Applications for Community Oncology

Lung Cancer Data Review

April 23, 2022

cornerstone specialty network™

2022 Lung Key Studies

(Neo)adjuvant NSCLC and Actionable NSCLC	Metastatic NSCLC and Actionable NSCLC	SCLC
• CheckMate -816 • IMpower010 • KEYNOTE-091	• CheckMate -9LA • ATEZO-BRAIN • DESTINY-Lung01 • EMPOWER-Lung1 • POSEIDON	• IMpower133 • CASPIAN • ATLANTIS • KEYNOTE-604 • CheckMate -451

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FDA APPROVAL

CheckMate-816

On March 4 2022, the Food and Drug Administration approved nivolumab (Opdivo, Bristol-Myers Squibb Company) with platinum-doublet chemotherapy for adult patients with resectable non-small cell lung cancer (NSCLC) in the neoadjuvant setting. This represents the first FDA approval for neoadjuvant therapy for early-stage NSCLC.

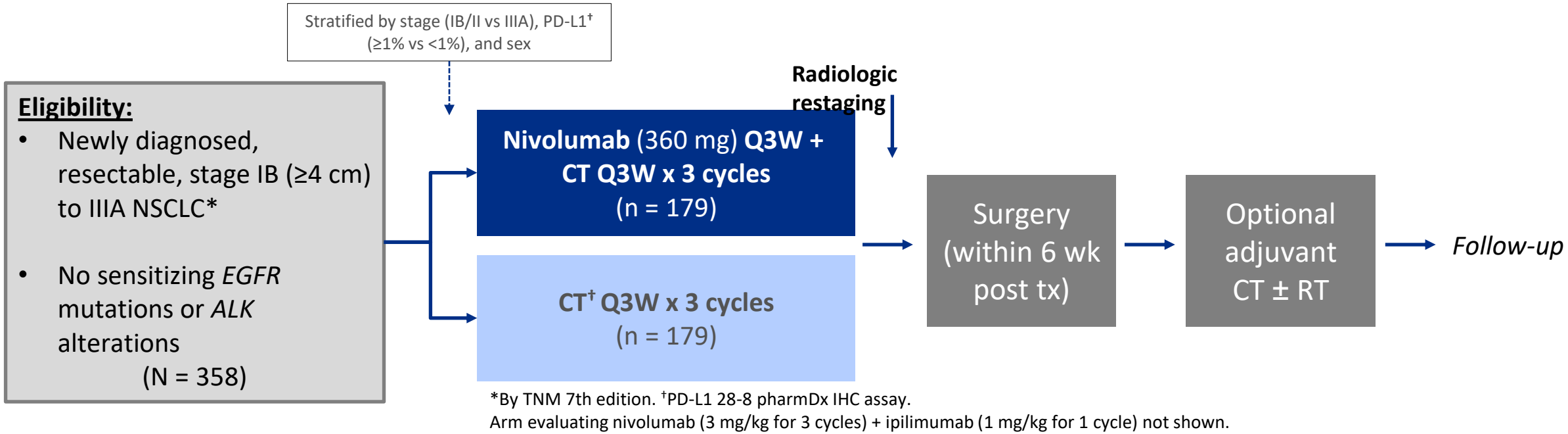
CLINICAL QUESTION

CheckMate-816

Does neoadjuvant immunotherapy (Nivolumab + Platinum chemotherapy) benefit patients with resectable stage IB–IIIA NSCLC?

CheckMate-816

Study Design: Randomized, open-label phase III trial neoadjuvant nivolumab + platinum chemotherapy for resectable Stage IB-IIIA NSCLC



*By TNM 7th edition. †PD-L1 28-8 pharmDx IHC assay.
Arm evaluating nivolumab (3 mg/kg for 3 cycles) + ipilimumab (1 mg/kg for 1 cycle) not shown.

Primary endpoints: pCR (by BIPR), EFS (by BICR)
Key secondary endpoints: OS, MPR (by BIPR), time to death or distant metastasis
Key exploratory endpoints: ORR (by BICR), surgery feasibility, peri/postoperative surgery-related AEs

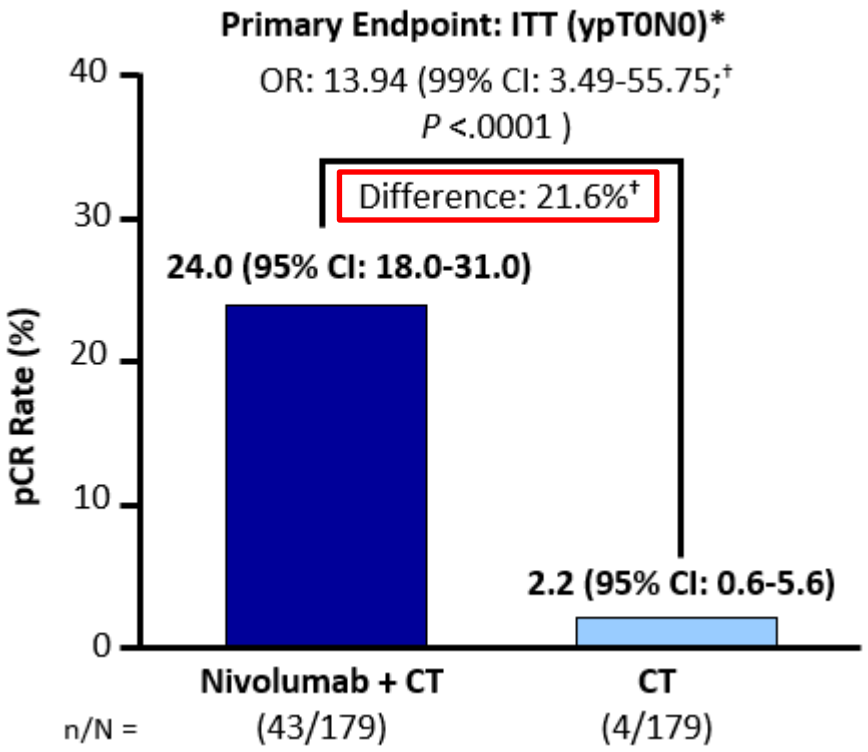
Data cutoff: October 20, 2021; min follow up: 29.5 months

AACR 2021. Abstr CT003. ASCO 2021. Abstr 8503.
AACR 2022. Abstr CT012

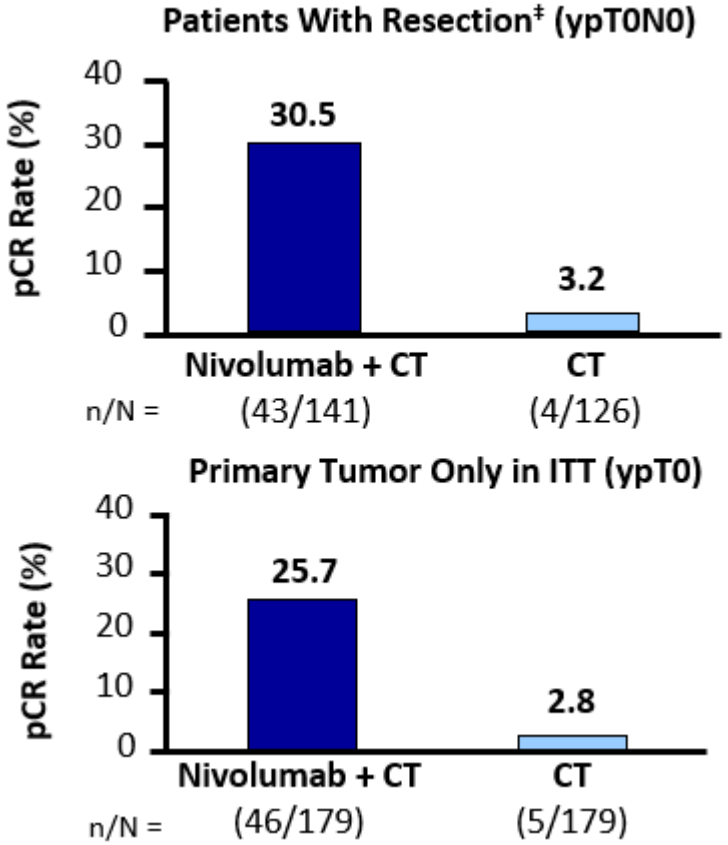
KEY DATA

CheckMate-816

pCR Rate per BICR (Primary Endpoint)



83.2% completed surgery on Nivo/Chemo vs 75.4% on chemo arm



- pCR rate in exploratory nivolumab + ipilimumab arm (ITT): 20.4% (95% CI: 13.4% to 29.0%)

pCR (pathologic complete response) defined as 0% residual viable tumor cells in primary lung tumor and sampled LNs. *In ITT population, those who did not undergo surgery categorized as nonresponders in primary analysis. †Calculated using stratified Cochran–Mantel–Haenszel method. ‡Patients who underwent definitive surgery with evaluable pathology sample.

Forde. AACR 2021. Abstr CT003.

KEY DATA

CheckMate-816

Event-free Survival

Subgroups	Median EFS, mo (95% CI) NIVO + chemo	Chemo	HR (95% CI)
Overall (n = 358)	**31.6 (30.2-NR)**	**20.8 (14.0-26.7)**	**0.63 (0.43-0.91)[a]**
Baseline disease stage			
IB-II (n = 127)	NR (27.8-NR)	NR (16.8-NR)	0.87 (0.48-1.56)
IIIA (n = 228)	31.6 (26.6-NR)	15.7 (10.8-22.7)	**0.54** (0.37-0.80)
Tumor histology			
Squamous (n = 182)	30.6 (20.0-NR)	22.7 (11.5-NR)	0.77 (0.49-1.22)
Non-squamous (n = 176)	NR (27.8-NR)	19.6 (13.8-26.2)	**0.50** (0.32-0.79)
PD-L1 expression level			
< 1% (n = 155)	25.1 (14.6-NR)	18.4 (13.9-26.2)	0.85 (0.54-1.32)
≥ 1% (n = 178)	NR (NR-NR)	21.1 (11.5-NR)	**0.41** (0.24-0.70)
1-49% (n = 98)	NR (27.8-NR)	26.7 (11.5-NR)	**0.58** (0.30-1.12)
≥ 50% (n = 80)	NR (NR-NR)	19.6 (8.2-NR)	**0.24** (0.10-0.61)

[a]97.38% CI reported. Chemo, chemotherapy; CI, confidence interval; EFS, event-free survival; HR, hazard ratio; mo, months; NIVO, nivolumab; NR, not reached; PD-L1, programmed death ligand 1.

Girard. AACR 2022. Abstr CT012.

SUMMARY

CheckMate-816

- Neoadjuvant nivo plus platinum-doublet chemotherapy results in significant improvements compared with chemotherapy alone
  - Statistically significant improvement in EFS over chemotherapy alone with a 37% reduction in the risk of progression, recurrence or death (Hazard Ratio [HR] 0.63; 95% Confidence Interval [CI]: 0.45 to 0.87; P=0.0052)
  - Nivo plus chemotherapy showed a median EFS of 31.6 months compared to 20.8 months for patients treated with chemotherapy alone. The 2-year EFS rate was 64% and 45%, respectively.
  - A prespecified interim analysis for OS resulted in a HR of 0.57 (95% CI: 0.38 to 0.87), which did not cross the boundary for statistical significance.
  - Incidence of grade 3-4 treatment-related (33.5% vs 36.9%) and surgery-related AEs (11.4% vs 14.8%) was similar between the NIVO + chemo and chemo arms, as reported previously.

CheckMate-816

Neoadjuvant nivolumab in combination with platinum-doublet chemotherapy benefits patients with early stage NSCLC improving the chance of successful surgical treatment and reducing the risk of recurrence compared to neoadjuvant chemotherapy and should be considered as a standard of care for select patients with resectable NSCLC

Need to increase the rates of NSCLC screening and early detection

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FDA APPROVAL

IMpower010

On October 15, 2021, the Food and Drug Administration approved atezolizumab (Tecentriq, Genentech, Inc.) for adjuvant treatment following resection and platinum-based chemotherapy in patients with stage II to IIIA non-small cell lung cancer (NSCLC) whose tumors have PD-L1 expression on ≥ 1% of tumor cells, as determined by an FDA-approved test.

The FDA also approved the VENTANA PD-L1 (SP263) Assay (Ventana Medical Systems, Inc.) as a companion diagnostic device to select patients with NSCLC for adjuvant treatment with Tecentriq.

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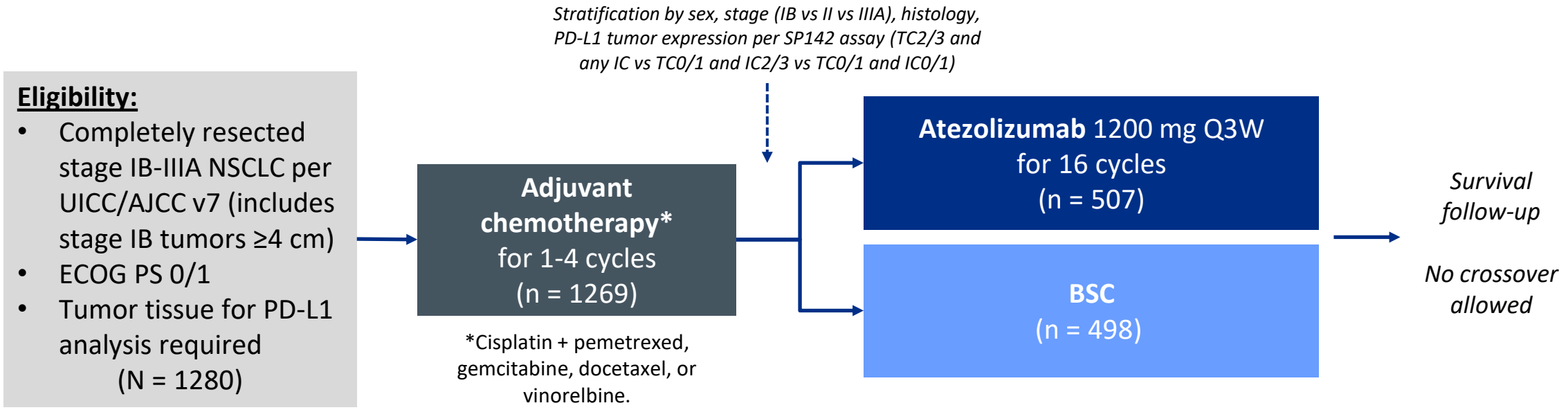
IMpower010

Does adjuvant atezolizumab, compared to SoC, provide benefit for patients with PD-L1-positive stage II-IIIA, fully resected NSCLC after adjuvant chemotherapy?

Subgroup analysis

IMpower010

Study Design: Randomized, open-label Phase 3



Primary endpoint: hierarchical evaluation of inv-assessed DFS in 3 populations: stage II-IIIA with PD-L1 TC ≥1%[†] → all randomized stage II-IIIA → ITT population (stage IB-IIIA)

Secondary endpoints: OS (ITT); DFS in stage II-IIIA with PD-L1 TC ≥50%[†]; 3-yr, 5-yr DFS in all 3 populations; safety

Exploratory endpoints: DFS across disease stages, nodal involvement, surgery types, and chemotherapy regimens

J Clin Oncol 39, 2021 (suppl 15; abstr 8500)

IMpower010

Patient and Treatment Characteristics

Characteristic	Atezolizumab (n = 507)	BSC (n = 498)
Median age, yr (range)*	62 (33-83)	62 (26-84)
Male, n (%)	337 (66.5)	335 (67.3)
ECOG PS 0/1, %	53.8/45.8	56.8/43.0
Nonsquamous histology, n (%)	328 (64.7)	331 (66.5)
PD-L1 TC ≥1%,† n (%)	283 (57.4)	252 (51.9)
Stage, n (%)		
• IB	65 (12.8)	58 (11.6)
• IIA	147 (29.0)	148 (29.7)
• IIB	90 (17.8)	84 (16.9)
• IIIA	205 (40.4)	208 (41.8)
Mediastinal LN dissection, n (%)	402 (79.3)	409 (82.1)
Mediastinal LN sampling, n (%)	93 (18.3)	88 (17.7)

Characteristic	Atezolizumab (n = 507)	BSC (n = 498)
Regional LN status (pN), n (%)		
▪ N0	183 (36.1)	169 (33.9)
▪ N1	170 (33.5)	178 (35.7)
▪ N2	154 (30.4)	151 (30.3)
Surgery type, n (%)		
• Lobectomy	394 (77.7)	391 (78.5)
• Pneumonectomy	77 (15.2)	83 (16.7)
• Bilobectomy	31 (6.1)	19 (3.8)
Median time from surgery to first atezolizumab/BSC treatment, mo (range)	**5.2** (2.4-7.7)	**5.1** (2.3-8.0)
Chemotherapy, n (%)		
• Cisplatin/docetaxel	77 (15.2)	75 (15.1)
• Cisplatin/gemcitabine	88 (17.4)	77 (15.5)
• Cisplatin/vinorelbine	152 (30.0)	151 (30.3)
• Cisplatin/pemetrexed	190 (37.5)	195 (39.2)

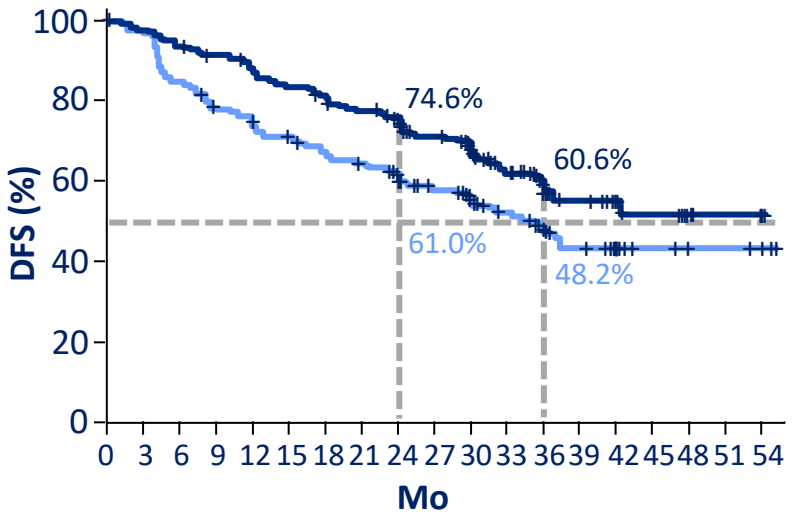
*Approximately 40% of patients in each arm were ≥65 yr of age.
†By PD-L1 SP263 IHC assay.

KEY DATA

IMpower010

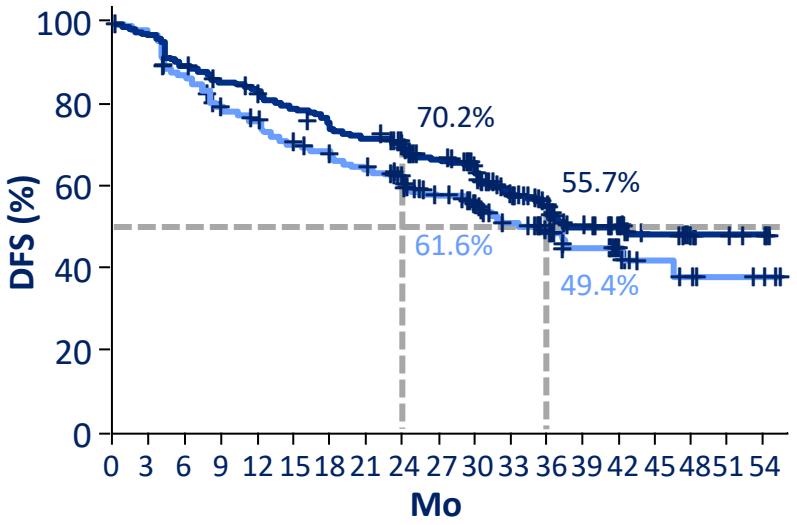
DFS benefit across subgroups, but primarily in patients with stage II-IIIA NSCLC and PD-L1 TC ≥1%

Stage II-IIIA NSCLC With PD-L1 TC ≥1%



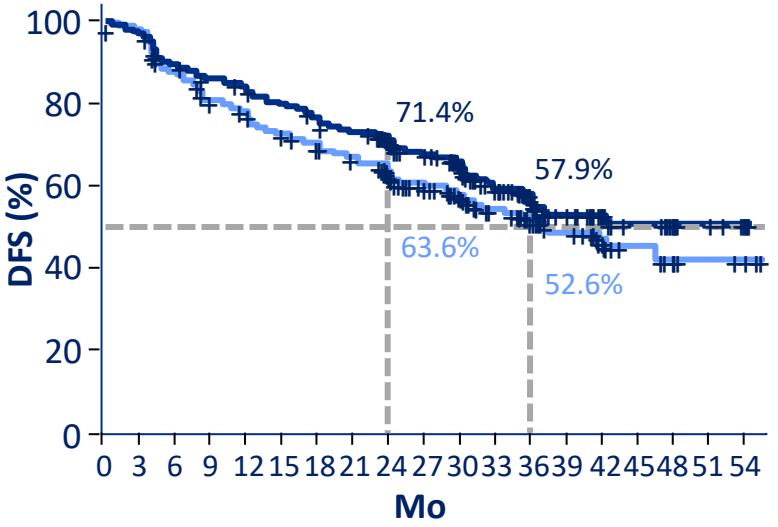
	Atezo (n = 248)	BSC (n = 228)
Median DFS, mo	NE	35.3
HR* (95% CI)	**0.66** (0.50-0.88)	
P Value	**0.004**	

All Randomized Stage II-IIIA NSCLC



	Atezo (n = 442)	BSC (n = 440)
Median DFS, mo	42.3	35.3
HR* (95% CI)	0.79 (0.64-0.96)	
P Value	0.02	

ITT (Stage IB-IIIA NSCLC)



	Atezo (n = 507)	BSC (n = 498)
Median DFS, mo	NE	37.2
HR* (95% CI)	0.81 (0.67-0.99)	
P Value	0.04†	

*Stratified. †Did not cross the prespecified boundary for significance.

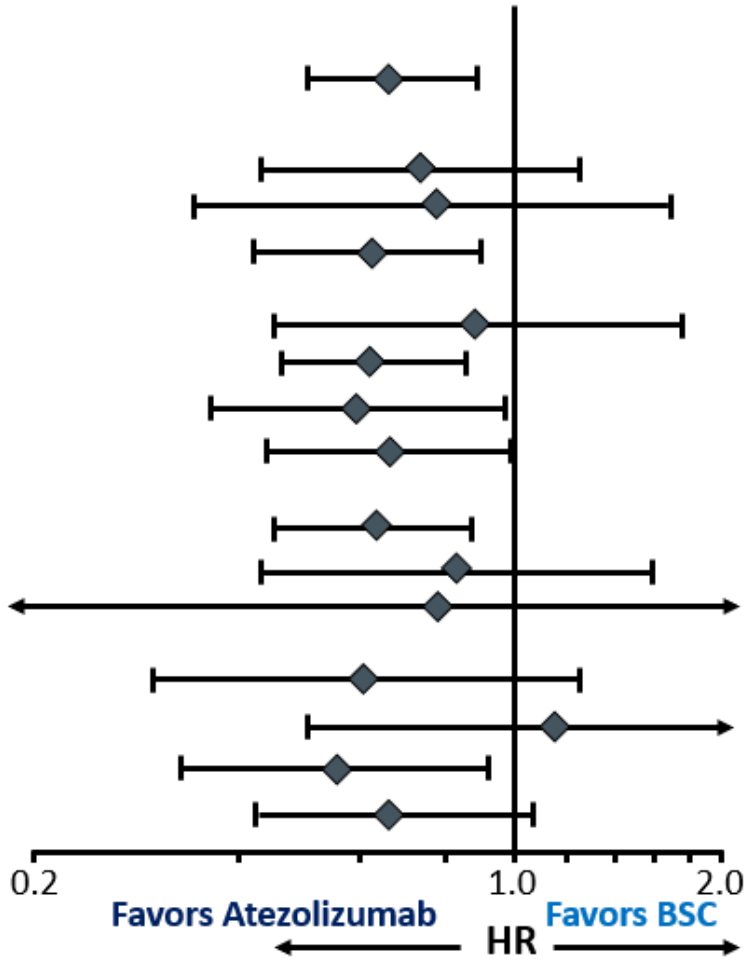
Wakelee. ASCO 2021. Abstr 8500.

KEY DATA

IMpower010

DFS in Patients with Stage II-IIIA NSCLC and PD-L1 TC ≥1%

Subgroup	n	HR (95% CI)	Atezolizumab	BSC
All patients	**476**	**0.66 (0.50-0.88)**	**NE**	**35.3**
Disease stage				
IIA	161	0.73 (0.43-1.24)	NE	NE
IIB	83	0.77 (0.35-1.69)	NE	NE
IIIA	232	0.62 (0.42-0.90)	42.3	26.7
Regional lymph node stage (pN)				
N0	106	0.88 (0.45-1.74)	36.7	NE
N+	370	0.62 (0.46-0.85)	NE	31.4
N1	194	0.59 (0.36-0.97)	NE	NE
N2	176	0.66 (0.44-0.99)	32.3	21.3
Type of surgery				
Lobectomy	359	0.63 (0.45-0.87)	NE	33.4
Pneumonectomy	85	0.83 (0.43-1.58)	36.1	NE
Bilobectomy	24	0.78 (0.18-3.33)	36.7	NE
CT regimen				
Cisplatin-docetaxel	71	0.60 (0.30-1.23)	36.1	18.0
Cisplatin-gemcitabine	75	1.14 (0.50-2.61)	36.1	NE
Cisplatin-vinorelbine	161	0.55 (0.33-0.92)	NE	34.2
Cisplatin-pemetrexed	169	0.66 (0.42-1.06)	NE	31.4



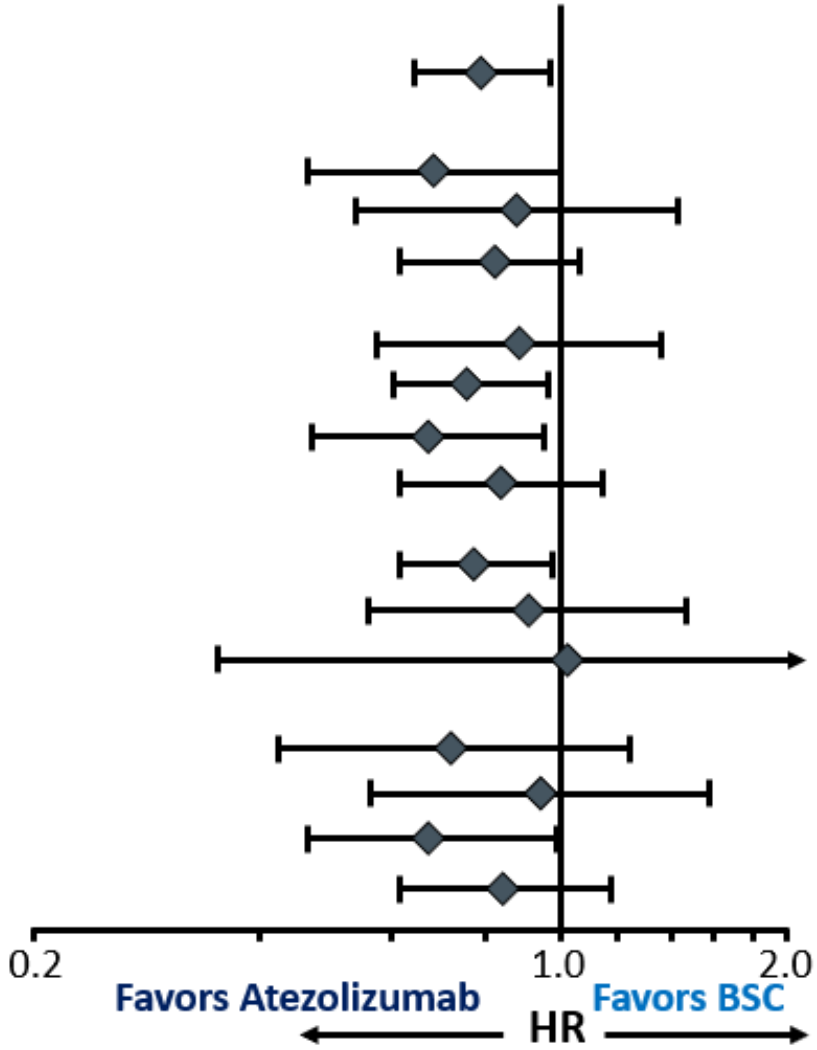
Altorki. WCLC 2021. Abstr PL02.05.

KEY DATA

IMpower010

DFS in All Randomized Patients With Stage II-IIIA NSCLC

Subgroup	n	HR (95% CI)	Atezo	BSC
All patients	**882**	**0.79 (0.64-0.96)**	**42.3**	**35.3**
Disease stage				
IIA	295	0.68 (0.46-1.00)	NE	NE
IIB	174	0.88 (0.54-1.42)	37.1	46.4
IIIA	413	0.81 (0.61-1.06)	32.3	29.7
Regional lymph node stage (pN)				
N0	229	0.88 (0.57-1.35)	NE	46.4
N+	653	0.76 (0.60-0.96)	42.3	31.4
N1	348	0.67 (0.47-0.95)	NE	36.0
N2	305	0.83 (0.61-1.13)	30.2	24.1
Type of surgery				
Lobectomy	675	0.77 (0.61-0.97)	42.3	32.0
Pneumonectomy	150	0.91 (0.56-1.47)	36.1	42.1
Bilobectomy	47	1.02 (0.35-2.98)	36.7	NE
CT regimen				
Cisplatin-docetaxel	124	0.72 (0.42-1.23)	36.1	37.3
Cisplatin-gemcitabine	138	0.94 (0.56-1.57)	36.1	46.4
Cisplatin-vinorelbine	271	0.67 (0.46-0.99)	NE	37.0
Cisplatin-pemetrexed	349	0.84 (0.61-1.16)	42.3	31.4



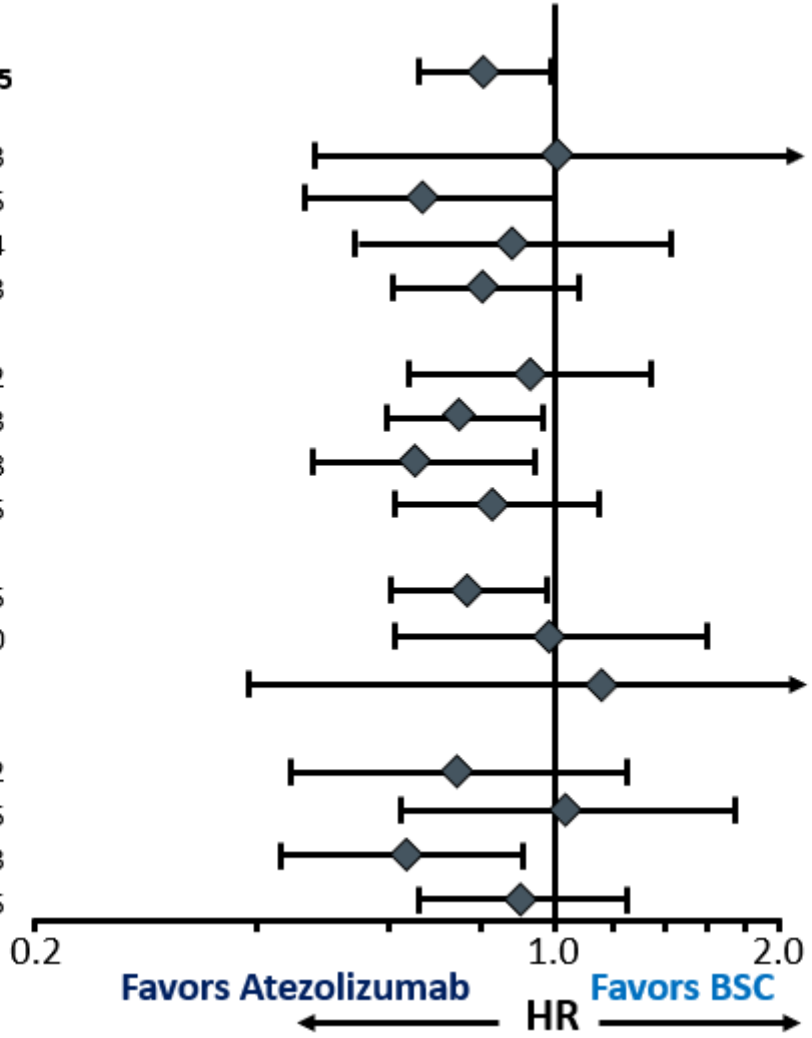
Altorki. WCLC 2021. Abstr PL02.05.

KEY DATA

IMpower010

DFS in All Randomized Patients With Stage IB-IIIA NSCLC (ITT)

Subgroup	n	HR (95% CI)	Atezo	BSC
All patients	**1005**	**0.81 (0.67-0.99)**	**NE**	**37.2**
Disease stage				
IB	123	1.01 (0.48-2.13)	NE	NE
IIA	295	0.68 (0.46-1.00)	NE	NE
IIB	174	0.88 (0.54-1.42)	37.1	46.4
IIIA	413	0.81 (0.61-1.06)	32.3	29.7
Regional lymph node stage (pN)				
N0	352	0.93 (0.64-1.36)	NE	NE
N+	653	0.76 (0.60-0.96)	42.3	31.4
N1	348	0.67 (0.47-0.95)	NE	36.0
N2	305	0.83 (0.61-1.13)	30.2	24.1
Type of surgery				
Lobectomy	785	0.78 (0.62-0.97)	NE	36.0
Pneumonectomy	160	0.98 (0.61-1.57)	36.1	42.1
Bilobectomy	50	1.14 (0.39-3.34)	36.7	NE
CT regimen				
Cisplatin-docetaxel	152	0.74 (0.45-1.23)	36.1	42.1
Cisplatin-gemcitabine	165	1.03 (0.62-1.70)	36.7	46.4
Cisplatin-vinorelbine	303	0.63 (0.43-0.91)	NE	37.0
Cisplatin-pemetrexed	385	0.91 (0.67-1.24)	42.3	36.0



Altorki. WCLC 2021. Abstr PL02.05.

SUMMARY

IMpower010

- For Stage II-IIIA, the risk of progression or death with atezolizumab versus BSC according to PD-L1 status among all randomized patients:
  - PD-L1 <1% HR 0.97 (95% CI 0.72–1.31)
  - PD-L1 1–49% HR 0.87 (95% CI 0.60–1.26)
  - PD-L1 ≥50% HR 0.43 (95% CI 0.27–0.68)

- Subgroup analysis demonstrated DFS improvement in the adjuvant NSCLC setting after platinum-based chemotherapy
  - PD-L1 TC ≥1% stage II-IIIA: HR 0.66; 95% CI: 0.50-0.88
  - All-randomized stage II-IIIA: HR 0.79; 85%CI: 0.64 -0.96

- Current exploratory subgroup analysis demonstrates benefit with adjuvant atezolizumab in patients with stage II - IIIA NSCLC
  - PD-L1 TC ≥1%, for most disease stages, for any nodal involvement, regardless of surgery type, and for most chemotherapy regimens (less favorable for cisplatin-gemcitabine)

- The safety profile consistent with prior experience across indications and lines of therapy

J Clin Oncol 39, 2021 (suppl 15; ASCO abstr 8500)

IMpower010

Atezolizumab continues to demonstrate benefit and should be a practice changing adjuvant treatment option for patients with PD-L1 TC ≥1%, stage II-IIIA NSCLC regardless of disease stage, level of nodal involvement, surgery type, and chemotherapy regimen

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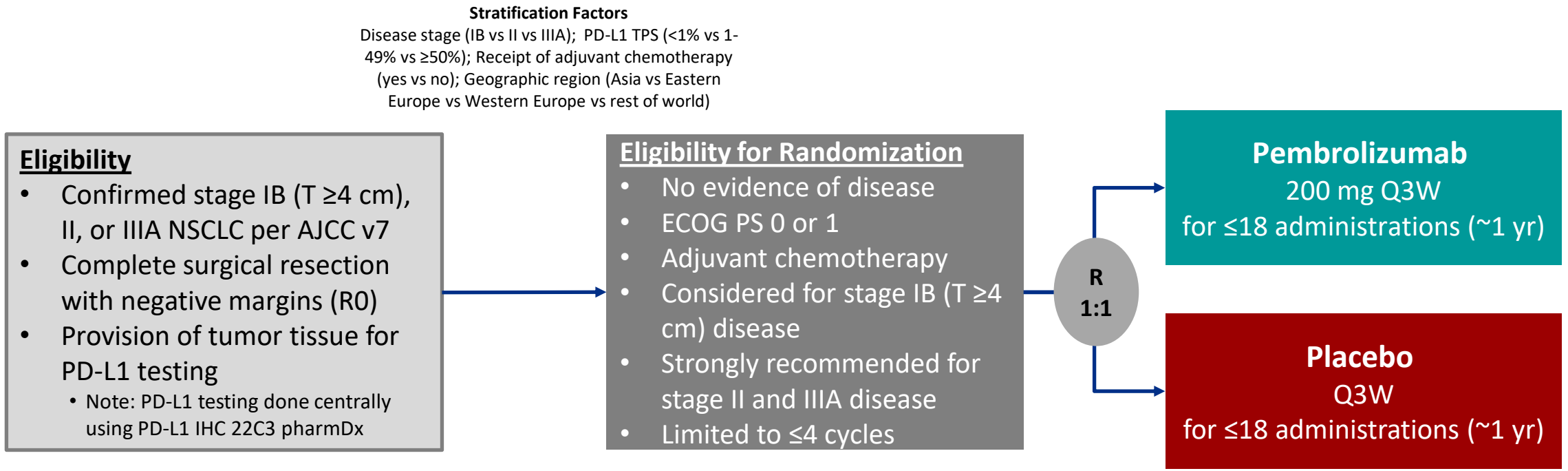
CLINICAL QUESTION

KEYNOTE-091

Does pembrolizumab provide benefit for patients with early stage NSCLC (stage I to IIIA) after resection and adjuvant chemotherapy?

KEYNOTE-091

Study Design: Randomized, triple-blind Phase 3 study



Primary endpoints: DFS in the overall population and DFS in the PD-L1 TPS ≥50% population
Secondary endpoints: DFS in the PD-L1 TPS ≥1% population, OS in the overall, PD-L1 TPS ≥50%, and PD-L1 TPS ≥1% populations, Lung cancer-specific survival in the overall population, and safety

Data cutoff date: September 20, 2021

KEYNOTE-091 also known as EORTC-1416-LCG/ETOP-8-15 – PEARLS

KEYNOTE-091

Overall Population, Baseline Characteristics

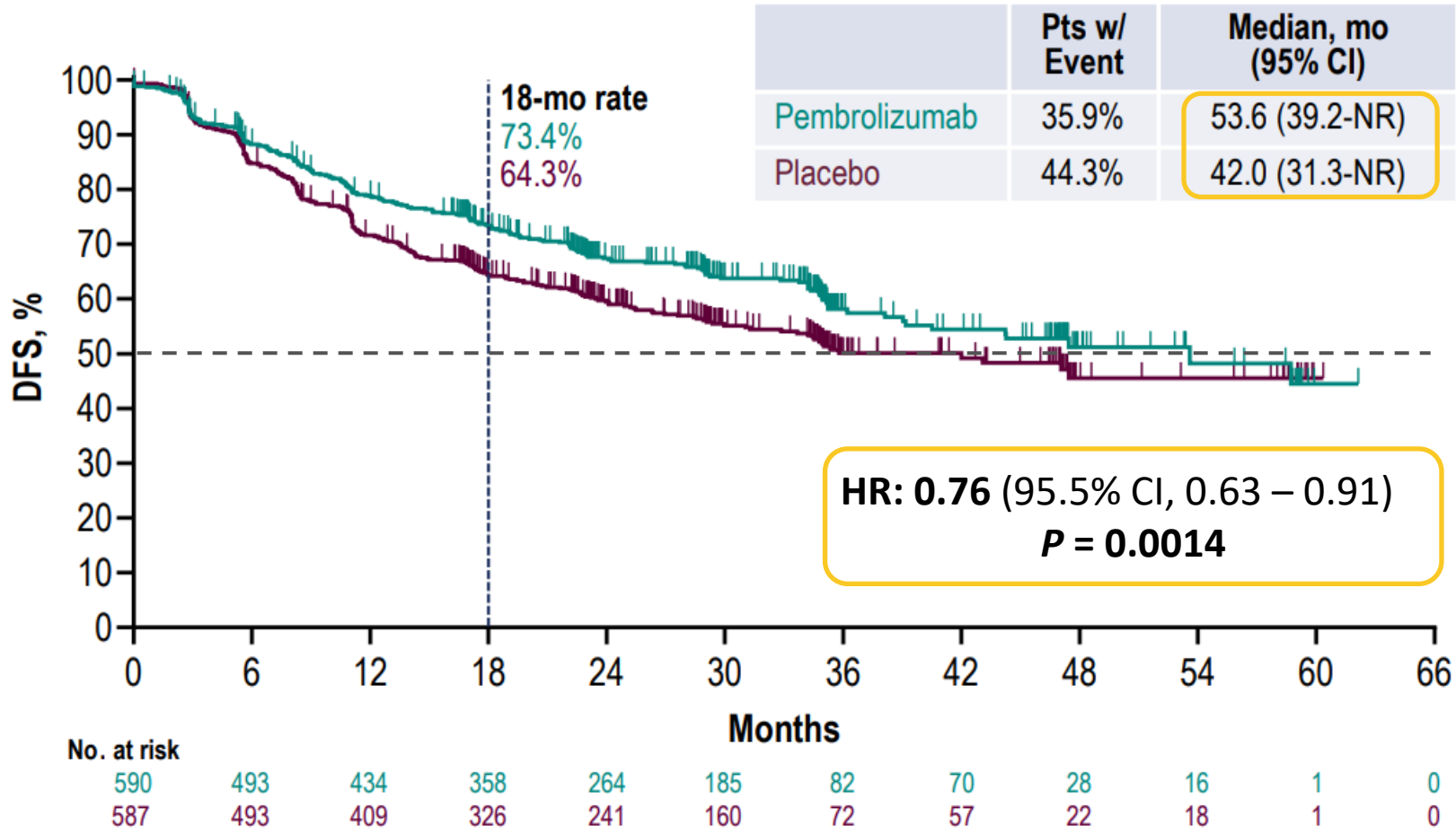
(%)	Pembrolizumab (n=590)	Placebo (n=587)
Age (Y) , Median (range)	65 (31-87)	65 (37-85)
Male	401 (68.0%)	403 (68.7%)
Geographic Region		
• Asia	106 (18.0%)	105 (17.9%)
• Eastern Europe	116 (19.7%)	113 (19.3%)
• Western Europe	303 (51.4%)	301 (51.3%)
• Rest of World	65 (11.0%)	68 (11.6%)
ECOG PS1	210 (35.6%)	244 (41.6%)
Current/former smoker	503 (85.3%)	521 (88.8%)
EGFR Mutation[a]	39 (6.6%)	34 (5.8%)
ALK translocation[b]	7 (1.2%)	7 (1.2%)

	Pembrolizumab (n=590)	Placebo (n=587)
Nonsquamous histology	398 (67.5%)	363 (61.8%)
Pathologic stage[c]		
• IB	84 (14.2%)	85 (14.5%)
• II	329 (55.8%)	338 (57.6%)
• IIIA	177 (30.0%)	162 (27.6%)
Received adjuvant chemo		
• Yes	506 (85.8%)	504 (85.9%)
• No	84 (14.2%)	83 (14.1%)
PD-L1 TPS		
• <1%	233 (39.5%)	232 (39.5%)
• 1 – 49%	189 (32.0%)	190 (32.4%)
• ≥50%	168 (28.5%)	165 (28.1%)

[a] EGFR status unknown for 333 (56.4%) in pembro arm and 337 (57.4%) in placebo arm.
[b] ALK status unknown for 357 (60.5%) in pembro arm and 390 (66.4%) in placebo arm.
[c] 2 (0.3%) participants in the placebo group had stage IV disease.

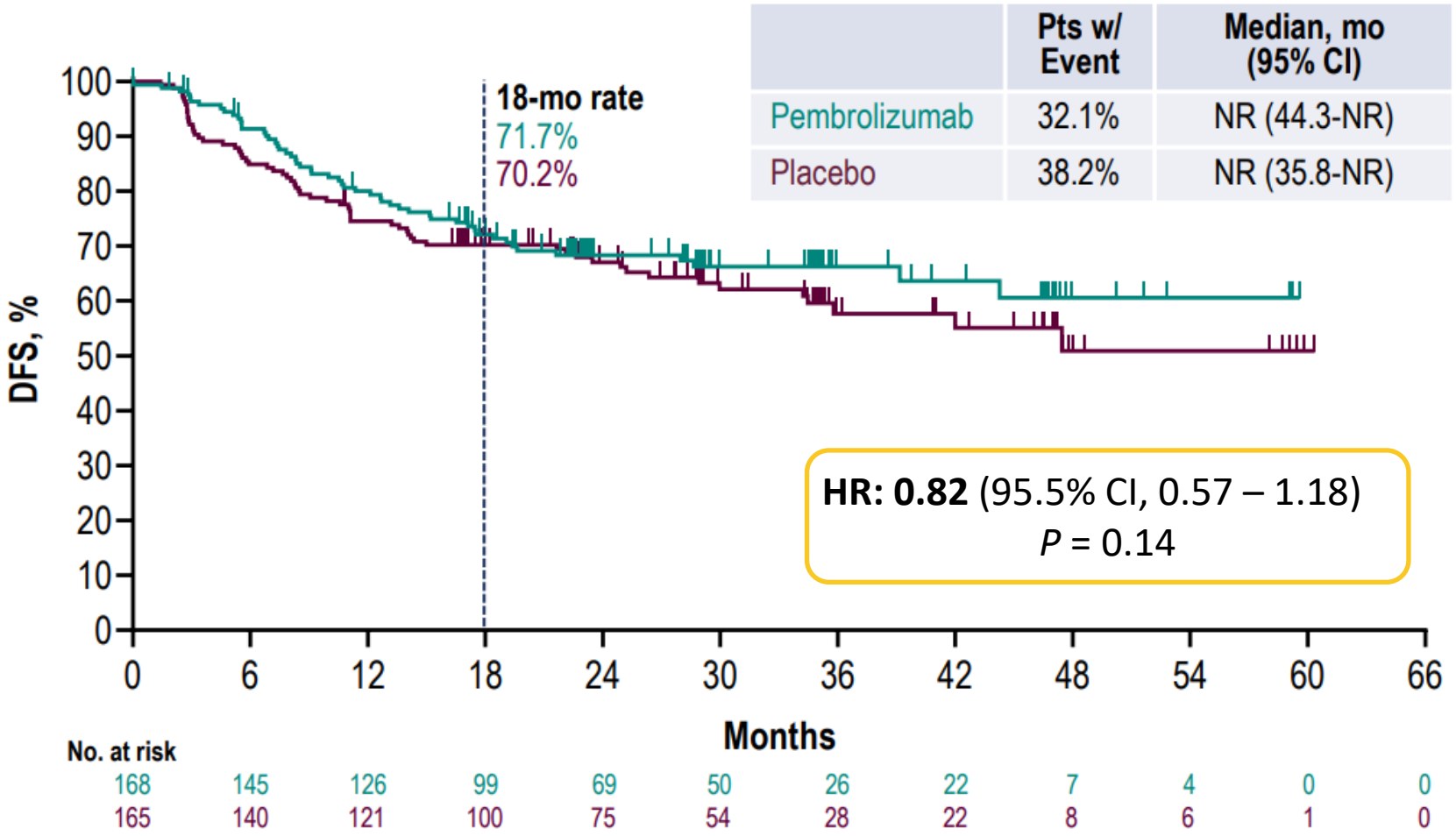
KEYNOTE-091

Overall Population, DFS



KEYNOTE-091

PD-L1 TPS ≥50% Population, DFS



	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	32.1%	NR (44.3-NR)
Placebo	38.2%	NR (35.8-NR)

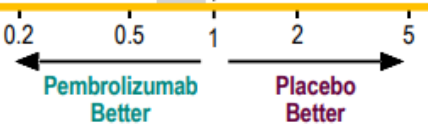
HR: 0.82 (95.5% CI, 0.57 – 1.18)
P = 0.14

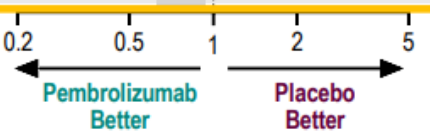
KEYNOTE-091

Overall Population, DFS in Key Subgroups

Subgroup	No. Events/ No. Participants	Hazard Ratio (95% CI)
Overall	472/1177	0.76 (0.63-0.91)
Age		
<65 years	213/558	0.73 (0.56-0.96)
≥65 years	259/619	0.84 (0.66-1.07)
Sex		
Female	158/373	0.73 (0.54-1.00)
Male	314/804	0.81 (0.65-1.01)
Geographic region		
Asia	96/211	0.74 (0.49-1.10)
Eastern Europe	90/229	0.84 (0.56-1.27)
Western Europe	245/604	0.77 (0.60-1.00)
Rest of world	41/133	0.74 (0.40-1.39)
ECOG performance status		
0	288/723	0.78 (0.62-0.99)
1	184/454	0.79 (0.59-1.06)
Smoking status		
Current	53/165	0.42 (0.23-0.77)
Former	340/859	0.84 (0.68-1.04)
Never	79/153	0.72 (0.47-1.13)

Subgroup	No. Events/ No. Participants	Hazard Ratio (95% CI)
Overall	472/1177	0.76 (0.63-0.91)
Pathologic stage		
IB	46/169	0.76 (0.43-1.37)
II	246/667	0.70 (0.55-0.91)
IIIA	178/339	0.92 (0.69-1.24)
Received adjuvant chemotherapy		
No	64/167	1.25 (0.76-2.05)
Yes	408/1010	0.73 (0.60-0.89)
Histology		
Nonsquamous	330/761	0.67 (0.54-0.83)
Squamous	142/416	1.04 (0.75-1.45)
PD-L1 TPS		
<1%	195/465	0.78 (0.58-1.03)
1-49%	160/379	0.67 (0.48-0.92)
≥50%	117/333	0.82 (0.57-1.18)
***EGFR* mutation**		
No	186/434	0.78 (0.59-1.05)
Yes	40/73	0.44 (0.23-0.84)
Unknown	246/670	0.82 (0.63-1.05)



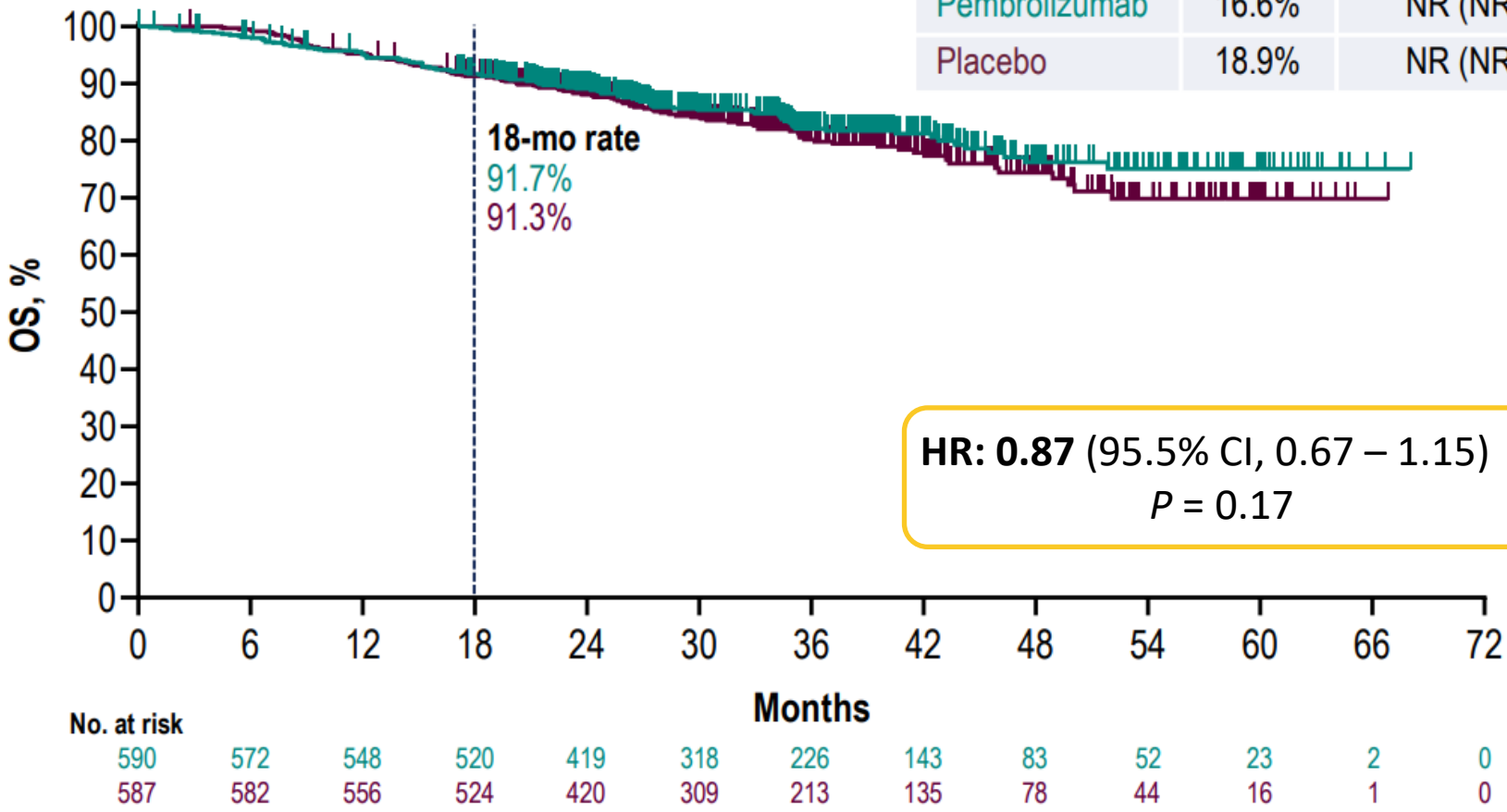


Response assessed per RECIST v1.1 by investigator review.

KEYNOTE-091

Overall Population, OS

	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	16.6%	NR (NR-NR)
Placebo	18.9%	NR (NR-NR)



HR: 0.87 (95.5% CI, 0.67 – 1.15)
P = 0.17

KEYNOTE-091

Adverse Events

	Pembrolizumab (n=580)	Placebo (n=581)
Any	556 (95.9%)	529 (91.0%)
Grade 3 – 5	198 (34.1%)	150 (25.8%)
Led to death	11 (1.9%)	6 (1.0%)
• Treatment related	4 (0.7%)*	0 (0%)
Serious	142 (24.5%)	90 (15.5%)
Treatment discontinuation	115 (19.8%)	34 (5.9%)
Treatment Interruption	221 (38.1%)	145 (25.0%)

* 1 participant each with myocarditis + cardiogenic shock, myocarditis + septic shock, pneumonia, and sudden death.

SUMMARY

KEYNOTE-091

- Adjuvant treatment with pembrolizumab significantly improved DFS in the overall population of patients with early-stage NSCLC following surgical resection
  - Reduced risk of disease recurrence or death by 24% compared to placebo regardless of PD-L1 status HR 0.76 [95% CI, 0.63-0.91]; p=0.0014)
  - Median DFS 53.6 months with pembrolizumab versus 42.0 months with placebo
- DFS in PD-L1 ≥50% did not meet statistical significance at time of interim analysis
- OS data immature at time of interim analysis
- The safety profile of pembrolizumab was consistent with prior experience across indications and lines of therapy

J Clin Oncol 39, 2021 (suppl 15; ASCO abstr 8500)

KEYNOTE-091

Pembrolizumab demonstrated benefit in the adjuvant setting for patients with early-stage NSCLC regardless of PD-L1 status and has the potential to reduce the risk of disease recurrence after surgery

More to come…

Advantages of Neoadjuvant vs Adjuvant

Neoadjuvant

- Higher chance of completion of chemo/immunotherapy
- Able to assess response to systemic treatment
- Potential downstaging

Adjuvant

- Faster local control with surgery
- Higher chance of completion of surgery
- Accurate upfront pathological staging

cornerstone specialty network™

Ongoing Immunotherapy Studies In The Neoadjuvant And Adjuvant Setting

Neoadjuvant Immunotherapy

Trial	Phase	Stage	Trial Design
CheckMate 816	3	IB-IIIA	CT vs. CT + Nivolumab
Impower 030	3	IB-IIIA	CT+ Atezolizumab vs. CT + Placebo
Keynote 671	3	II-IIIB	CT + Pembrolizumab vs. CT
Aegean	3	II-IIIB	CT + Durvalumab vs. CT + placebo
NEOSTAR	2	IA-IIIA	Nivo vs. Nivo + Ipi vs. Nivo + CT vs. Ipi + Nivo + CT
NADIM II	2	IIIA	Nivo + CT vs. CT
NEOMUN	2	II-IIIA	Pembrolizumab
Pilot Study	2	IIIA	Durvalumab ± Tremelimumab + RT

Adjuvant Immunotherapy

Trial	Phase	Stage	Trial Design
ANVIL	3	IB-IIIA	Nivo vs. observation
PEARLS (KEYNOTE-091)	3	IB/II-IIIA	Pembro vs. placebo
BR.31	3	IB-IIIA	MEDI4736
IMpower010	3	IB-IIIA	Atezolizumab vs. BSC
ALCHEMIST	3	II-IIIB	Pembro (sequential or in combination) + Chemo

BSC: best supportive care

Q&A

(Neo)Adjuvant NSCLC

2022 Lung Key Studies

(Neo)Adjuvant NSCLC and Actionable NSCLC	Metastatic NSCLC and Actionable NSCLC	SCLC
• CheckMate -816 • IMpower010 • KEYNOTE-091	• CheckMate -9LA • ATEZO-BRAIN • DESTINY-Lung01 • EMPOWER-Lung1 • POSEIDON	• IMpower133 • CASPIAN • ATLANTIS • KEYNOTE-604 • CheckMate -451

CheckMate -9LA and ATEZO-BRAIN

Does immunotherapy in combination with chemotherapy benefit patients with metastatic NSCLC and brain metastases?

CheckMate -9LA: a post hoc analysis
and
ATEZO-BRAIN: a phase II study

SUMMARY

CheckMate -9LA and ATEZO-BRAIN

	CheckMate -9LA		ATEZO-BRAIN
Treatment Arms	**NIVO + IPI + Chemo** (pemetrexed + cisplatin or carboplatin or paclitaxel + carboplatin) (n=51)	**Chemo** (pemetrexed + cisplatin or carboplatin or paclitaxel + carboplatin) (n=50)	**ATEZO + Chemo** (Pemetrexed + Carboplatin) (n=40)
NSCLC type	Squamous or Non-squamous NSCLC		Non-Squamous NSCLC
Systemic Median OS, HR (95% CI)	19.3 months	6.8 months 0.43 (0.27-0.67)	13.6 months (9.7-NR)
OS rate, 2 yr %	35%	12%	32%
Systemic Median PFS HR (95% CI)	10.6 months	4.1 months 0.40 (0.25 – 0.64)	8.9 (6.7-13.8) 18-mo, 24.9%
Intracranial Median PFS HR (95% CI)	13.5 months	4.6 months 0.36 (0.22 – 0.60)	6.9 months (4.7-12.1) 18-mo, 10.4%
ORR Systemic, n (%)	22 (43%)	12 (24%)	19 (47.5%)
ORR Intracranial, n (%)	20 (39%)	10 (20%)	16 (40%)

WCLC 2021; Abstract OA09.01.
WCLC 2021; Abstract OA09.02.

CheckMate -9LA and ATEZO-BRAIN

Immunotherapy plus chemotherapy in the first-line setting provides benefit to patients regardless of brain mets status

2022 Lung Key Studies

(Neo)Adjuvant NSCLC and Actionable NSCLC	Metastatic NSCLC and Actionable NSCLC	SCLC
• CheckMate -816 • IMpower010 • KEYNOTE-091	• CheckMate -9LA • ATEZO-BRAIN • DESTINY-Lung01 • EMPOWER-Lung1 • POSEIDON	• IMpower133 • CASPIAN • ATLANTIS • KEYNOTE-604 • CheckMate -451

DESTINY-Lung01

Does trastuzumab deruxtecan (T-DXd) provide benefit for patients with *HER2*-mutated (*HER2*m) metastatic NSCLC?

KEY DATA

DESTINY-Lung01

Study Design: Multicenter, international, 2-cohort phase 2 trial

Key eligibility criteria

- Unresectable/metastatic nonsquamous NSCLC
- Relapsed from or is refractory to standard treatment
- Measurable disease by RECIST v1.1
- Asymptomatic CNS metastases at baseline[a]
- ECOG PS of 0 or 1
- Locally reported *HER2* mutation (for Cohort 2)[b]

Cohort 1:
HER2-overexpressing[c] (IHC 3+ or IHC 2+)
T-DXd
6.4 mg/kg q3w
N = 49

Cohort 1a:
HER2-overexpressing[c] (IHC 3+ or IHC 2+)
T-DXd
5.4 mg/kg q3w
N = 41

Cohort 2:
***HER2*-mutated**
T-DXd
6.4 mg/kg q3w
N = 42

Cohort 2 expansion:
***HER2*-mutated**
T-DXd
6.4 mg/kg q3w
N = 49

Primary end point
- Confirmed ORR by ICR[d]

Secondary end points
- DOR
- PFS
- OS
- DCR
- Safety

Exploratory end point
- Biomarkers of response

Data cutoff: May 3, 2021
- 91 patients with *HER2*m NSCLC were enrolled and treated with T-DXd
- 15 patients (16.5%) remain on treatment to date
- 76 patients (83.5%) discontinued, primarily for progressive disease (37.4%) and adverse events (29.7%)

[a]Patients with asymptomatic brain metastases not requiring ongoing steroid or anticonvulsant therapy were allowed to enroll [b]*HER2* mutation documented solely from a liquid biopsy could not be used for enrolment [c]HER2 overexpression without known *HER2* mutation was assessed by local assessment of archival tissue and centrally confirmed [d]Per RECIST v1.1

DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; ICR, independent central review; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1.

ESMO Congress 2021; Abstract LBA45; NEJM 2022; 386:241-251

KEY DATA

DESTINY-Lung01

Demographics and Baseline Characteristics

	T-DXd (N = 91)
Age, median (range), years	60.0 (29.0-88.0)
Female, %	65.9
Race, %	
Asian	34.1
White	44.0
Black	1.1
Other	20.9
Region, %	
Asia	25.3
Europe	36.3
North America	38.5
ECOG PS, %	
0 | 1	25.3 | 74.7
***HER2* mutation, %**	
Kinase domain	93.4
Extracellular domain	6.6
Asymptomatic CNS metastases at baseline, %	36.3
Smoking status, %	
Never | Former | Current	57.1 | 40.7 | 2.2
History of prior lung resection, %	22.0

ESMO Congress 2021; Abstract LBA45; NEJM 2022; 386:241-251

DESTINY-Lung01

Prior Therapies

	Patients (N = 91)
History of any prior systemic cancer therapy, n (%)	**90 (98.9)**
Prior lines of treatment, median (range)	2 (0-7)[a]
Prior treatment, n (%)	
Platinum-based therapy	86 (94.5)
Anti–PD-(L)1 therapy	60 (65.9)
Platinum-based and anti–PD-(L)1 therapy[b]	57 (62.6)
Docetaxel	18 (19.8)
HER2 TKI[c]	13 (14.3)

[a]One patient was enrolled without receiving prior cancer therapy
[b]Given separately or in combination
[c]Patients previously treated with a HER2 antibody or an antibody-drug conjugate were ineligible, but those who previously received a HER2 TKI such as afatinib, pyrotinib, or poziotinib were allowed

ESMO Congress 2021; Abstract LBA45; NEJM 2022; 386:241-251

DESTINY-Lung01

Confirmed ORR, Best Overall Response and DoR

	Patients (N = 91)
Confirmed ORR[a], n (%)	**50 (54.9)** (95% CI, 44.2-65.4)
Best overall response, n (%)	
CR	**1 (1.1)**
PR	**49 (53.8)**
SD	34 (37.4)
PD	3 (3.3)
Not evaluable	4 (4.4)
DCR, n (%)	84 (92.3) (95% CI, 84.8-96.9)
Median DoR, months	**9.3** (95% CI, 5.7-14.7)
Median follow up, months	13.1 (range, 0.7-29.1)

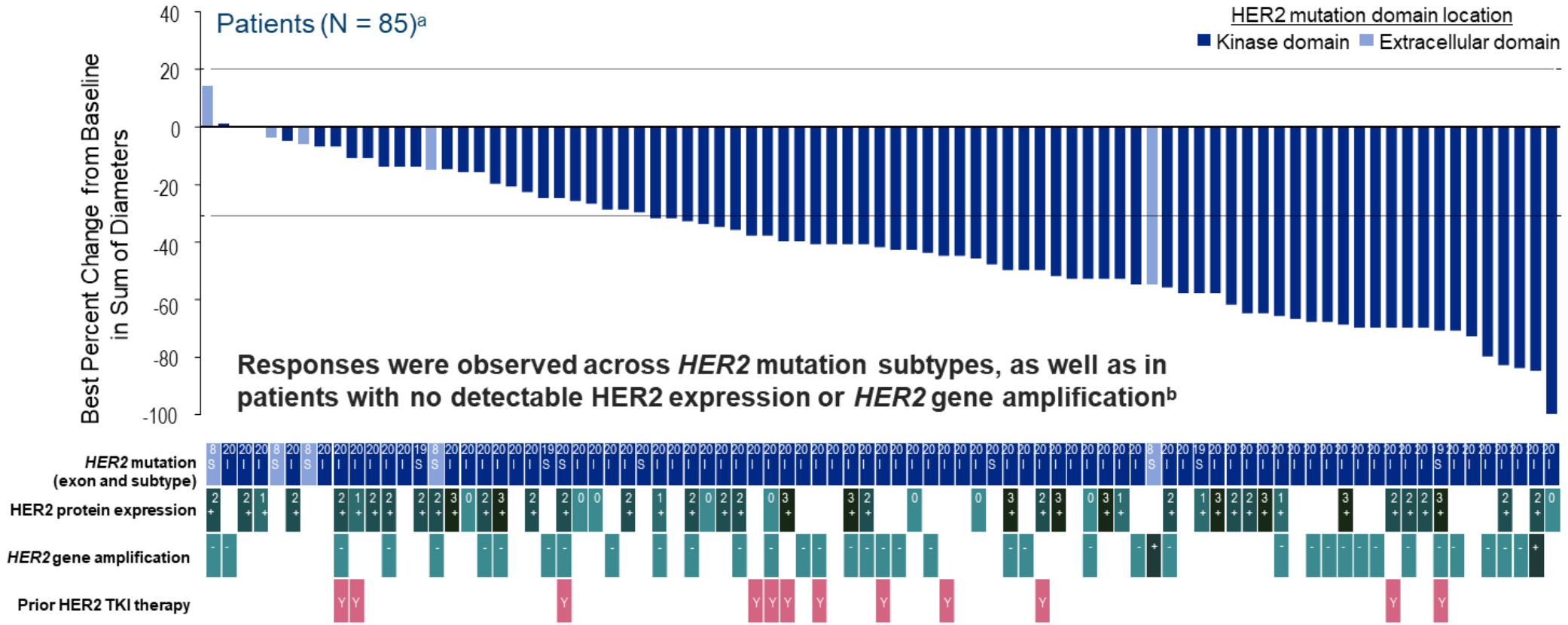
[a]Primary endpoint

CR, complete response; DoR, duration of response; PD, progressive disease; PR, partial response; SD, stable disease.

KEY DATA

DESTINY-Lung01

Best Percentage Change of Tumor Size From Baseline



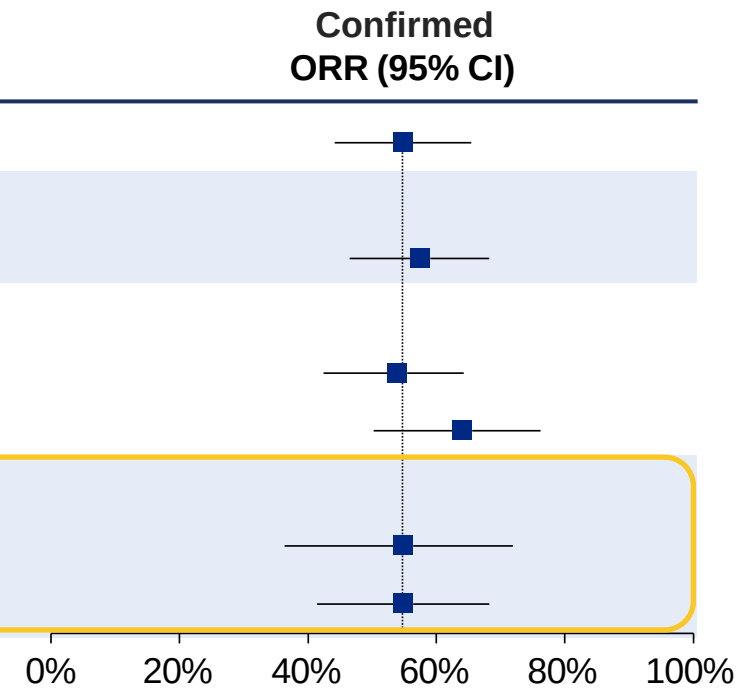
[a]Best change in tumor size by ICR for 85 of 91 patients for whom baseline and postbaseline data were available. Baseline is last measurement taken before enrollment. [b]The Oncomine™ Dx Target Test (Thermo Fisher Scientific) was used to confirm local HER2 mutation status and to determine HER2 amplification status. HER2 protein expression status was determined by immunohistochemistry using a modified PATHWAY anti-HER2 (4B5) (Ventana Medical Systems, Inc.) assay. Shown is best (minimum) percentage change from baseline in the sum of diameters for all target lesions; (-), negative; (+), positive; I, insertion; N, no; S, substitution; Y, yes. Blank cells (except for the prior HER2 TKI therapy row) indicate pati ents whose tumor samples were not evaluable or assessed. The upper dashed horizontal line indicates a 20% increase in tumor size in the patients who had disease progression and the lower dashed line indicates a 30% decrease in tumor size (partial response).

ESMO Congress 2021; Abstract LBA45; NEJM 2022; 386:241-251

DESTINY-Lung01

Response to T-DXd in Subgroups

	No. of Responders	Confirmed ORR (95% CI)
All patients	50/91	54.9 (44.2-65.4)
***HER2* mutation domain**		
Kinase domain	49/85	57.6 (46.5-68.3)
Prior treatment received		
Platinum-based therapy	46/86	53.5 (42.4-64.3)
Platinum-based therapy and anti-PD-(L)1 therapy[a]	**37/57**	**64.9 (51.1-77.1)**
Asymptomatic CNS metastasis at baseline[b]		
Yes	18/33	54.5 (36.4-71.9)
No	32/58	55.2 (41.5-68.3)

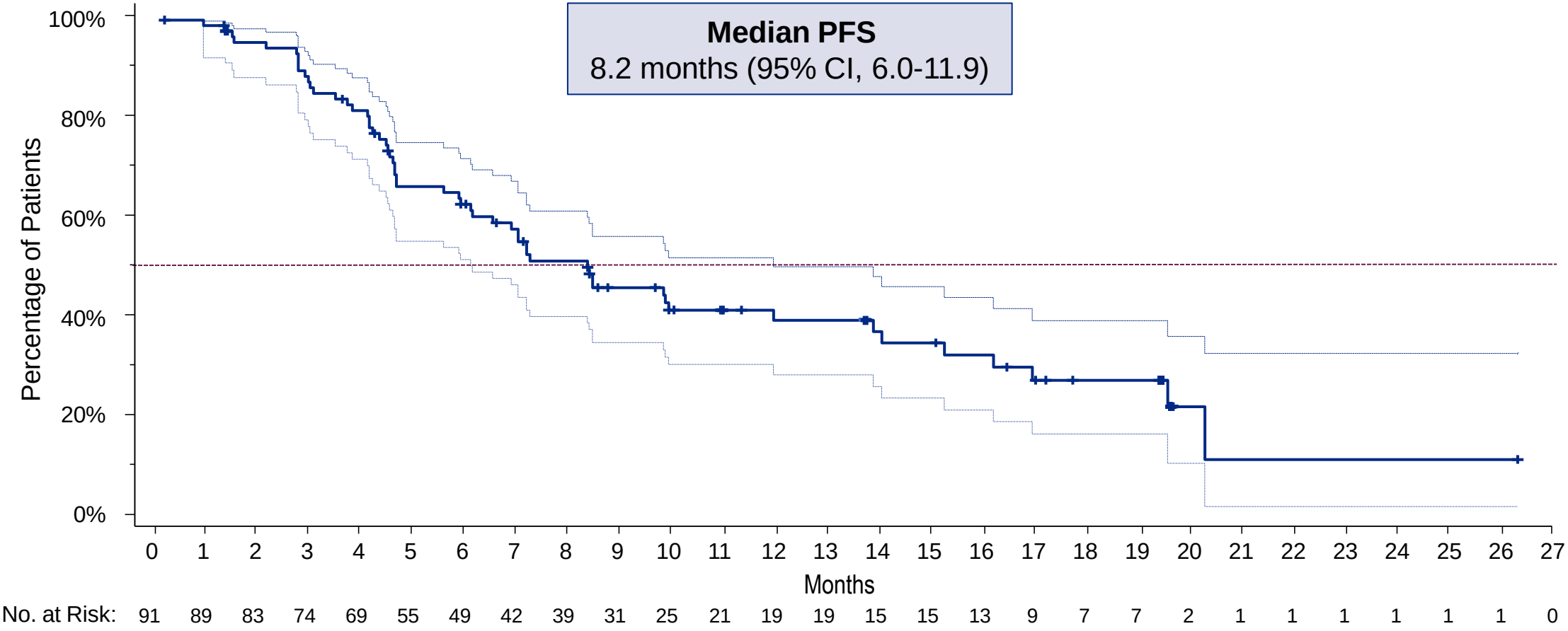


[a]Given separately or in combination
[b]Patients had asymptomatic brain metastases not requiring ongoing steroid or anticonvulsant therapy

KEY DATA

DESTINY-Lung01

Progression-free Survival



Median follow-up was 13.1 months (range, 0.7-29.1)

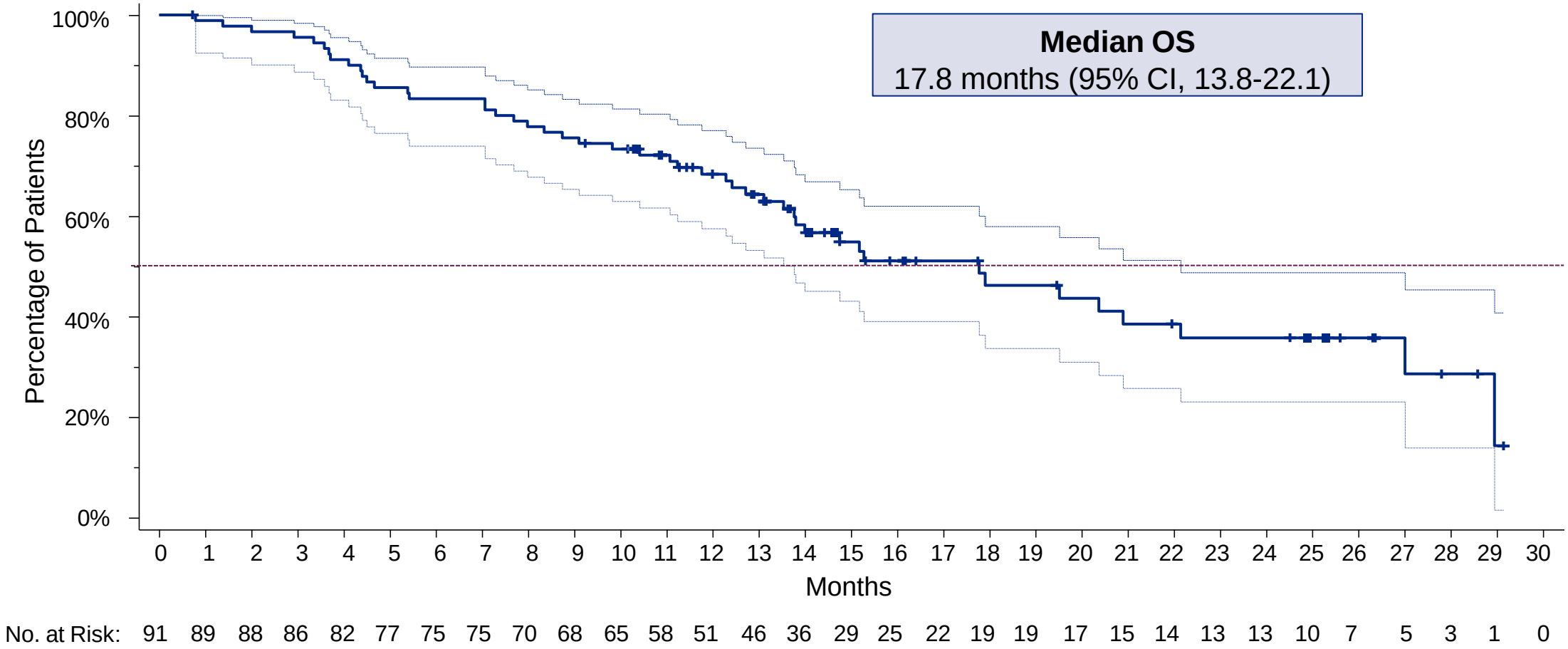
PFS assessed by ICR using RECIST v1.1., the median was based on Kaplan-Meier estimate, and 95% CI for median was computed using the Brookmeyer-Crowley method, and dashed lines indicate the 95% CI. Of 91 patients, 41 had progressive disease and 15 had died by the data cutoff date. Data for 35 patients were censored as indicated by tick marks; patients were censored if they discontinued treatment.

ESMO Congress 2021; Abstract LBA45; NEJM 2022; 386:241-251

KEY DATA

DESTINY-Lung01

Overall Survival



Median follow-up was 13.1 months (range, 0.7-29.1 months)
Dashed lines indicate the 95% CI. Of 91 patients, 47 had died by the data cutoff date. Data for 44 patients were censored as indicated by tick marks; patients were censored if they discontinued treatment.

ESMO Congress 2021; Abstract LBA45; NEJM 2022; 386:241-251

KEY DATA

DESTINY-Lung01

Overall Safety Summary

n (%)	Patients (N = 91)
Any drug-related TEAE	88 (96.7)
Drug-related TEAE Grade ≥3	42 (46.2)
Serious drug-related TEAE	18 (19.8)
Drug-related TEAE associated with discontinuation[a]	23 (25.3)
Drug-related TEAE associated with dose reduction	31 (34.1)
Drug-related TEAE associated with an outcome of death	2 (2.2)[c]

Relationship to study drug was determined by the treating investigator. [a]Pneumonitis (n = 12) and interstitial lung disease (n = 5) were among the drug-related TEAEs associated with discontinuation. [b]1 patient experienced grade 3 ILD as reported by investigator and died. The reported ILD was subsequently adjudicated as grade 5 by the interstitial lung disease adjudication committee.
ILD, interstitial lung disease; TEAE, treatment-emergent adverse event.

- Median treatment duration was 6.9 months (range, 0.7-26.4 months)
- The most common drug-related TEAEs associated with treatment discontinuation were investigator-reported pneumonitis (13.2%) and ILD (5.5%)
- The most common drug-related TEAEs associated with dose reduction were nausea (11.0%) and fatigue (8.8%)

DESTINY-Lung01

Adjudicated Drug-Related ILD/Pneumonitis

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
n (%)	3 (3.3)	15 (16.5)	4 (4.4)	0	2 (2.2)	24 (26.4)

- The median time to onset of first reported drug-related ILD/pneumonitis was 141 days (range, 14- 462 days), with a median duration of 43 days (95% CI, 24-94 days)
- 75% of adjudicated drug-related ILD/pneumonitis[a] cases were of low grade (Grade 1/2)
- 21 of 24 patients with adjudicated drug-related ILD/pneumonitis received ≥1 dose of glucocorticoids. However, not all glucocorticoid treatment was administered per the ILD/pneumonitis management guidelines[b]
- At the time of data cutoff, 54% (13/24) of investigator-reported cases had fully resolved

[a]Drug-related ILD/pneumonitis was determined by the Independent Adjudication Committee based on the current MedDRA version for the narrow ILD standard MedDRA query (SMQ), selected terms from the broad ILD SMQ, and respiratory failure and acute respiratory failure. [b]Events of ILD/pneumonitis in the present study were actively managed based on the protocol-defined ILD/pneumonitis management guidelines.

SUMMARY

DESTINY-Lung01

- T-DXd demonstrated efficacy consistently across subgroups, including in those patients with stable CNS metastases
  - Exploratory analyses demonstrated anticancer activity across different *HER2* mutation subtypes, as well as in patients with no detectable *HER2* expression or *HER2* gene amplification

- Overall, the safety profile was consistent with previously reported studies
  - Most adjudicated drug-related ILD/pneumonitis cases were of low grade
  - ILD/pneumonitis remains an important identified risk
    - Effective early detection and management are critical in preventing high-grade ILD/pneumonitis

- The 5.4 mg/kg dose is being explored in future studies to evaluate the optimal dosing regimen in patients with *HER2*m NSCLC (DESTINY-Lung02; NCT04644237)

ESMO Congress 2021; Abstract LBA45; NEJM 2022; 386:241-251

DESTINY-Lung01

Trastuzumab deruxtecan (T-DXd) provides benefit in the 2L+ setting and supports development as a potential new treatment standard for patients with HER2-mutated (HER2m) metastatic NSCLC

April 19th 2022, acceptance of the supplemental Biologics License Application (sBLA) of ENHERTU® (fam-trastuzumab deruxtecan-nxki) for the treatment of adult patients in the U.S. with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have a HER2 (ERBB2) mutation and who have received a prior systemic therapy; granted Priority Review.

2022 Lung Key Studies

(Neo)Adjuvant NSCLC and Actionable NSCLC	Metastatic NSCLC and Actionable NSCLC	SCLC
• CheckMate -816 • IMpower010 • KEYNOTE-091	• CheckMate -9LA • ATEZO-BRAIN • DESTINY-Lung01 • EMPOWER-Lung1 • POSEIDON	• IMpower133 • CASPIAN • ATLANTIS • KEYNOTE-604 • CheckMate -451

FDA APPROVAL

EMPOWER-Lung 1 Clinical Trial

On February 22, 2021, the Food and Drug Administration approved cemiplimab-rwlc (Libtayo, Regeneron Pharmaceuticals, Inc.) for the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) (locally advanced who are not candidates for surgical resection or definitive chemoradiation or metastatic) whose tumors have high PD-L1 expression (Tumor Proportion Score [TPS] > 50%) as determined by an FDA-approved test, with no EGFR, ALK or ROS1 aberrations.

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EMPOWER-Lung 1 Clinical Trial

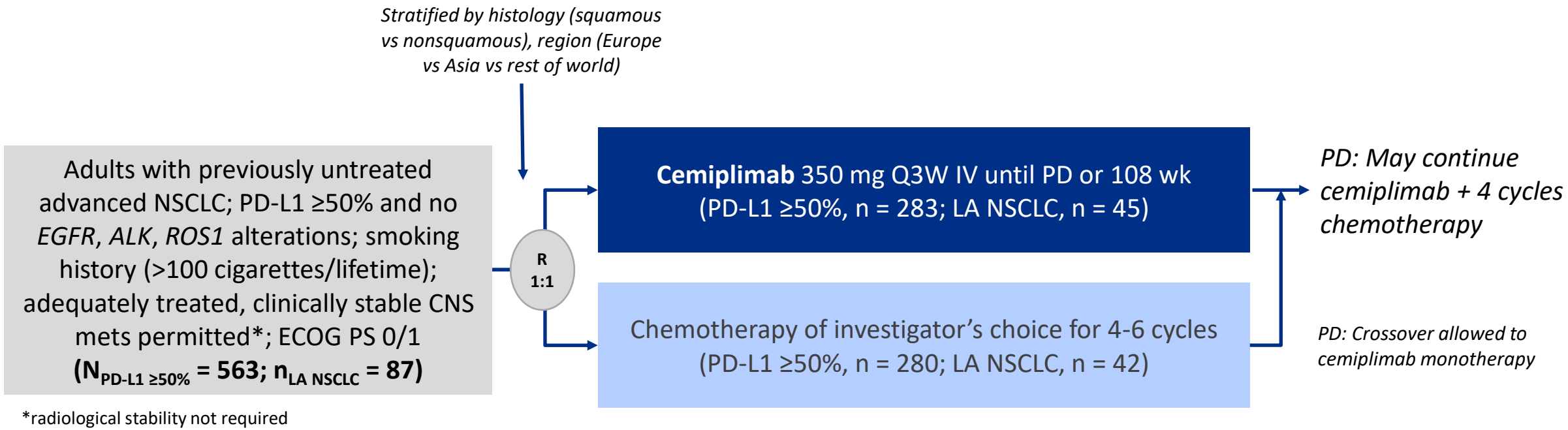
Does cemiplimab provide benefit for patients with locally advanced NSCLC with PD-L1 ≥50%?

Post hoc subgroup analysis

KEY DATA

EMPOWER-Lung 1 Clinical Trial

Study Design: Phase 3 study of locally advanced NSCLC defined as patient with stage IIIB or IIIC NSCLC either ineligible for definitive concurrent CRT or with recurrence after initial treatment with concurrent CRT



Primary endpoints: OS, PFS
Secondary endpoints: ORR, DoR, HRQoL, safety

WCLC 2021. Abstr FP04.03. Lancet. 2021;397:592.

KEY DATA

EMPOWER-Lung 1 Clinical Trial

Baseline Characteristics of LA NSCLC Subgroup

Characteristic, n (%)	Cemiplimab (n = 45)	CT (n = 42)
Median age, yr (range)	63 (31.0-79.0)	63.5 (43.0-81.0)
• ≥65 yr, n (%)	17 (37.8)	19 (45.2)
Male	41 (91.1)	34 (81.0)
ECOG PS 0	16 (35.6)	13 (31.0)
Smoking status		
• Active tobacco use	22 (48.9)	16 (38.1)
• History of active tobacco use	23 (51.1)	26 (61.9)

Characteristic, n (%)	Cemiplimab (n = 45)	CT (n = 42)
Histology		
• Squamous	27 (60.0)	28 (66.7)
• Nonsquamous	18 (40.0)	14 (33.3)
Stage at screening		
• IIIB	36 (80.0)	33 (78.6)
• IIIC	9 (20.0)	9 (21.4)
PD-L1 expression		
• ≥90%	18 (40.0)	18 (42.9)
• >60% to <90%	11 (24.4)	10 (23.8)
• ≥50% to ≤60%	16 (35.6)	14 (33.3)

WCLC 2021. Abstr FP04.03. Lancet. 2021;397:592.

KEY DATA

EMPOWER-Lung 1 Clinical Trial

LA NSCLC Subgroup

	Cemiplimab (n = 45)	CT (n = 42)
Median duration of exposure, wk (IQR)	30.7 (11.9-43.6)	17.7 (13.0-20.0)
Median follow-up, mo (IQR)	12.2 (7.2-21.8)	11.6 (7.8-17.4)
Duration of follow-up, n (%)		
• ≥6 mo	35 (77.8)	32 (76.2)
• ≥12 mo	23 (51.1)	19 (45.2)
• ≥18 mo	13 (28.9)	9 (21.4)
• ≥24 mo	8 (17.8)	5 (11.9)
• ≥30 mo	0	0

Overall median follow-up: 11.6 mo (IQR: 7.2-18.2)

WCLC 2021. Abstr FP04.03. Lancet. 2021;397:592.

KEY DATA

EMPOWER-Lung 1 Clinical Trial

Efficacy in LA NSCLC Subgroup

Outcome	Cemiplimab (n = 45)	CT (n = 42)	HR (95% CI)
OS			
• Median, mo (95% CI)	NE (17.7-NE)	15.5 (9.6-NE)	**0.48**
• 12-mo, %	**78.5**	**57.8**	(0.20-1.14; nominal *P*=0.09)
PFS			
• Median, mo (95% CI)	8.4 (4.5-15.3)	6.2 (4.6-6.6)	**0.49**
• 12-mo, %	**38.5**	**5.8**	(0.27-0.88; nominal *P*=0.02)
ORR, n (%) [95% CI]	**20 (44.4)** [29.6-60.0]	**13 (31.0)** [17.6-47.1]	
Best overall response, n (%)			
• CR	1 (2.2)	1 (2.4)	
• PR	**19 (42.2)**	**12 (28.6)**	
• SD	10 (22.2)	18 (42.9)	
• Non-CR/Non-PD	0	1 (2.4)	
• PD	7 (15.6)	1 (2.4)	
• Not evaluable	8 (17.8)	9 (21.4)	
Median DoR, mo	**12.5 (6.4-21.0)**	**6.2 (3.4-8.5)**	

WCLC 2021. Abstr FP04.03. Lancet. 2021;397:592.

NE: not evaluable

SUMMARY

EMPOWER-Lung 1 Clinical Trial

- First-line cemiplimab significantly improved PFS with a 51% reduction in risk of progression (HR: 0.49; 95% CI: 0.27-0.88; nominal P = 0.02)
- Improvements in OS and ORR were also observed

WCLC 2021. Abstr FP04.03. Lancet. 2021;397:592.

EMPOWER-Lung 1 Clinical Trial

First-line cemiplimab improved outcomes for patients with locally advanced NSCLC with PD-L1 ≥ 50% and no EGFR, ALK, or ROS1 alterations and is a beneficial treatment option for this subset of patients

SUMMARY

	EMPOWER-Lung1†	KEYNOTE-042	IMpower110
Treatment Arms	**Cemiplimab** vs chemotherapy	**Pembrolizumab** vs chemotherapy	**Atezolizumab** vs chemotherapy
n	710 (PD-L1 ≥50% n= 563)	1274 (PD-L1 ≥50% n= 599)	572 (PD-L1 high n=207)
Median OS,	NE (17.9-NE) vs 14.2 months	20.0 vs 12.2 months	20.2 vs 13.1 months
HR (95% CI)	HR 0.57 (0.42-0.77; nominal *P*=0.0002)	HR 0.68 (95% CI: 0.57 – 0.81; *P*=0.0006)	HR 0.59 (95% CI: 0.40 – 0.89; *P*=0.0106)
Median PFS	8.2 vs 5.7 months	6.9 vs 6.4 months	8.1 vs 5.0 months
HR (95% CI)	HR 0.54 (0.43-0.68; nominal *P*<0.0001)	HR 0.82 (0.68 – 0.99; *P*=NS)	HR 0.63 (95% CI 0.45–0.88)
ORR, n (%)	39% vs 20%	39.1% vs 32.3%	38.3% vs 28.6%
Median DoR	16.7 vs 6.0 months	28.1 vs 10.8 months	Not reached vs 6.7 months
Reference	WCLC 2021; Abstract OA09.01. WCLC 2021; Abstract OA09.02.	JCO 2019; 37, 7: 537-546. Journal for ImmunoTherapy of Cancer 2021;9	N Engl J Med 2020; 383:1328-1339

(†Efficacy results updated to reflect PD-L1 ≥50% ITT; results for the laNSCLC PD-L1 ≥50% subgroup were presented on 04/23/2022 in error)

2022 Lung Key Studies

(Neo)Adjuvant NSCLC and Actionable NSCLC	Metastatic NSCLC and Actionable NSCLC	SCLC
• CheckMate -816 • IMpower010 • KEYNOTE-091	• CheckMate -9LA • ATEZO-BRAIN • DESTINY-Lung01 • EMPOWER-Lung1 • POSEIDON	• IMpower133 • CASPIAN • ATLANTIS • KEYNOTE-604 • CheckMate -451

CLINICAL QUESTION

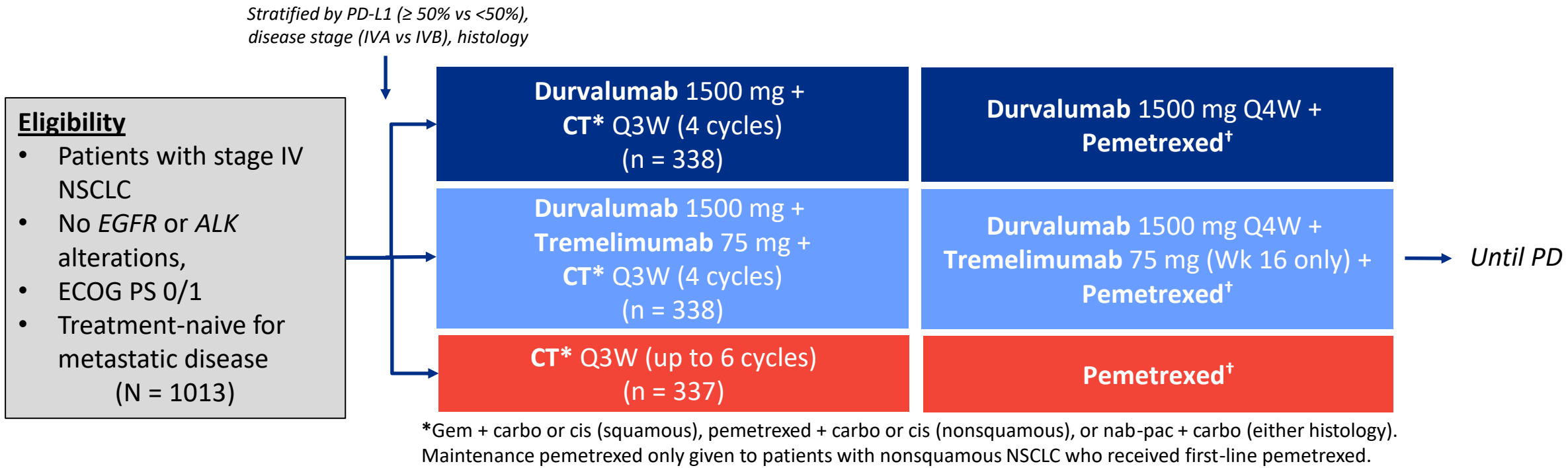
POSEIDON Clinical Trial

Does front-line durvalumab, with or without tremelimumab and chemotherapy, provide benefit for patients with metastatic NSCLC?

KEY DATA

POSEIDON Clinical Trial

Study Design: Open-label, multicenter, randomized phase III trial



*Gem + carbo or cis (squamous), pemetrexed + carbo or cis (nonsquamous), or nab-pac + carbo (either histology). Maintenance pemetrexed only given to patients with nonsquamous NSCLC who received first-line pemetrexed.

Primary endpoints: PFS by BICR, OS (D + CT vs CT); positivity for either triggered analysis of key secondary endpoints

Key secondary endpoints: PFS by BICR, OS, OS in patients with bTMB ≥20 mut/Mb (D + T + CT vs CT)

Other secondary endpoints: ORR, DoR, BOR by BICR; 12-mo PFS; HRQoL; safety/tolerability

Johnson. WCLC 2021. Abstr PL02.01

KEY DATA

POSEIDON Clinical Trial

Baseline Characteristics

Characteristic	Durvalumab + CT (n = 338)	Durvalumab + Tremelimumab + CT (n = 338)	CT (n = 337)
Median age, yr (range)	64.5 (32-87)	63.0 (27-87)	64.0 (32-84)
Male, %	74.9	79.6	73.6
White/Asian/other, %	53.8/36.4/9.8	60.7/29.3/10.1	53.1/38.0/8.9
E Europe/Asia/N Am/W Europe/other, %	30.5/35.5/13.6/7.7/12.7	36.1/28.4/13.0/8.6/13.9	28.2/36.8/11.9/8.3/14.8
ECOG PS 0/1, %	32.3/67.8	32.5/67.5	35.3/64.4
Squamous/non-squamous histology, %	37.9/61.8	36.7/63.3	36.2/63.5
AJCC disease stage IVA/IVB, %	50.3/49.4	50.6/48.8	49.3/50.4
Current or former/never smoker, %	75.1/24.9	82.5/17.5	76.3/23.4
PD-L1 expression ≥ 50%/≥ 1%, %	27.8/66.3	29.9/63.0	28.8/61.4
CNS metastases, %	8.3	9.8	13.4
Liver metastases, %	18.3	20.4	23.7

Johnson. WCLC 2021. Abstr PL02.01

KEY DATA

POSEIDON Clinical Trial

Efficacy

	D + CT vs Chemo	D + T + CT vs Chemo
Median PFS, months	**5.5** vs 4.8	**6.2** vs 4.8
HR (95% CI; *P* value)	HR 0.74 (95% CI: 0.62-0.89; *P* = 0.0093)	HR 0.72 (95% CI: 0.60-0.86; *P* = 0.00031)
1-year PFS rate	24.4% vs 13.1%	26.6% vs 13.1%
Median OS, months	13.3 vs 11.7	14.0 vs 11.7
HR (95% CI; *P* value)	HR 0.86 (95% CI, 0.72-1.02; *P* = 0.07581)	HR 0.77 (95% CI, 0.65-0.92; *P* = 0.00304)
2-year OS rates	29.6% vs 22.1%	32.9% vs 22.1%

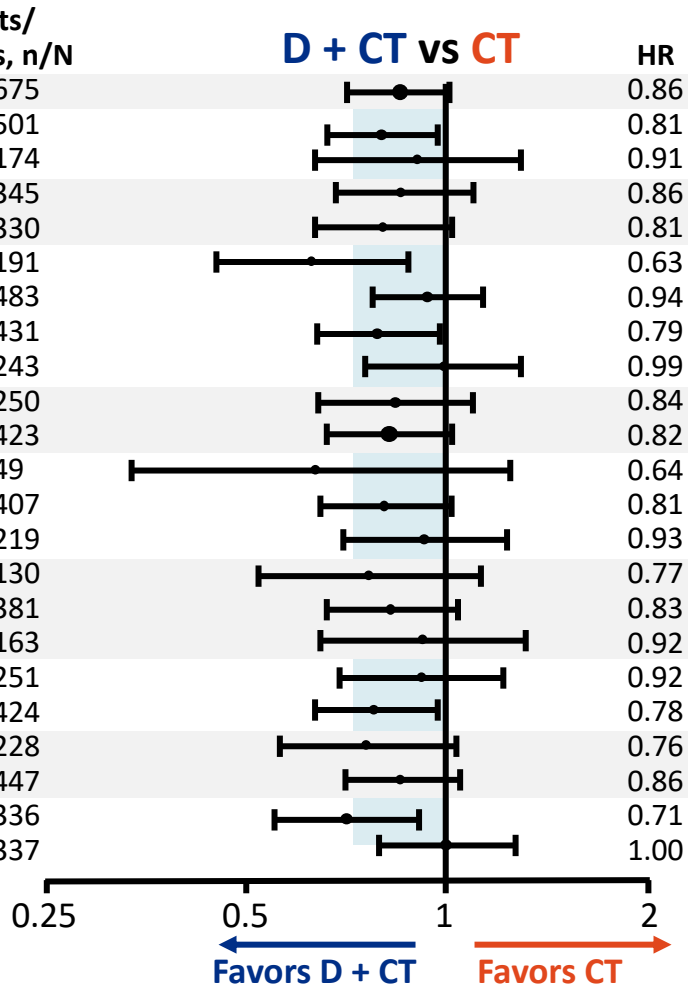
Johnson. WCLC 2021. Abstr PL02.01

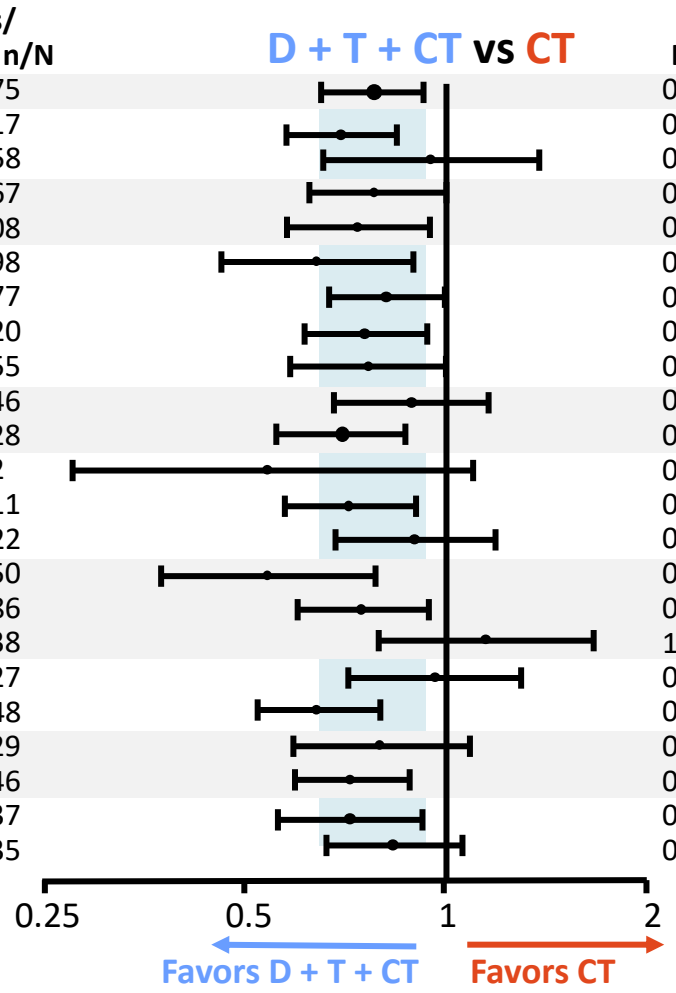
KEY DATA

POSEIDON Clinical Trial

OS by Subgroup

		Events/ patients, n/N	D + CT	HR	Events/ patients, n/N	D + T + CT	HR
All patients		549/675		0.86	536/675		0.77
Sex	Male	423/501		0.81	422/517		0.70
	Female	126/174		0.91	114/158		0.96
Age	<65 years	273/345		0.86	280/367		0.79
	≥65 years	276/330		0.81	256/308		0.74
Tumor PD-L1 expression	TC ≥50%	144/191		0.63	149/198		0.65
	TC <50%	405/483		0.94	387/477		0.82
	TC ≥1%	335/431		0.79	321/420		0.76
	TC <1%	214/243		0.99	215/255		0.77
Histology	Squamous	220/250		0.84	217/246		0.88
	Nonsquamous	327/423		0.82	318/428		0.70
Planned CT	Nab-paclitaxel doublet	40/49		0.64	33/42		0.55
	Pemetrexed doublet	311/407		0.81	304/411		0.72
	Gemcitabine doublet	198/219		0.93	199/222		0.90
Smoking history	Current	107/130		0.77	115/150		0.54
	Former	314/381		0.83	306/386		0.75
	Never	127/163		0.92	114/138		1.15
Race	Asian	195/251		0.92	175/227		0.97
	Non-Asian	354/424		0.78	361/448		0.65
ECOG PS	0	168/228		0.76	166/229		0.80
	1	381/447		0.86	370/446		0.72
AJCC disease stage	IVA	259/336		0.71	259/337		0.72
	IVB	288/337		1.00	276/335		0.84



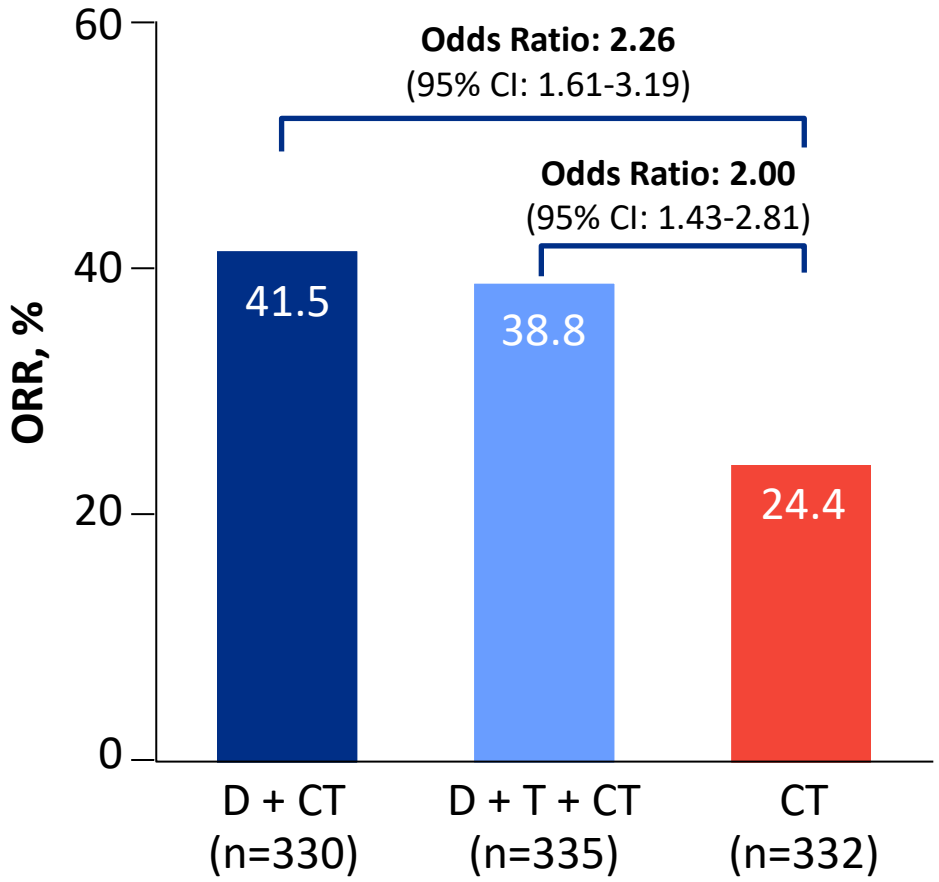


Johnson. WCLC 2021. Abstr PL02.01

KEY DATA

POSEIDON Clinical Trial

Response: Confirmed ORR



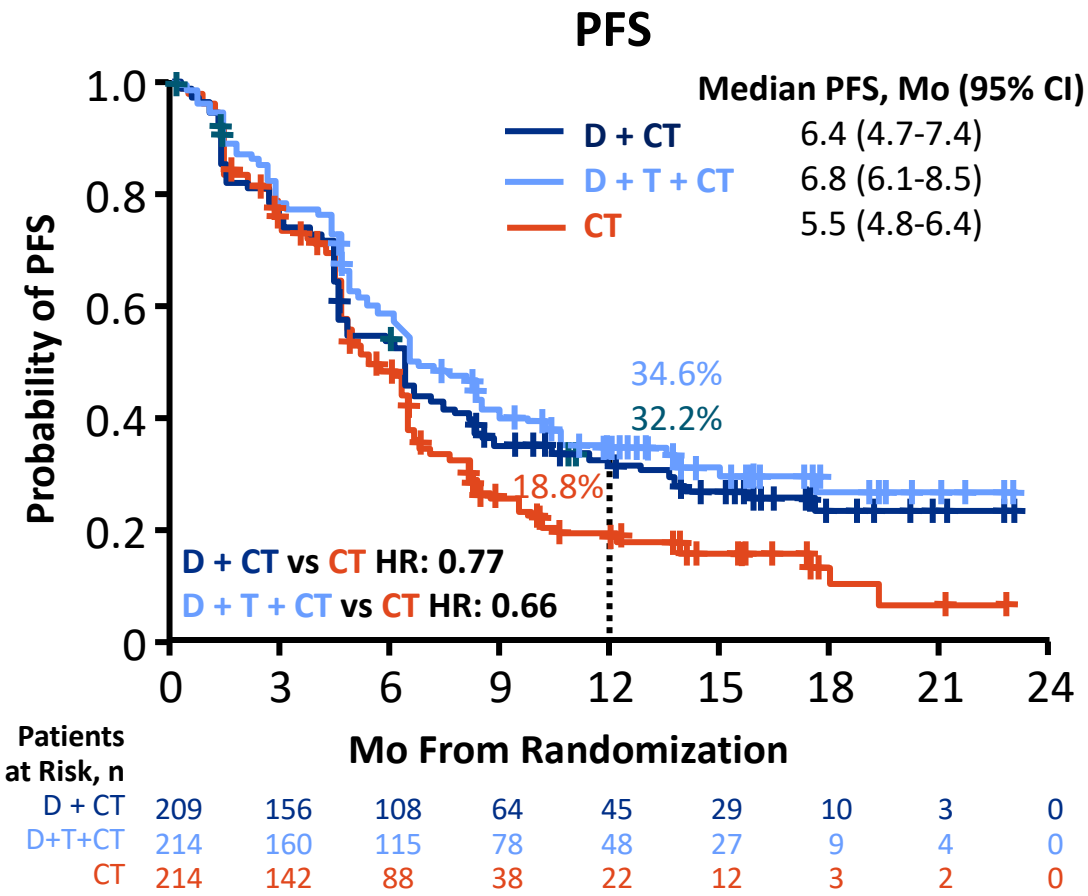
Duration of Response	D + CT (n = 330)	D + T + CT (n = 335)	CT (n = 332)
Responders, n	137	130	81
Median DoR, mo (95% CI)	7.0 (5.7-9.9)	9.5 (7.2-NE)	5.1 (4.4-6.0)
Still in response at 12 mo, %	38.9	49.7	21.4

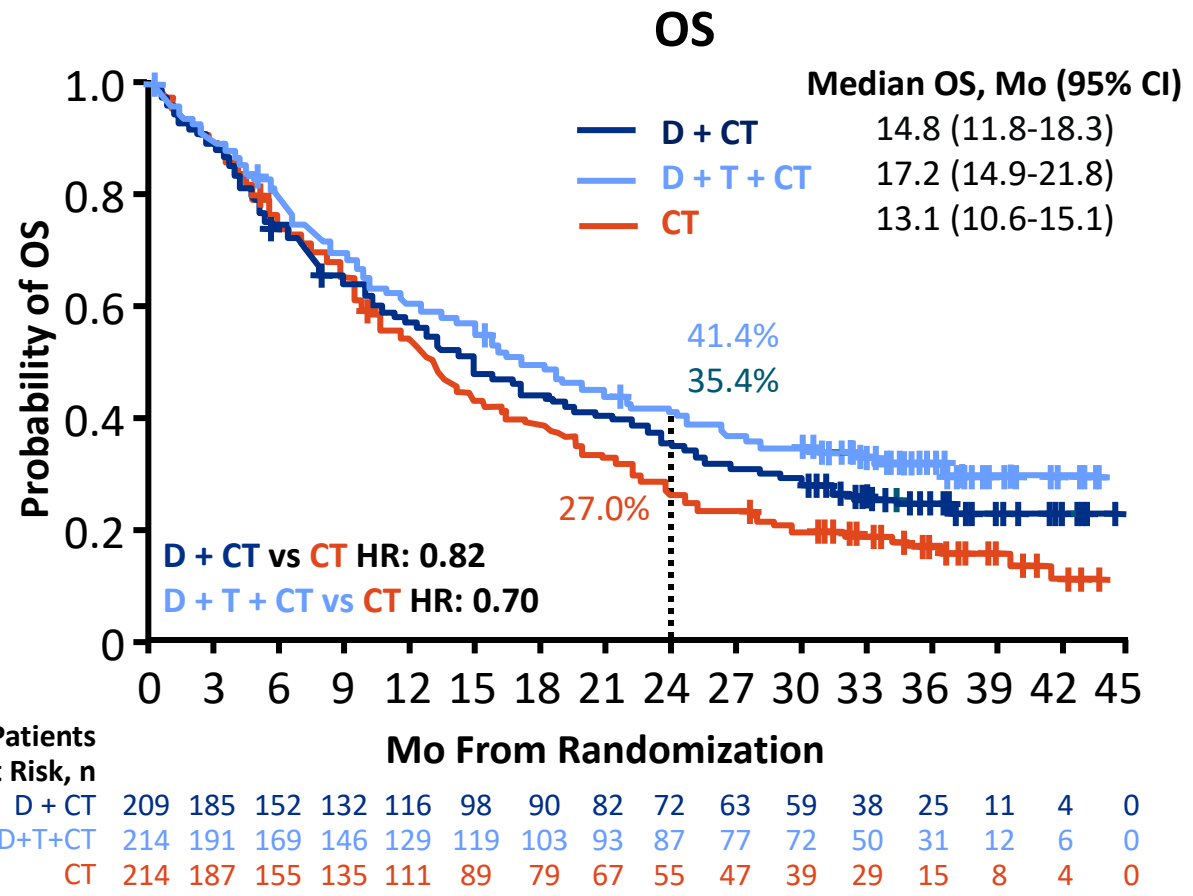
Johnson. WCLC 2021. Abstr PL02.01

KEY DATA

POSEIDON Clinical Trial

Efficacy: Non-squamous histology





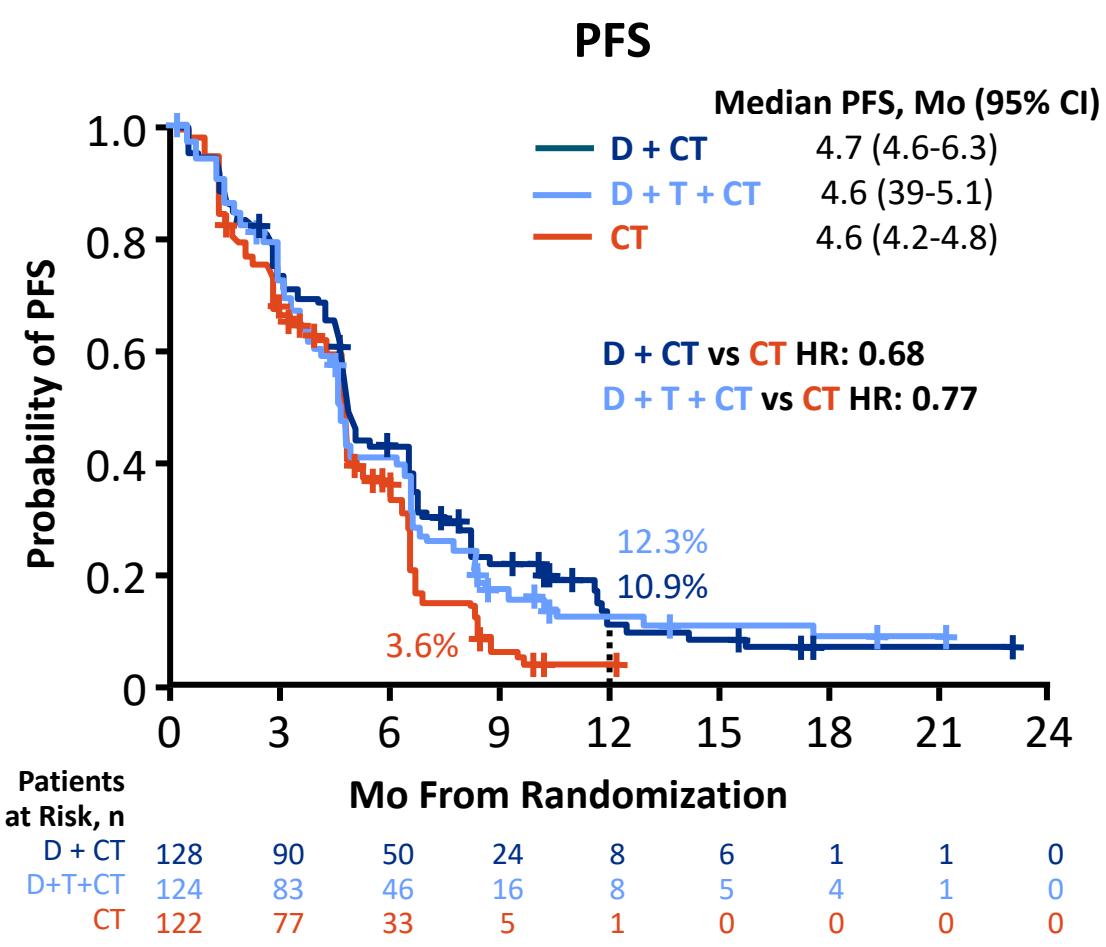
Note: 95.5% of patients with non-squamous histology who received CT had pemetrexed + platinum

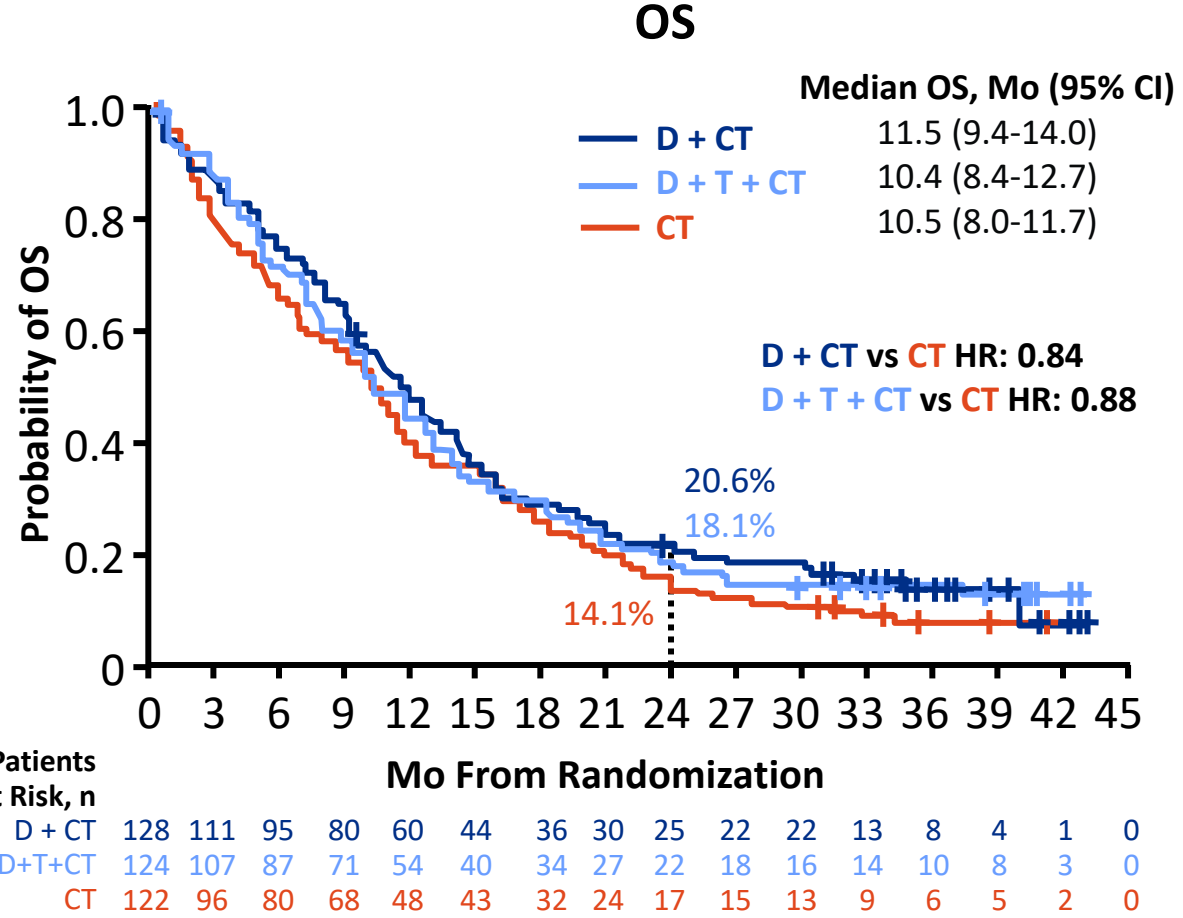
Johnson. WCLC 2021. Abstr PL02.01

KEY DATA

POSEIDON Clinical Trial

Efficacy: Squamous histology





Note: 88.3% of patients with squamous histology who received CT had gemcitabine + platinum

Johnson. WCLC 2021. Abstr PL02.01

KEY DATA

POSEIDON Clinical Trial

Response by Histology

Non-squamous: Response Outcome	**Durvalumab + CT (n = 203)**	**Durvalumab + Tremelimumab + CT (n = 211)**	**CT (n = 211)**
Confirmed ORR, %	**44.3**	**45.5**	**23.7**
Median DoR, mo (95% CI)	10.6 (6.6-NE)	16.4 (9.3-NE)	6.0 (4.4-8.7)

Squamous: Response Outcome	**Durvalumab + CT (n = 126)**	**Durvalumab + Tremelimumab + CT (n = 124)**	**CT (n = 121)**
Confirmed ORR, %	**37.3**	**27.4**	**25.6**
Median DoR, mo (95% CI)	5.5 (4.9-6.7)	5.6 (4.3-7.2)	4.8 (3.7-5.2)

Johnson. WCLC 2021. Abstr PL02.01

KEY DATA

POSEIDON Clinical Trial

Safety

Adverse Event, n (%)	Durvalumab + CT (n = 334)	Durvalumab + Tremelimumab + CT (n = 330)	CT (n = 333)
Any-grade all-cause AEs	321 (96.1)	321 (97.3)	320 (96.1)
• Grade 3/4 AE	183 (54.8)	176 (53.3)	172 (51.7)
• Serious AE	134 (40.1)	146 (44.2)	117 (35.1)
• AE leading to treatment discontinuation	68 (20.4)	73 (22.1)	51 (15.3)
• AE leading to death	34 (10.2)	41 (12.4)	30 (9.0)
Any-grade treatment-related AEs	296 (88.6)	306 (92.7)	298 (89.5)
• Grade 3/4 AE	149 (44.6)	171 (51.8)	148 (44.4)
• Serious AE	65 (19.5)	91 (27.6)	59 (17.7)
• AE leading to treatment discontinuation	47 (14.1)	51 (15.5)	33 (9.9)
• AE leading to death	7 (2.1)	11 (3.3)	8 (2.4)

Johnson. WCLC 2021. Abstr PL02.01

KEY DATA

POSEIDON Clinical Trial

Immune-Mediated Adverse Events

	Durvalumab + CT (n = 334)		Durvalumab + Tremelimumab + CT (n = 330)		CT (n = 333)	
Immune-Mediated AE*, n (%)	**Any Grade**	**Grade 3/4**	**Any Grade**	**Grade 3/4**	**Any Grade**	**Grade 3/4**
Any immune-mediated AE	64 (19.2)	23 (6.9)	111 (33.6)	33 (10.0)	17 (5.1)	5 (1.5)
Hypothyroid events	20 (6.0)	0	27 (8.2)	0	3 (0.9)	0
Pneumonitis	10 (3.0)	4 (1.2)	12 (3.6)	3 (0.9)	2 (0.6)	2 (0.6)
Rash	5 (1.5)	2 (0.6)	13 (3.9)	3 (0.9)	6 (1.8)	2 (0.6)
Hepatic events	11 (3.3)	8 (2.4)	12 (3.6)	7 (2.1)	0	0
Dermatitis	4 (1.2)	1 (0.3)	14 (4.2)	1 (0.3)	1 (0.3)	0
Colitis	4 (1.2)	1 (0.3)	13 (3.9)	5 (1.5)	0	0
Hyperthyroid events	4 (1.2)	1 (0.3)	9 (2.7)	0	1 (0.3)	0
Adrenal insufficiency	4 (1.2)	1 (0.3)	8 (2.4)	2 (0.6)	0	0
Rare/miscellaneous	1 (0.3)	1 (0.3)	11 (3.3)	3 (0.9)	2 (0.6)	1 (0.3)

Johnson. WCLC 2021. Abstr PL02.01

SUMMARY

POSEIDON Clinical Trial

Durvalumab plus chemotherapy significantly prolonged PFS vs chemotherapy alone

- PFS HR: 0.74 (95% CI: 0.62-0.89; *P* = 0.00093)
- Combination showed a trend toward longer OS that did not reach statistical significance (HR: 0.86; 95% CI: 0.72-1.02; *P* = 0.07581)
- Survival benefits were more prominent in patients with non-squamous histology

- Durvalumab plus tremelimumab and chemotherapy significantly improved both PFS and OS vs chemotherapy alone
  - PFS HR: 0.72 (95% CI: 0.60-0.86; *P* = 0.00031)
  - OS HR: 0.77 (95% CI: 0.65-0.92; *P* = 0.00304)
  - Survival benefits were more prominent in patients with non-squamous histology

Johnson. WCLC 2021. Abstr PL02.01

POSEIDON Clinical Trial

Durvalumab plus tremelimumab and chemotherapy is a potential new first-line treatment option for metastatic NSCLC

Q&A

Metastatic NSCLC

cornerstone specialty network™

2022 Lung Key Studies

(Neo)adjuvant NSCLC and Actionable NSCLC	Metastatic NSCLC and Actionable NSCLC	SCLC
• CheckMate -816 • IMpower010 • KEYNOTE-091	• CheckMate -9LA • ATEZO-BRAIN • DESTINY-Lung01 • EMPOWER-Lung1 • POSEIDON	• IMpower133 • CASPIAN • ATLANTIS • KEYNOTE-604 • CheckMate -451

IMpower133

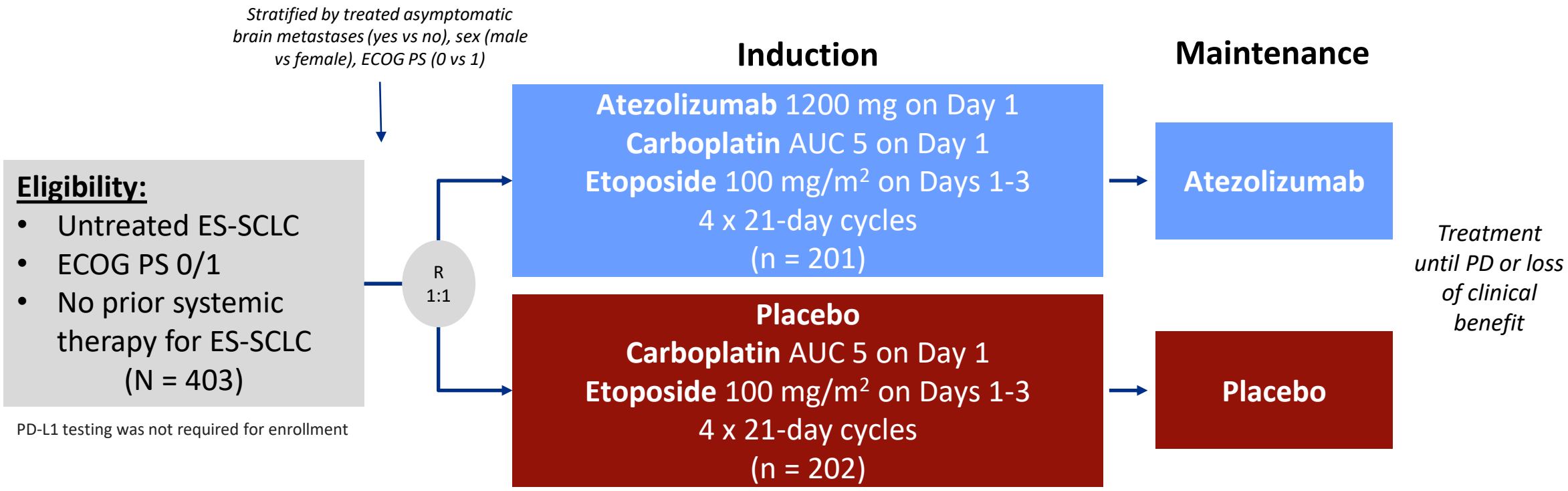
Does atezolizumab plus chemotherapy provide benefit for patients with extensive-stage SCLC in the first-line setting?

Updated OS and Subgroup Analysis
and
Real-world comparison study

cornerstone specialty network™

IMpower133

Study Design: Randomized, double-blind, placebo-controlled Phase 3 trial



Primary endpoints: investigator-assessed PFS, OS

Secondary endpoints: ORR, DoR, safety

Update median follow-up for OS was 22.9 months; 302 deaths had occurred.

Clinical cutoff date: January 24, 2019

ESMO 2019 Abstr: 2374; J Clin Oncol. 2021 Feb 20;39(6):619-630

IMpower133

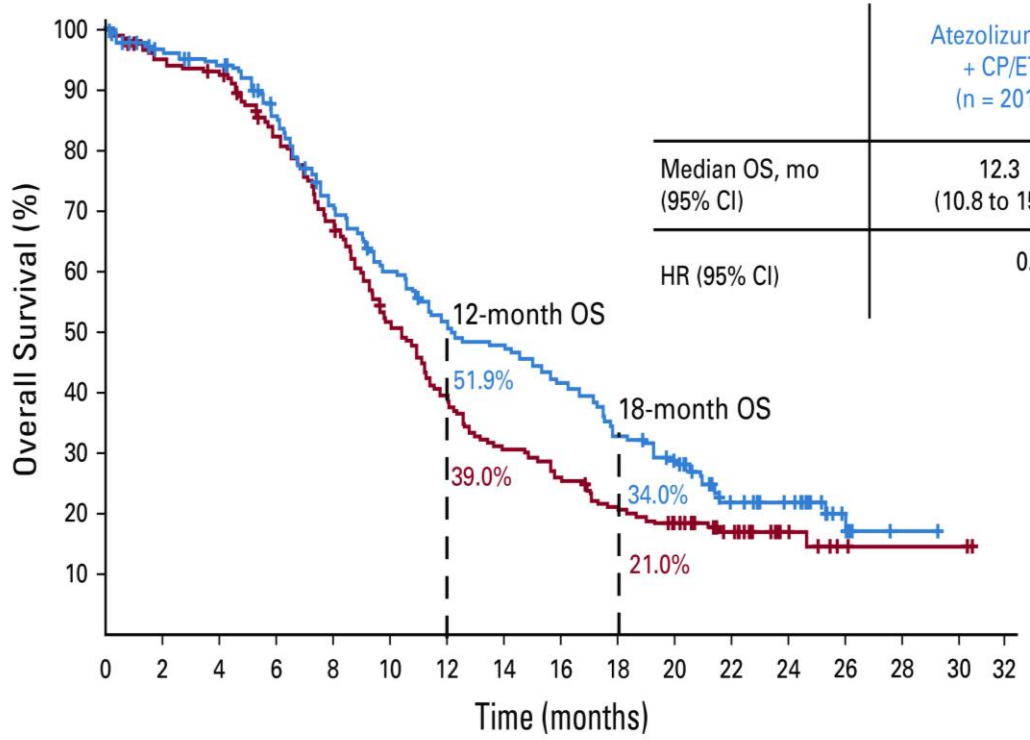
Baseline Characteristics

Characteristic	Atezolizumab + Carboplatin/Etoposide (n = 201)	Placebo + Carboplatin/Etoposide (n = 202)
Median age, yrs (range)	64 (28-90)	64 (26-87)
< 65 yrs, n (%)	111 (55)	106 (52)
≥ 65 yrs, n (%)	90 (45)	96 (48)
Male, n (%)	129 (64)	132 (65)
White, n (%)	163 (81)	159 (79)
Asian, n (%)	33 (16)	36 (18)
ECOG PS 0, n (%)	73 (36)	67 (33)
ECOG PS 1, n (%)	128 (64)	135 (67)
Current smoker, n (%)	74 (36.8)	75 (37.1)
Former smoker, n (%)	118 (58.7)	126 (61.4)
Brain metastases, n (%)	17 (8)	18 (9)
Liver metastases, n (%)	77 (38)	72 (36)

ESMO 2019 Abstr: 2374; J Clin Oncol. 2021 Feb 20;39(6):619-630

IMpower133

Updated Overall Survival



	Atezolizumab + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8 to 15.8)	10.3 (9.3 to 11.3)
HR (95% CI)	0.76 (0.60 to 0.95) *P* = .0154*	

No. of Patients at Risk

Atezolizumab + CP/ET	201	187	180	159	130	109	93	86	75	61	51	28	21	8	1
Placebo + CP/ET	202	189	183	160	131	97	74	58	49	39	33	20	8	3	2	2

	Atezo + CP/ET		Placebo + CP/ET
6-month OS	86% (n=159)		83% (n=160)
12-month OS	52% (n=93)	Δ 13%	39% (n=74)
18-month OS (Exploratory)	34% (n=61)	Δ 13%	21% (n=39)
24-months OS (Subject to change with longer follow-up)	22% (n=21)		17% (n=8)

The safety observed in the updated analysis was generally consistent with the safety observed in the initial analysis.

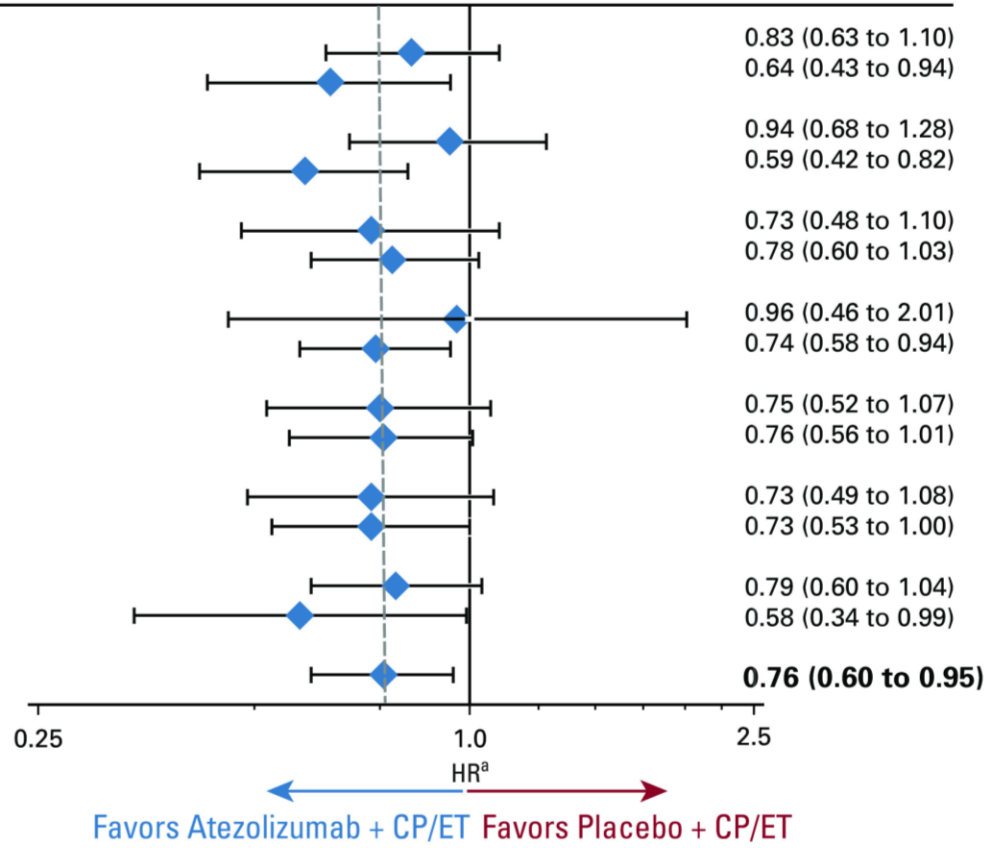
Clinical cutoff date: January 24, 2019

ESMO 2019 Abstr: 2374; J Clin Oncol. 2021 Feb 20;39(6):619-630

IMpower133

Updated Overall Survival

Subgroup	Median OS (months) Atezolizumab + CP/ET	Placebo + CP/ET	OS HR[a] (95% CI)
Male (n = 261)	12.2	10.9	0.83 (0.63 to 1.10)
Female (n = 142)	13.6	9.5	0.64 (0.43 to 0.94)
< 65 years (n = 217)	12.1	11.5	0.94 (0.68 to 1.28)
≥ 65 years (n = 186)	14.4	9.6	0.59 (0.42 to 0.82)
ECOG PS 0 (n = 140)	16.8	12.6	0.73 (0.48 to 1.10)
ECOG PS 1 (n = 263)	11.3	9.3	0.78 (0.60 to 1.03)
Brain metastases (n = 35)	8.5	9.7	0.96 (0.46 to 2.01)
No brain metastases (n = 368)	12.6	10.4	0.74 (0.58 to 0.94)
Liver metastases (n = 149)	9.3	7.8	0.75 (0.52 to 1.07)
No liver metastases (n = 254)	16.3	11.2	0.76 (0.56 to 1.01)
bTMB < 10 (n = 134)	11.8	9.4	0.73 (0.49 to 1.08)
bTMB ≥ 10 (n = 212)	14.9	11.2	0.73 (0.53 to 1.00)
bTMB < 16 (n = 266)	12.5	10.0	0.79 (0.60 to 1.04)
bTMB ≥ 16 (n = 80)	17.1	11.9	0.58 (0.34 to 0.99)
ITT (N = 403)	**12.3**	**10.3**	**0.76 (0.60 to 0.95)**



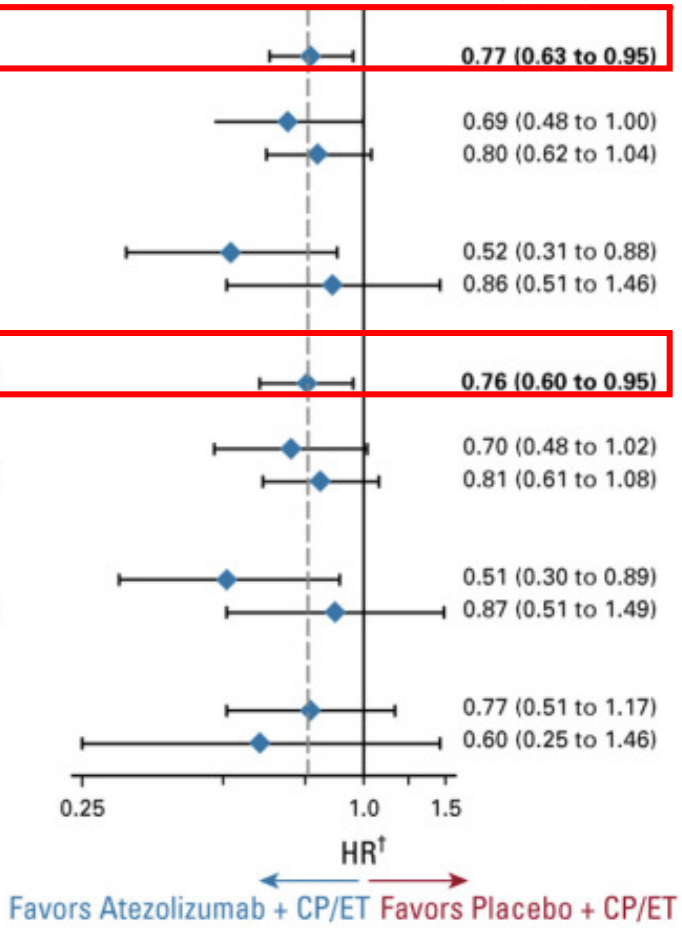
A total of 57 patients had unknown bTMB (blood-based tumor mutational burden) score. These patients comprised the nonbiomarker evaluable population, which included 28 patients who had a bTMB result with a maximum somatic allele frequency < 1%, 15 patients who had a sample that either failed quality control at the testing vendor or had median exon coverage < 800, and 14 patients who did not submit a plasma sample at baseline.

ESMO 2019 Abstr: 2374; J Clin Oncol. 2021 Feb 20;39(6):619-630

IMpower133

Updated Subgroup Analysis

Subgroup	Atezolizumab + CP/ET	Placebo + CP/ET	HR[a] (95% CI)
PFS (months)			
All patients (N = 403)	**5.2**	**4.3**	**0.77 (0.63 to 0.95)**
ITT-BEP			
BEP (n = 137)	5.2	4.2	0.69 (0.48 to 1.00)
Non-BEP (n = 266)	5.2	4.3	0.80 (0.62 to 1.04)
PD-L1 expression 1%			
< 1% PD-L1 (n = 65)	5.4	4.2	0.52 (0.31 to 0.88)
≥ 1% PD-L1 (n = 72)	5.1	5.5	0.86 (0.51 to 1.46)
OS (months)			
All patients (N = 403)	**12.3**	**10.3**	**0.76 (0.60 to 0.95)**
ITT-BEP			
BEP (n = 137)	9.9	8.9	0.70 (0.48 to 1.02)
Non-BEP (n = 266)	14.6	11.2	0.81 (0.61 to 1.08)
PD-L1 expression 1%			
< 1% PD-L1 (n = 65)	10.2	8.3	0.51 (0.30 to 0.89)
≥ 1% PD-L1 (n = 72)	9.7	10.6	0.87 (0.51 to 1.49)
PD-L1 expression 5%			
< 5% PD-L1 (n = 108)	9.2	8.9	0.77 (0.51 to 1.17)
≥ 5% PD-L1 (n = 29)	21.6	9.2	0.60 (0.25 to 1.46)



Subgroup analysis of PFS (clinical cutoff date: April 4, 2018) and **OS (clinical cutoff date: January 24, 2019)** by programmed death-ligand 1 (PD-L1) expression in the biomarker-evaluable population (BEP)

ESMO 2019 Abstr: 2374; J Clin Oncol. 2021 Feb 20;39(6):619-630

IMpower133

Real world, retrospective comparison using The US Oncology Network EHR data

	IMpower133	Real-World Study
Baseline Characteristic	**Atezolizumab + Carboplatin/Etoposide (n = 201)**	**Atezolizumab + Carboplatin/Etoposide (n=267)**
Median age, yrs (range)	**64 (28-90)**	**68 (32-88)**
Male, n (%)	**129 (64.2)**	**121 (45.3)**
White, n (%)	**163 (81.1)**	**195 (73.0)**
ECOG PS 0, n (%)	73 (36.3)	16 (6.0)
ECOG PS 1, n (%)	128 (63.7)	143 (53.6)
ECOG PS 2+, n (%)	**0**	**65 (24.3)**
ECOG not documented	---	43 (16.1)
Current smoker, n (%)	74 (36.8)	54 (20.2)
Former smoker, n (%)	118 (58.7)	63 (23.6)
Never smoked	9 (4.5)	3 (1.1)
Smoking Not documented	---	147 (55.1)
Brain metastases at baseline, n (%)	**17 (8.5)**	**61 (22.8)**

ASCO 2021 Abstr: 8561;
J Clin Oncol. 2021 Feb 20;39(6):619-630

SUMMARY

IMpower133

Real world, retrospective comparison using The US Oncology Network EHR data

IMpower133 Atezolizumab + Carboplatin/Etoposide (n = 201)	Real-World Study Atezolizumab + Carboplatin/Etoposide (n=267)
Median follow-up: (data cut-off April 24, 2018) 13.9 months	Median follow-up: 5.45 months (range 0.72 – 14.36)
Median duration of treatment: **4.7 months** (range 0 – 21)	K-M median time to treatment discontinuation: **4.9 months** (95% CI: 4.2-5.3)
% still on treatment > 6 months: **31.33%**	% still on treatment at 6 months (K-M): **35.1%** (95%CI: 28.4 – 41.9)
K-M Median progression-free survival (PFS): **5.2 months** (95% CI: 4.4 – 5.6)	K-M Median time to next treatment/death (TTNT): **6.9 months** (95% CI: 6.4 – 8.2)
PFS (RECIST criteria) at 6 months: 30.9% (95% CI: 24.3 – 37.5)	% not initiated on 2L at 6 months: 64.5 % (95% CI: 56.7 – 71.3)

ASCO 2021 Abstr: 8561;
J Clin Oncol. 2021 Feb 20;39(6):619-630

IMpower133

Atezolizumab plus chemotherapy continues to provide benefit for patients with extensive-stage SCLC in the first-line setting and should be considered practice-changing

2022 Lung Key Studies

(Neo)adjuvant NSCLC and Actionable NSCLC	Metastatic NSCLC and Actionable NSCLC	SCLC
• CheckMate -816 • IMpower010 • KEYNOTE-091	• CheckMate -9LA • ATEZO-BRAIN • DESTINY-Lung01 • EMPOWER-Lung1 • POSEIDON	• IMpower133 • CASPIAN • KEYNOTE-604 • CheckMate-451 • ATLANTIS

CASPIAN

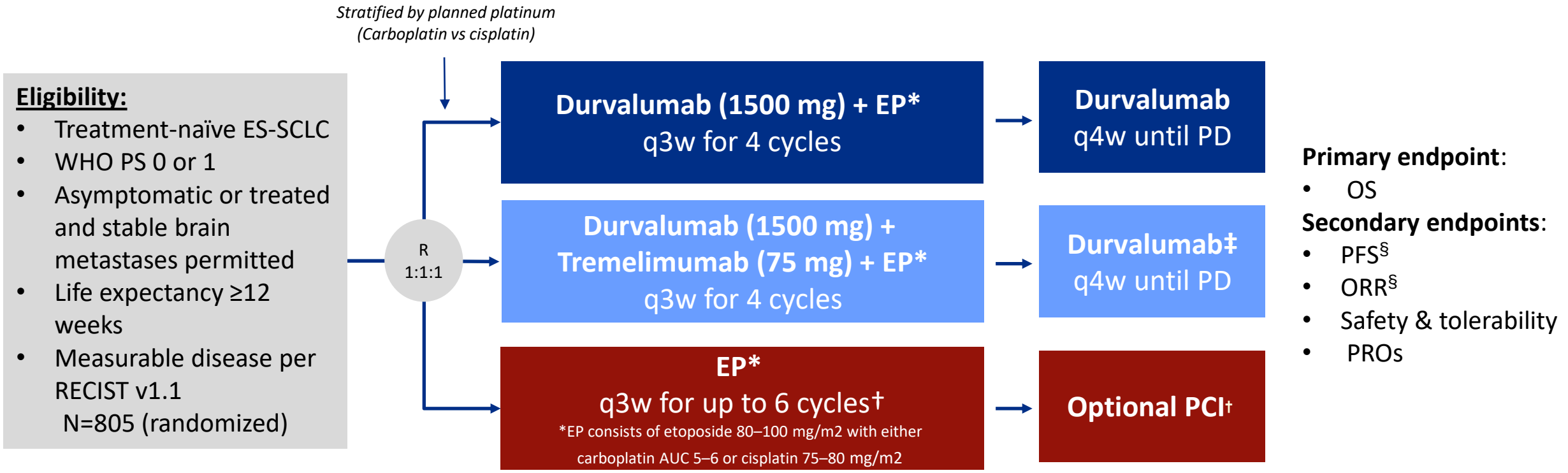
Does durvalumab in combination with chemotherapy, with or without tremelimumab, benefit patients with extensive-stage SCLC?

3-year Overall Survival Update

KEY DATA

CASPIAN

Study Design: Randomized, open-label, global Phase 3 trial



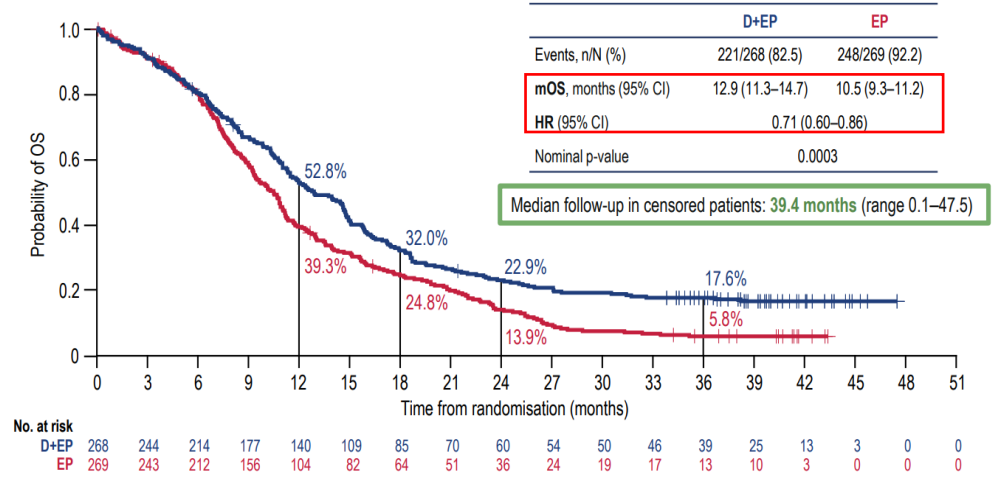
Updated analysis of OS after median follow-up of approximately 3 years was a planned exploratory analysis. Data cutoff: 22 March 2021. PFS and ORR data were not collected since the previous data cutoff. Serious AEs (including deaths) were analyzed, but other safety data were not collected.

†Patients could receive an additional 2 cycles of EP (up to 6 cycles total) and PCI at the investigator's discretion; ‡Patients received an additional dose of tremelimumab post-EP; §By investigator assessment per RECIST v1.1 AEs, adverse events; AUC, area under the curve; ORR, objective response rate; PCI, prophylactic cranial irradiation; PD, disease progression; PFS, progression-free survival; PROs, patient-reported outcomes; PS, performance status; q3w, every 3 weeks; q4w, every 4 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

KEY DATA

CASPIAN

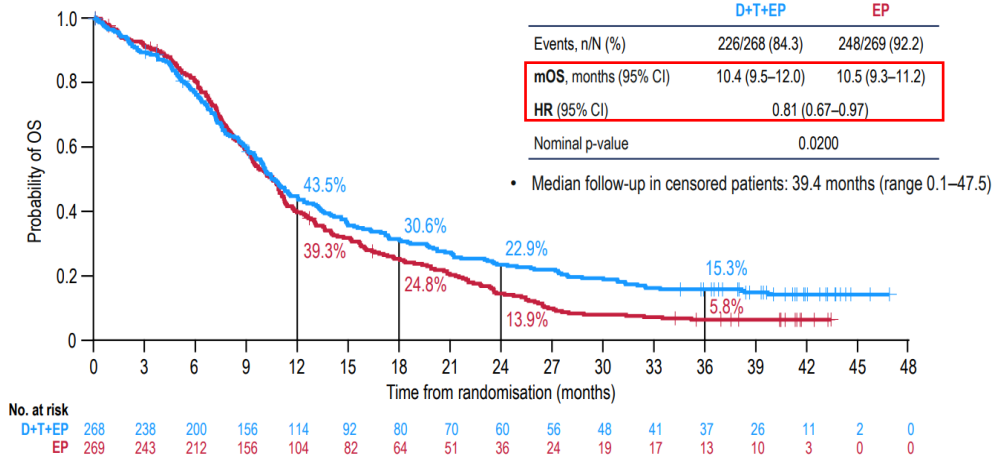
3-year Overall Survival Update: D+EP vs EP



	D+EP	EP
Events, n/N (%)	221/268 (82.5)	248/269 (92.2)
mOS, months (95% CI)	12.9 (11.3–14.7)	10.5 (9.3–11.2)
HR (95% CI)	0.71 (0.60–0.86)	
Nominal p-value	0.0003	

Median follow-up in censored patients: 39.4 months (range 0.1–47.5)

3-year Overall Survival Update: D+T+EP vs EP



	D+T+EP	EP
Events, n/N (%)	226/268 (84.3)	248/269 (92.2)
mOS, months (95% CI)	10.4 (9.5–12.0)	10.5 (9.3–11.2)
HR (95% CI)	0.81 (0.67–0.97)	
Nominal p-value	0.0200	

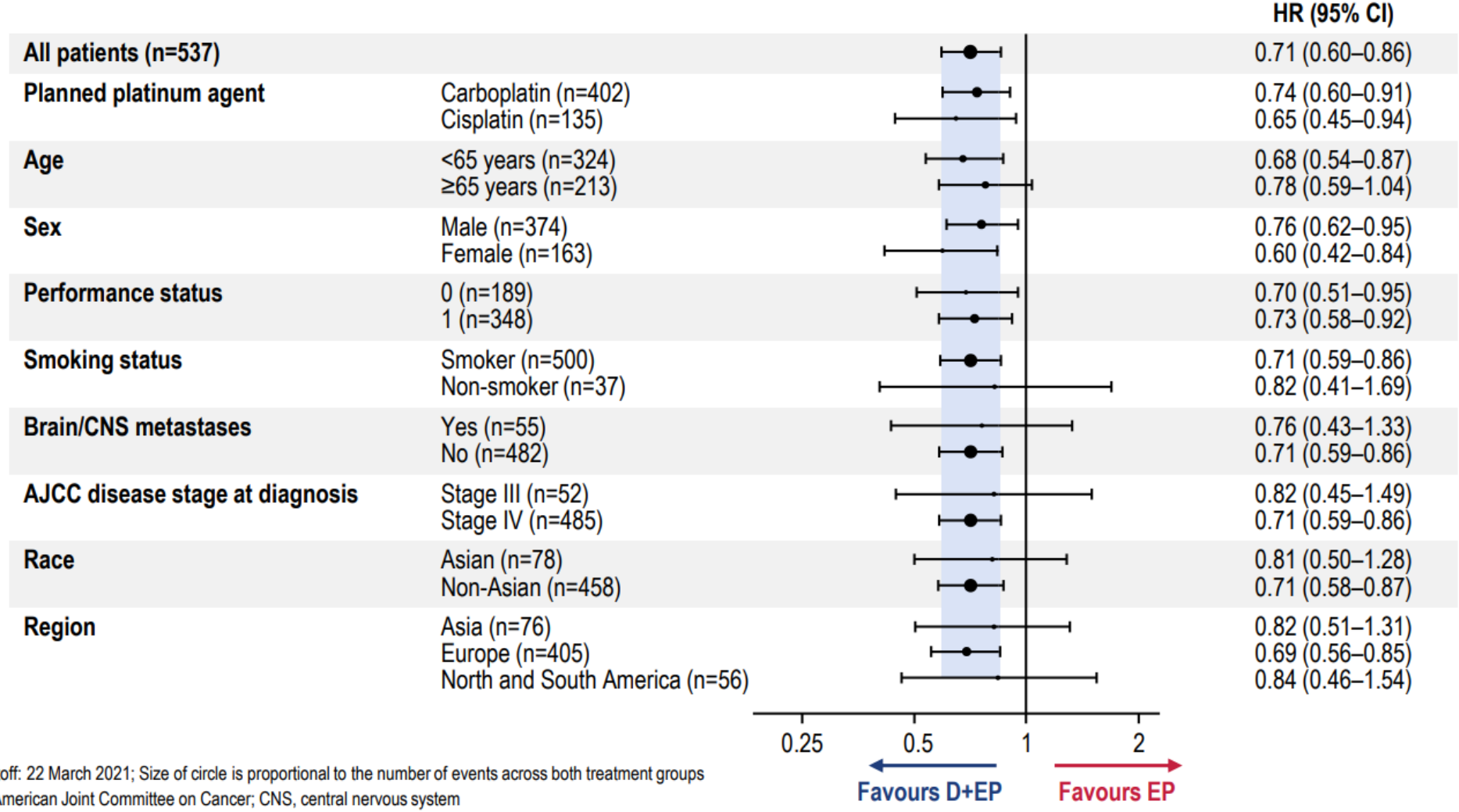
- Median follow-up in censored patients: 39.4 months (range 0.1–47.5)

OS (%)	D+EP	D+T+EP	EP
12 months	52.8%	43.5%	39.3%
18 months	32.0%	30.6%	24.8%
24 months	22.9%	22.9%	13.9%
36 months	17.6%	15.3%	5.8%

ESMO 2021 Abstr LBA61

CASPIAN

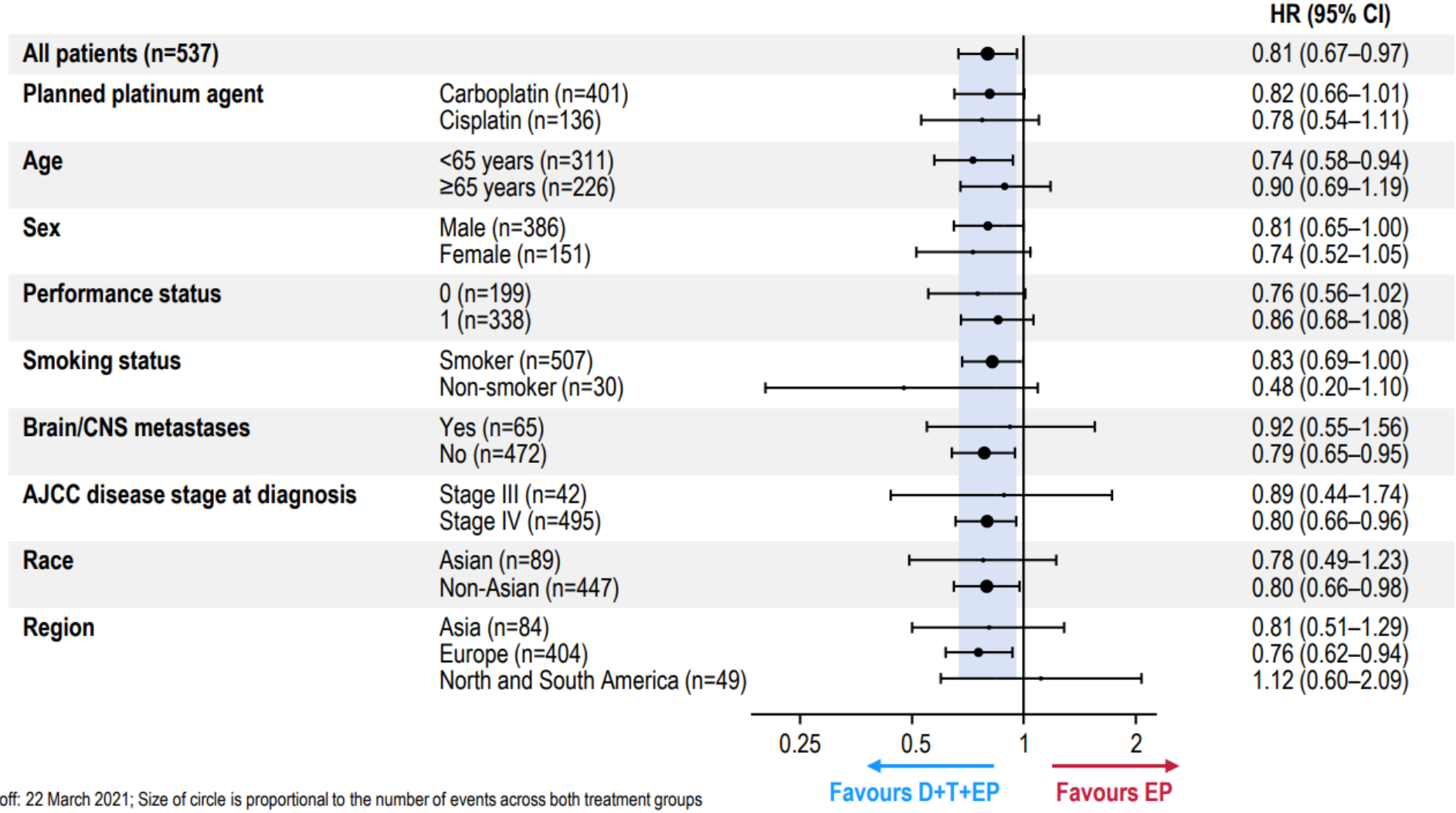
3-year Overall Survival Update: D+EP vs EP Subgroup Analysis



Data cutoff: 22 March 2021; Size of circle is proportional to the number of events across both treatment groups
AJCC, American Joint Committee on Cancer; CNS, central nervous system

CASPIAN

3-year Overall Survival update: D+T+EP vs EP Subgroup Analysis



Data cutoff: 22 March 2021; Size of circle is proportional to the number of events across both treatment groups

CASPIAN

Treatment Exposure: D+EP vs D+T+EP

	D+EP (n=265)	D+T+EP (n=266)
Ongoing durvalumab at data cutoff, n (%)	27 (10.2)	19 (7.1)
Median number of durvalumab doses (range)	7.0 (1–52)	6.0 (1–46)
Total duration of durvalumab exposure, n (%)		
≥1 year	54 (20.4)	49 (18.4)
≥2 years	32 (12.1)	30 (11.3)
≥3 years	24 (9.1)	21 (7.9)
Median total duration of durvalumab, weeks (range)	28.0 (0.3–198.7)	23.1 (0.1–190.0)

CASPIAN

3-year Serious Adverse Events Update

	D+EP (n=265)	D+T+EP (n=266)	EP (n=266)
Serious AEs (all cause), n (%)*	**86 (32.5)**	**126 (47.4)**	**97 (36.5)**
Febrile neutropenia	12 (4.5)	11 (4.1)	12 (4.5)
Pneumonia	6 (2.3)	16 (6.0)	11 (4.1)
Anaemia	5 (1.9)	9 (3.4)	12 (4.5)
Thrombocytopenia	1 (0.4)	6 (2.3)	9 (3.4)
Hyponatremia	2 (0.8)	9 (3.4)	4 (1.5)
Neutropenia	2 (0.8)	5 (1.9)	7 (2.6)
Diarrhea	2 (0.8)	7 (2.6)	4 (1.5)
Pulmonary embolism	1 (0.4)	7 (2.6)	0
AEs leading to death (all cause), n (%)†	**14 (5.3)**	**29 (10.9)**	**16 (6.0)**
Treatment-related AEs leading to death	6 (2.3)	12 (4.5)	2 (0.8)

*Serious AEs occurring in ≥2% patients in any treatment arm are shown; †Four additional deaths were reported since the previous analysis (none considered treatment related): one in the D+EP arm (aspiration), two in the D+T+EP arm (drowning and pneumocystis jirovecii pneumonia), and one in the EP arm (small intestine leiomyosarcoma)

SUMMARY

CASPIAN

- First-line durvalumab in combination with EP demonstrated ongoing improvement in overall survival vs EP with 3 years of follow-up
  - 12.9 months vs 10.5 months; HR: 0.71 (95% CI: 0.60-0.86; *P* = 0.0003)
  - OS benefit was maintained across subgroups
- No significant improvement in outcomes with addition of tremelimumab to durvalumab with EP
- No new safety concerns; consistent with previous findings

CASPIAN

Durvalumab in combination with chemotherapy continues to provide benefit for patients with extensive-stage SCLC and should be considered practice changing in the first-line setting

2022 Lung Key Studies

(Neo)adjuvant NSCLC and Actionable NSCLC	Metastatic NSCLC and Actionable NSCLC	SCLC
• CheckMate -816 • IMpower010 • KEYNOTE-091	• CheckMate -9LA • ATEZO-BRAIN • DESTINY-Lung01 • EMPOWER-Lung1 • POSEIDON	• IMpower133 • CASPIAN • ATLANTIS • KEYNOTE-604 • CheckMate -451

CLINICAL QUESTION

ATLANTIS

Does lurbinectedin in combination with doxorubicin benefit patients with relapsed SCLC after 1 prior line of chemotherapy?

ATLANTIS

Study Design: Multicenter, randomized phase III trial

Stratified by ECOG PS (0 vs 1-2), CTFI (≥180 vs 90-179 vs <90 days), CNS involvement (yes vs no), prior PD-1/PD-L1 inhibitor (yes vs no), investigator preference for control arm

Eligibility

- SCLC with 1 prior line of chemotherapy (other biologic lines allowed)
- ECOG PS 0-2
- Patients with chemotherapy-free interval (CTFI) <30 days excluded

(N = 613)

Doxorubicin* 40 mg/m^2 Day 1 **+**
Lurbinectedin† 2 mg/m^2 Day 1 Q3W
(n = 307)

Topotecan 1.5 mg/m^2 Days 1-5 Q3W or
CAV‡ Day 1 Q3W
(n = 306)

PD or unacceptable toxicity

*Maximum 10 cycles of doxorubicin.
†Lurbinectedin continued as maintenance at 3.2 mg/m^2 Day 1 Q3W.
‡CAV, cyclophosphamide/doxorubicin/vincristine.
G-CSF prophylaxis mandatory in both arms.

Primary endpoint: OS

Secondary endpoints: PFS, tumor response, DoR, safety

Paz-Ares. WCLC 2021. Abstr PL02A.03.

ATLANTIS

Baseline Characteristics

Parameter	Lurbinectedin + Doxorubicin (n = 307)	Topotecan or CAV (n = 306)
Male, %	57.3	56.5
Median age, yr (range)	63.0 (19-83)	63.0 (37-82)
Median BSA, m^2 (range)	1.8 (1.4-2.5)	1.8 (1.3-2.8)
ECOG PS 0/1/2, %	30.9/64.2/4.9	31.0/66.7/2.3
Smoking status former/current/never, %	29.6/64.2/6.2	29.1/65.0/5.9
Median time since SCLC diagnosis, mo (range)	9.3 (2.5-55.5)	9.1 (2.3-42.3)
Bulky disease (1 lesion ≥50 mm), %	46.9	41.5
CNS involvement, %	15.0	16.0
1 prior line treatment, %	97.1	98.7
Best response prior chemotherapy CR/PR/SD, %	5.5/62.5/23.1	4.9/62.4/20.6
Prior anti–PD-1 or PD-L1, %	6.2	5.6
Median TTP to prior chemotherapy, mo (range)	7.4 (0.8-40.2)	7.4 (1.6-33.7)
Median CTFI, days (range) • **<90/90-179/≥180**	115.0 (0-1094) 32.2/37.5/30.3	120.5 (13-960) 33.0/37.9/29.1

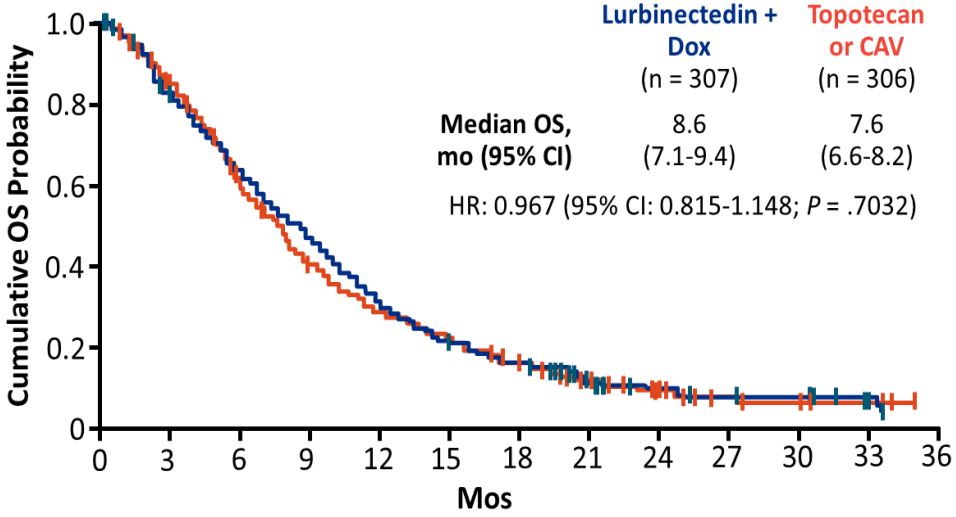
Paz-Ares. WCLC 2021. Abstr PL02A.03.

KEY DATA

ATLANTIS

Efficacy

OS in ITT Population

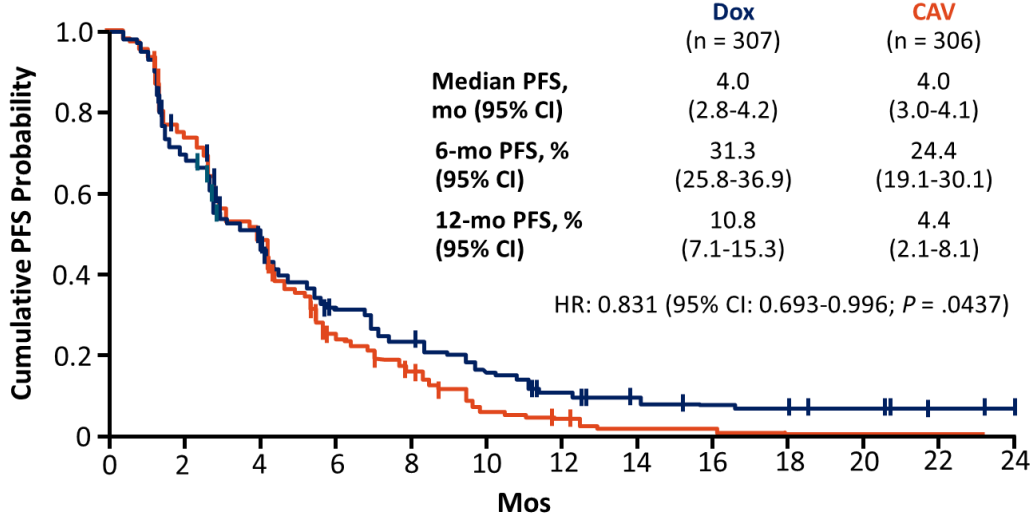


	Lurbinectedin + Dox (n = 307)	Topotecan or CAV (n = 306)
Median OS, mo (95% CI)	8.6 (7.1-9.4)	7.6 (6.6-8.2)

HR: 0.967 (95% CI: 0.815-1.148; *P* = .7032)

Lurbinectedin + Dox	307	247	188	138	91	62	43	25	14	10	9	5
Topotecan or CAV	306	244	168	111	77	62	42	24	15	8	6	4

PFS by Independent Review



	Lurbinectedin + Dox (n = 307)	Topotecan or CAV (n = 306)
Median PFS, mo (95% CI)	4.0 (2.8-4.2)	4.0 (3.0-4.1)
6-mo PFS, % (95% CI)	31.3 (25.8-36.9)	24.4 (19.1-30.1)
12-mo PFS, % (95% CI)	10.8 (7.1-15.3)	4.4 (2.1-8.1)

HR: 0.831 (95% CI: 0.693-0.996; *P* = .0437)

Lurbinectedin + Dox	307	198	134	72	52	34	21	16	12	11	9	6	5
Topotecan or CAV	306	196	119	50	32	11	7	3	3	1	1	1	

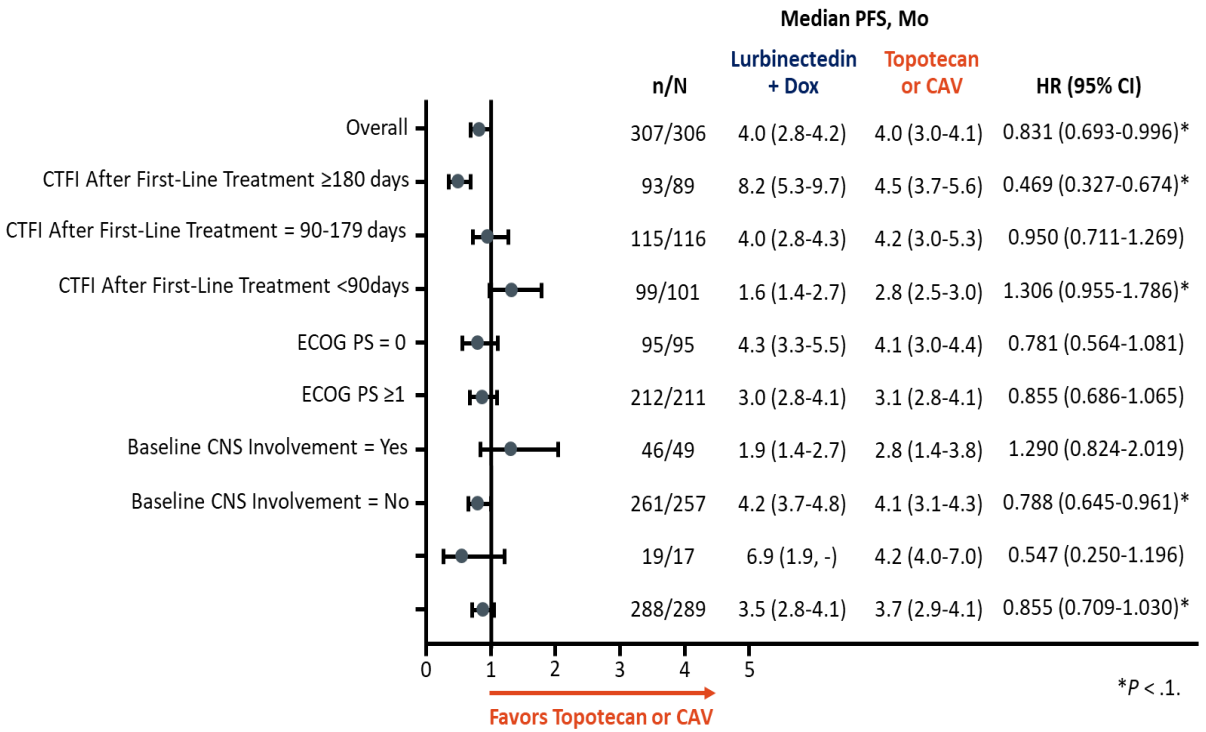
Paz-Ares. WCLC 2021. Abstr PL02A.03.

KEY DATA

ATLANTIS

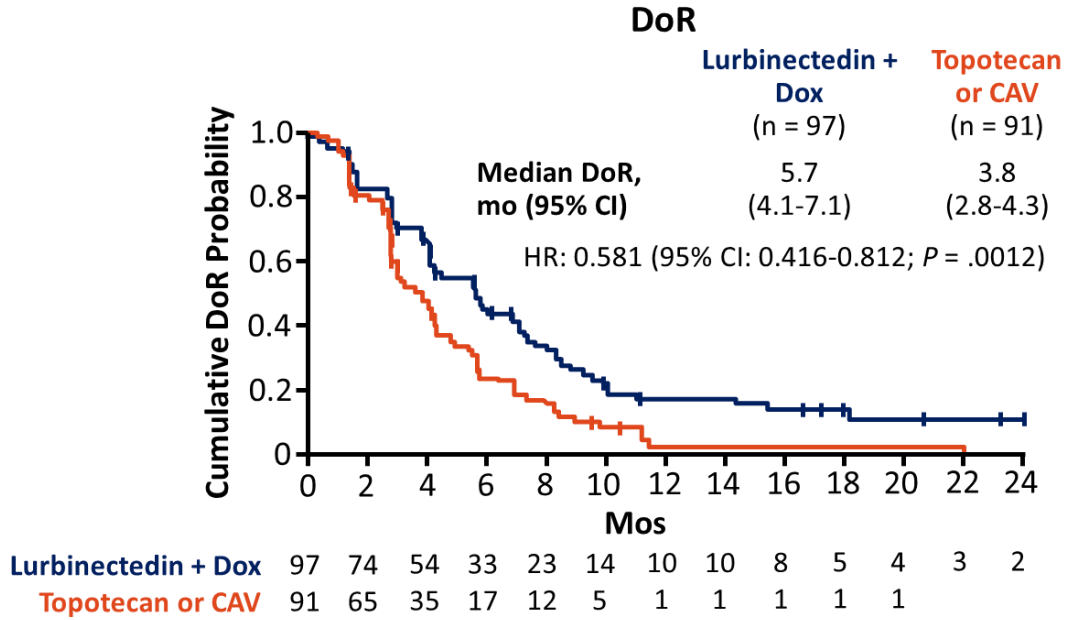
Efficacy

PFS by Stratification Factors



CTFI: Chemotherapy-free interval

Response



ORR	Lurbinectedin + Doxorubicin		Topotecan or CAV	
	n	ORR, %	n	ORR, %
All Patients	307	**31.6**	306	**29.7**
CTFI after 1L tx				
<90 days	99	20.2	101	18.8
90-179 days	115	33.0	116	39.7
≥180 days	93	41.9	89	29.9

Paz-Ares. WCLC 2021. Abstr PL02A.03.

KEY DATA

ATLANTIS

Safety

Grade ≥3 AE	Lurbinectedin + Doxorubicin (n = 303)	Topotecan or CAV (n = 289)	P Value
Hematologic, n (%)			
Anemia	44 (14.5)	90 (31.1)	<0.0001
Neutropenia	112 (37.0)	200 (69.2)	<0.0001
Febrile neutropenia	12 (4.0)	24 (8.3)	0.0377
Thrombocytopenia	42 (13.9)	90 (31.1)	<0.0001
Nonhematologic, n (%)			
ALT increased	6 (2.0)	3 (1.0)	0.5057
AP increased	2 (0.7)	3 (1.0)	0.6783
AST increased	7 (2.3)	4 (1.4)	0.5463
Fatigue	26 (8.6)	31 (10.7)	0.4051
Nausea	6 (2.0)	4 (1.4)	0.7525
Vomiting	4 (1.3)	0	0.1242

AE-Related Outcome, n (%)	Lurbinectedin + Doxorubicin (n = 303)	Topotecan or CAV (n = 289)
Any TRAE	268 (88.4)	266 (92.0)
Any grade ≥3 AE	143 (47.2)	218 (75.4)
Any grade 4 AE	49 (16.2)	158 (54.7)
Any grade ≥3 SAE	38 (12.5)	83 (28.7)
Death due to AE	1 (0.3)	10 (3.5)
Discontinuations due to AE	23 (7.6)	45 (15.6)
Delays due to AEs	79 (26.1)	99 (34.3)
Reductions due to AEs	66 (21.8)	138 (47.8)

Paz-Ares. WCLC 2021. Abstr PL02A.03.

ATLANTIS

Lurbinectedin in combination with doxorubicin did not provide overall survival benefit in patients with relapsed SCLC

- *June 15th, 2020: FDA accelerated approval for lurbinectedin monotherapy for the treatment of adult patients with metastatic SCLC with disease progression, after platinum-based chemotherapy*
  - *ORR of 35% and a median DoR of 5.3 months*
  - *Higher dose used in monotherapy trial compared to dose used in combination in ATLANTIS*

2022 Lung Key Studies

(Neo)adjuvant NSCLC and Actionable NSCLC	Metastatic NSCLC and Actionable NSCLC	SCLC
• CheckMate -816 • IMpower010 • KEYNOTE-091	• CheckMate -9LA • ATEZO-BRAIN • DESTINY-Lung01 • EMPOWER-Lung1 • POSEIDON	• IMpower133 • CASPIAN • ATLANTIS • KEYNOTE-604 • CheckMate -451

SUMMARY

	KEYNOTE-604		CheckMate -451		
Trial	Randomized, double-blind, multicenter Phase 3 trial		Randomized, double-blind, multicenter Phase 3 trial		
Eligibility	Stage IV SCLC; No previous systemic therapy; ECOG PS 0/1 with adequate organ function; Life expectancy ≥ 3 mos; No unstable brain metastases		ED-SCLC; ECOG PS 0/1; At least stable disease following 4 cycles of first-line platinum-based CT; No symptomatic CNS mets		
Arms	**Pembrolizumab + Etoposide + Platinum CT** (n = 228)	**Placebo + Etoposide + Platinum CT** (n=225)	**Nivolumab + Ipilimumab** (n = 279)	**Placebo** (n = 275)	**Nivolumab** (n= 280)
Median PFS, months	4.8	4.3	1.7	1.4	1.9
	HR 0.73 (95% CI: 0.60 – 0.88)		HR 0.72 (95% CI 0.60 -0.87)		HR 0.67 (95% CI, 0.56 to 0.81)
Median OS, months	**10.8**	**9.7**	**9.2**	**9.6**	**10.4**
	HR 0.78 (95% CI: 0.63 – 0.97; *P* = 0.0124)		HR 0.92 (0.8-1.1; *P* = 0.37)		HR 0.84 (0.7-1.0)
ORR, % (95% CI)	70.6 (64.2-76.4)	61.8 (55.1-68.2)	9.1% (5.9 to 13.2)	4.2% (2.1 – 7.4)	11.5% (7.9 – 16.0)
Median DoR, months (range)	4.2 (1.0 – 26+)	3.7 (1.4 – 26.8+)	10.2 (3.5 to 16.1)	8.1 (2.1 to nr)	11.2 (7.3 to nr)
Outcome	Did not meet primary OS endpoint Indication withdrawn March 2021		Did not meet primary OS endpoint Indication withdrawn December 2020		

Rudin. ASCO 2020. Abstr 9001.

Owonikoko. ELCC 2019. Abstr LBA1.
Journal of Clinical Oncology 2021, 39, 12: 1349-1359.

Q&A

SCLC

Thank you