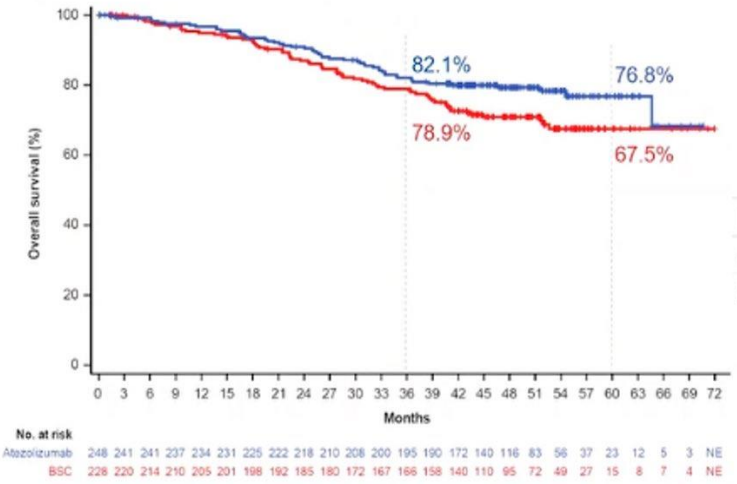
Impower-010 OS Data from WCLC 2022

Results of OS IA: PD-L1 TC ≥1%[a] (stage II-IIIA)

(data cutoff: 18 Apr '22, median follow-up: 46 months)

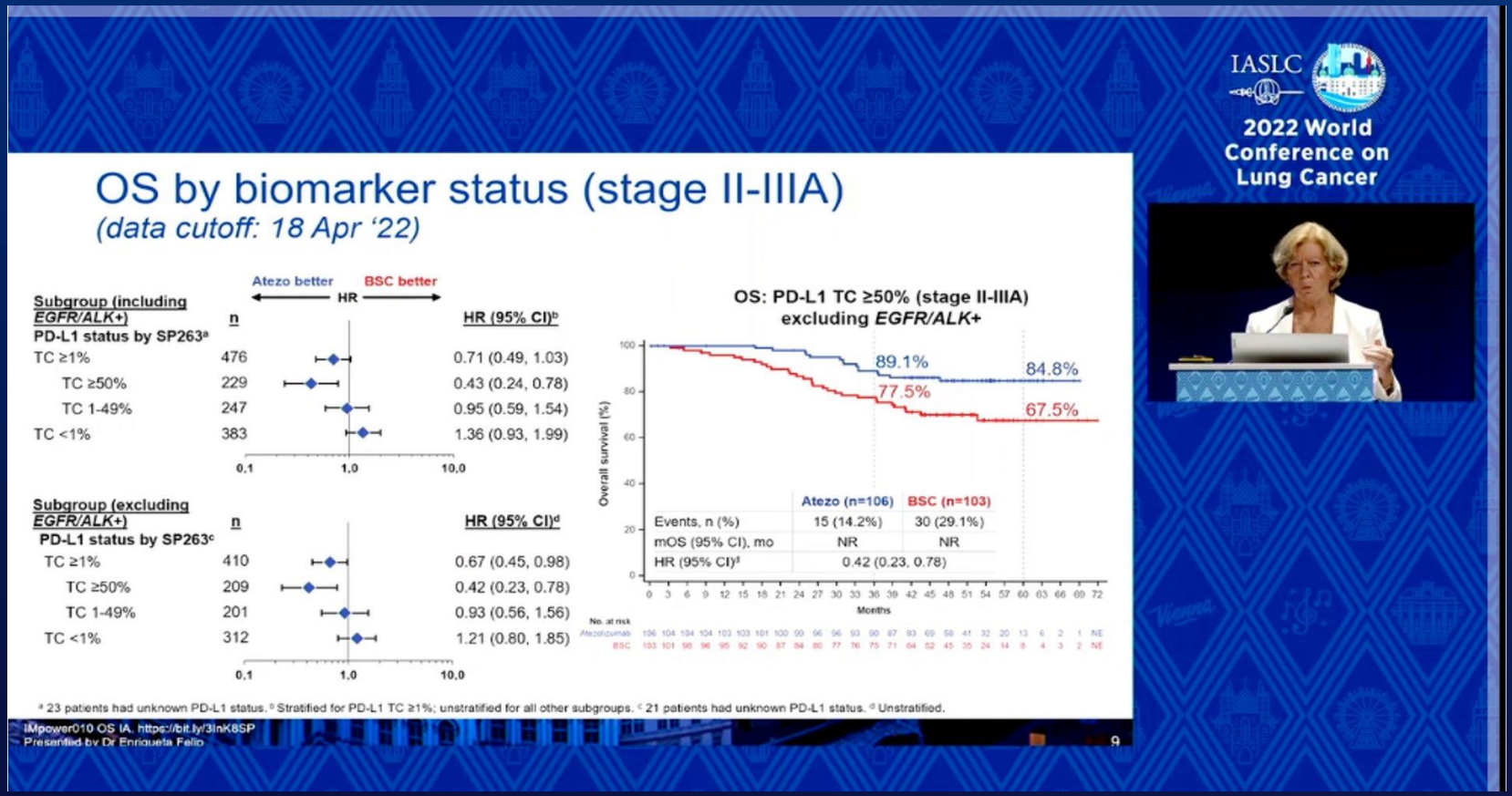


	Atezo (n=248)	BSC (n=228)
Events, n (%)	52 (21.0%)	64 (28.1%)
mOS (95% CI), mo	NR	NR
HR (95% CI)[b]	0.71 (0.49, 1.03)	

mOS, median overall survival; NR, not reached. [a]By SP263 assay. [b]Stratified.

IASLC 2022 World Conference on Lung Cancer

Impower-010 OS Data from WCLC 2022



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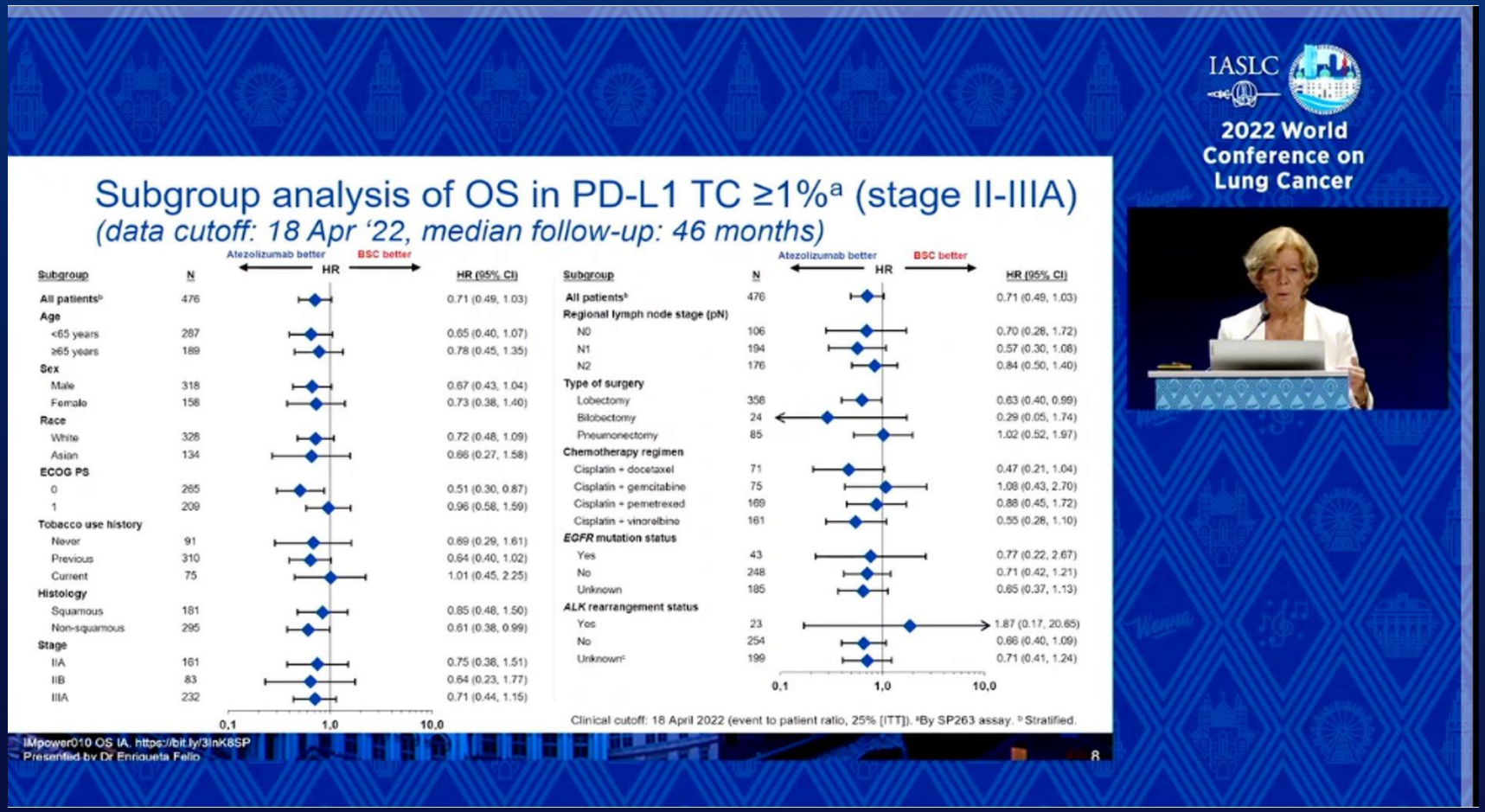
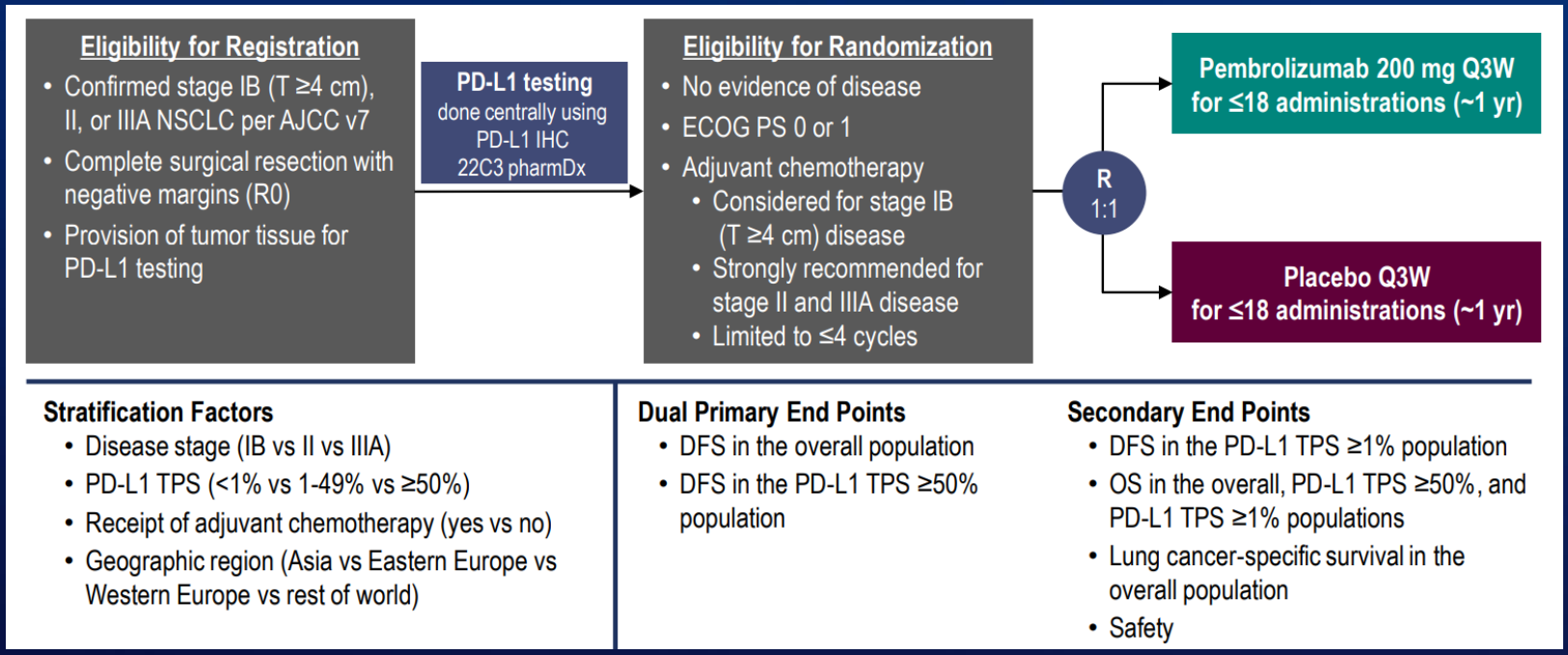
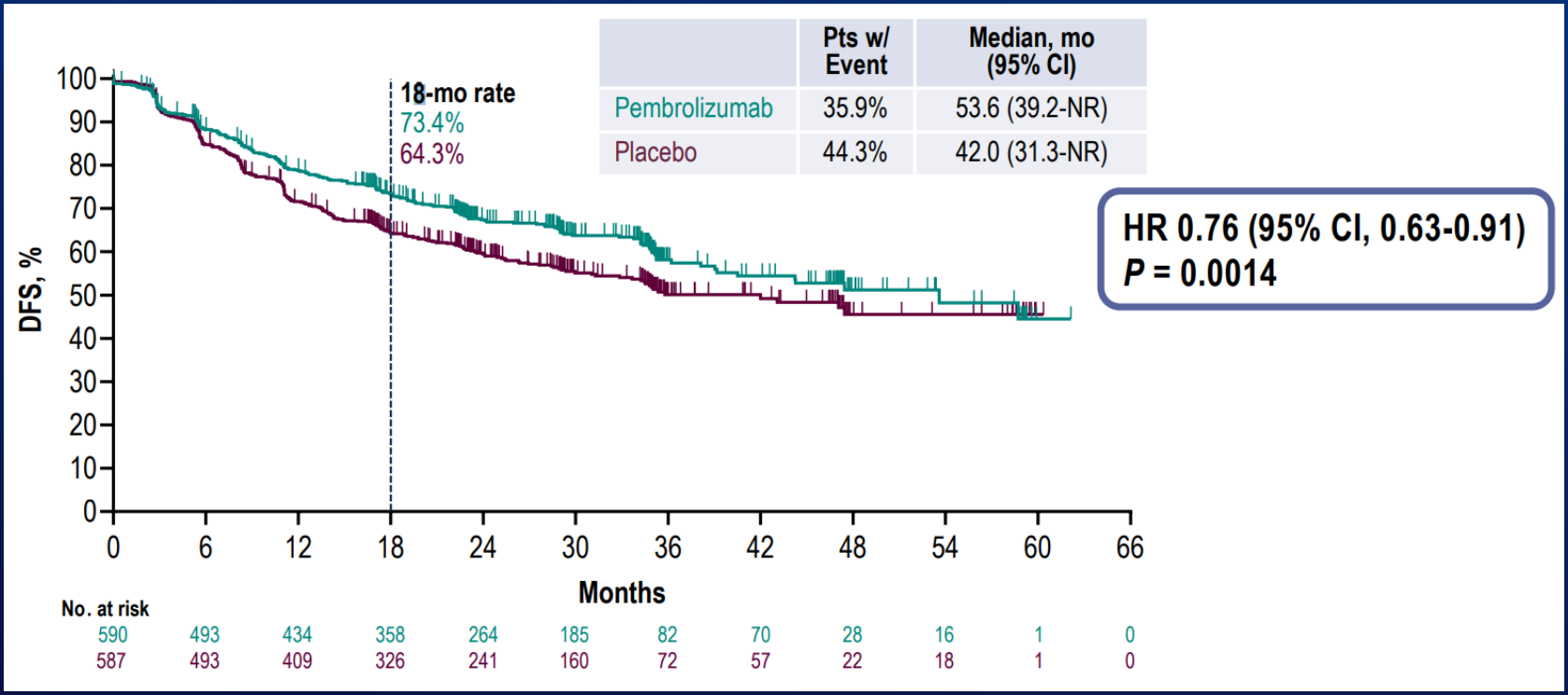


Pearls/Keynote-091: Adjuvant Pembrolizumab



Paz-Ares, ESMO Virtual Plenary 2022

Disease-free survival



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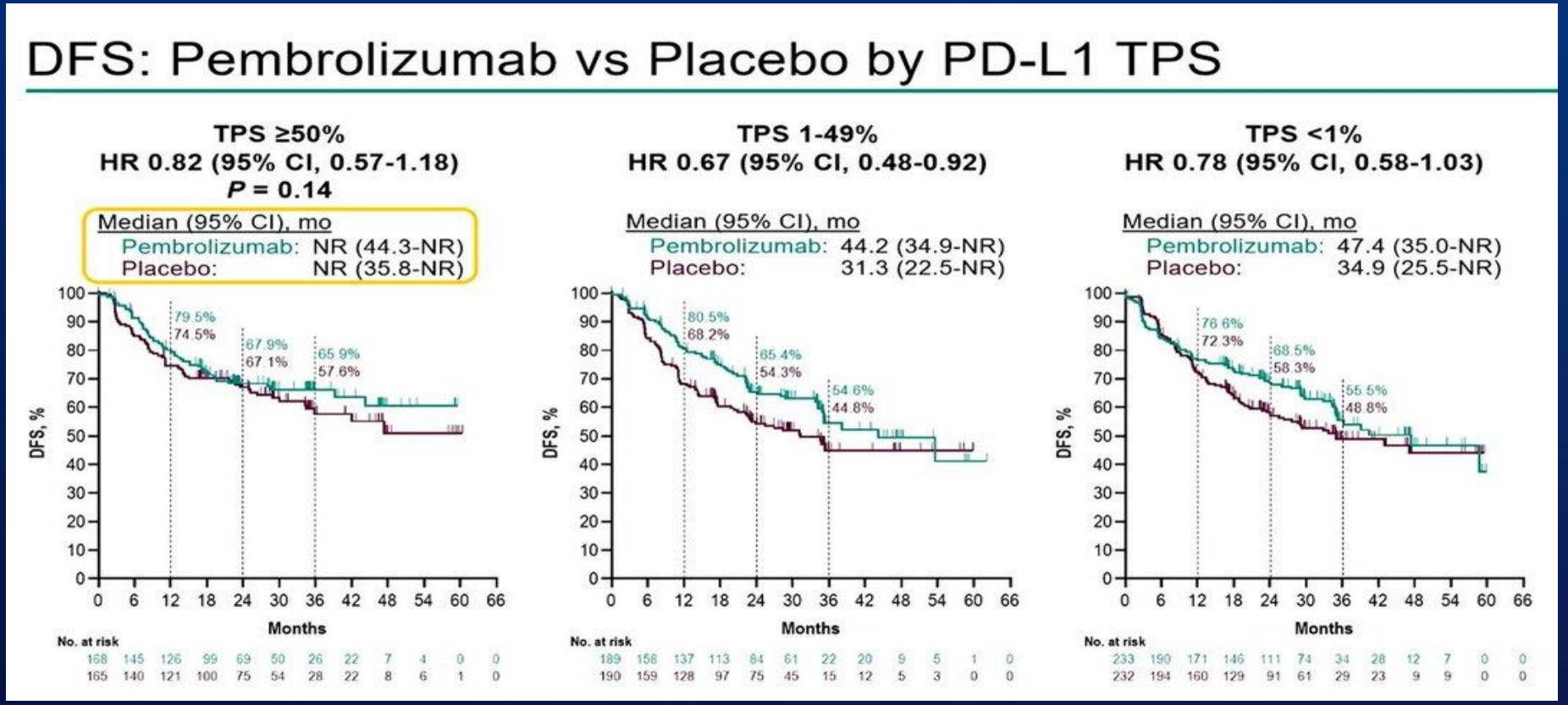
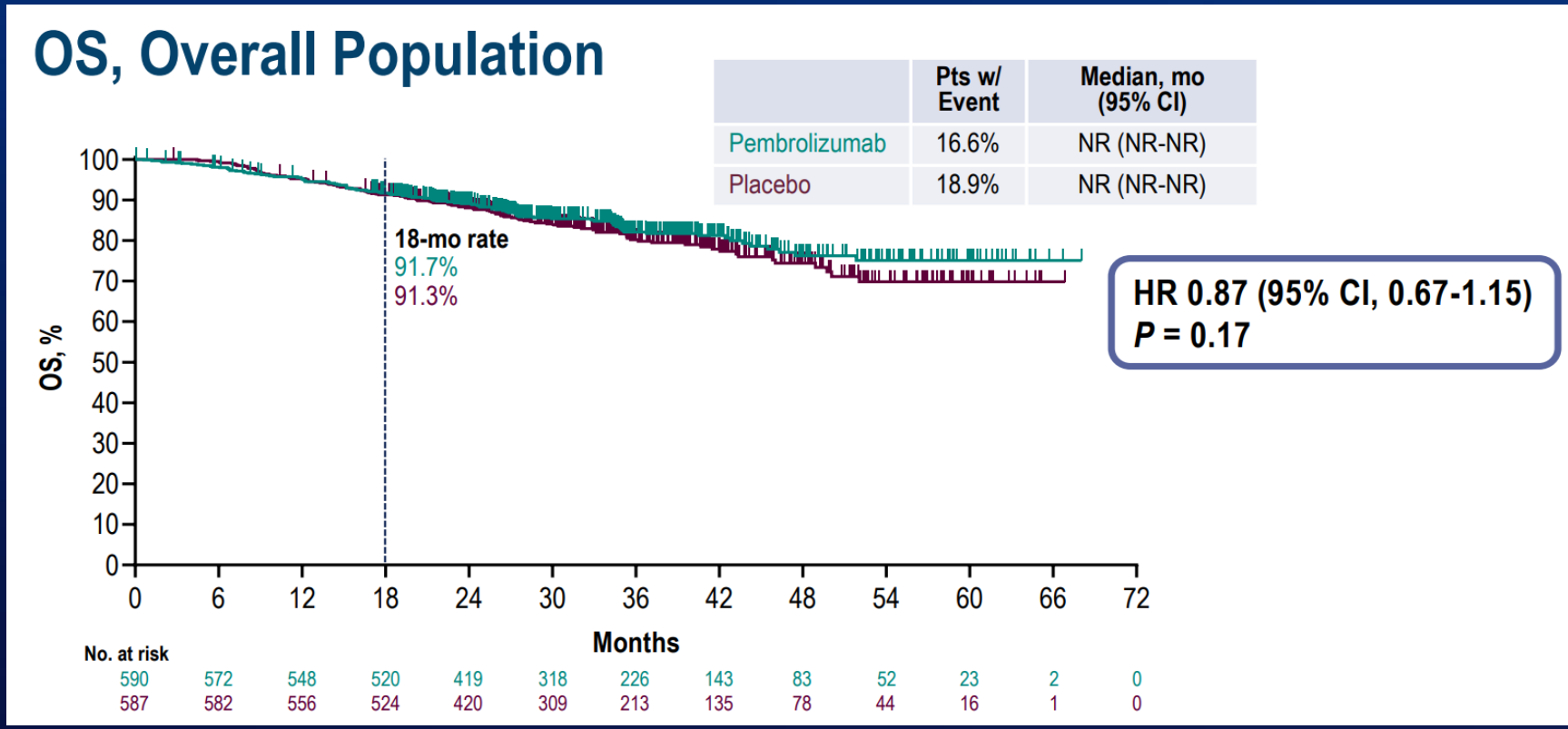


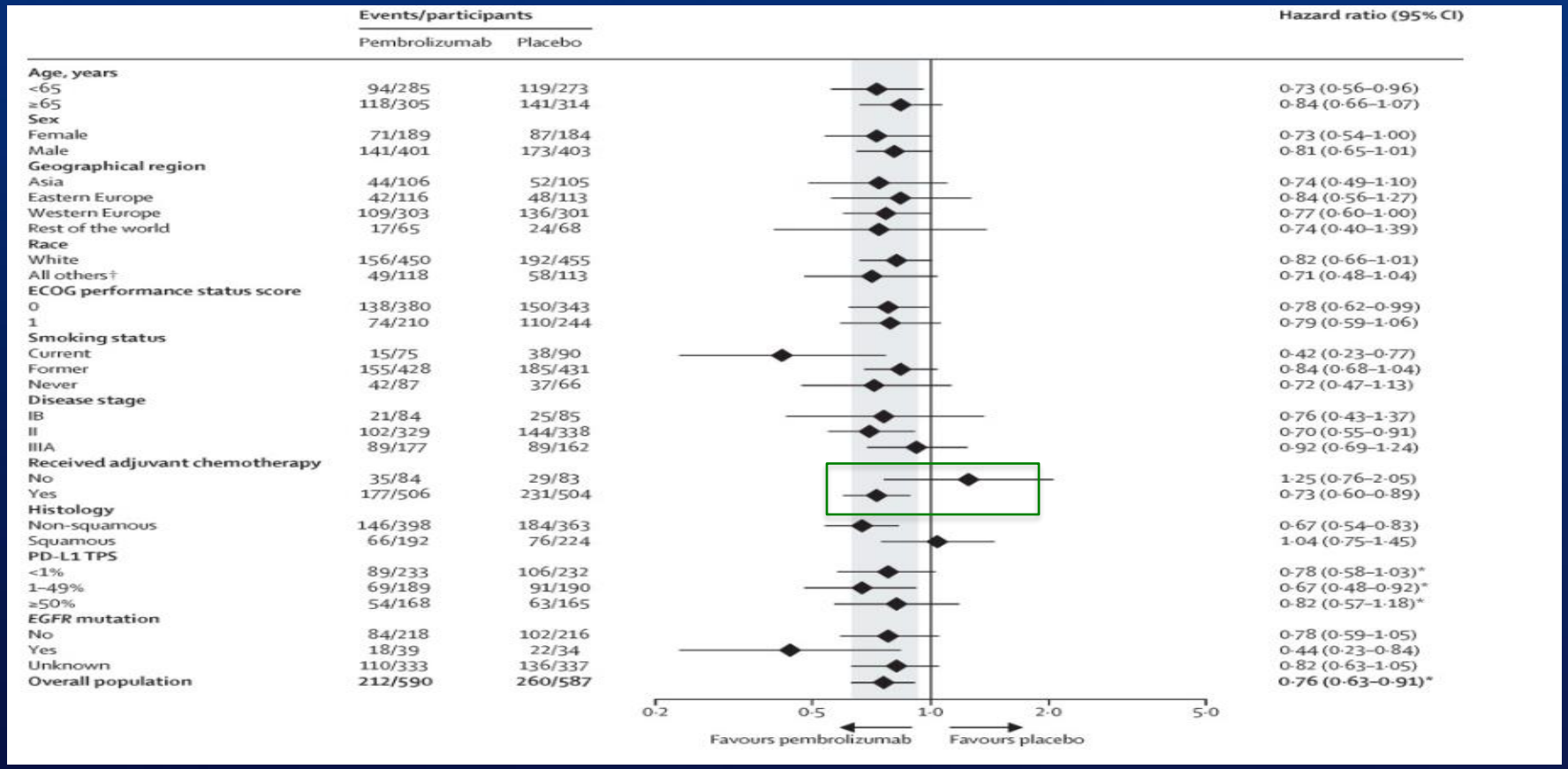
Paz-Ares, ESMO Virtual Plenary 2022

Overall survival



Paz-Ares, ESMO Virtual Plenary 2022

Benefit mainly in patients who received adjuvant chemo



	Events/participants		Hazard ratio (95% CI)
	Pembrolizumab	Placebo	
Age, years			
<65	94/285	119/273	0·73 (0·56–0·96)
≥65	118/305	141/314	0·84 (0·66–1·07)
Sex			
Female	71/189	87/184	0·73 (0·54–1·00)
Male	141/401	173/403	0·81 (0·65–1·01)
Geographical region			
Asia	44/106	52/105	0·74 (0·49–1·10)
Eastern Europe	42/116	48/113	0·84 (0·56–1·27)
Western Europe	109/303	136/301	0·77 (0·60–1·00)
Rest of the world	17/65	24/68	0·74 (0·40–1·39)
Race			
White	156/450	192/455	0·82 (0·66–1·01)
All others†	49/118	58/113	0·71 (0·48–1·04)
ECOG performance status score			
0	138/380	150/343	0·78 (0·62–0·99)
1	74/210	110/244	0·79 (0·59–1·06)
Smoking status			
Current	15/75	38/90	0·42 (0·23–0·77)
Former	155/428	185/431	0·84 (0·68–1·04)
Never	42/87	37/66	0·72 (0·47–1·13)
Disease stage			
IB	21/84	25/85	0·76 (0·43–1·37)
II	102/329	144/338	0·70 (0·55–0·91)
IIIA	89/177	89/162	0·92 (0·69–1·24)
Received adjuvant chemotherapy			
No	35/84	29/83	1·25 (0·76–2·05)
Yes	177/506	231/504	0·73 (0·60–0·89)
Histology			
Non-squamous	146/398	184/363	0·67 (0·54–0·83)
Squamous	66/192	76/224	1·04 (0·75–1·45)
PD-L1 TPS			
<1%	89/233	106/232	0·78 (0·58–1·03)*
1–49%	69/189	91/190	0·67 (0·48–0·92)*
≥50%	54/168	63/165	0·82 (0·57–1·18)*
***EGFR* mutation**			
No	84/218	102/216	0·78 (0·59–1·05)
Yes	18/39	22/34	0·44 (0·23–0·84)
Unknown	110/333	136/337	0·82 (0·63–1·05)
Overall population	**212/590**	**260/587**	**0·76 (0·63–0·91)***

O'brien et al, The Lancet Oncology Sep 2022

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What Should We do?

Adjuvant Immunotherapy

Vs

Neoadjuvant Immunotherapy

What Should We do?

Adjuvant Immunotherapy

Vs

Neoadjuvant Immunotherapy

Happy to come for another 2 hours talk to cover this

Osimertinib as adjuvant therapy in patients with stage IB–IIIA EGFR mutation positive NSCLC after complete tumor resection: ADAURA

Roy S. Herbst[1], Masahiro Tsuboi[2], Thomas John[3], Christian Grohe[4], Margarita Majem[5], Jonathan W. Goldman[6], Sang-We Kim[7], Dominika Marmol[8], Yuri Rukazenkov[8], Yi-Long Wu[9]

[1] Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA; [2] Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [3] Department of Medical Oncology, Austin Health, Melbourne, Australia; [4] Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; [5] Medical Oncology Services, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6] David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, USA; [7] Department of Oncology, Asan Medical Center, Seoul, South Korea; [8] Oncology Research & Development, AstraZeneca, Cambridge, United Kingdom; [9] Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China

PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20

PRESENTED BY: Roy S. Herbst

Presented By Roy Herbst at TBD

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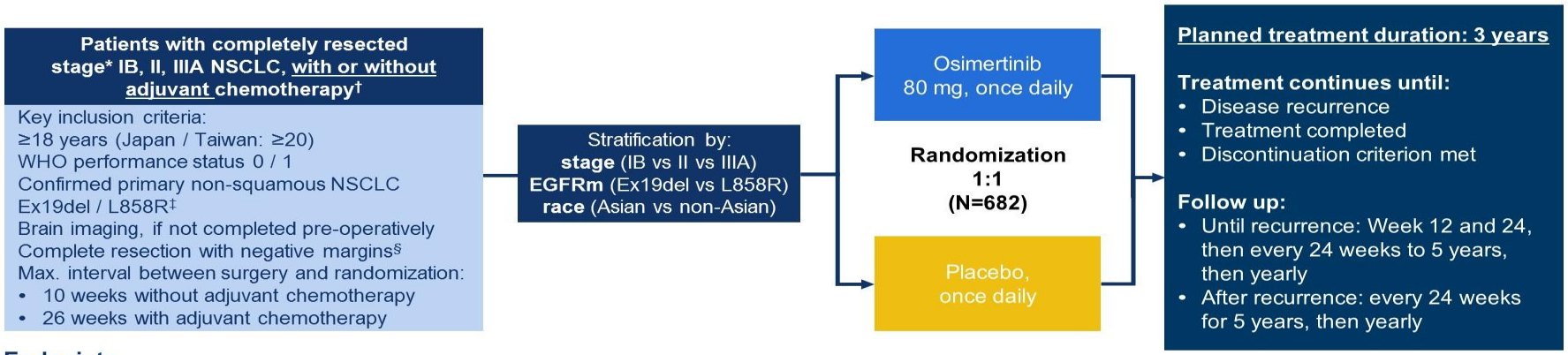
ADAURA Phase III double-blind study design



Endpoints

- **Primary**: DFS, by investigator assessment, in stage II/IIIA patients; designed for superiority under the assumed DFS HR of 0.70
- **Secondary**: DFS in the overall population¶, DFS at 2, 3, 4, and 5 years, OS, safety, health-related quality of life

- **Following IDMC recommendation, the study was unblinded early due to efficacy; here we report an unplanned interim analysis**
- **At the time of unblinding the study had completed enrollment and all patients were followed up for at least 1 year**

NCT02511106; ADAURA data cut-off: January 17, 2020. *AJCC 7th edition; †Prior, post, or planned radiotherapy was not allowed; ‡Centrally confirmed in tissue; §Patients received a CT scan after resection and within 28 days prior to treatment; ¶Stage IB / II / IIIA. CT, computed tomography; Ex19del, exon 19 deletion; IDMC, Independent Data Monitoring Committee; WHO, World Health Organization.

Presented By Roy Herbst at TBD

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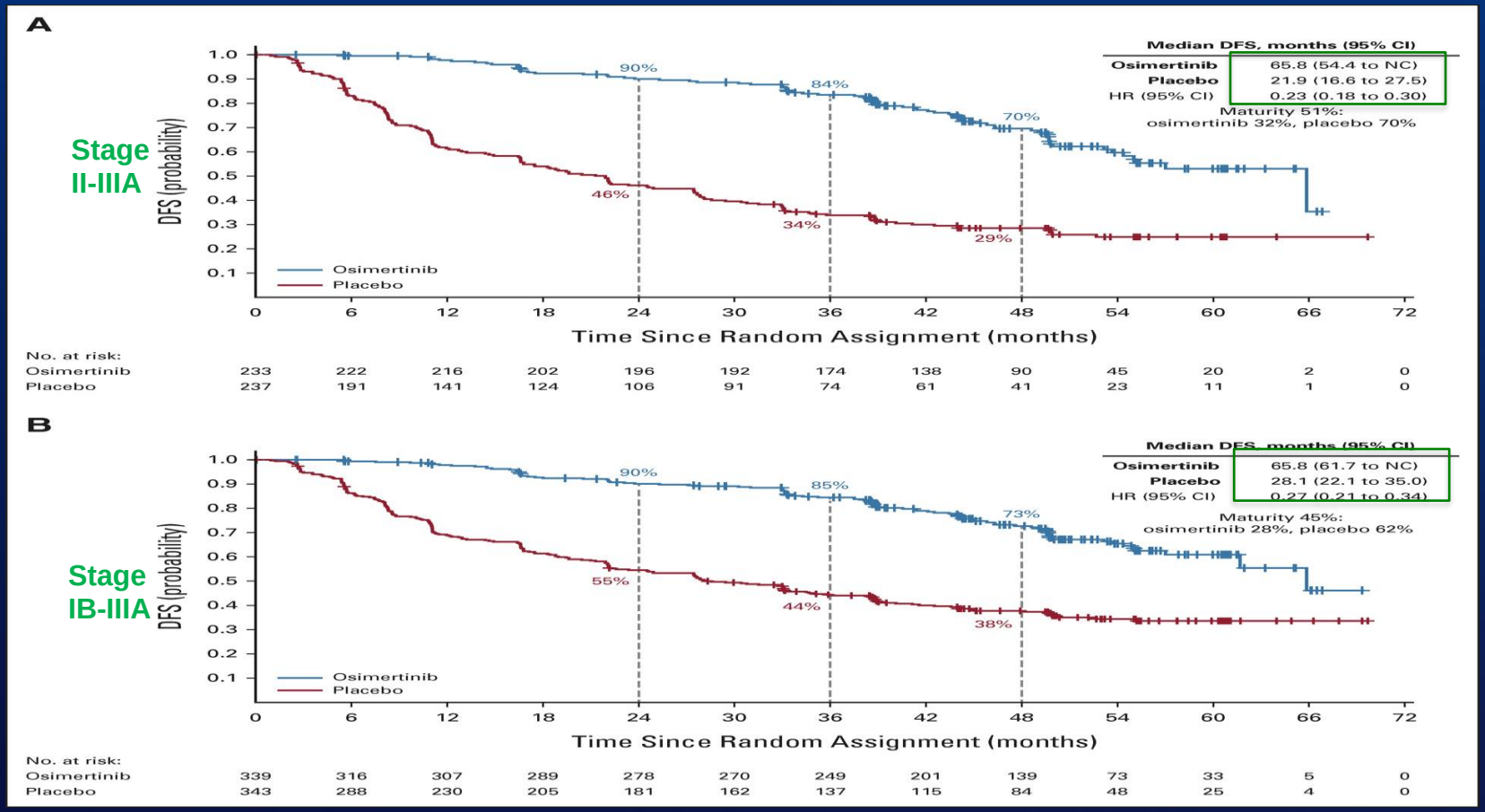
HOT OFF THE PRESS
Updated DFS



Herbst et al, JCO Jan 2023

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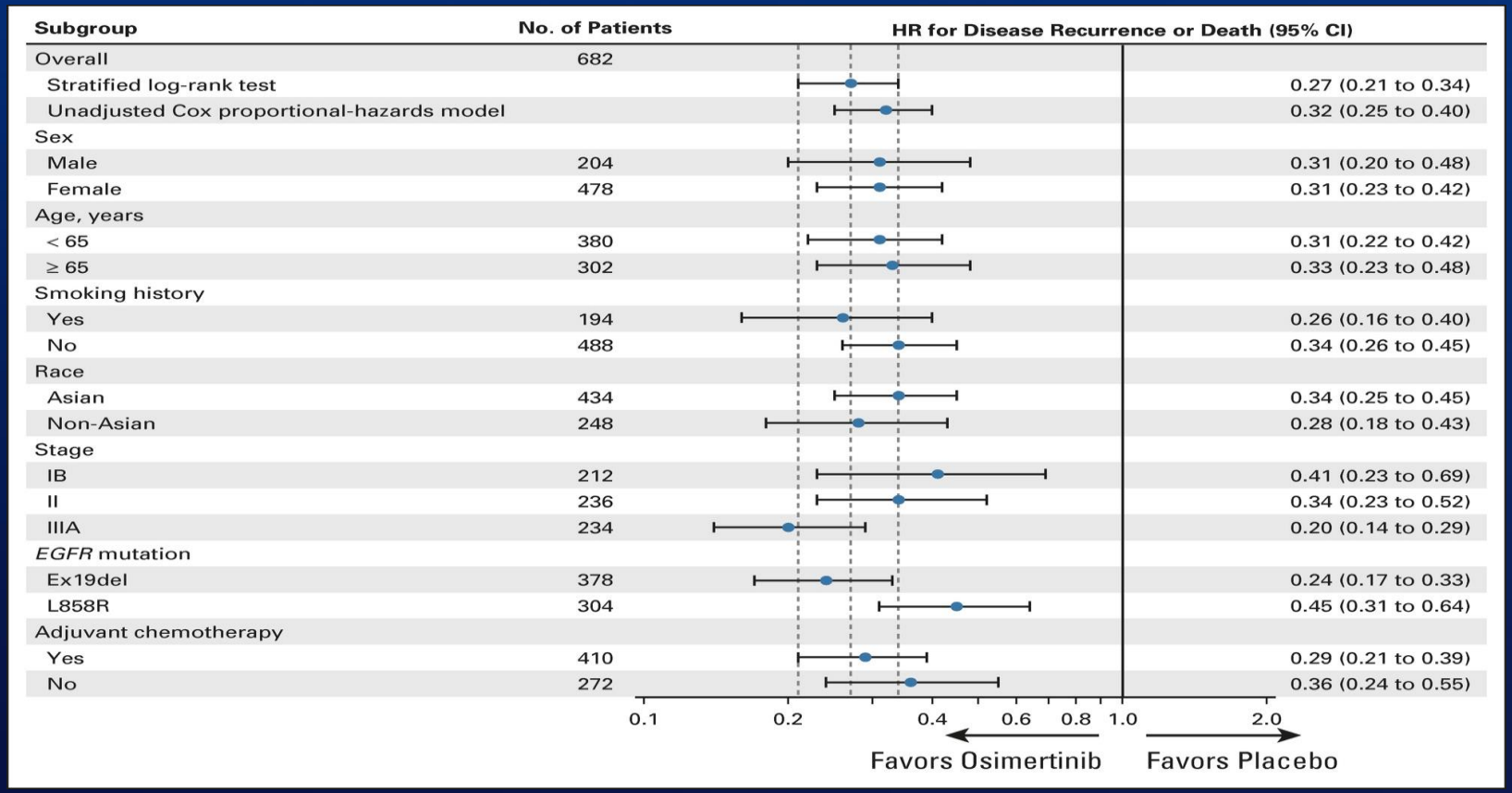
DFS subgroups analysis



Herbst et al, JCO Jan 2023

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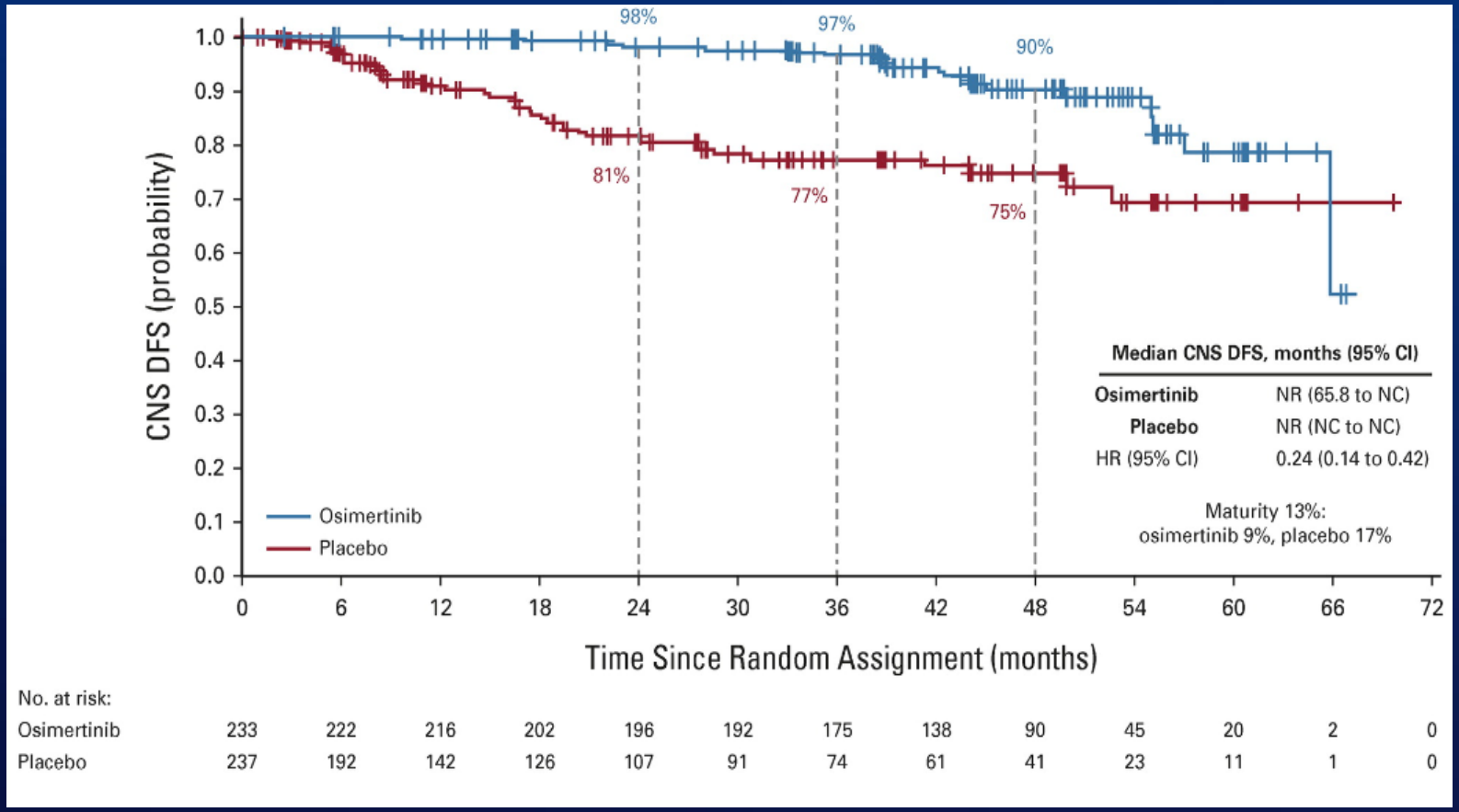
CNS DFS



Herbst et al, JCO Jan 2023

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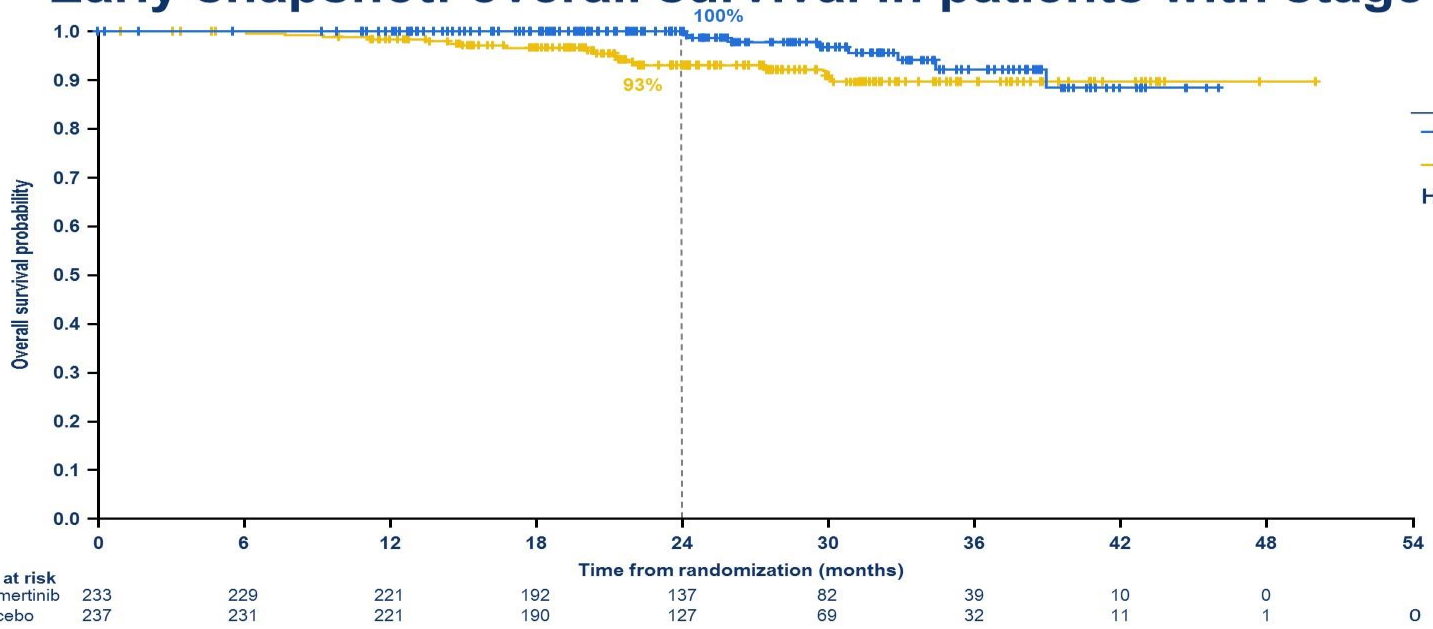
Early snapshot: overall survival in patients with stage II/IIIA disease



No. at risk										
Osimertinib	233	229	221	192	137	82	39	10	0	
Placebo	237	231	221	190	127	69	32	11	1	0

Median OS, months (95% CI)	
– Osimertinib	NR (NC, NC)
– Placebo	NR (NC, NC)
HR (95% CI)	**0.40 (0.18, 0.90)**

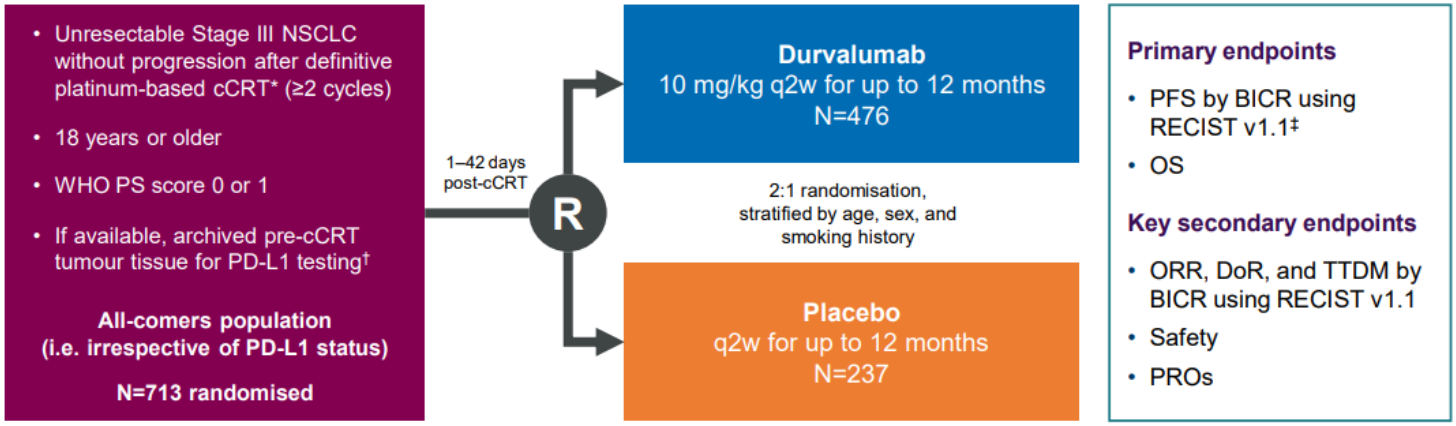
Maturity 5%:
osimertinib 3%, placebo 7%

ADAURA data cut-off: January 17, 2020.
Median follow-up: osimertinib 26.1, placebo 24.7 months.
Tick marks indicate censored data.

Presented By Roy Herbst

Unresectable stage III NSCLC

Unresectable stage III NSCLC- Pacific trial



- Updated analyses of OS and PFS (~4 years after the last patient was randomised; planned exploratory update)
  - Treatment effects for the ITT population were estimated using a stratified log-rank approach (with trial stratification factors)
  - Treatment effects for patient subgroups were estimated from unstratified Cox proportional-hazards models (with treatment as the only covariate)

Antonia, NEJM 2018; Spigel JCO 2022

Pacific trial

PFS:

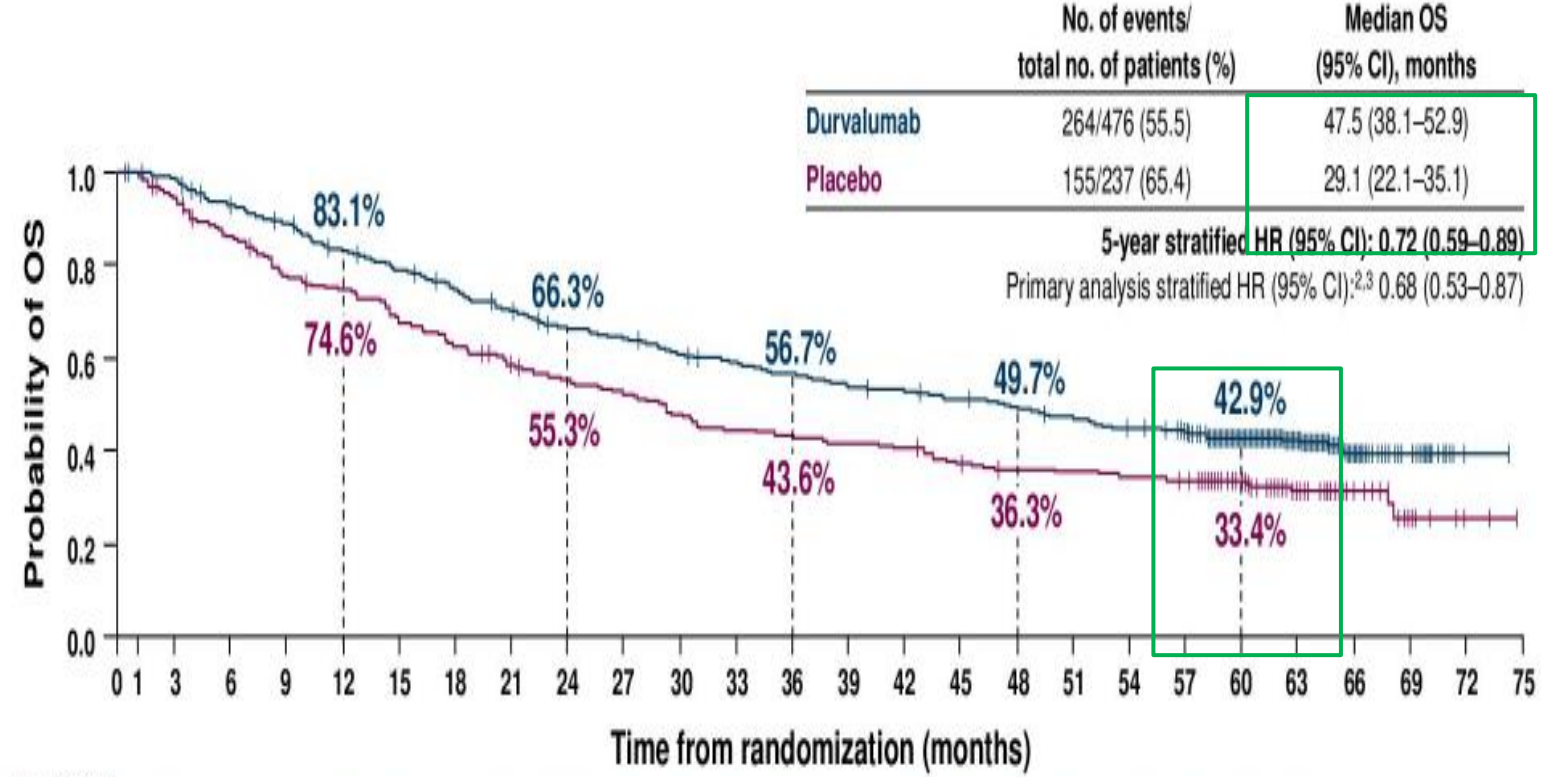
Median:

16.9 months

Vs

5.6 months

OS:



Antonia, NEJM 2018; Spigel JCO 2022

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Outline

- Epidemiology of lung cancer
- Updates on management of early-stage NSCLC
- Updates on management of stage IV NSCLC

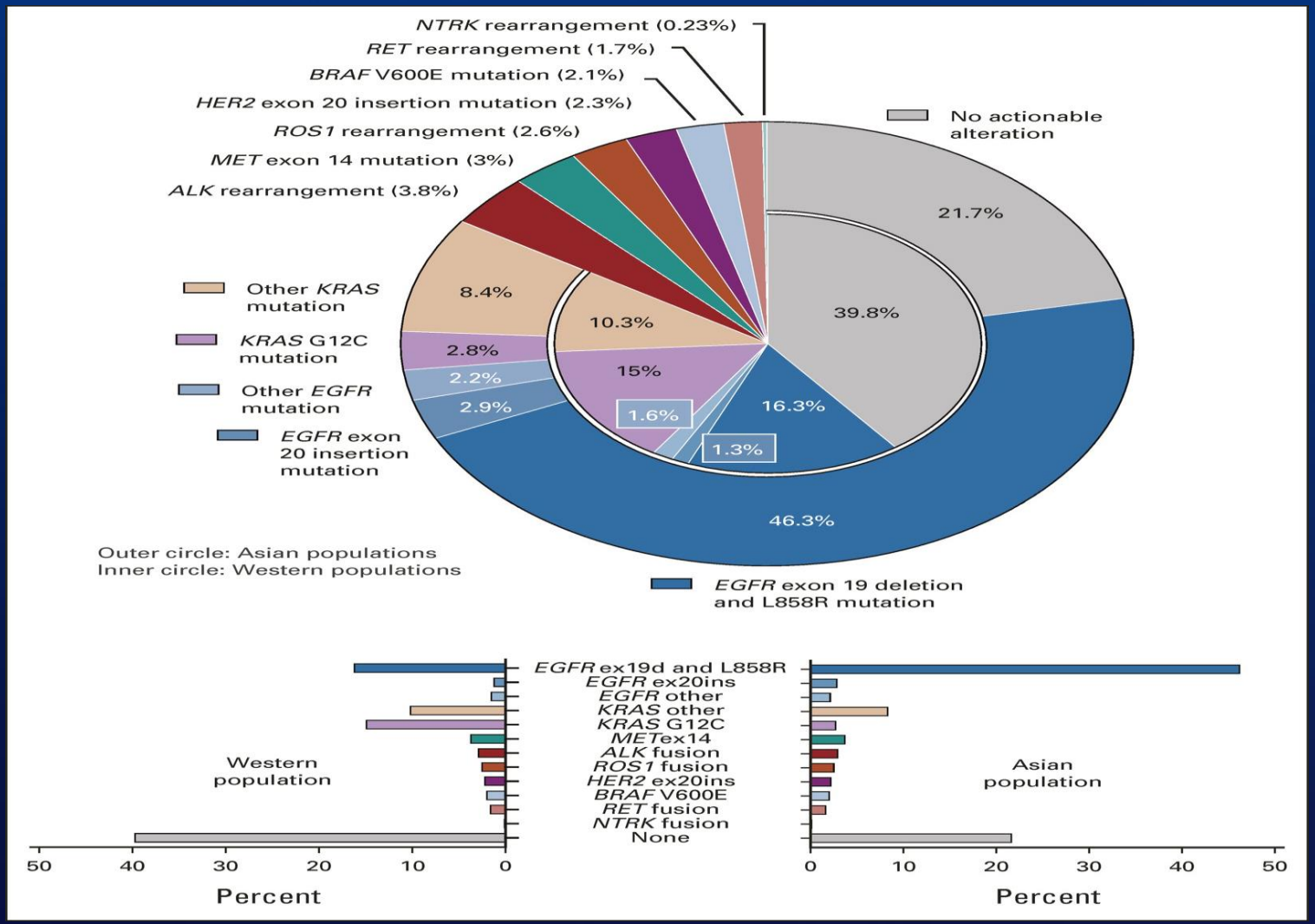
Treatment options for stage IV NSCLC

Chemotherapy

Targeted therapy

Immunotherapy

Molecular Profiling of Lung Adenocarcinoma



Tan et al; *JCO* 2022

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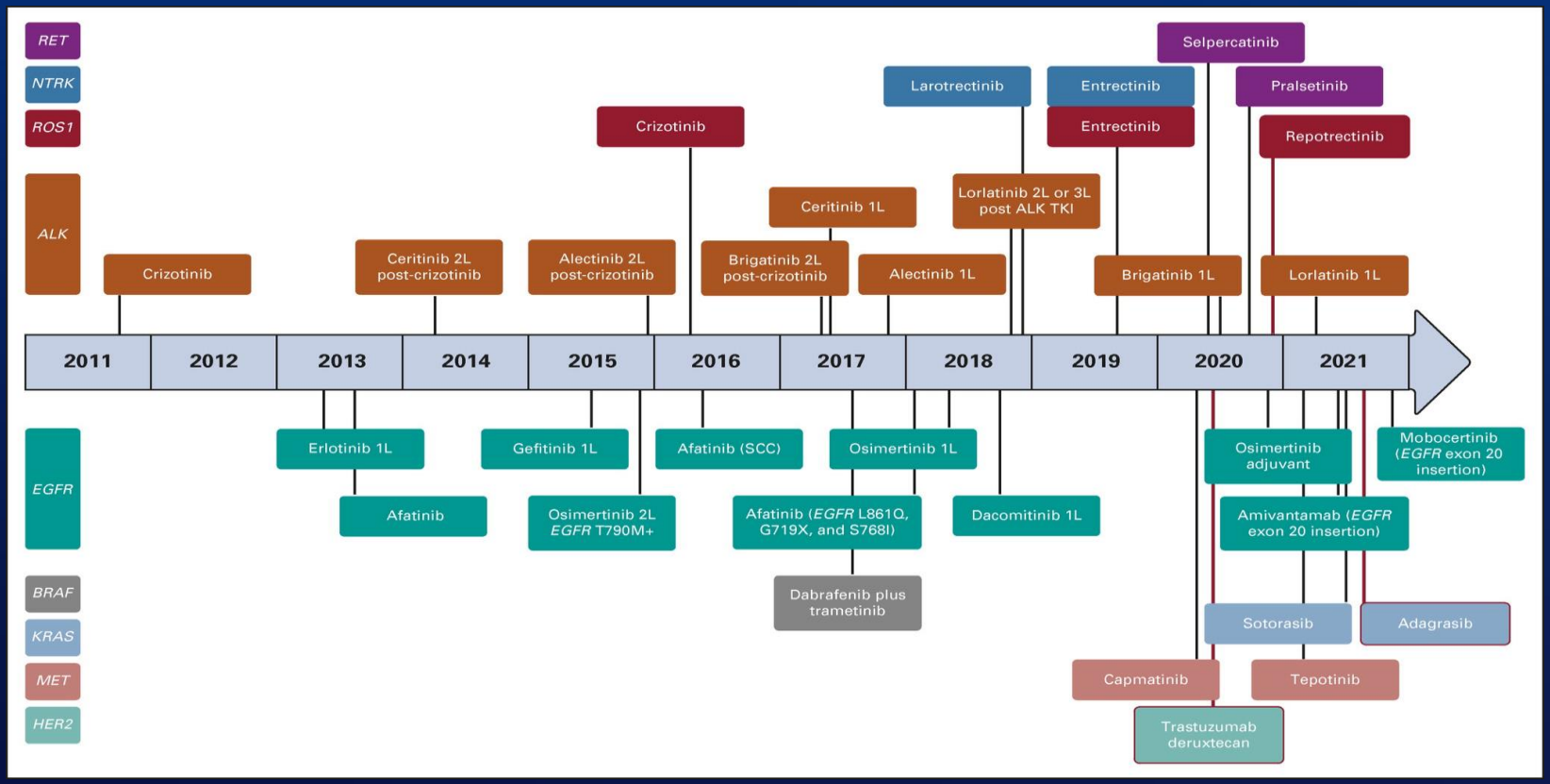
Timeline of FDA-approved targeted therapies for oncogene-driven NSCLC



Tan et al; *JCO* 2022

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FDA approved Targeted therapeutic agents in Lung Adenocarcinoma *(as of Feb 2023)*

Gene	FDA approved Therapeutic Agents
ALK	Alectinib, Brigatinib, Ceritinib, Crizotinib, Lorlatinib
BRAF V600E	Dabrafenib plus Trametinib
EGFR	Osimertinib, Erlotinib, Afatinib, Gefitinib, Dacomatinib, Erlotinib + Ramucirumab
EGFR Exon 20	Amivantamab, Mobocertinib *(in 2nd line)*
KRAS (G12C)	Sotorasib, Adagrasib *(in 2nd line)*
MET exon 14	Capmatinib, Tepotinib
NTRK	Larotrectinib, Entrectinib
RET	Selpercatinib, Pralsetinib
ROS-1	Crizotinib, Entrectinib
Her-2	Trastuzumab Deruxtecan *(in 2nd line)*

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Molecular Testing

Every patient with advanced NSCLC (at least non-squamous) SHOULD have full NGS testing

Data shows we are doing better with NGS testing, but we are not there yet

We can, we need to, and we should DO EVEN BETTER with NGS testing

Highly recommend to wait for results of NGS before starting Tx (due to toxicity when giving targeted therapy after IO)

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Molecular Testing

- Multiplexed next genetic sequencing (NGS) panels are preferred over single- gene tests (tell you more and cost less)

- Test all non-squamous histologies and any NSCLC histology when clinical features indicate a higher probability of an oncogenic driver (eg, young age; light or absent tobacco Hx).

- In some clinical settings in which tissue is limited and/or insufficient for molecular testing, physicians could/should use a cfDNA assay (liquid biopsy)

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- In some clinical settings in which tissue is limited and/or insufficient for molecular testing, physicians could/should use a cfDNA assay (liquid biopsy)

I recommend using both and I usually send both

2022 ASCO® ANNUAL MEETING

Association of comprehensive molecular genotyping and overall survival in patients with advanced non-squamous non-small cell lung cancer

Charu Aggarwal, Melina E. Marmarelis, Wei-Ting Hwang, Dylan G. Scholes, Tara L. McWilliams, Aditi P. Singh, Lova Sun, John Kosteva, Michael R. Costello, Roger B. Cohen, Corey J. Langer, Peter E. Gabriel, Lawrence N. Shulman, Jeffrey C. Thompson, Erica L. Carpenter

Abramson Cancer Center,
University of Pennsylvania
Philadelphia, PA, United States

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Comprehensive molecular genotyping and overall survival

Patients with comprehensive molecular genotyping had superior OS (22.1 months, 95% CI 14.62 – NA), compared to those with incomplete or no testing (11.6 months, 95% CI 3.61 – NA), p=0.02, likely mediated by delivery of targeted therapy

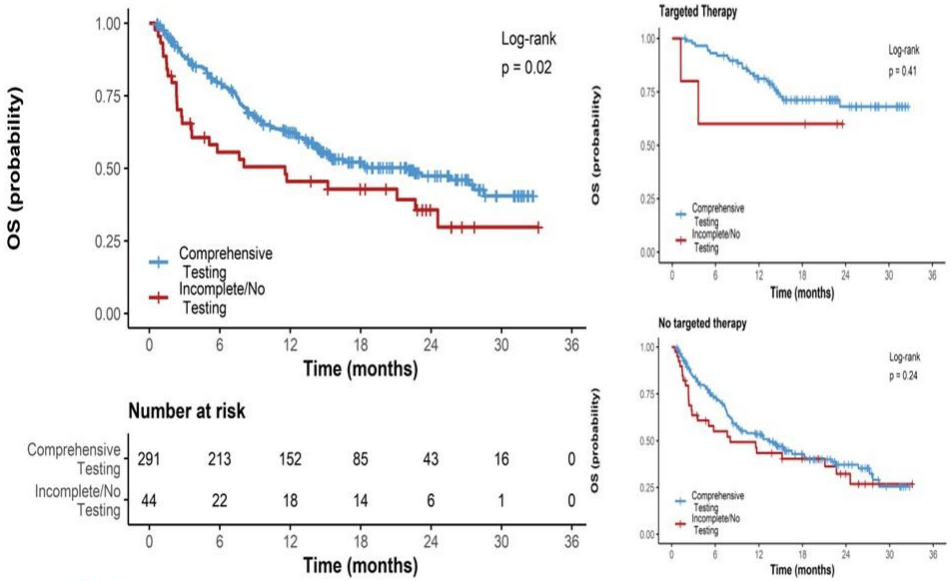

Fig 1.
Kaplan-Meier curve for OS of patients with comprehensive testing compared to patients with incomplete/no testing.

Availability of molecular genotyping results prior to first line therapy was associated with an improvement in OS (24.57 months, 95% CI, 18.56– NR), compared to patients without results available prior to first line therapy (6.18 months, 95% CI, 2.83 – 10.3), p<0.0001

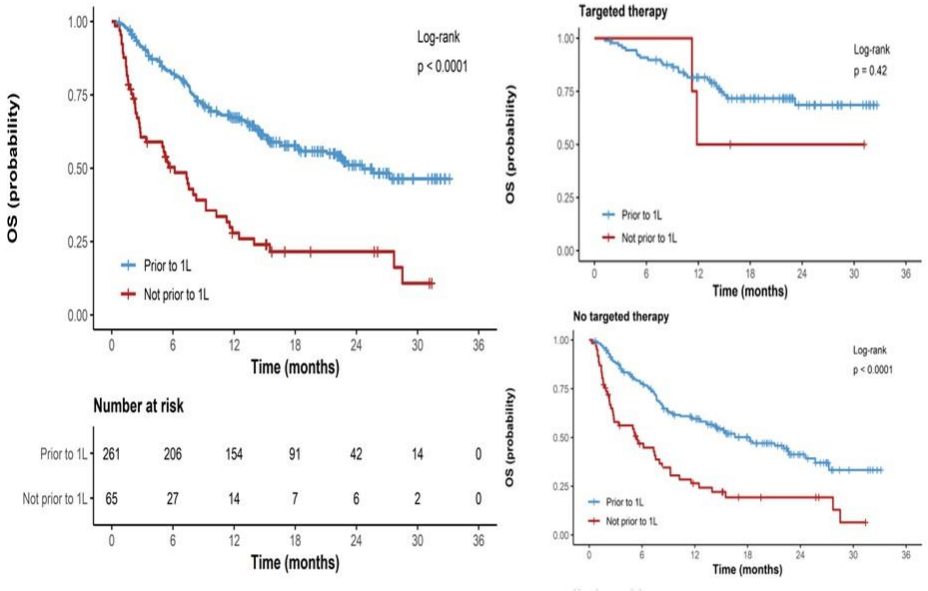

Fig 2.
Kaplan-Meier curve for OS of patients with comprehensive testing back prior to first line treatment compared to patients with results not back prior to first line treatment.

Newly approved therapy for Her 2 mutation

The NEW ENGLAND JOURNAL of MEDICINE

Trastuzumab Deruxtecan in *HER2*-Mutant Non–Small-Cell Lung Cancer

MULTICENTER, INTERNATIONAL, PHASE 2 STUDY

91

Adults with metastatic *HER2*-mutant NSCLC refractory to standard treatment (median follow-up, 13 mo)

Confirmed objective response (assessed by independent central review)	55% (95% CI, 44–65)
Duration of response	9.3 mo
Progression-free survival	8.2 mo
Overall survival	17.8 mo

Grade 3 or higher drug-related adverse events occurred in 46% of patients.

Trastuzumab deruxtecan showed durable anticancer activity.

B.T. Li et al. 10.1056/NEJMoa2112431

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Li et al, NEJM Jan 2022

Immunotherapy

- IO has become standard of care in 1st line systemic therapy for stage IV, either alone or in combination with chemo

- **Options:**

Atezolizumab

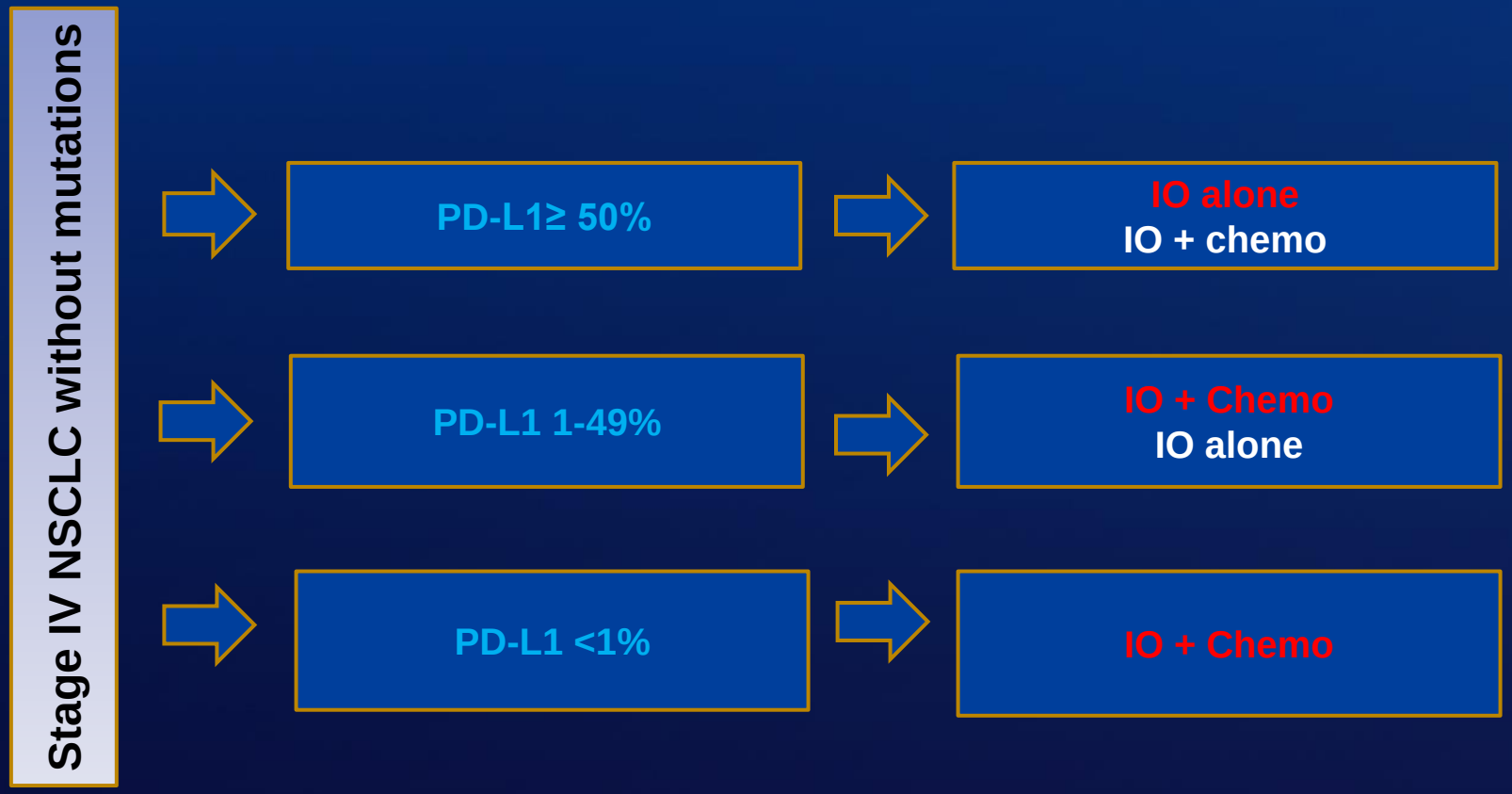
Cemiplimab-rwlc

Ipilimumab + Nivolumab

Pembrolizumab

Tremelimumab + Durvalumab

Treatment algorithm for stage IV NSCLC



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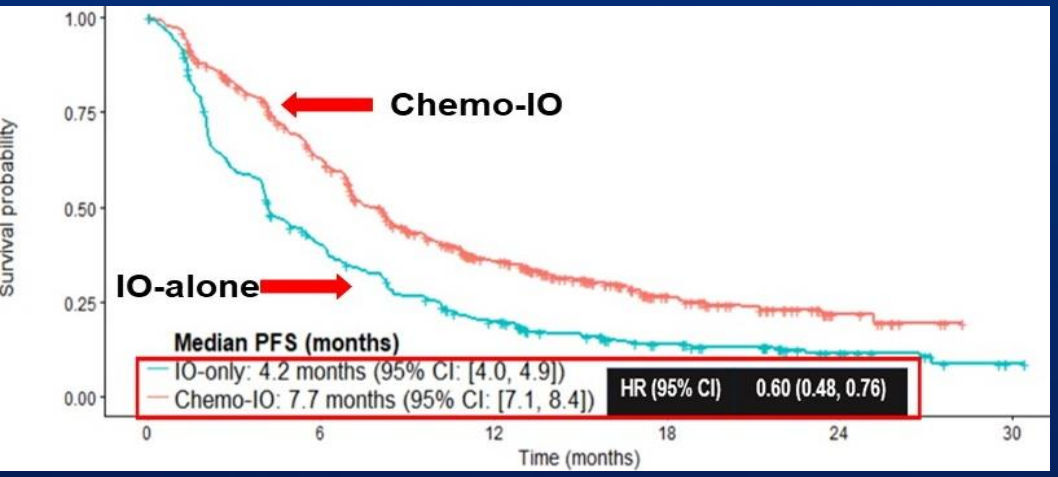
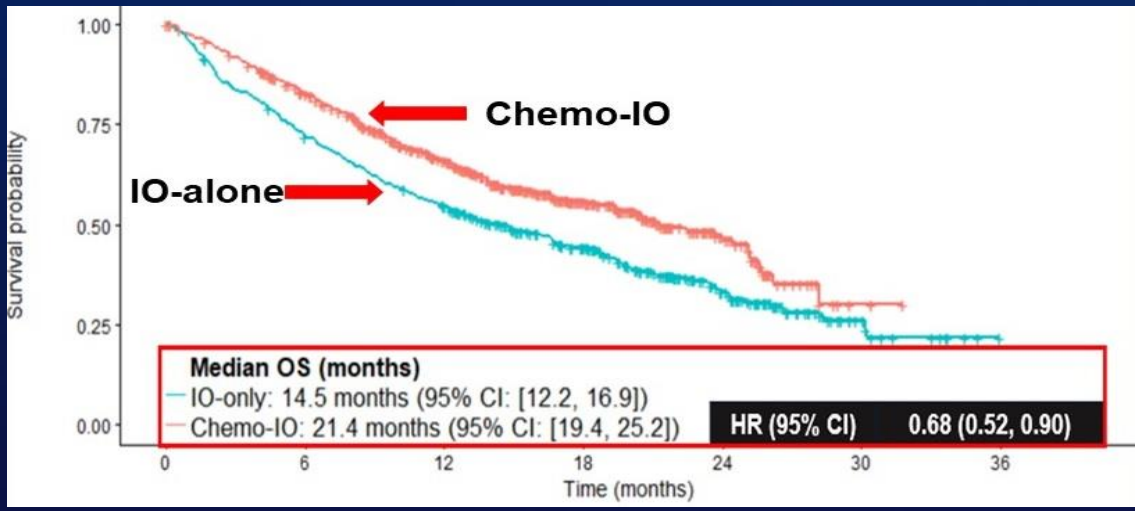
META ANALYSIS: CHEMO-IO VS IO: PD-L1 ≥1-49%





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Akinboro, et al. ASCO, 2021

META ANALYSIS: CHEMO-IO VS IO: PD-L1 ≥1-49%

	Subgroup	N[1]	Median OS in months	OS HR[2] (95% CI)	Median PFS in months	PFS HR[2] (95% CI)
Age	<65	580	23.7 vs 16.1	0.63 (0.43, 0.92)	7.1 vs 4.0	0.55 (0.40, 0.76)
	65-74	443	22.5 vs 14.8	0.61 (0.38, 0.97)	9.5 vs 4.5	0.60 (0.40, 0.88)
	≥75	132	13.9 vs 10.3	0.95 (0.42, 2.14)	6.4 vs 4.9	0.85 (0.42, 1.71)
ECOG	0	415	25.2 vs 20.0	0.65 (0.38, 1.10)	9.6 vs 5.8	0.57 (0.38, 0.86)
	1+	751	16.8 vs 11.0	0.68 (0.50, 0.94)	7.0 vs 4.0	0.65 (0.49, 0.86)
Smoking	Never	160	28.2 vs 18.0	0.57 (0.22, 1.46)	8.1 vs 4.1	0.44 (0.21, 0.92)
	Ever	1005	20.8 vs 13.5	0.68 (0.51, 0.91)	7.6 vs 4.2	0.62 (0.49, 0.80)

Akinboro, et al. ASCO, 2021

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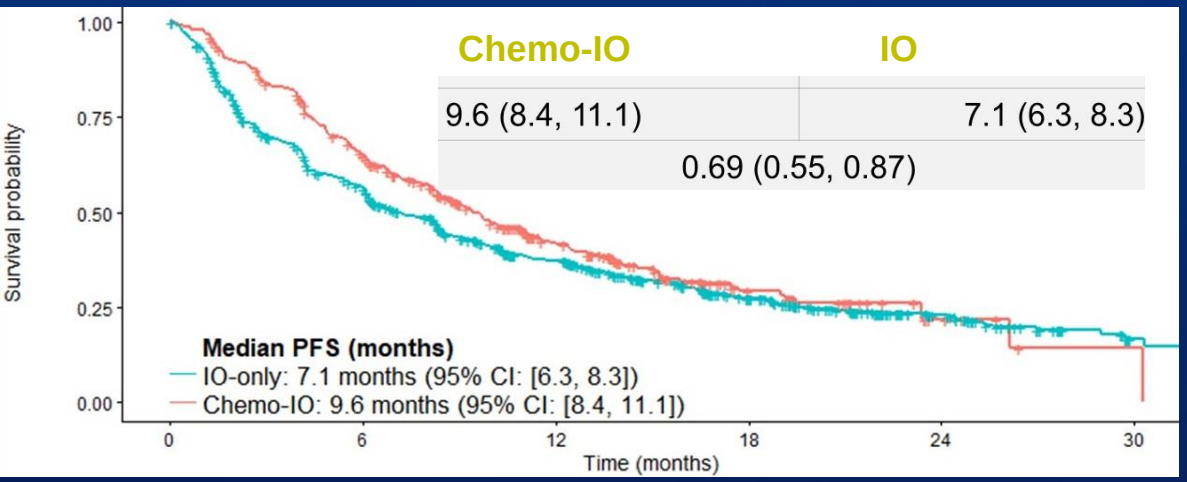
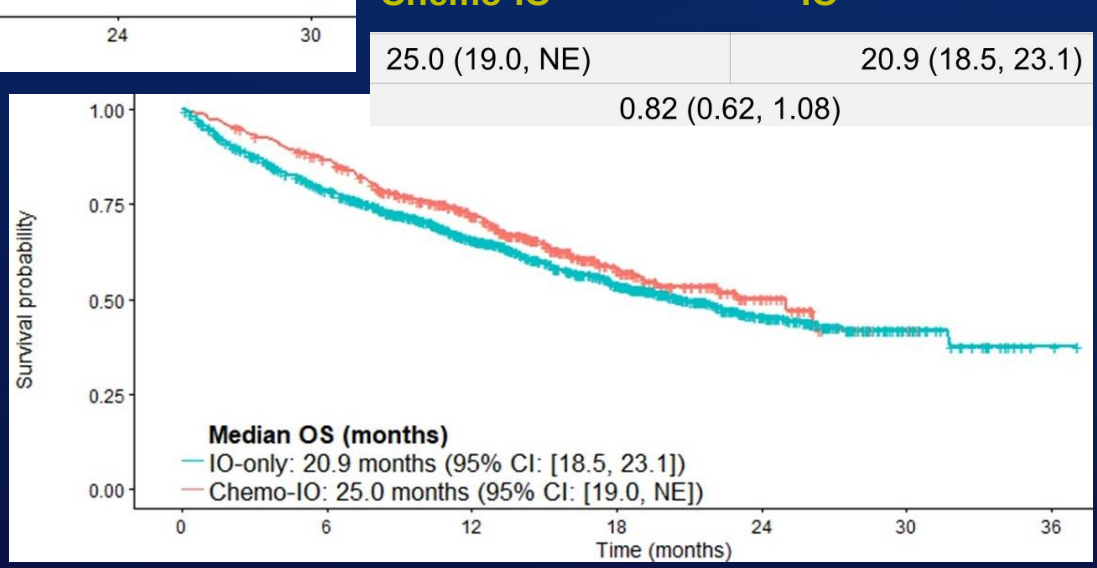
Cancer Center

META ANALYSIS: CHEMO-IO VS IO: PD-L1 ≥50%





Akinboro, et al. ASCO, 2022

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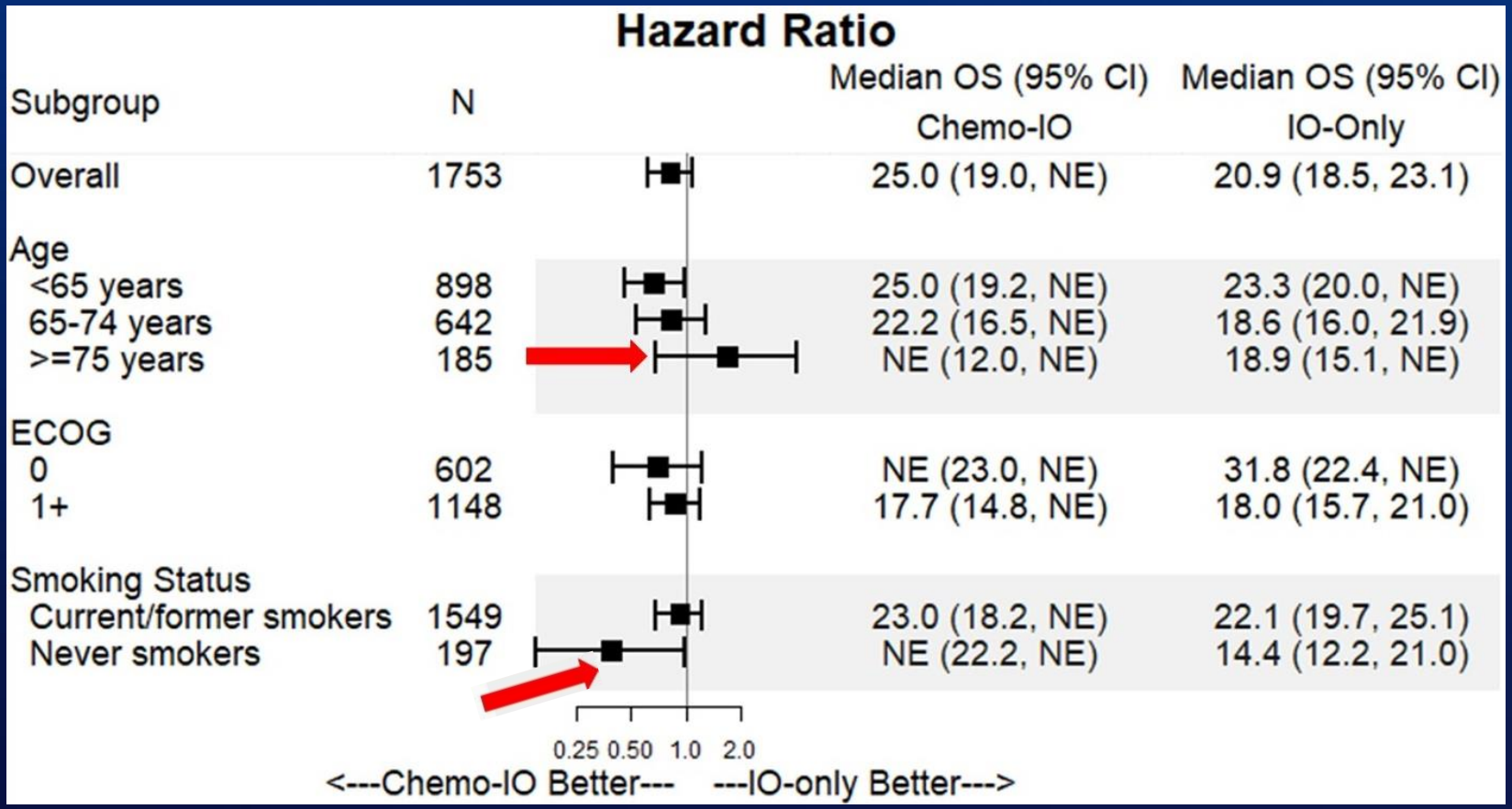
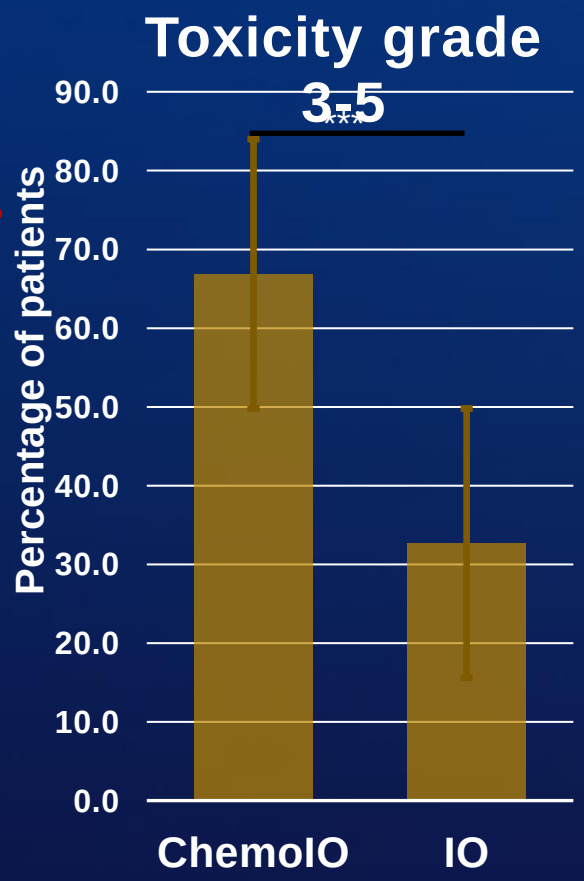
META ANALYSIS: CHEMO-IO VS IO: PD-L1 ≥50%



Akinboro, et al. ASCO, 2022

CHEMO-IO VS IO-ALONE: TOXICITY

	All Grade Toxicities (P+C vs P)			Grade 3-5 Toxicities (P+C vs P)		
	RD (%)	95% CI	p	RD (%)	95% CI	p
Any	17.3	8.7, 25.8	< 0.01	23.3	4.7, 41.9	0.014
Led to Discontinuation	12	1.9, 22	0.02	7.4	0.5, 14.3	0.035
Neutropenia	25.9	17.2, 34.5	< 0.01	14.7	5.3, 24.1	0.002
Vomiting	20.5	12.2, 28.7	< 0.01	-0.8	-4.7, 3.1	0.69
Thrombocytopenia	16.5	9.6, 23.4	< 0.01	6	1.3, 107	0.012
Any irAE	-9.1	-25.8, 7.6	0.29	-3.1	-9.1, 2.8	0.30
Hypothyroidism	-2.7	-8.1, 2.8	0.34		NA	
Severe skin reaction	-3.2	-7.1, 0.7	0.11	-3.4	-6.7, -0.1	0.045



Doherty, et al. ASCO, 2019; Zhang lab, unpublished

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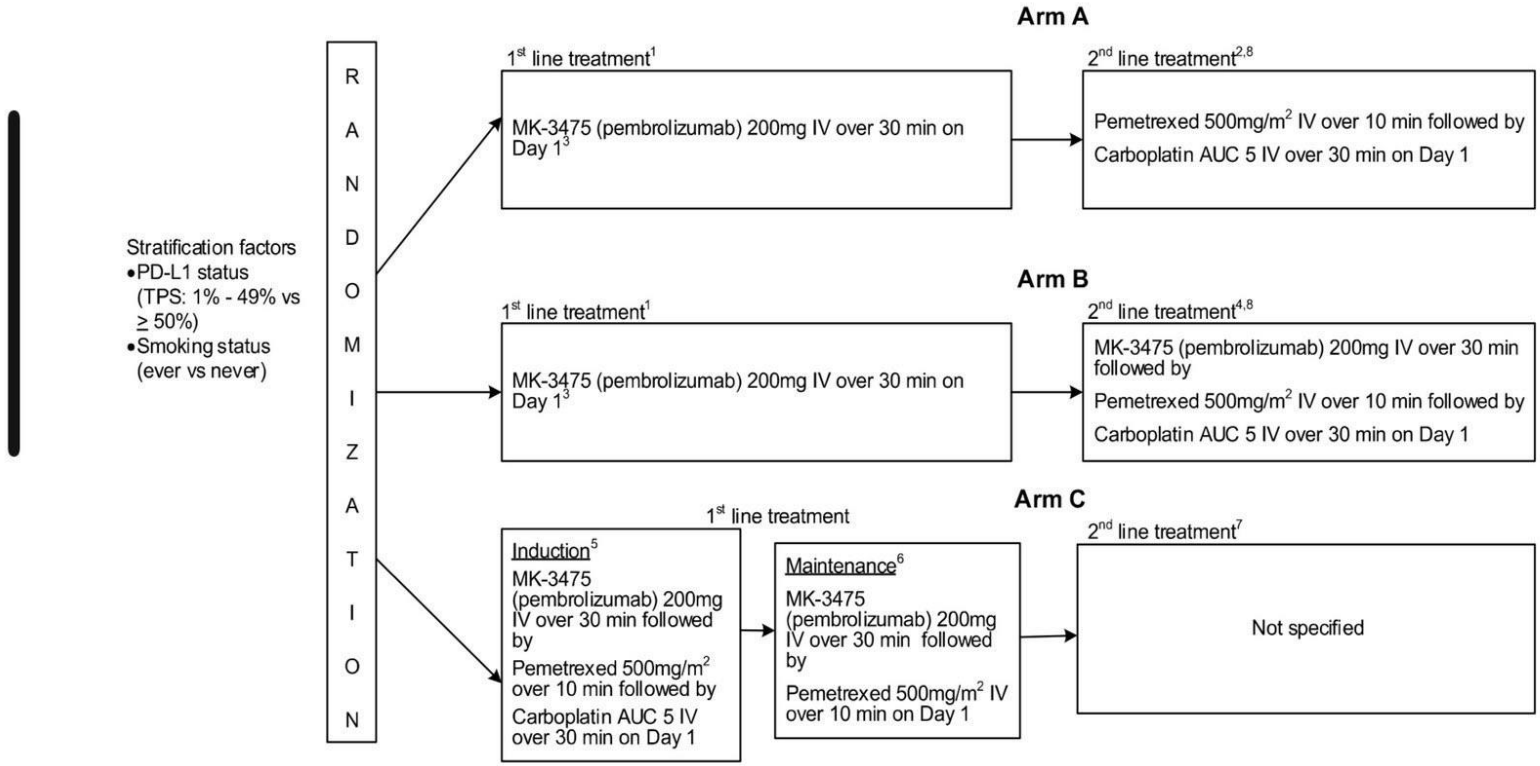
ECOG-ACRIN EA 5163 CLINICAL TRIAL CHEMO-IO VS IO-ALONE:

ECOG-ACRIN
Cancer Research Group

EA5163
Version Date: October 25, 2021

Schema



Treatment options for stage IV NSCLC

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

MOLECULAR AND BIOMARKER-DIRECTED THERAPY FOR ADVANCED OR METASTATIC DISEASE[a,b]

PD-L1 ≥50% First-line Therapy

ADENOCARCINOMA, LARGE CELL, NSCLC NOS

Preferred
- Pembrolizumab (category 1)[46,47]
- (Carboplatin or cisplatin) + pemetrexed + pembrolizumab (category 1)[48,49]
- Atezolizumab (category 1)[50]
- Cemiplimab-rwlc (category 1)[51]

Other Recommended
- Carboplatin + paclitaxel + bevacizumab[c,d] + atezolizumab (category 1)[52]
- Carboplatin + albumin-bound paclitaxel + atezolizumab[53]
- Nivolumab + ipilimumab + pemetrexed + (carboplatin or cisplatin) (category 1)[54]
- Cemiplimab-rwlc + paclitaxel + (carboplatin or cisplatin) (category 1)[55]
- Cemiplimab-rwlc + pemetrexed + (carboplatin or cisplatin) (category 1)[55]
- Tremelimumab-actl + durvalumab + carboplatin + albumin-bound paclitaxel (category 2B)[56]
- Tremelimumab-actl + durvalumab + (carboplatin or cisplatin) + pemetrexed (category 2B)[56]

Useful in Certain Circumstances
- Nivolumab + ipilimumab (category 1)[57]

SQUAMOUS CELL CARCINOMA

Preferred
- Pembrolizumab (category 1)[46,47]
- Carboplatin + (paclitaxel or albumin-bound paclitaxel) + pembrolizumab (category 1)[58]
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PD-L1 ≥1-49% First-line Therapy
Continuation Maintenance

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Treatment options for stage IV NSCLC

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Non-Small Cell Lung Cancer

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- Pembrolizumab (category 2B)[e,46,47]

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PD-L1 ≥50% First-line Therapy

Continuation Maintenance

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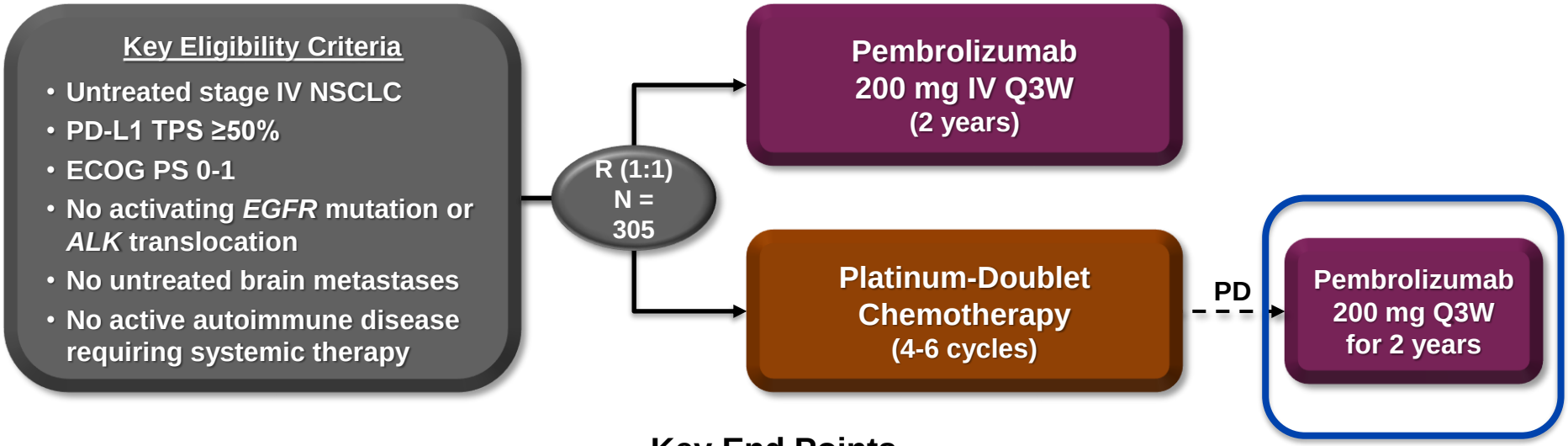
KEYNOTE-024



Key End Points

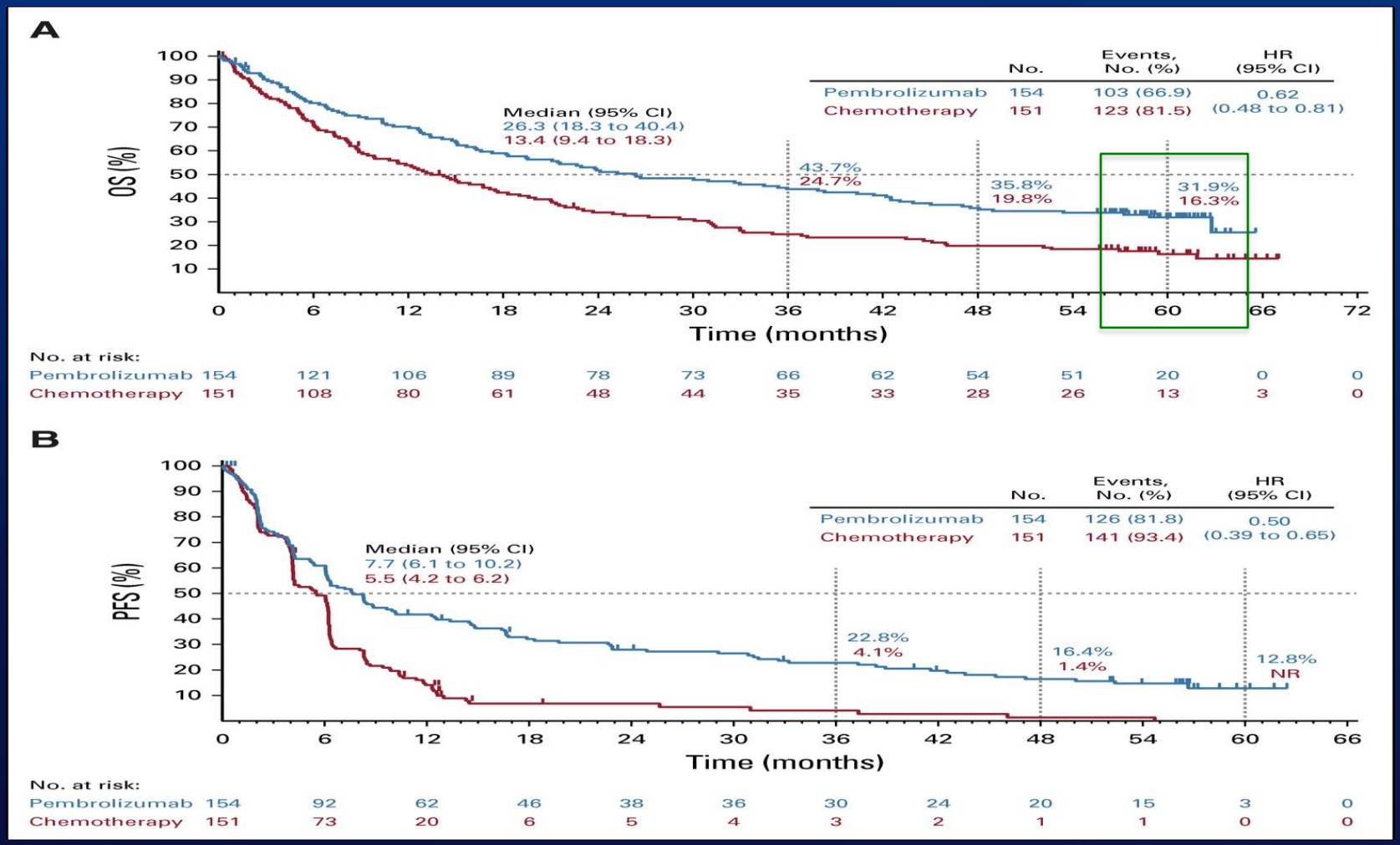
Primary: PFS (RECIST v1.1 per blinded, independent central review)

Secondary: OS, ORR, safety

Exploratory: DOR, Quality of life

Reck M et al, NEJM 2016; 375 (19): 1823-1833
Reck M et al, J Clin Oncol 2019

Updated survival data from Keynote 024



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De Castro Jr et al, JCO Oct 2022

FDA Approvals for lung cancer 2022/2023

- Adjuvant Pembrolizumab JAN 23
  **Stage IB-IIIA NSCLC (post chemo/post resection)*
- Adagrasib (accelerated approval) DEC 22
  *Advanced *+KRAS NSCLC (2nd line)*
- Tremelimumab + Durvalumab + chemo NOV 22
  **Advanced NSCLC (1st line)*
- Cemiplimab-rwlc + chemo NOV 22
  **Advanced NSCLC (1st line)*
- Fam-Trastuzumab Deruxtecan-nxki AUG 22
  ** HER-2 + mutation NSCLC (2nd line)*
- Neoadjuvant Nivolumab + Chemo MAR 22
  *Resectable NSCLC
- *Regular Approval for Selpercatinib* (had initial accelerated approval) SEP 22
  * Advanced RET+ NSCLC

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Thank You

Acknowledgment: Patients and their families

“The human spirit is much stronger than anything that could happen to it”

George Scott

Twitter: @RMManochakian

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