ASCO Direct Highlights: Lung

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Disclosures

- Mirati Therapeutics – research funding
- Lilly/NCCN – grant reviewer

2022 ASCO® ANNUAL MEETING

Phase II Randomized Study Comparing Proton Craniospinal Irradiation with Photon Involved-Field Radiotherapy for Patients with Solid Tumor Leptomeningeal Metastasis

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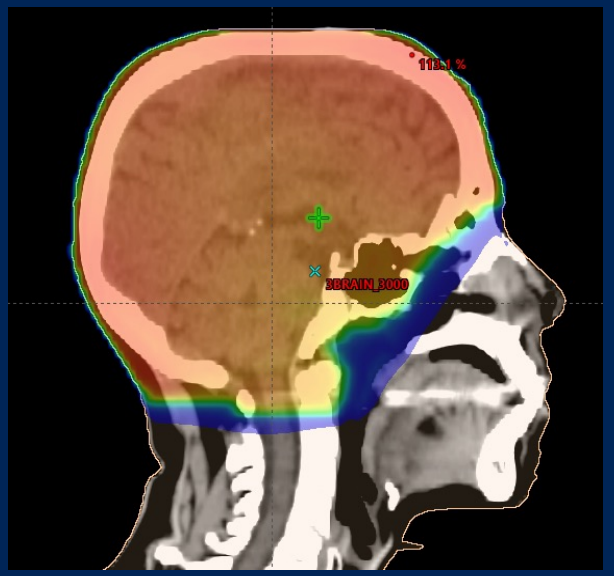
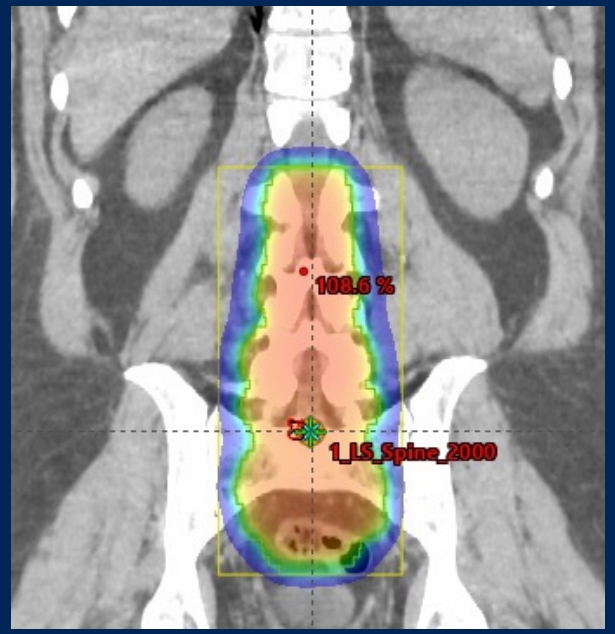
Memorial Sloan Kettering Cancer Center

Introduction

- Leptomeningeal Metastasis (LM) involves seeding of the cerebrospinal fluid (CSF)-filled leptomeningeal space surrounding the brain and spinal cord.
  - Associated with marked morbidity and mortality
  - Can lead to death within 4-6 weeks without treatment or 4-6 months with standard therapies
- Standard-of-care photon involved-field radiotherapy (IFRT), such as whole brain radiotherapy or focal spine radiotherapy, is effective for relieving symptoms but does not halt progression of disease along the leptomeningeal space
  - Supported by NCCN guidelines
  - Does not seem to improve survival

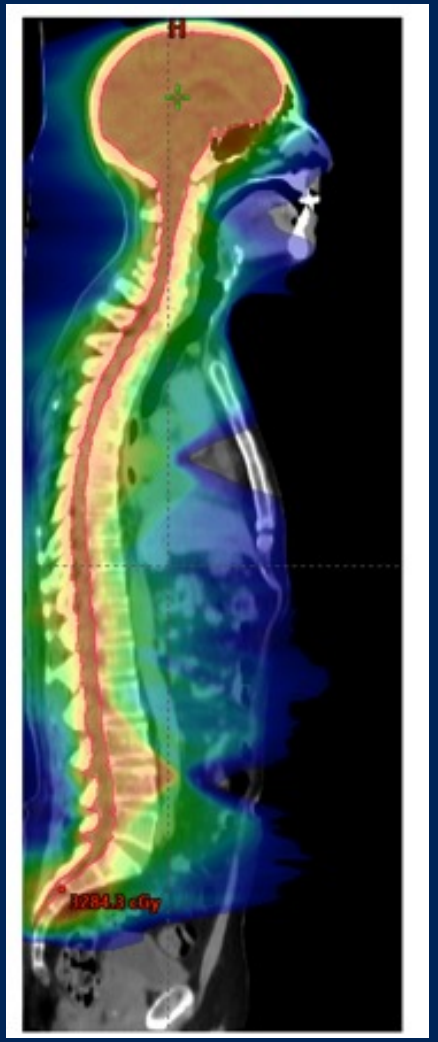




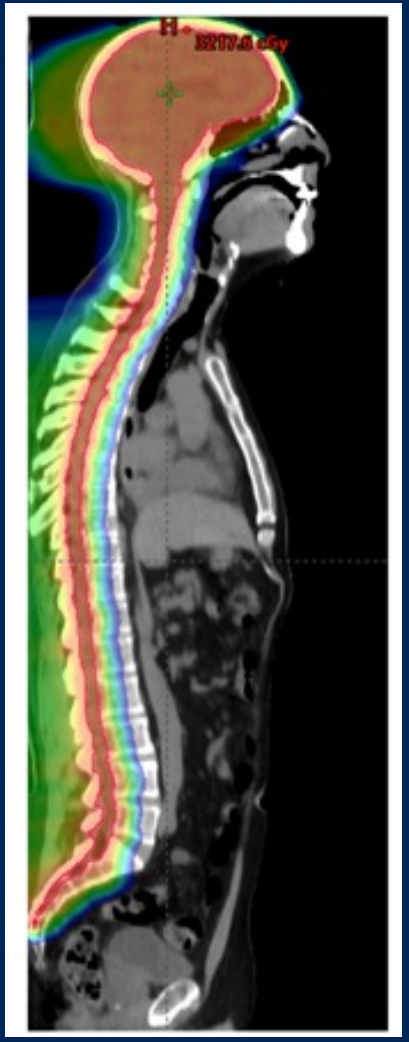
Herrlinger et al., J Neurol Sci 2004; Siegel RL et al., CA Cancer J Clin 2020; Kesari et al., Lancet Oncol 2010; Figura NB et al. BCRT 2019; Le Rhun E. et al. Annals of Oncology 2018; Zhen et al., Radiation Oncology 2020; Morris et al., JTO 2012; Hendriks et al., EJC 2019; Gani et al. Stralentherapie and Onkologie 2012; Brown et al. IJROBP 2013; Yang et al. Neuro Oncology 2020

Introduction

- Craniospinal irradiation (CSI) may potentially be beneficial in disease control as the entire leptomeningeal space is targeted.
- Proton CSI (pCSI) significantly less toxic compared to x-ray-based photon CSI evaluated prospectively in patients with medulloblastoma
  - >5% weight loss 64% photon vs. 16% proton
  - Grade 2+ nausea and vomiting 71% vs. 26%
  - Grade 3+ esophagitis 57% vs. 5%



Photon CSI

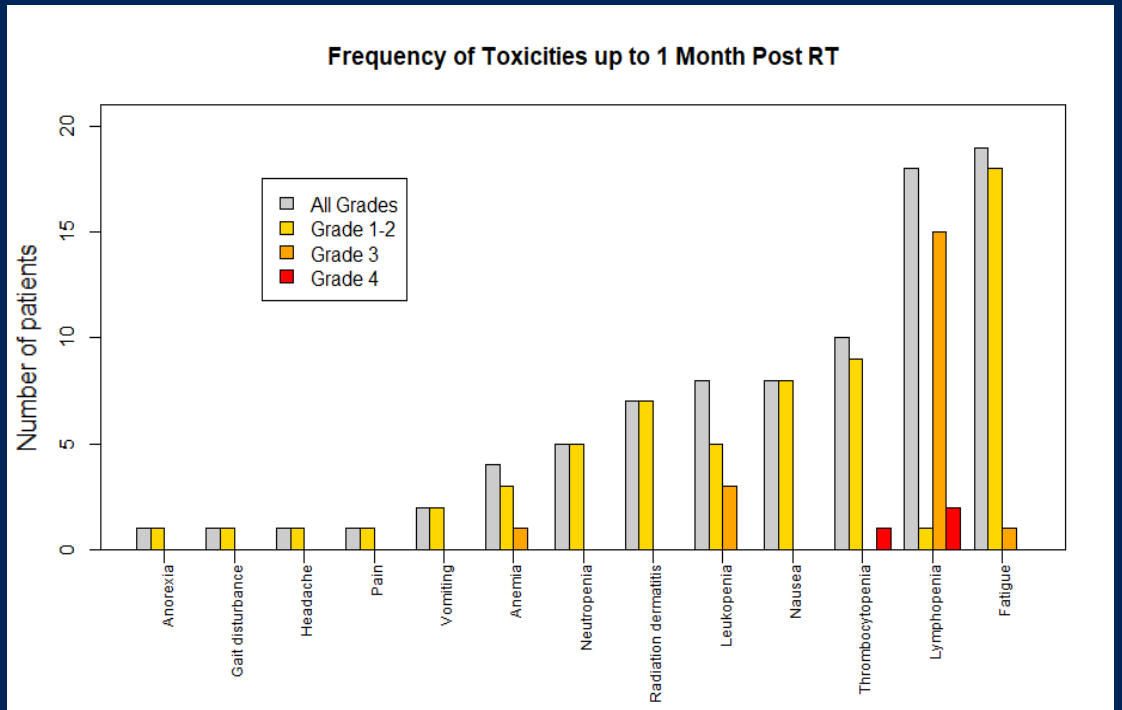


Proton CSI

Brown et al. IJROBP 2013

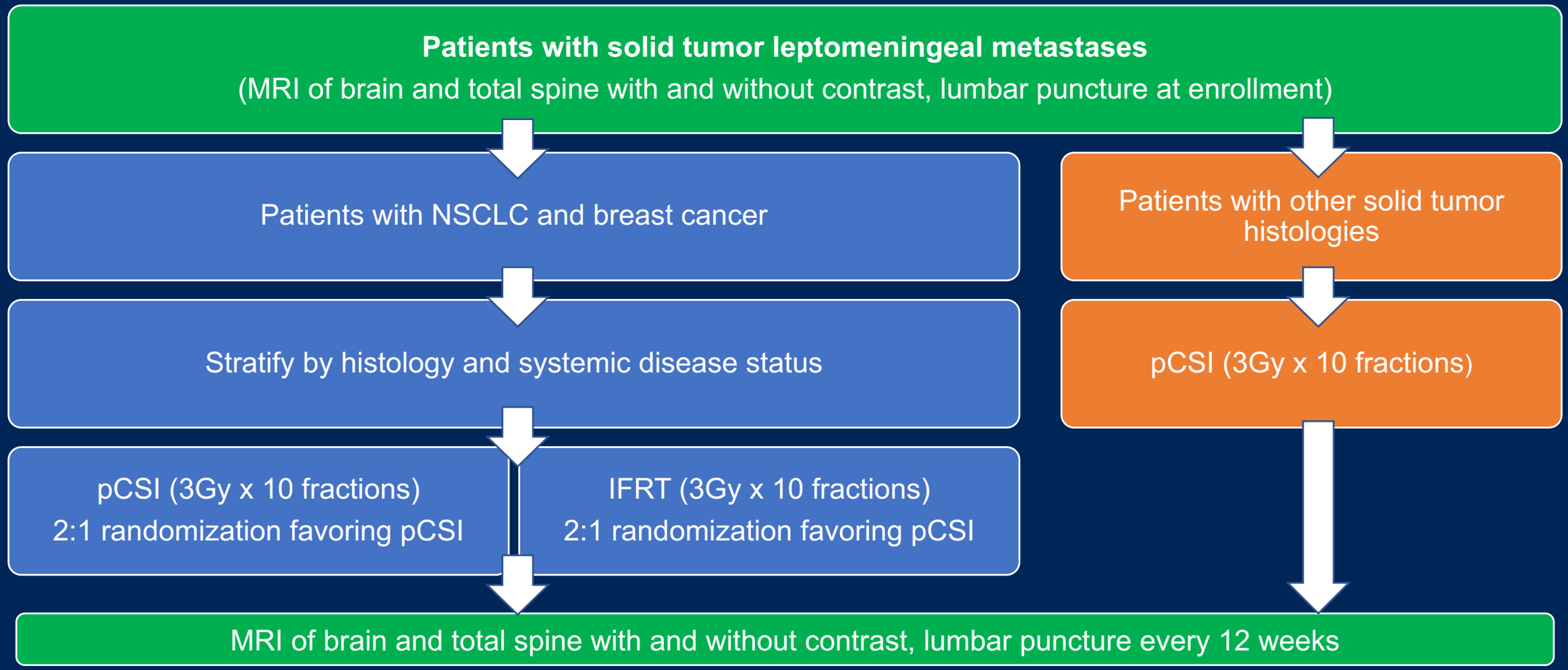
Introduction

- Phase IB study of proton craniospinal irradiation for patients with solid tumor LM (NCT03520504)
  - 21 patients enrolled 06/2018- 04/2019
  - 3Gy x 10 daily fractions
- Limited toxicities
- Promising outcomes
  - Last patient censored at 24 months
  - Median central nervous system progression-free survival (CNS PFS) 7 months (95% CI 5-13 months)
  - Median overall survival (OS) 9 months (95% CI 6-22 months)



Symptoms	Grade 3	Grade 4
Anemia	1 (5%)	0 (0%)
Leukopenia	3 (15%)	0 (0%)
Thrombocytopenia	0 (0%)	**1 (5%)**
Lymphopenia	15 (75%)	**2 (10%)**
Fatigue	**1 (5%)**	0 (0%)

Phase II Trial Design



Study Objectives

- Primary:
  - To compare CNS PFS of pCSI and photon IFRT in patients with metastatic NSCLC or breast cancer LM
- Secondary:
  - To compare OS of pCSI and photon IFRT for patients with metastatic NSCLC or breast cancer LM
  - To characterize treatment-related adverse events (TAEs, CTCAE v5.0)
- Exploratory
  - To evaluate CNS PFS, OS, and TAEs in patients with other solid tumor histology enrolled on the exploratory pCSI group

Patient Eligibility and Progression Criteria

- Patient Criteria
  - Inclusion Criteria:
    - LM established radiographically and/or with CSF cytology
    - KPS $\geq$ 60
  - Exclusion Criteria:
    - Multiple, serious major neurologic deficits including encephalopathy
    - Extensive systemic disease without reasonable systemic treatment options
- Progression of disease in the CNS defined as 1 or more below:
  - Clinical: new neurologic deficit
  - Radiographic: progressive disease using Leptomeningeal Assessment in Neuro-Oncology scale
  - Cytologic: new positive cytology in patients with previously negative cytology

Patient Characteristics- Randomized Groups

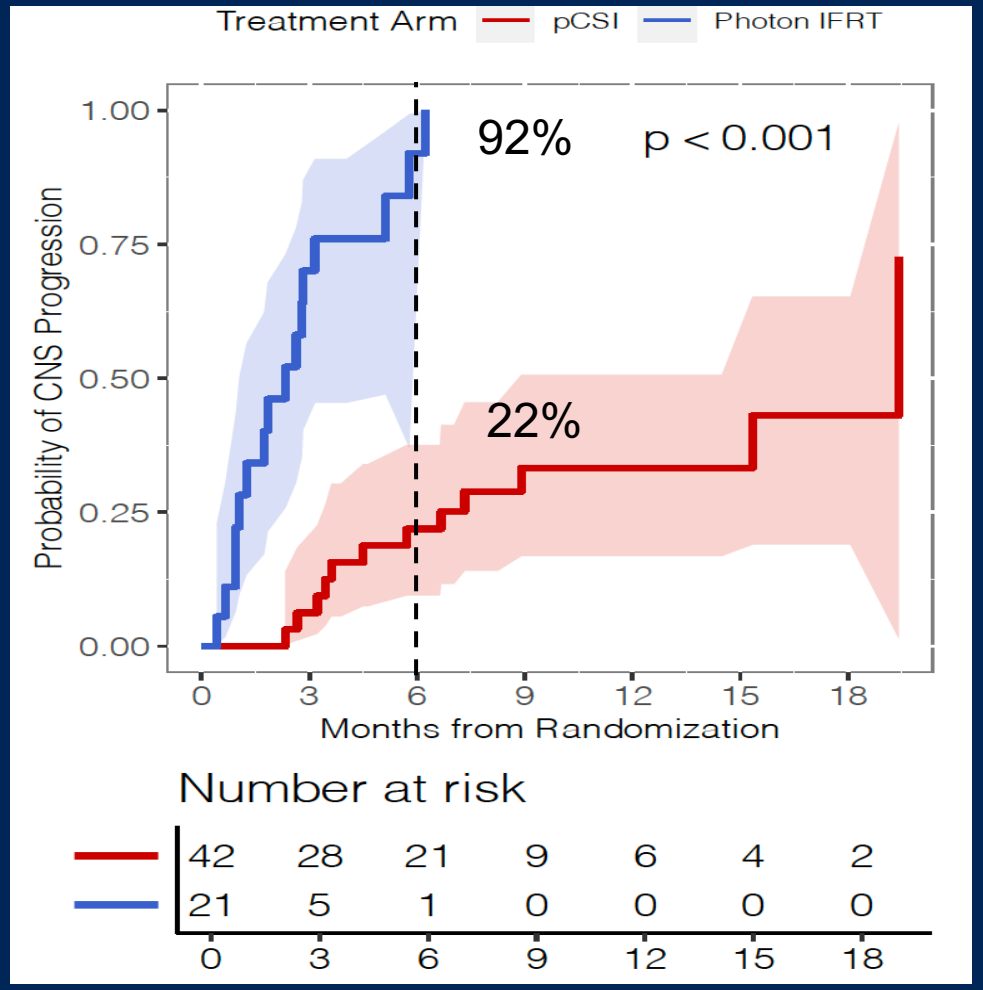
Characteristic	pCSI (N=42)	Photon IFRT (N=21)
Age (median, range)	56 (49-55)	61 (54-65)
Sex		
Female	34 (81%)	18 (86%)
Male	8 (19%)	3 (14%)
Primary Disease		
NSCLC	24 (57%)	12 (57%)
EGFR+	12 (29%)	7 (33%)
Breast	18 (43%)	9 (43%)
HER2+	6 (14%)	4 (19%)
Systemic Disease Status		
Active	22 (52%)	11 (52%)
Stable/None	20 (48%)	10 (48%)

Characteristic	pCSI (N=42)	Photon IFRT (N=21)
KPS (median, range)	80 (60-90)	80 (60-90)
At Enrollment		
Positive MRI	38 (91%)	21 (100%)
Positive Cytology	28 (67%)	11 (52%)
Positive CSF CTC	36 (86%)	17 (81%)
Brain Metastases		
Yes	28 (67%)	15 (71%)
No	14 (33%)	6 (29%)
Median Lines of Prior Systemic Therapy	2 (0-8)	2 (0-8)
IFRT Fields		
WBRT		9 (43%)
Spinal RT		1 (5%)
Both		8 (38%)

Interim Analysis Results

- Median follow up 9.3 months (95% CI 7.8-17.6 months)
- Randomized pCSI group (N=42):
  - 12 patients with CNS progression
  - 16 patients died
    - 8 with systemic progression
    - 4 with CNS progression
    - 4 with CNS and systemic progression
- Randomized IFRT group (N=21):
  - 16 patients with CNS progression
  - 14 patients died
    - 9 with CNS progression
    - 5 with CNS and systemic progression

CNS PROGRESSION RATE



PRESENTED BY:
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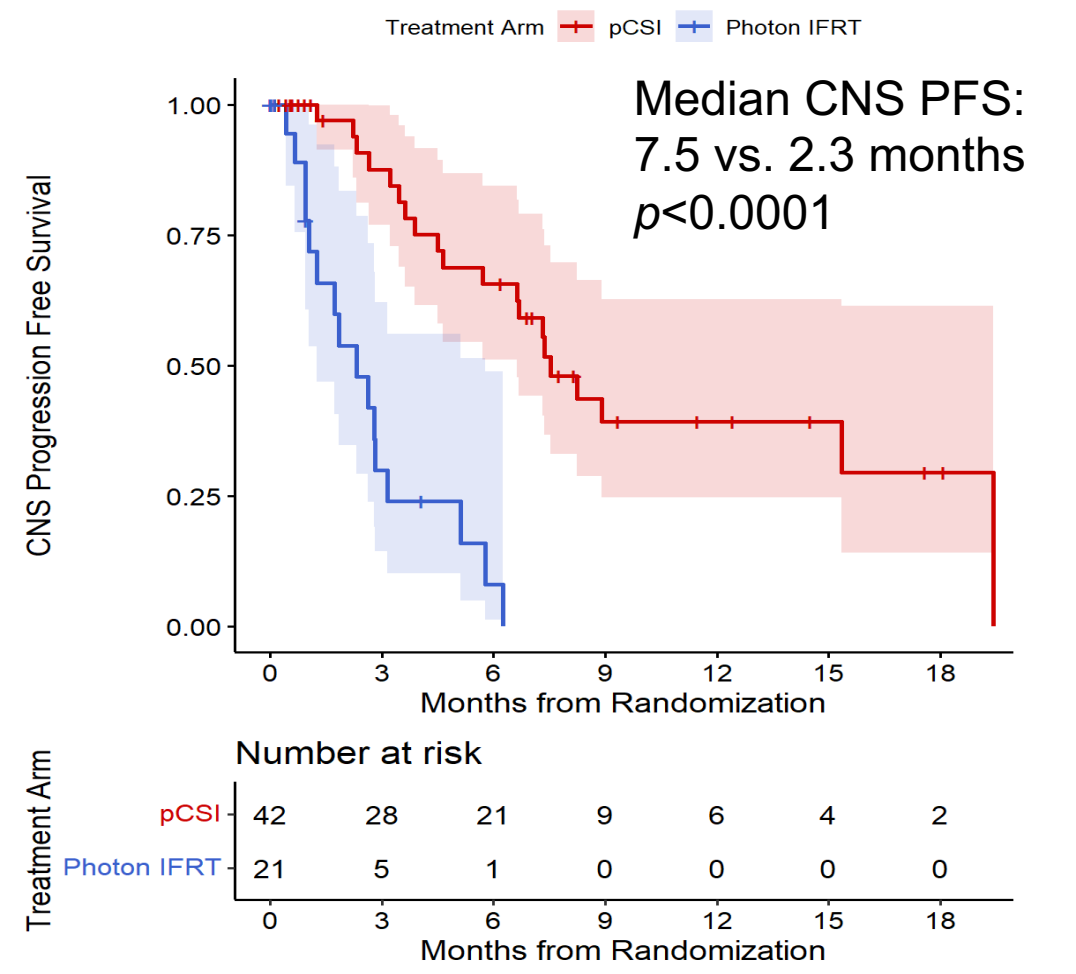
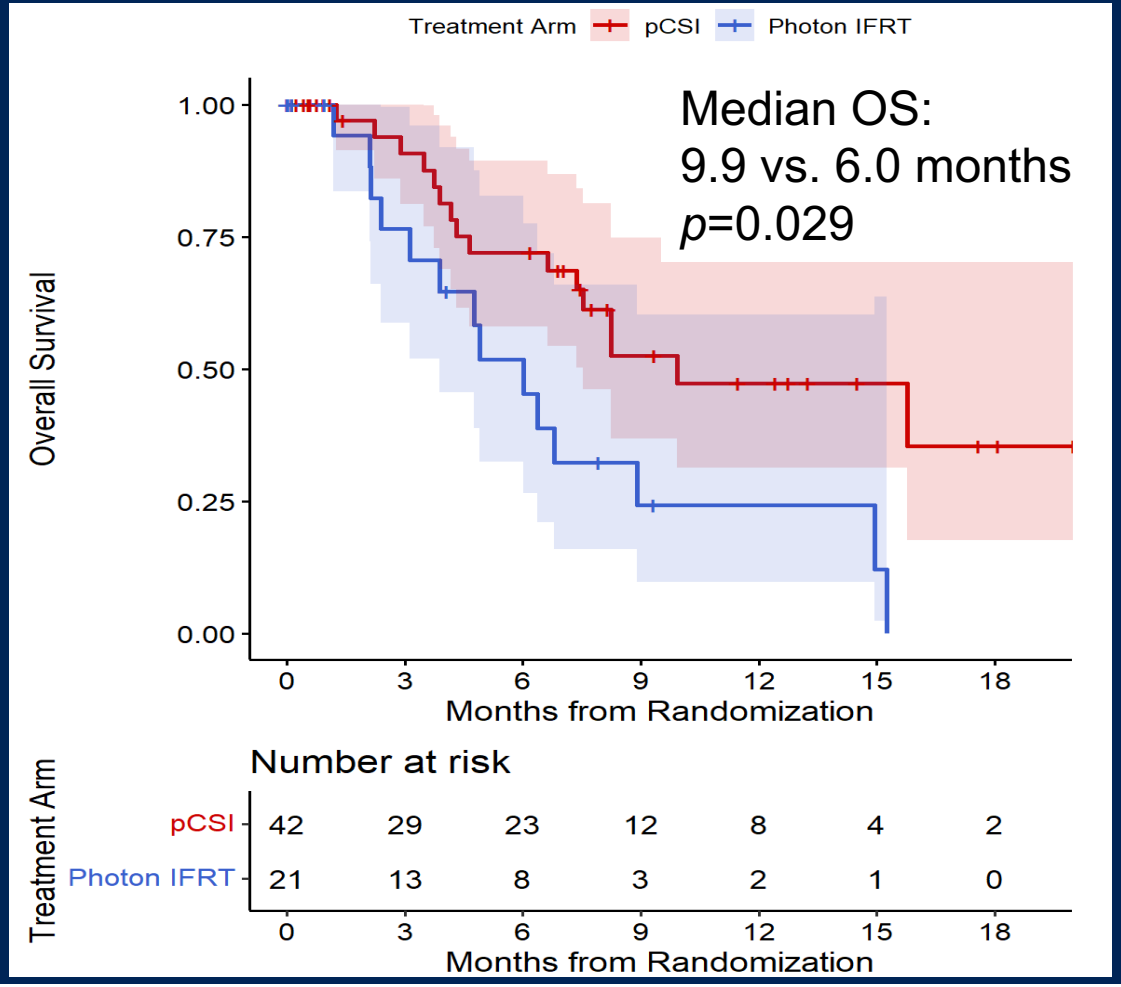
Interim Analysis Results





Interim Analysis Results

	CNS PFS			OS		
Variables	HR	95% CI	p-value	HR	95% CI	p-value
pCSI (reference: photon IFRT)	0.15	0.07-0.35	<0.001	0.43	0.21-0.92	0.029
Age at randomization	1.01	0.71-1.43	>0.9	1.26	0.86-1.84	0.2
KPS ≥80 (reference: <80)	0.97	0.46-2.06	>0.9	0.99	0.46-2.15	>0.9
Stable/non systemic disease (reference: active)	0.50	0.23-1.06	0.072	0.44	0.20-1.01	0.053
Breast histology (reference: NSCLC)	0.96	0.46-1.98	>0.9	1.03	0.47-2.30	>0.9

	Randomized pCSI group (N=42)		Randomized IFRT group (N=21)		Exploratory pCSI group (N=35)	
Symptoms	**Grade 3**	**Grade 4**	**Grade 3**	**Grade 4**	**Grade 3**	**Grade 4**
Fatigue	1 (2%)		2 (10%)			
Gait Disturbance			1 (5%)			
Headache			1 (5%)		1 (3%)	
Muscle Weakness					1 (3%)	
Nausea					1 (3%)	
Pain	1 (2%)					
Vomiting	1 (2%)				1 (3%)	
Lymphopenia		4 (10%)		4 (19%)		6 (17%)

Conclusion

- **First randomized study of optimal radiotherapy approach for solid tumor LM**
- Compared to standard-of-care photon IFRT, **pCSI significantly improved CNS PFS** (median 7.5 months vs. 2.3 months), for patients with NSCLC and breast cancer LM, meeting the primary endpoint of the study
- pCSI also had a significant **OS benefit** (median 9.9 vs. 6.0 months) compared to photon IFRT in patients with NSCLC and breast cancer LM with our data to date
- High-grade toxicities were comparable between pCSI and photon IFRT
- Yang JT et al. J Clin Oncol. 2022 Jul 8. PMID: 35802849.

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Comparison of quality of life in patients randomized to high-dose once daily (QD) thoracic radiotherapy (TRT) with standard twice daily (BID) TRT in limited stage small cell lung cancer (LS-SCLC) on CALGB 30610 (NCT00632853)

(Alliance for Clinical Trials in Oncology, Sub-study CALGB 70702)

Apar Kishor Ganti, Amylou C. Dueck, Briant Fruth, Andreas Rimner, Saiama Naheed Waqar, Michael D Mix, William J. Petty, Jeffrey A. Bogart

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Apar Kishor Ganti, MD

Background

- CALGB 30610 trial - 70Gy QD TRT was not associated with a superior overall survival compared to 45Gy BID TRT in limited stage small cell lung cancer
- Since both arms appeared to provide similar clinical benefit, other factors such as quality of life may help oncologists decide on the best treatment approach for their patients.

Patients and Methods

- Questionnaires - FACT-L, FACT Trial Outcome Index-Lung Cancer (FACT-L TOI), FACT-Esophageal Cancer Eating and Swallowing Indices, ECOG Acute Esophagitis Scale, Hospital Anxiety and Depression Scale (HADS), the EQ-5D and a single item assessing difficulty swallowing
- Time points - Baseline, 3, 5, 7, 12, 26, and 52 weeks after starting radiation therapy

Patients and Methods

- Assess treatment inconvenience at these time points.
- Primary endpoints - FACT-L TOI and FACT eating and swallowing subscales at 12 weeks
- Mean changes from baseline were compared between arms using general linear mixed models

Results

- CALGB 30610 – 646 patients
- 417 patients consented to participate in the patient-reported outcomes substudy
- Baseline PROs – 364 patients
- 342 patients – at least one follow-up PRO
- 340 patients – baseline and at least 1 follow-up PRO
- The completion rate of the questionnaires was 87% at baseline and 71% at week 52

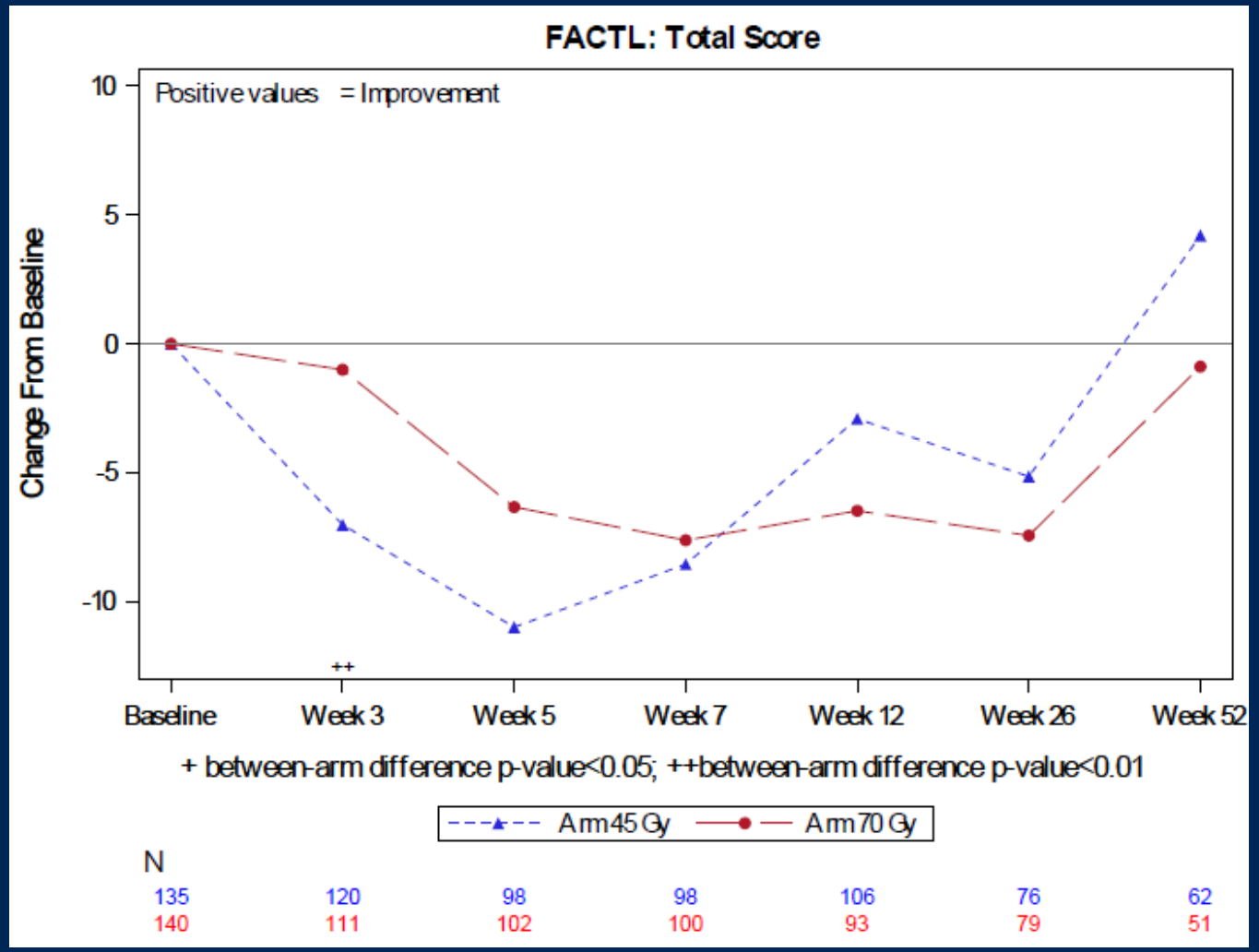
Results - Demographics

	Treatment Arm	
	45 Gy (N=167)	70 Gy (N=171)
Median Age (yrs) (Range)	64 (42.0, 81.0)	62.0 (37.0, 78.0)
Gender, n (%)		
Male	85 (50.9%)	79 (46.2%)
Female	82 (49.1%)	92 (53.8%)
Race, n (%)		
White	148 (88.6%)	146 (85.4%)
Black or African American	13 (7.8%)	17 (9.9%)
Asian	0 (0.0%)	1 (0.6%)
American Indian or Alaska Native	2 (1.2%)	1 (0.6%)
Ethnicity, n (%)		
Hispanic or Latino	6 (3.6%)	5 (2.9%)
Non-Hispanic	156 (93.4%)	156 (91.2%)
ECOG PS, n (%)		
0	78 (46.7%)	84 (49.1%)
1	82 (49.1%)	76 (44.4%)
2	7 (4.2%)	11 (6.4%)

Results

- The FACT-L total score mean worsening was significantly less in the QD arm at week 3 (-1.0 vs -7.0; P=.003)

Physical, social/family, emotional, and functional well-being; lung cancer subscale (symptoms, cognitive function, regret of smoking)



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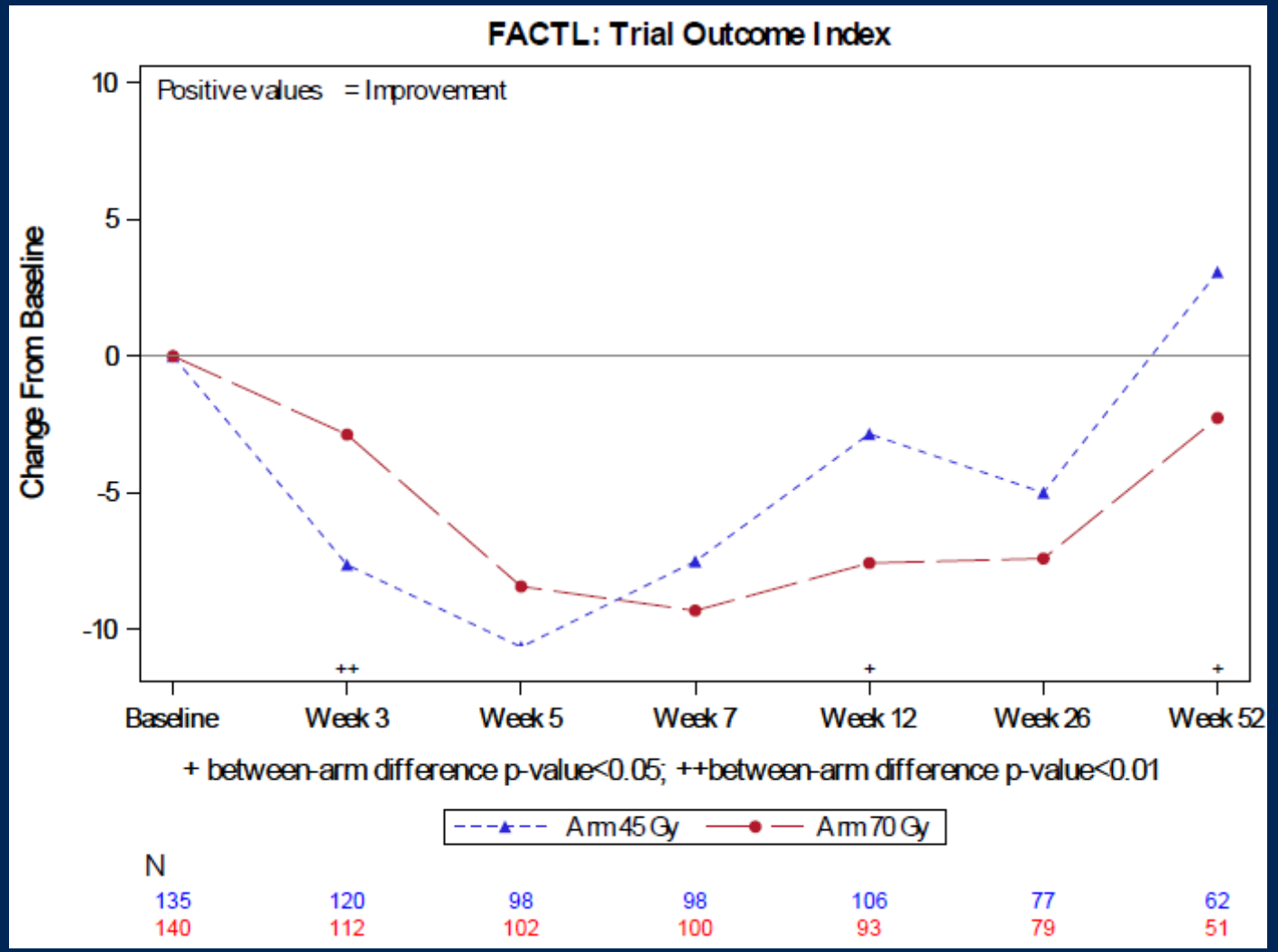
Results

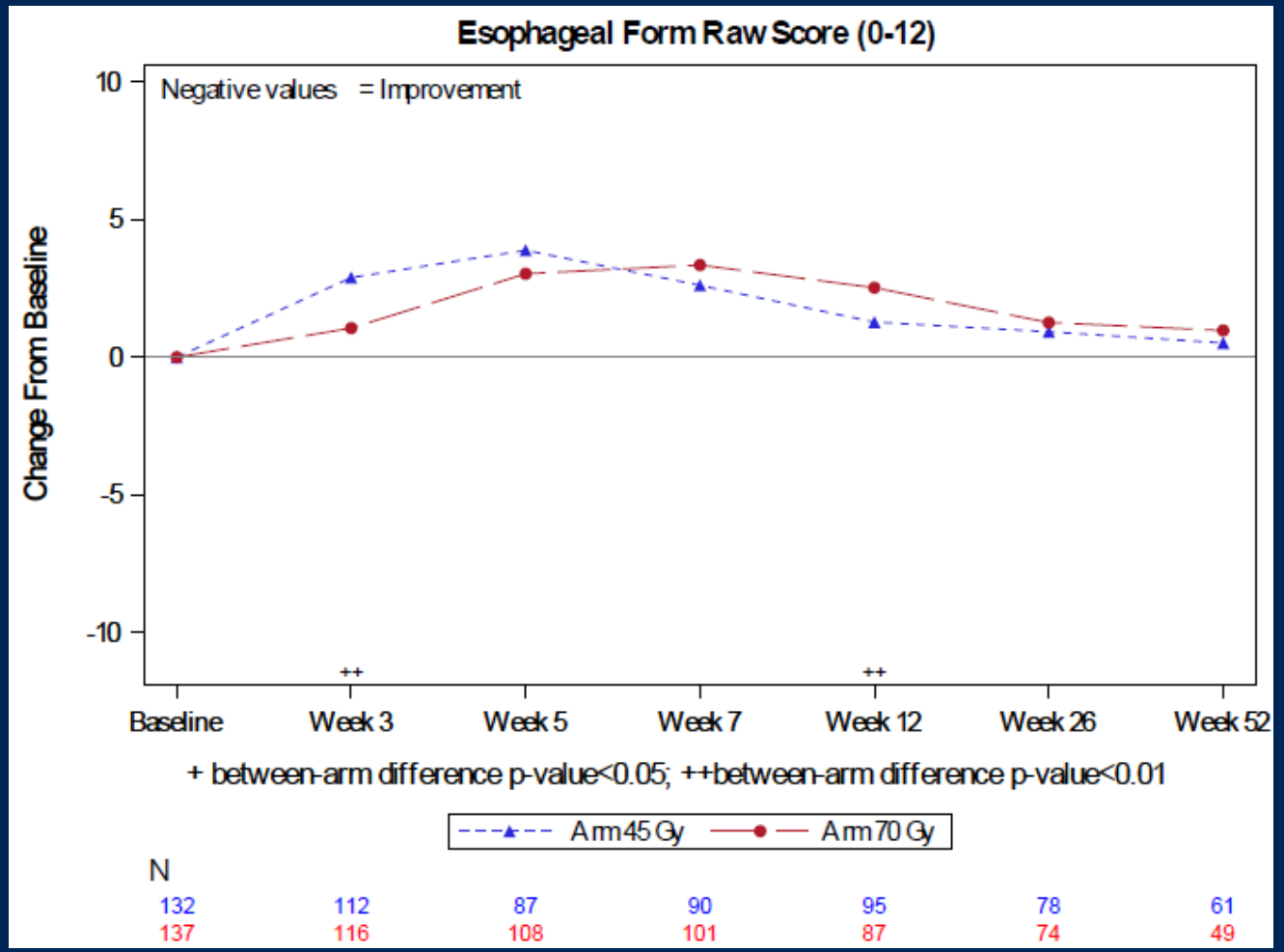
- FACT-L TOI mean worsening
  - Less in the QD arm at week 3 (-2.9 vs -7.6; P=.003)
  - Greater in the QD arm at week 12 (-7.6 vs -2.8; P=.03).

Trial Outcome Index (TOI), is the sum of the Physical, Functional, and Lung Cancer Subscales.



Results

- Acute esophagitis score
  - Worse in the BID arm at week 3 (2.89 vs. 1.06; p<.001)
  - Worse in the QD arm at week 12 (2.52 vs. 1.27; p=0.002)



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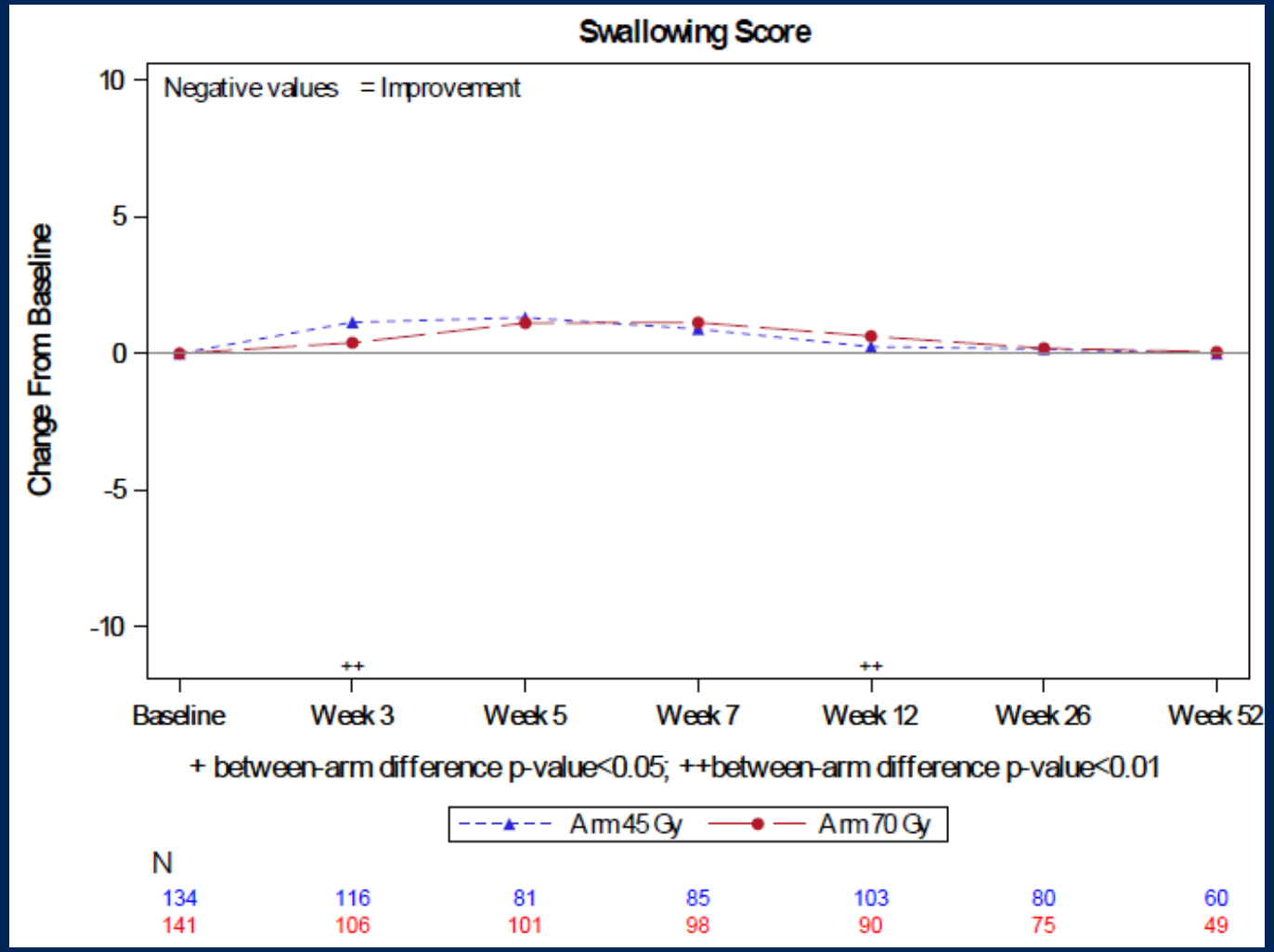
Results

- Difficulty swallowing
  - Greater in BID arm at week 3 (1.14 vs. 0.39; p<.001)
  - Greater in the QD arm at week 12 (0.63 vs. 0.24; p=.005)



Results – Treatment Convenience

	Treatment Arm		
	45 Gy (N=352)	70 Gy (N=376)	Total (N=1485)
Tx Convenience Score, n (%)			
Very inconvenient	53 (15.1%)	74 (19.7%)	127 (17.4%)
Somewhat inconvenient	63 (17.9%)	22 (5.9%)	85 (11.7%)
Somewhat convenient	75 (21.3%)	88 (23.4%)	163 (22.4%)
Very convenient	161 (45.7%)	192 (51.1%)	353 (48.5%)
Convenience Category, n (%)*			
Inconvenient	116 (33.0%)	96 (25.5%)	212 (29.1%)
Convenient	236 (67.0%)	280 (74.5%)	516 (70.9%)

* $p<.05$

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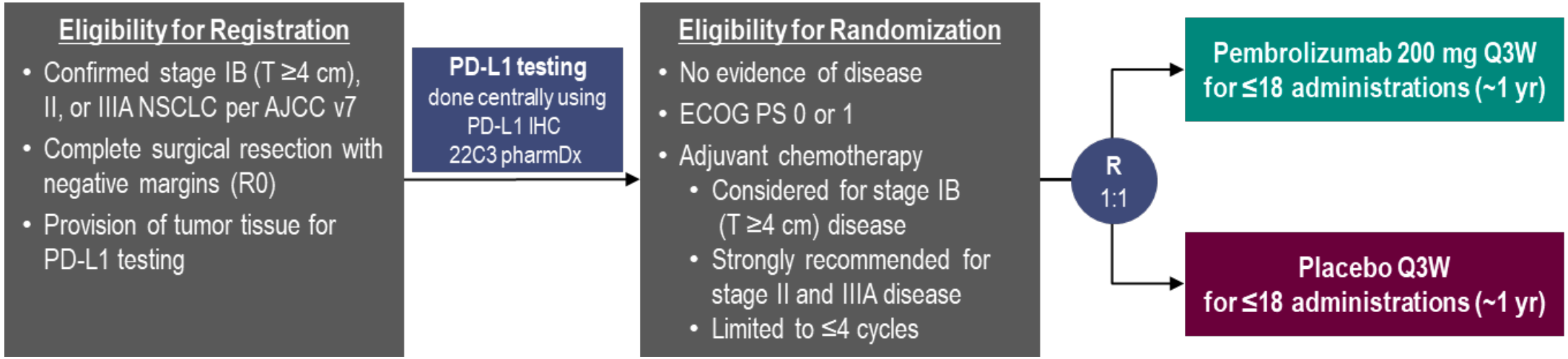
Conclusions

- Both QD and BID radiation regimens were well tolerated.
- The QD arm had better quality of life scores at week 3, but worse scores at week 12
- The QD arm was perceived to be less inconvenient

Abstract 8512: EORTC-1416-LCG/ETOP 8-15 –PEARLS/KEYNOTE-091 Study of Pembrolizumab versus Placebo for Completely Resected Early-Stage NSCLC: Outcomes in Subgroups Related to Surgery, Disease Burden, and Adjuvant Chemotherapy Use - O'Brien et. al.



Primary endpoints: DFS overall population, DFS in PDL1 >= 50%
Secondary: DFS in PDL1>=1%, OS, …
Stratification by stage, PDL1, chemotherapy, geographic region

Patient Characteristics

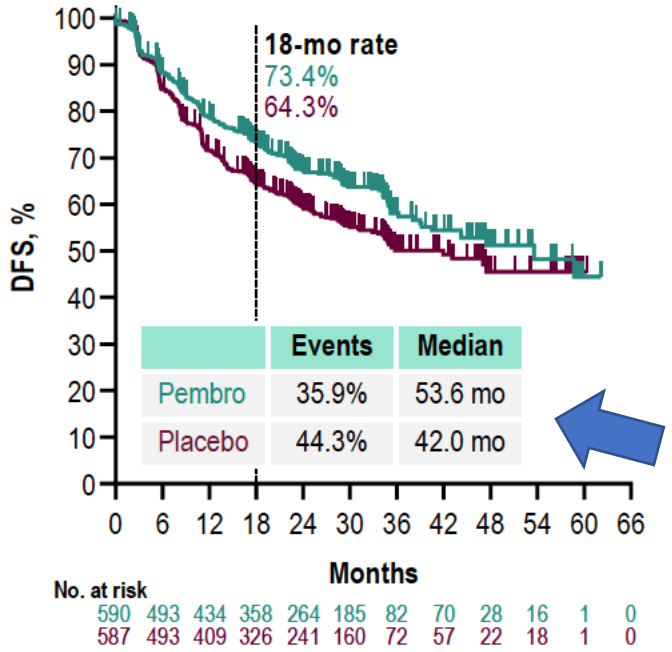
Characteristic	Overall		PD-L1 TPS ≥50%	
	Pembro (N = 590)	Placebo (N = 587)	Pembro (N = 168)	Placebo (N = 165)
Age, median (range), y	65.0 (31-87)	65.0 (37-85)	64.5 (38-82)	65.0 (37-85)
Male sex	68.0%	68.7%	72.0%	70.3%
Geographic region				
Asia	18.0%	17.9%	17.3%	17.6%
Eastern Europe	19.7%	19.3%	18.5%	18.2%
Western Europe	51.4%	51.3%	53.6%	53.9%
Rest of world	11.0%	11.6%	10.7%	10.3%
ECOG PS 1	35.6%	41.6%	31.0%	38.8%

Patient Characteristics

Characteristic	Overall		PD-L1 TPS ≥50%	
	Pembro (N = 590)	Placebo (N = 587)	Pembro (N = 168)	Placebo (N = 165)
Current/former smoker	85.3%	88.8%	91.7%	92.1%
Nonsquamous histology	67.5%	61.8%	61.3%	63.6%
Received adjuvant chemotherapy	85.8%	85.9%	85.1%	85.5%
Pathologic stage[a]				
IB	14.2%	14.5%	12.5%	13.3%
II	55.8%	57.6%	56.5%	56.4%
IIIA	30.0%	27.6%	31.0%	30.3%
EGFR mutation[b]	6.6%	5.8%	3.6%	3.0%
ALK translocation[c]	1.2%	1.2%	1.8%	0.0%

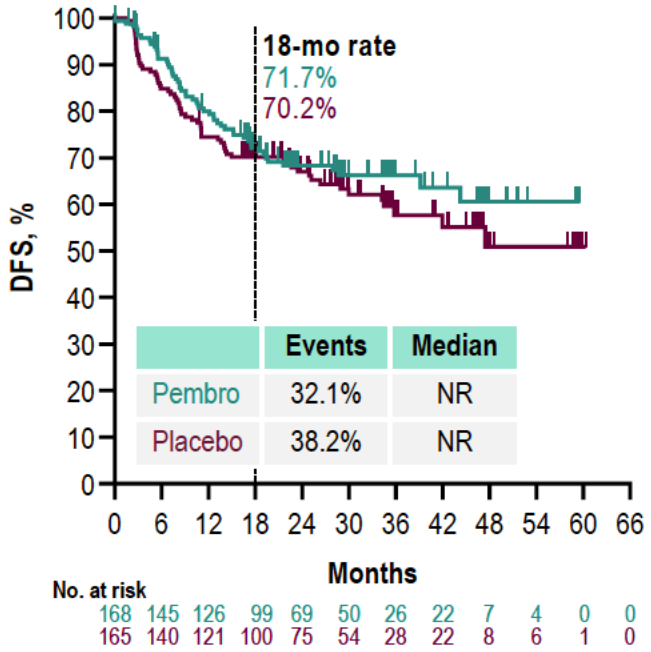
PEARLS/KEYNOTE-091:
Primary Results From the Protocol-Specified Second Interim Analysis (IA2)

DFS, Overall Population
HR 0.76 (95% CI 0.63-0.91)
***P* = 0.0014**



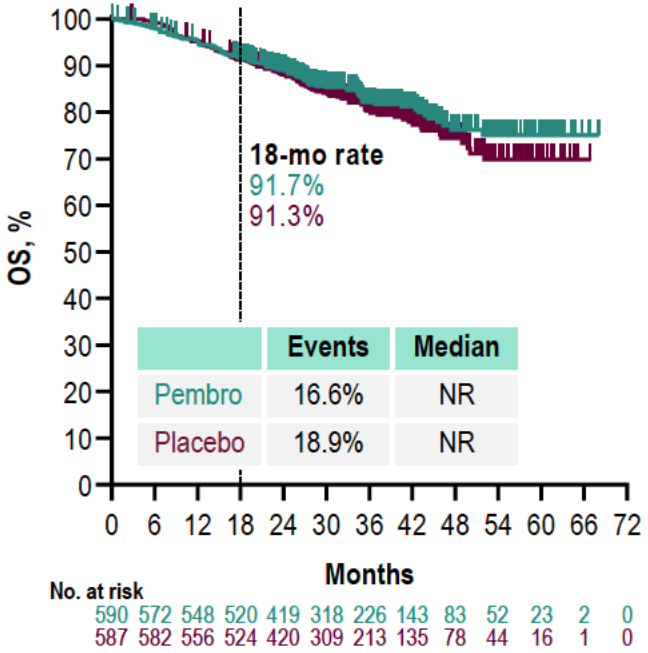
	Events	Median
Pembro	35.9%	53.6 mo
Placebo	44.3%	42.0 mo

DFS, PD-L1 TPS ≥50% Population
HR 0.82 (95% CI 0.57-1.18)
***P* = 0.14**



	Events	Median
Pembro	32.1%	NR
Placebo	38.2%	NR

OS, Overall Population
HR 0.87 (95% CI 0.67-1.15)
***P* = 0.17**



	Events	Median
Pembro	16.6%	NR
Placebo	18.9%	NR

DFS benefit generally consistent across most protocol-specified subgroups, including PD-L1 TPS <1% (HR 0.78, 95% CI 0.58-1.03) and 1-49% (HR 0.67, 95% CI 0.48-0.92)

Overall safety profile generally as expected for pembrolizumab monotherapy

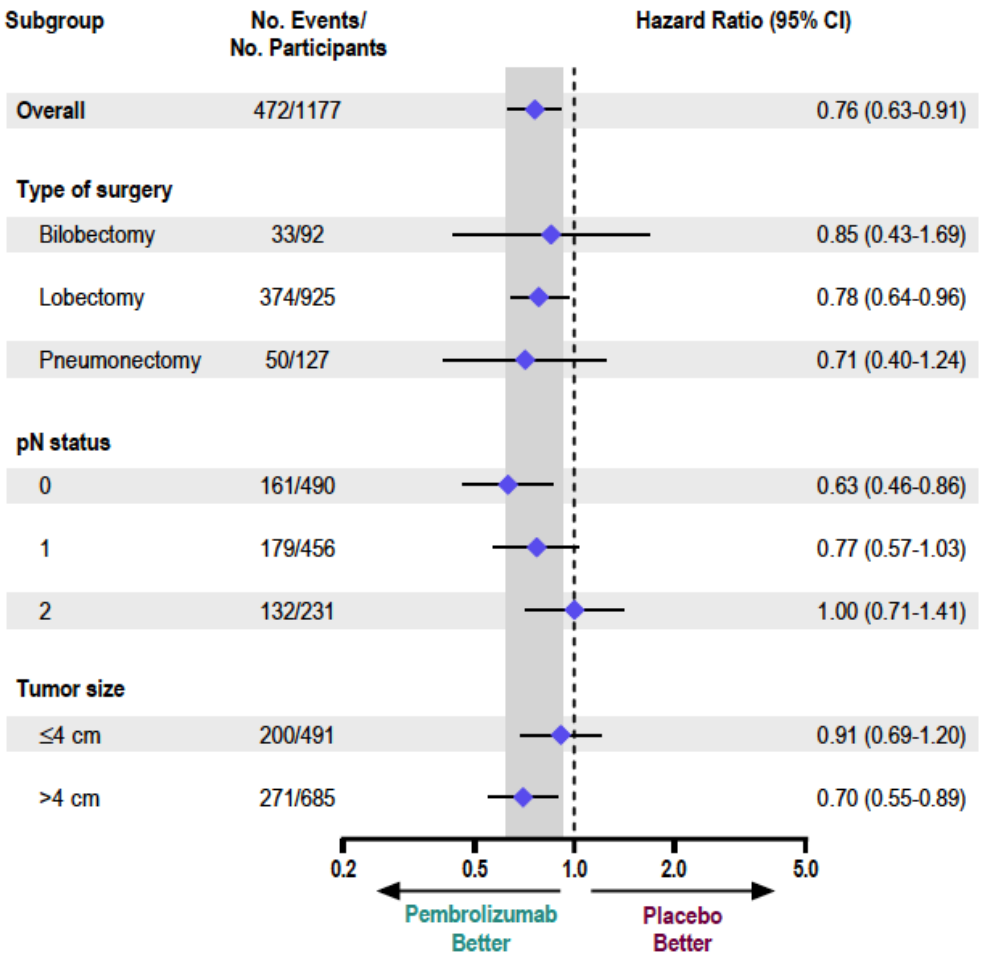
Objective: Explore the Potential Impact of the Type of Surgical Resection, Baseline Disease Burden, and Use of Adjuvant Chemotherapy on DFS at IA2

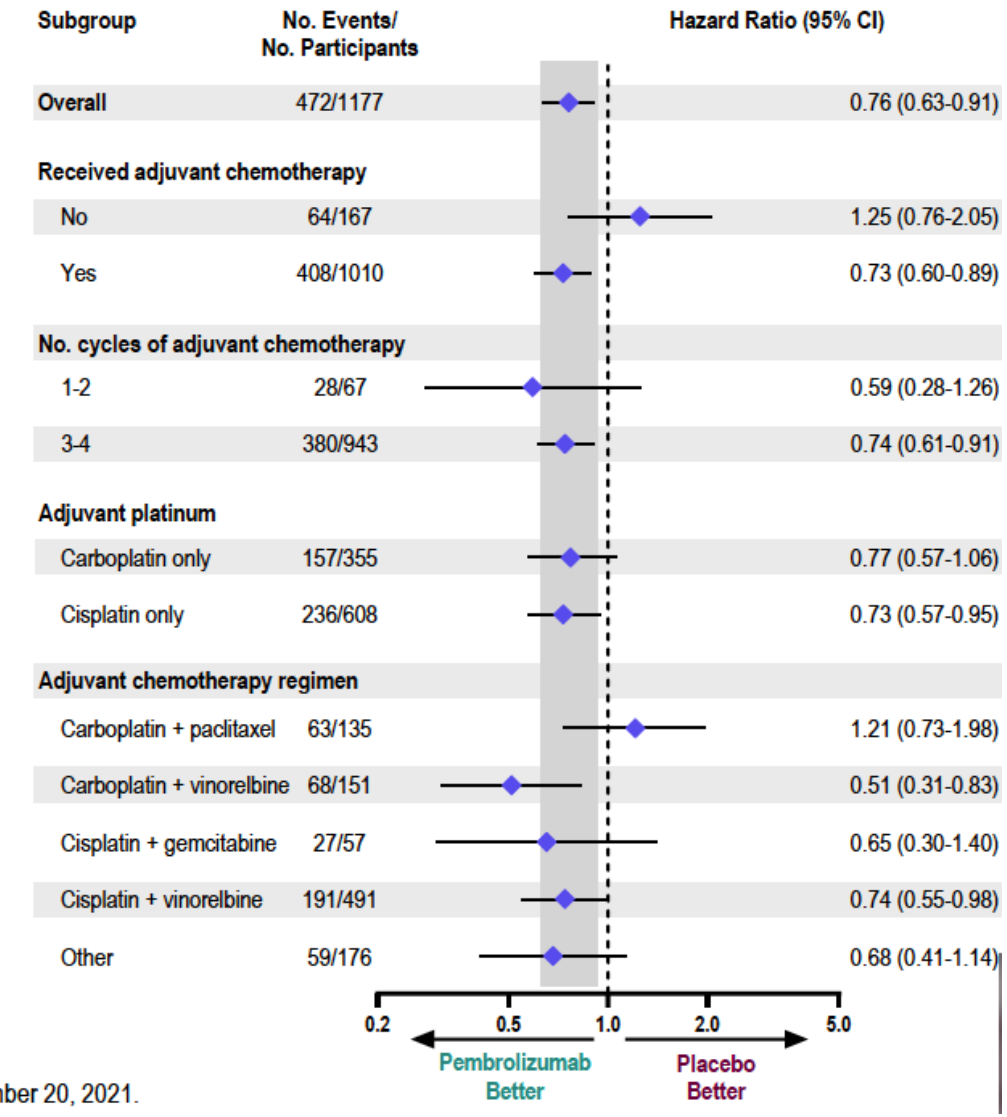
	Pembro (N = 590)	Placebo (N = 587)
Type of surgery, n (%)		
Bilobectomy	47 (8.0)	45 (7.7)
Lobectomy	461 (78.1)	464 (79.0)
Pneumonectomy	65 (11.0)	62 (10.6)
Other	17 (2.9)	16 (2.7)
pN status, n (%)		
0	233 (39.5)	257 (43.8)
1	233 (39.5)	223 (38.0)
2	124 (21.0)	107 (18.2)
Tumor size, n (%)		
≤4 cm	252 (42.7)	239 (40.7)
>4 cm	337 (57.1)	348 (59.3)
Missing	1 (0.2)	0

	Pembro (N = 590)	Placebo (N = 587)
Received adjuvant chemotherapy		
No, n (%)	84 (14.2)	83 (14.1)
Reason for not receiving, n		
Participant refused	36	30
Physician decision[a]	46	47
Unknown	2	6
Disease stage in those who did not receive, n		
IB	24	30
II	48	43
IIIA	12	10
Yes, n (%)	506 (85.8)	504 (85.9)
1-2 cycles	35 (5.9)	32 (5.5)
3-4 cycles	471 (79.8)	472 (80.4)

	Pembro (N = 590)	Placebo (N = 587)
Type of adjuvant platinum, n (%)		
Carboplatin-based only	184 (31.2)	171 (29.1)
Cisplatin-based only	301 (51.0)	307 (52.3)
Carboplatin- and cisplatin-based	21 (3.6)	26 (4.4)
Adjuvant regimen, n (%)		
Carboplatin + paclitaxel	60 (10.2)	75 (12.8)
Carboplatin + vinorelbine	81 (13.7)	70 (11.9)
Cisplatin + gemcitabine	27 (4.6)	30 (5.1)
Cisplatin + vinorelbine	241 (40.8)	250 (42.6)
Other	97 (16.4)	79 (13.5)

Results: DFS in Subgroups Related to Surgical Resection, Disease Burden, and Use of Adjuvant Chemotherapy





95% CIs of all subgroups overlapped the 95% CI of the overall population and included the overall HR of 0.76. Data cutoff date: September 20, 2021.

Conclusions

- In this exploratory analysis, pembrolizumab generally improved DFS regardless of the type of surgical resection, degree of lymph node involvement, tumor size, and type and extent of adjuvant chemotherapy
  - Exploratory subgroup analysis results should be interpreted with caution due to the lack of power and lack of multiplicity adjustment
- Together with the overall efficacy and safety findings, these data support the benefit of adjuvant pembrolizumab for stage IB (T ≥4 cm) to IIIA NSCLC following complete resection and, if recommended, adjuvant chemotherapy

Pembrolizumab adjuvant therapy remains investigational – FDA review by 1/29/2023
NCCN 2A /FDA indicated immunotherapy (neo)adjuvant therapy for NSCLC

1. Nivolumab in combination with platinum doublet chemotherapy with resectable (tumors ≥4 cm or node positive)
2. Atezolizumab for patients with completely resected stage IIB-IIIA or high-risk stage IIA PD-L1+ (≥1%) NSCLC

2022 ASCO® ANNUAL MEETING

FDA

Outcomes of anti-PD-(L)1 therapy with or without chemotherapy (chemo) for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 score ≥50%: FDA Pooled Analysis

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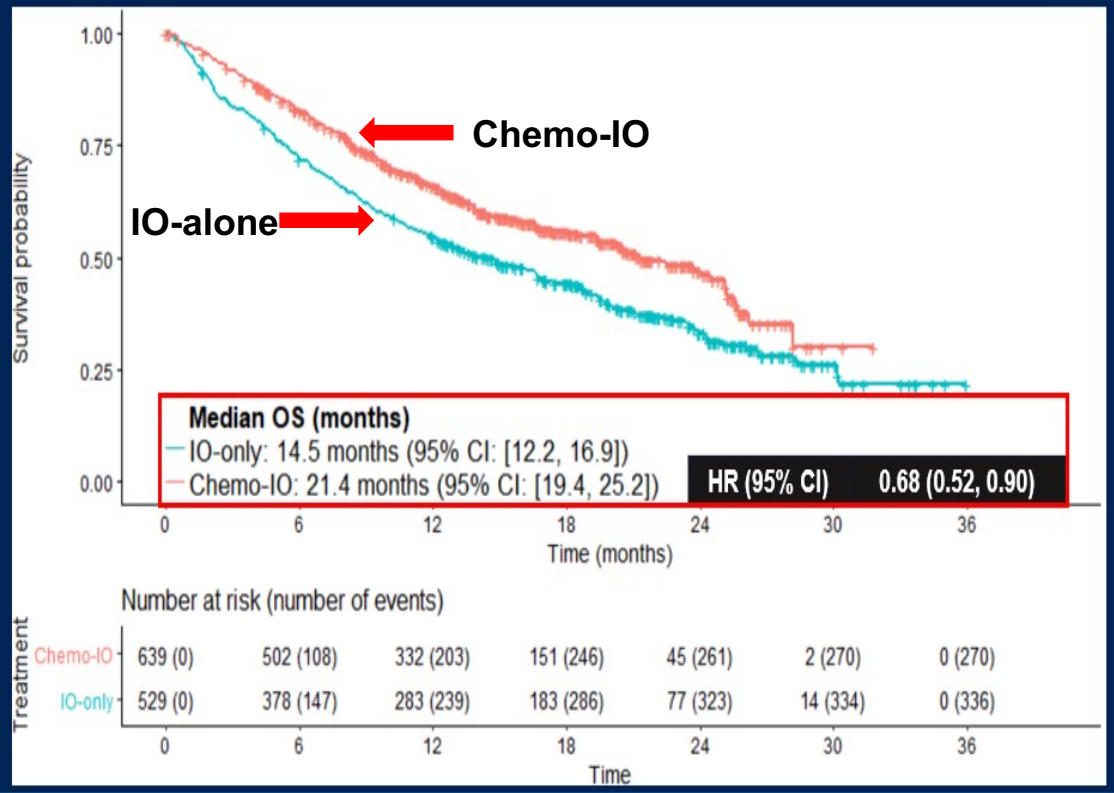
FDA-approved regimens for advanced/metastatic NSCLC not harboring tumor genomic alterations

PD-L1 level	Regimen	Histology	Approval endpoint
≥ 50%	**Pembrolizumab**	NSCLC	**OS** & PFS
	Atezolizumab [a]	NSCLC	**OS**
	Cemiplimab	NSCLC	**OS** & PFS
≥ 1%	**Pembrolizumab**	NSCLC	**OS**
	Nivolumab + Ipilimumab	NSCLC	**OS**
None	**Pembrolizumab** + Platinum + Pemetrexed [b]	NSq-NSCLC	**OS** & PFS
	Pembrolizumab + Carboplatin + Paclitaxel	Sq-NSCLC	**OS** & PFS
	Atezolizumab + Bevacizumab + Carboplatin + Paclitaxel	NSq-NSCLC	**OS** & PFS
	Atezolizumab + Carboplatin + Nab-paclitaxel	NSq-NSCLC	**OS** & PFS
	Nivolumab + Ipilimumab + Platinum doublet	NSCLC	**OS**

Abbreviations: NSCLC=non-small cell lung cancer; Nsq=non-squamous; OS=overall survival; PD-L1=programmed death ligand-1; PFS=progression-free survival; Sq=squamous.
[a] PD-L1 high population for atezolizumab defined as PD-L1 staining ≥ 50% of tumor cells or tumor-infiltrating immune cells covering ≥ 10% of the tumor area.
[b] Initial Accelerated approval in 2017 based on PFS.

Prior Work presented at 2021 Meeting PDL1 1-49%

Exploratory OS: NSCLC PDL1 1-49%



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Oladimeji Akinboro; June 4, 2021

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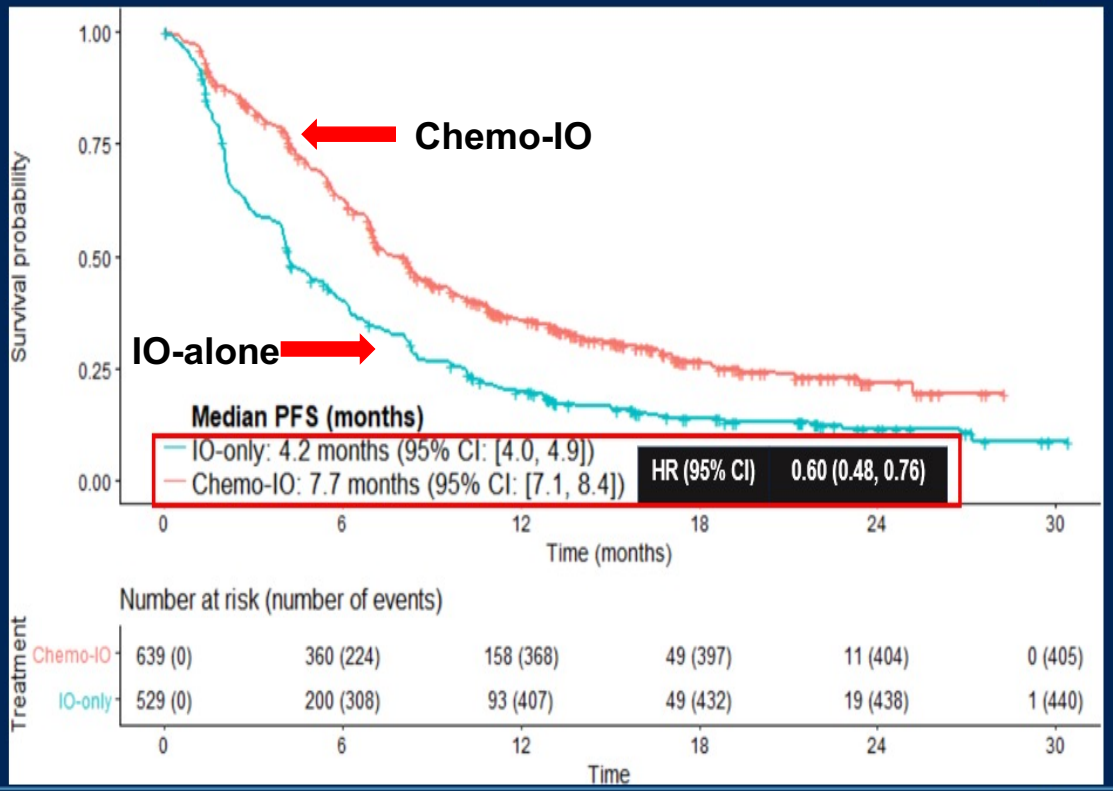
Exploratory PFS: NSCLC PDL1 1-49%



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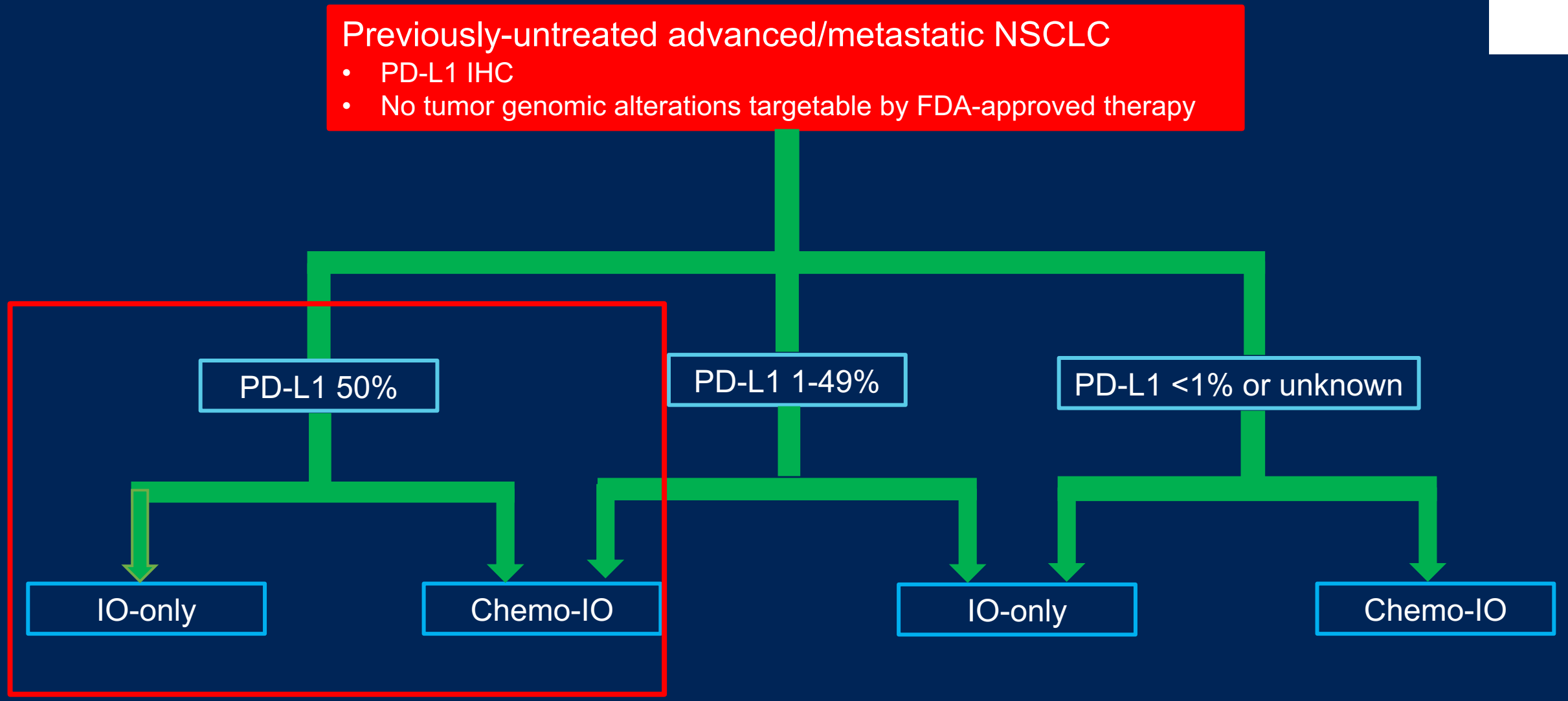

Abbreviations: Chemo-IO=platinum-based doublet chemotherapy plus immunotherapy; IO=immunotherapy; NSCLC=non-small-cell lung cancer; PD-L1=programmed death ligand-1.

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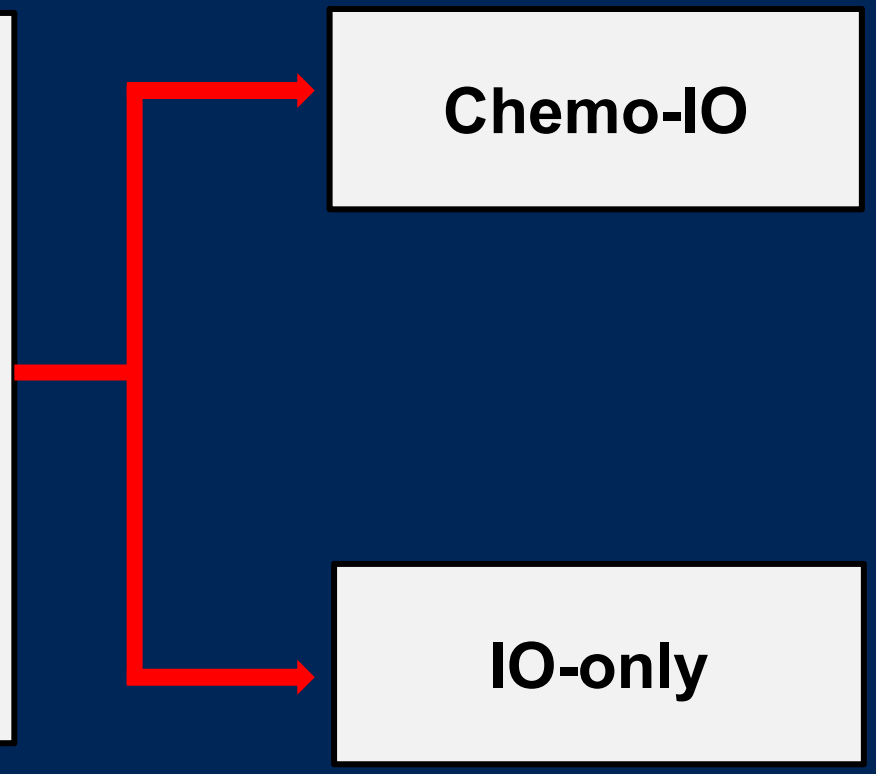
Study Design

Pooled Analysis Population

- Advanced NSCLC
- PD-L1 TPS ≥50%
  - Excluded staining by tumor-infiltrating immune cells
- No sensitizing *EGFR* mutations or *ALK* alterations
- Clinical trial supported FDA approval of IO-based regimen



Exploratory Primary Outcome measure

- OS

Other exploratory outcome measures

- PFS
- ORR

Sub-group analyses

- Age (yrs): *<65 vs 65-75 vs ≥75*
- ECOG PS: *0 vs. ≥ 1*
- Smoking history: *Never vs. Ever*

Abbreviations: *ALK*=anaplastic lymphoma kinase gene; Chemo-IO= platinum-based doublet chemotherapy plus immunotherapy; ECOG PS=Eastern Cooperative Oncology Group Performance Status; *EGFR*=epidermal growth factor receptor gene; FDA=U.S. Food and Drug Administration; IO=immunotherapy; NSCLC=non-small-cell lung cancer; ORR=objective response rate; OS=overall survival; PD-L1=programmed death ligand-1; PFS=progression-free survival; TPS=tumor proportion score; yrs=years.

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Statistical analysis

- OS and PFS:
  - Medians estimated with Kaplan-Meier methods
  - Hazard ratios estimated with Cox proportional hazards model stratified by trial

- ORR:
  - Odds ratios estimated with a logistic regression model with trial as a covariate

- All analyses were covariate-adjusted for:
  - Age, sex, race, ECOG PS, histology and smoking history

Abbreviations: ECOG PS=Eastern Cooperative Oncology Group Performance Status; ORR=objective response rate; OS=overall survival; PFS=progression-free survival.

Clinical trials of first-line Chemo-IO and IO regimens included in FDA pooled analysis

Chemo-IO Trials		IO-only Trials	
Trial	Investigational Regimen	Trial	Investigational Regimen
KEYNOTE-021*	**Pembrolizumab** + Chemo**	CheckMate 026	**Nivolumab****
KEYNOTE-189	**Pembrolizumab** + Chemo**	KEYNOTE-024	**Pembrolizumab****
KEYNOTE-407	**Pembrolizumab** + Chemo**	KEYNOTE-042	**Pembrolizumab****
IMpower150	**Atezolizumab** + Bevacizumab + Chemo***	IMpower110	**Atezolizumab****
IMpower130	**Atezolizumab** + Chemo**	CheckMate 227	**Nivolumab** + **Ipilimumab****
CheckMate-9LA	**Nivolumab** + **Ipilimumab** + Chemo**	EMPOWER-Lung 1	**Cemiplimab****

Abbreviations: Chemo-IO=platinum-based doublet chemotherapy immunotherapy; IO=immunotherapy.
* Cohort G
** Control arms: Platinum-based doublet chemotherapy
*** Control arm in IMpower150: Bevacizumab plus platinum-based doublet chemotherapy

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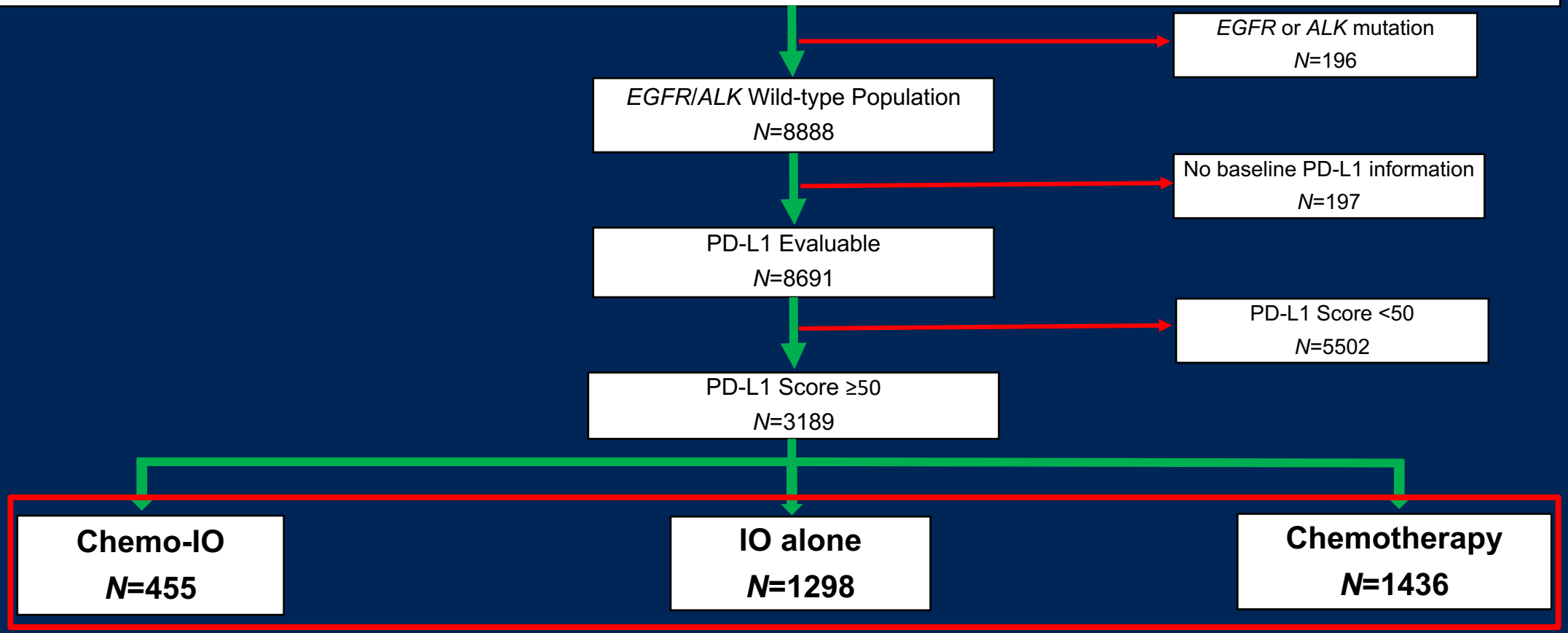
Consort Diagram

All patients in the Chemo-IO, IO-Only, and Chemotherapy arms from randomized controlled trials which supported FDA approvals in advanced NSCLC (12 Studies)

N=9084



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Demographic and baseline characteristics

		Chemo-IO (*N*=455)	IO alone (*N*=1,298)	Chemo (*N*=1,436)	Overall (*N*=3,189)
Age	Median, years	65	64	64	64
	<65 years, %	49	53	50	51
	65-74 years, %	41	36	39	38
	≥75 years, %	10	11	11	11
Sex	Female	37	29	31	31
Race	White, %	91	77	80	80
	Black, %	1	1	2	1
	Asian, %	8	20	16	16
Smoking history	Ever smoked, %	87	89	88	89
ECOG PS	≥1, %	59	68	67	66
Histology	Non-squamous, %	78	69	68	70

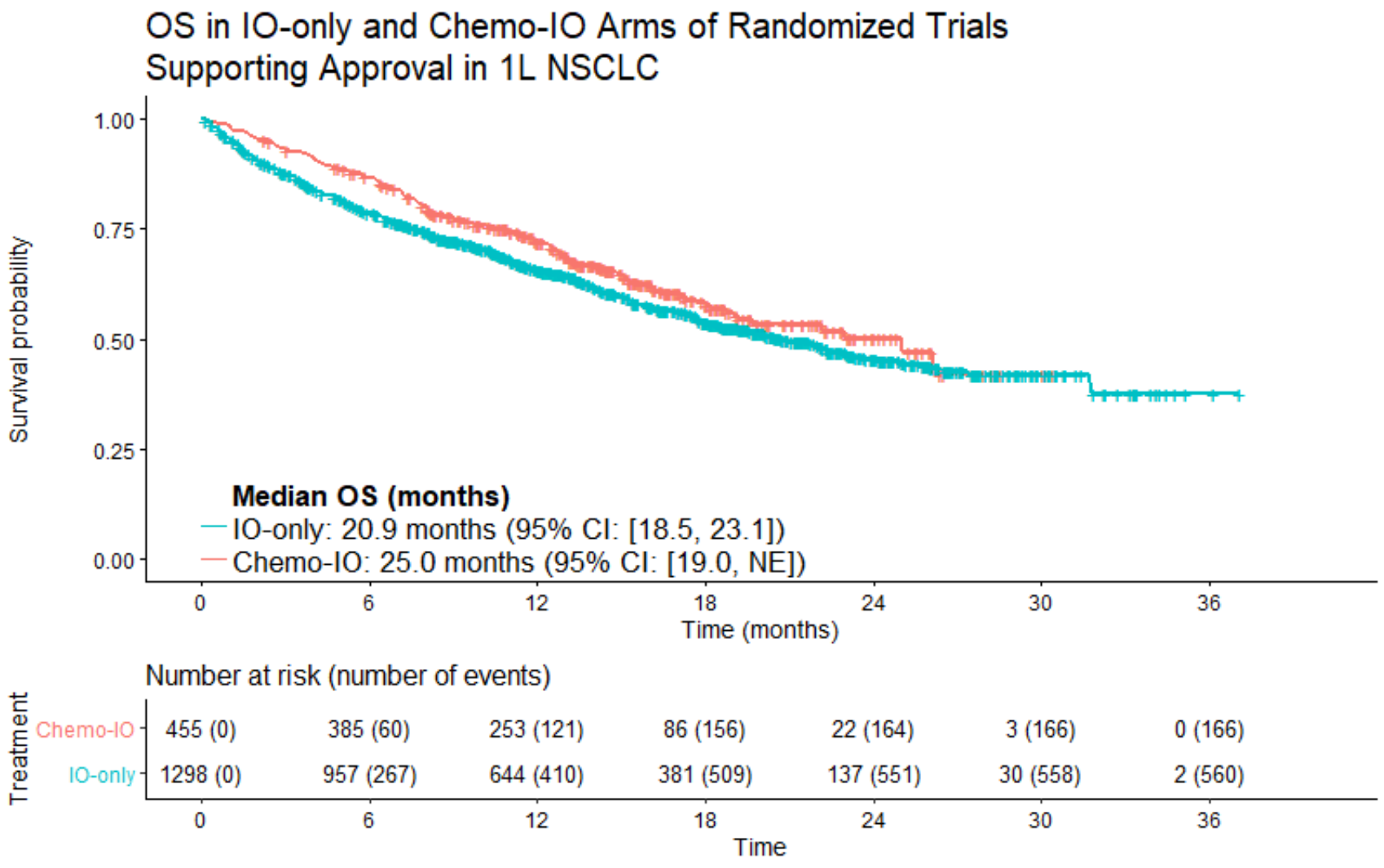
Abbreviations: Chemo-IO=platinum-based doublet chemotherapy plus immunotherapy; ECOG PS=Eastern Cooperative Oncology Group Performance Status; IO=immunotherapy; *N*=number.

Exploratory OS, PFS, and ORR: NSCLC PD-L1 ≥50%

	Chemo-IO (*N*=455)	IO-alone (*N*=1,298)
OS		
Median, months (95% CI)	25.0 (19.0, NE)	20.9 (18.5, 23.1)
HR (95% CI)	0.82 (0.62, 1.08)	
PFS		
Median, months (95% CI)	9.6 (8.4, 11.1)	7.1 (6.3, 8.3)
HR (95% CI)	0.69 (0.55, 0.87)	
ORR		
% (95% CI)	61 (56, 66)	43 (41, 46)
Odds ratio	1.2 (1.1, 1.3)	

Abbreviations: Chemo-IO=platinum-based doublet chemotherapy plus immunotherapy; CI=confidence interval; HR-hazards ratio; IO=immunotherapy; *N*=number; NSCLC=non-small-cell lung cancer; NE=not estimable; ORR=objective response rate; OS=overall survival; PD-L1=programmed death ligand-1; PFS=progression-free survival.

Exploratory OS: Chemo-IO vs IO in NSCLC PD-L1 ≥50%



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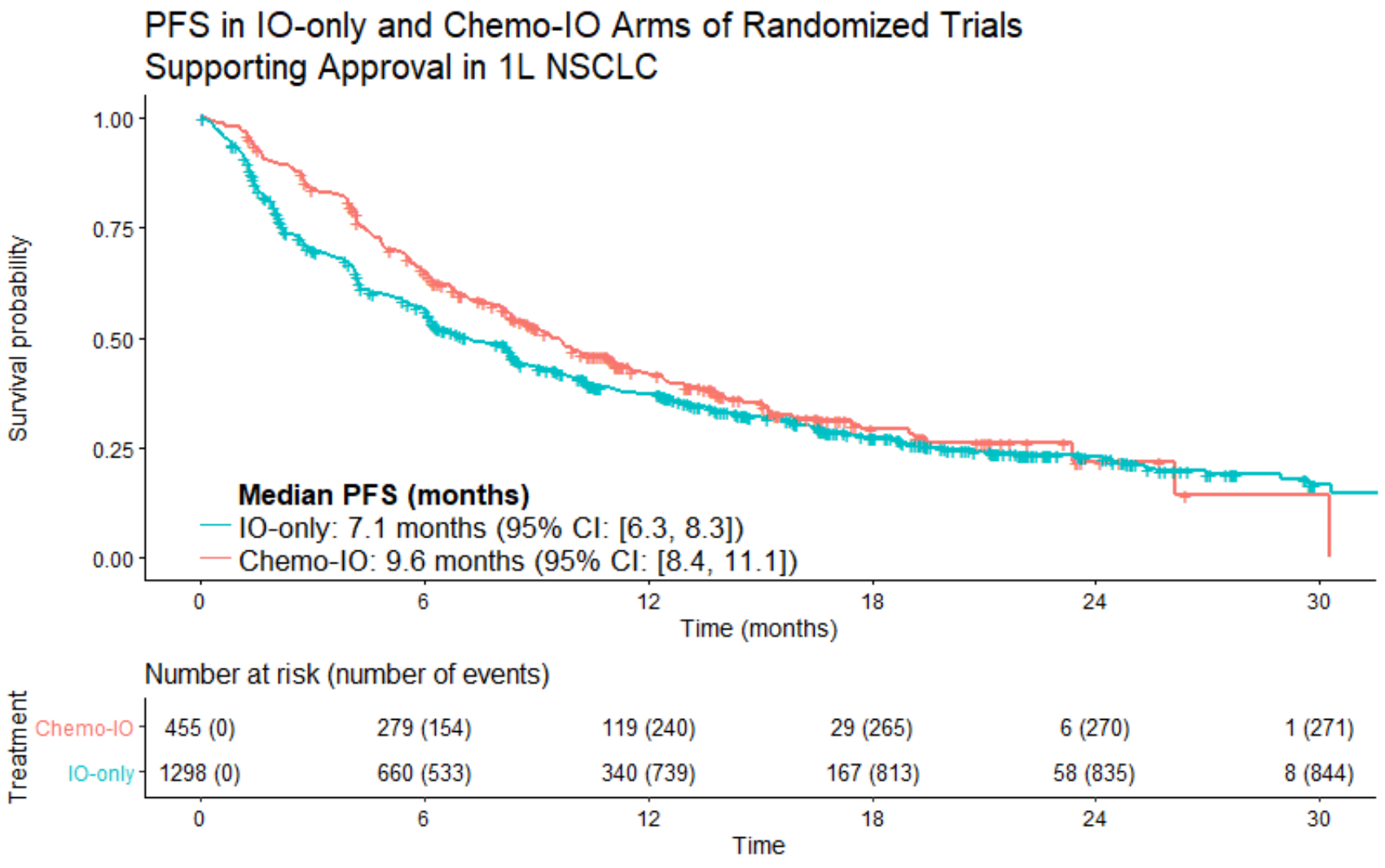
Exploratory PFS: Chemo-IO vs IO in NSCLC PD-L1 ≥50%



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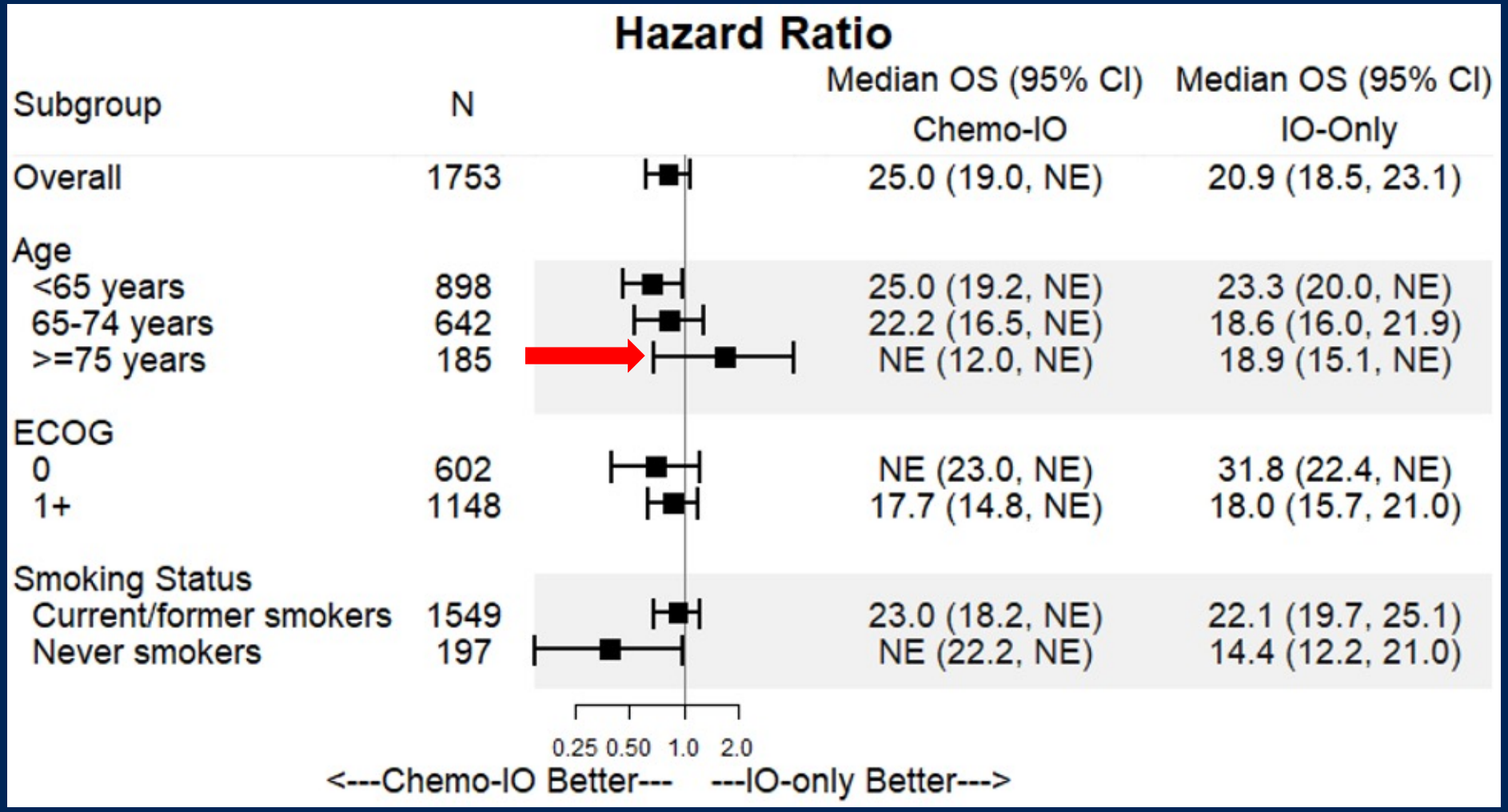
OS in NSCLC PD-L1 ≥50% in selected subgroups



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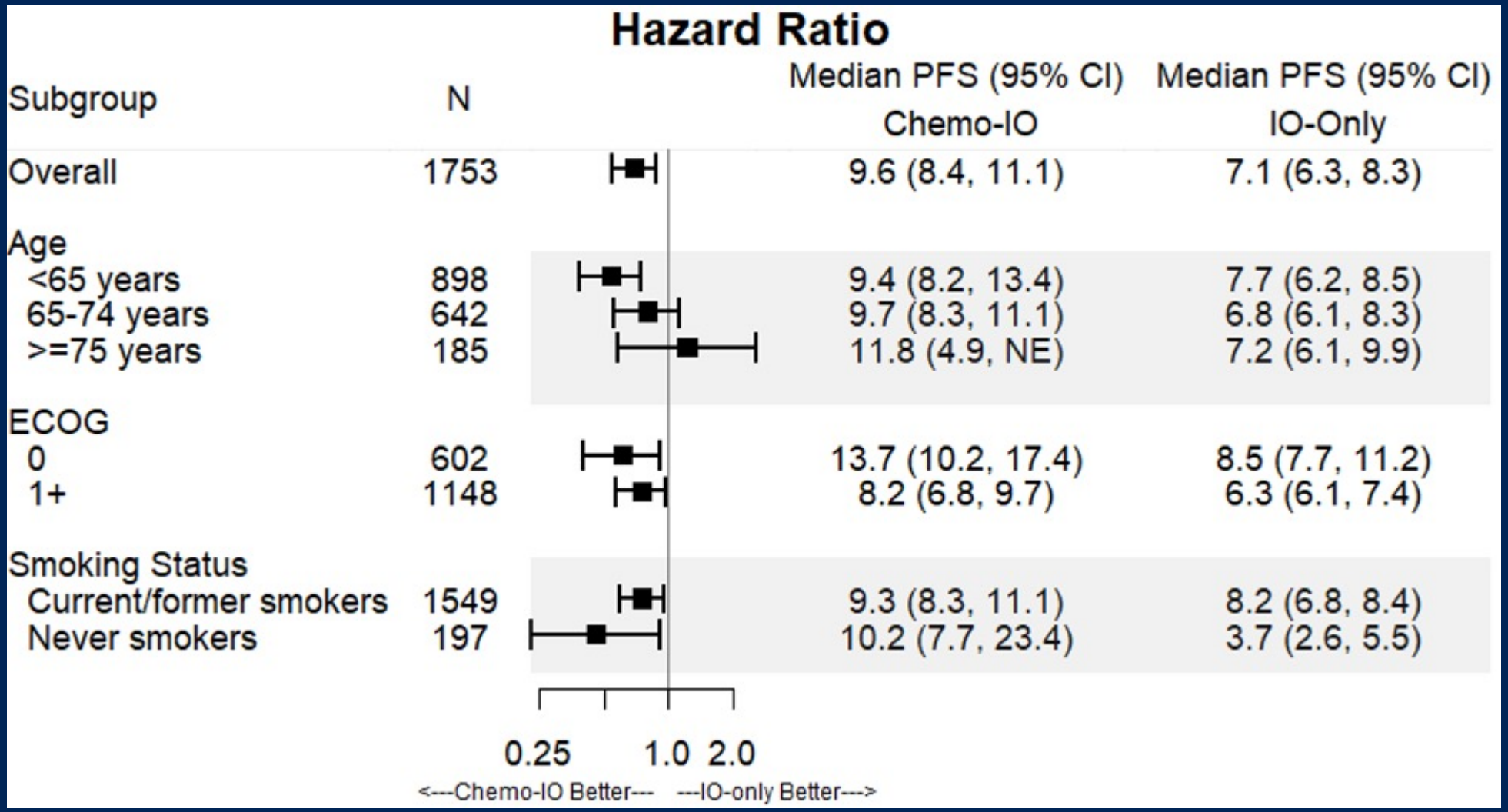
PFS in NSCLC PD-L1 ≥50% in selected subgroups



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Limitations

- Retrospective exploratory pooled analyses
  - Results only hypothesis-generating
- Analyses do not explain the lack of concordance between OS and PFS/ORR results
  - Subsequent therapies in the IO-only arm
  - Deaths and treatment-discontinuation due to toxicity
- Potential heterogeneity across trials
  - Differences in PD-L1 assays
- Notable differences between clinical trial populations and real-world patients

Abbreviations: Chemo-IO=chemoimmunotherapy; IO=immunotherapy; ORR=objective response rate; OS=overall survival; PD-L1=programmed death ligand-1; PFS=progression-free survival.

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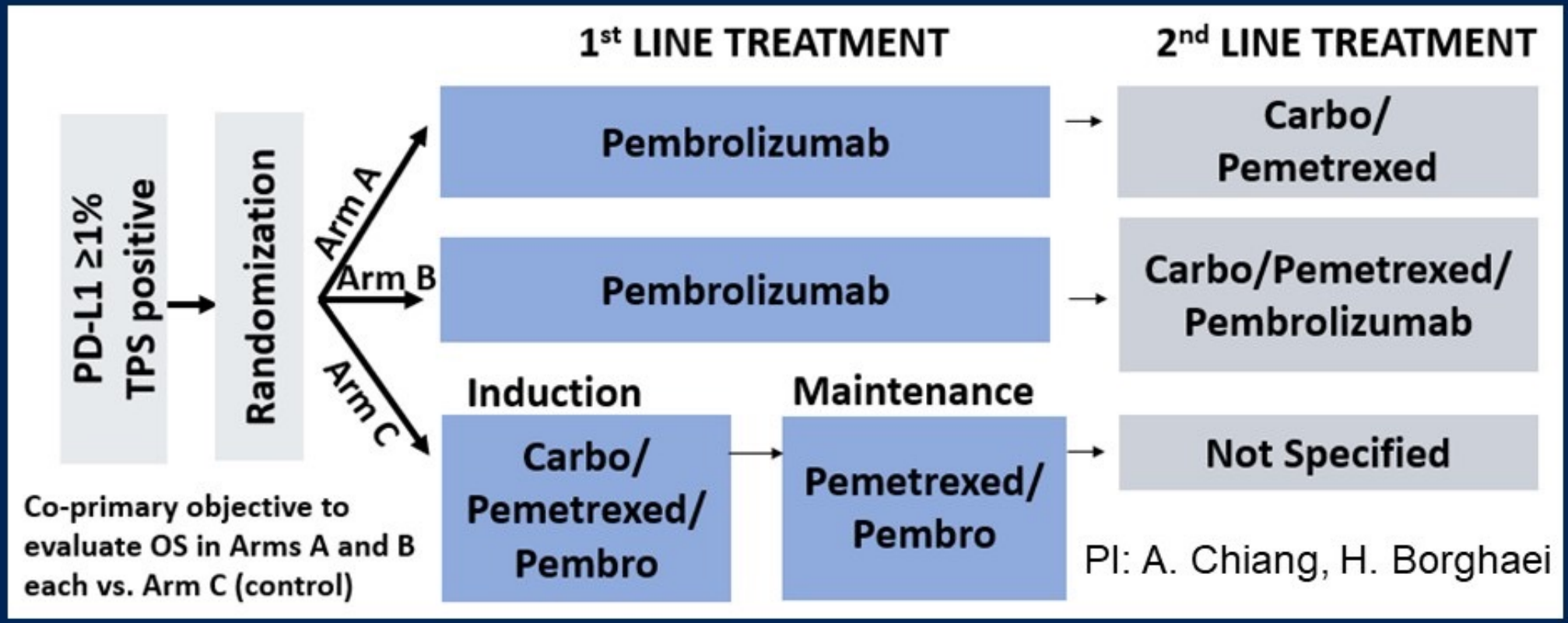

Summary: Advanced/Metastatic NSCLC PD-L1 ≥ 50%

- Our pooled analysis does not suggest a difference in OS for Chemo-IO vs IO-alone though there appears to be a slight numerical advantage favoring Chemo-IO
- Observed differences in PFS and ORR between Chemo-IO and IO-alone to be interpreted in the context of the OS findings and the exploratory nature of this analysis
- Older adults aged ≥75 years may have better OS and PFS outcomes with IO-only regimens
- These support shared decision-making in selecting a therapeutic approach

Abbreviations: Chemo-IO=platinum-based doublet chemotherapy plus immunotherapy; ECOG PS=Eastern Cooperative Oncology Group Performance Status; IO=immunotherapy; NSCLC=non-small-cell lung cancer; ORR=objective response rate; OS=overall survival; PD-L1=programmed death ligand-1.

Thank you!