

2022-08-27

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SC 컨벤션센터 12층 아나이스홀

Clinical trial and real-world data

: 1L Platinum-EPs combined with Atezolizumab
in Extensive-stage(ES)-SCLC

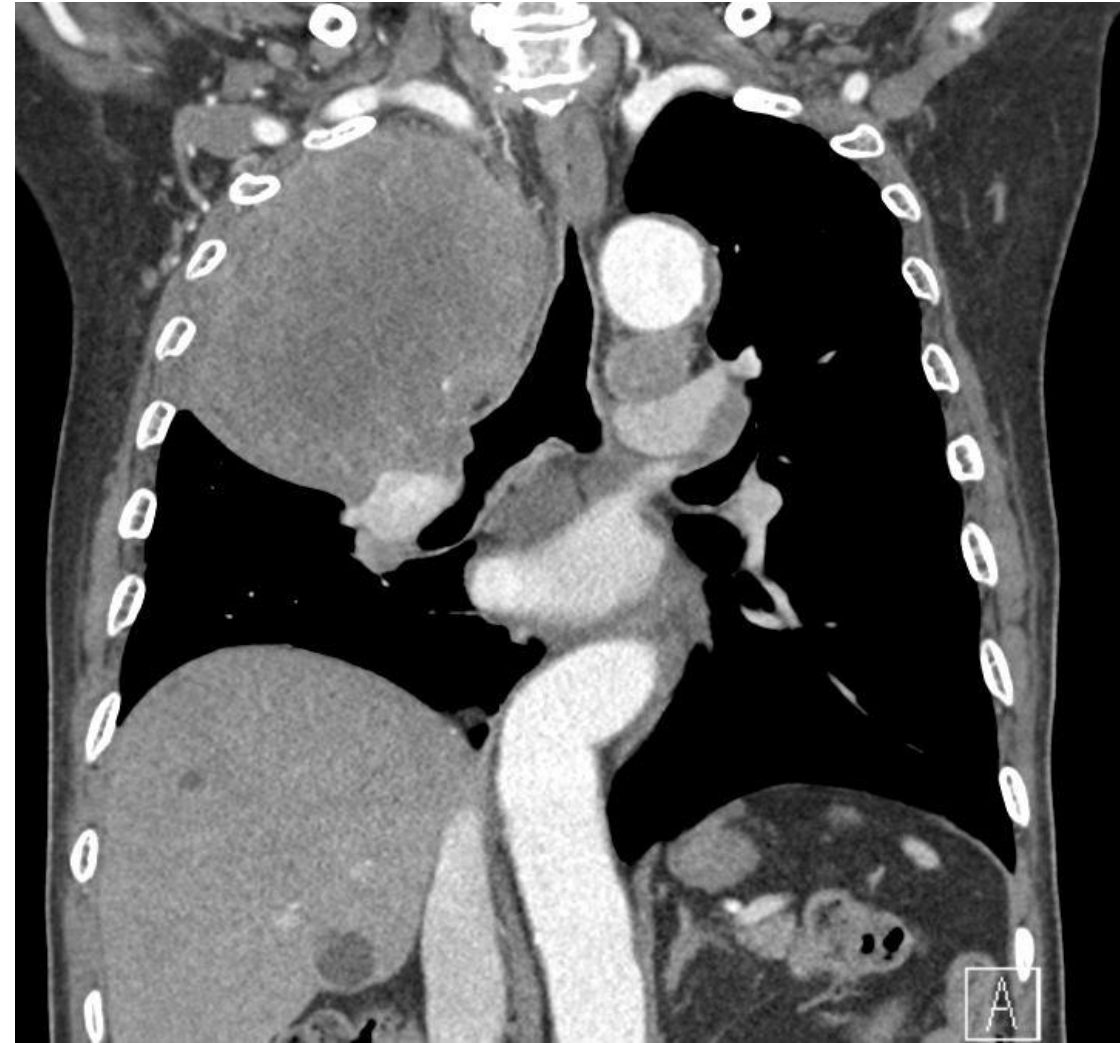
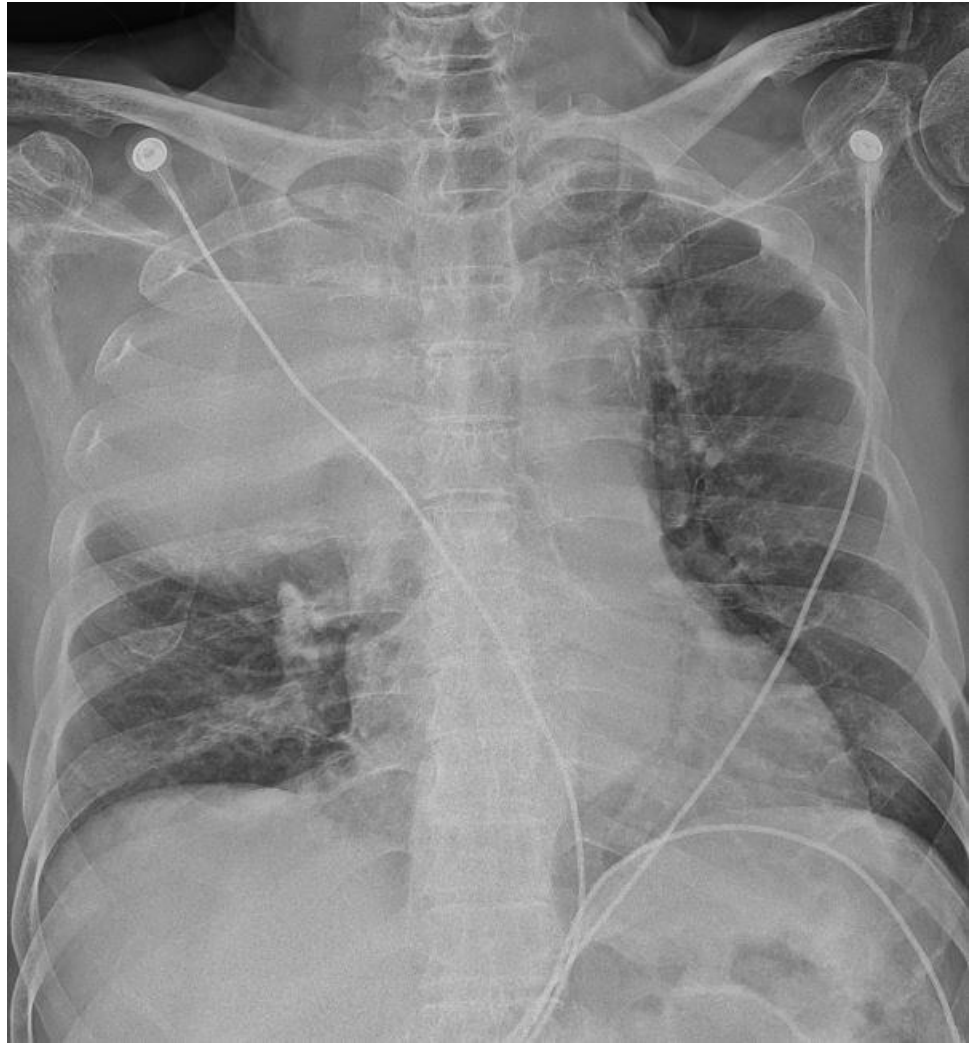
한양대학교 병원

호흡기알레르기내과

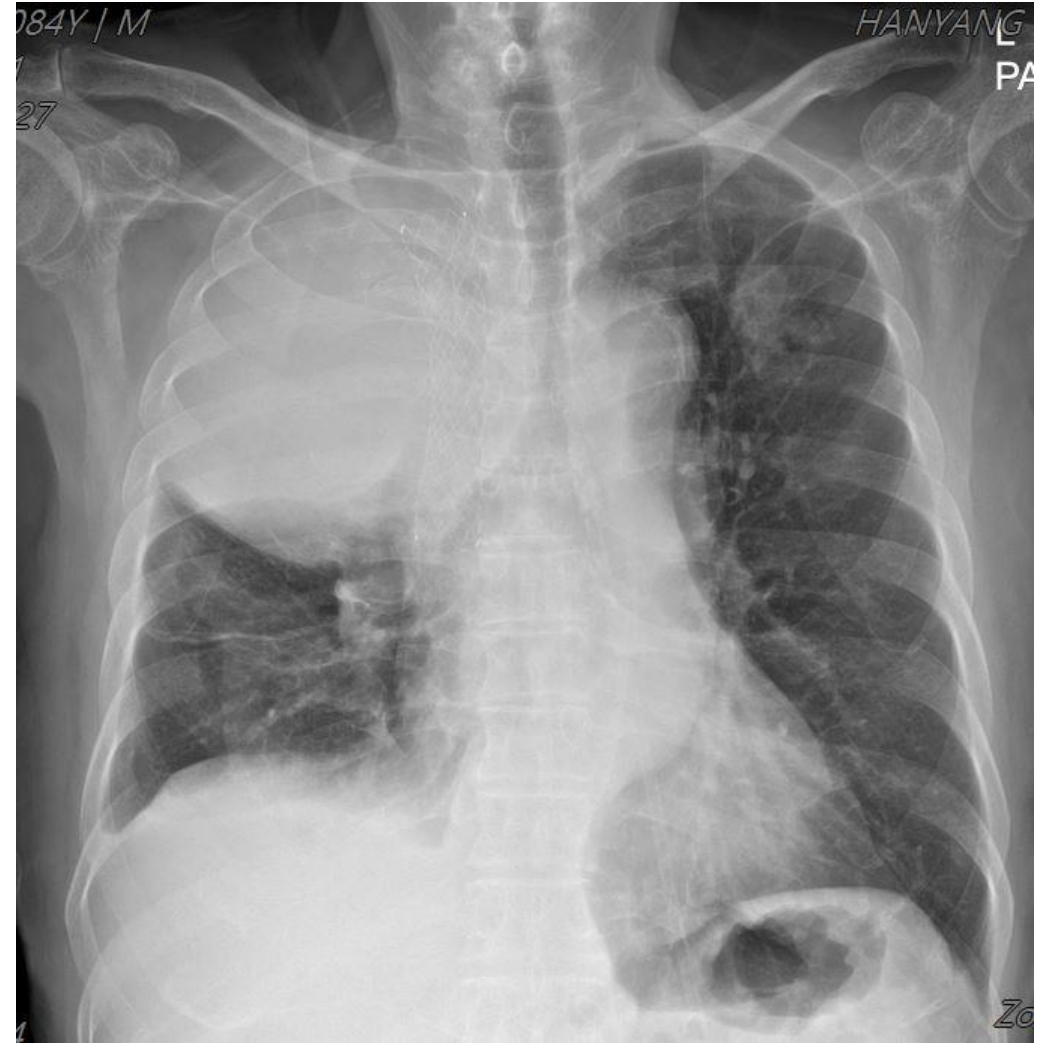
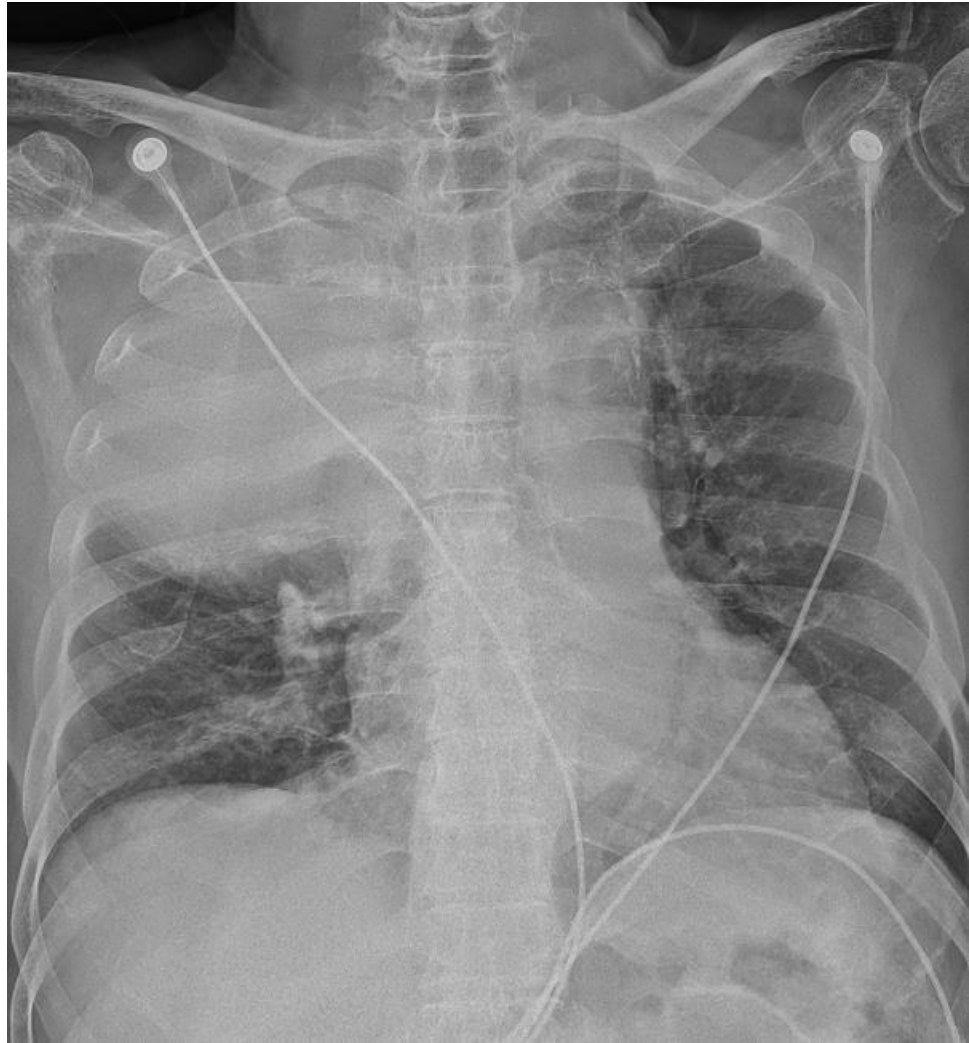
박동원

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M/84, 60PYS heavy smoker

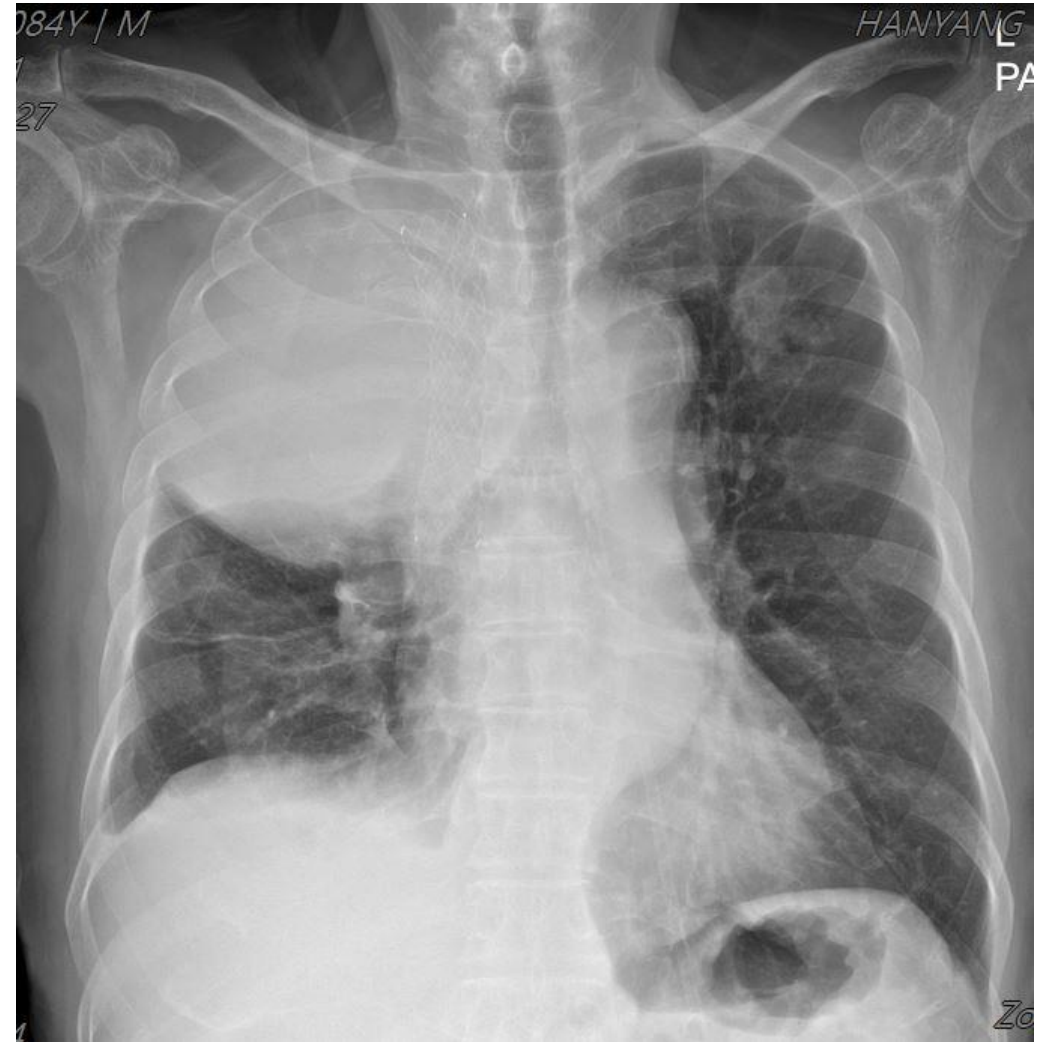


M/82, 60PYS heavy smoker



M/82, 60PYS heavy smoker

- 금일 RTx 예정
- 이전 병원에 전화
> 조직 검사 결과를 물어봄.



Latest version of NCCN guideline



National Comprehensive
Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Small Cell Lung Cancer

Version 2.2022 — November 24, 2021

NCCN.org

Today's topic



- Standard treatment of ES-SCLC
- Clinical trials of ES-SCLC
- Real-world data of ES-SCLC
- Further clinical trials

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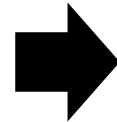
ES-SCLC treatment

* Preferred regimen

IO (Atezo) + EPS + Carbo #4
IO (Durva) + EPS + Carbo/Cis #4



IO (Atezo) maintenance
IO (Durva) maintenance



≥ 6M

Re-challenge with original regimen

< 6M

Topotecan
Lurbinectidin
Clinical trial

* Other regimen

- EPS + Carbo/cis
- Irinotecan + Carbo/cis

ES-SCLC treatment (South Korea)

가. 투여단계: 1차(first-line)

연번	항암요법	투여대상
1	etoposide + platinum (개정 제2021-46호: 2021.3.1)	LD, ED
	irinotecan + platinum	
3	atezolizumab ^{주1} + etoposide + carboplatin (개정 제2020-216호: 2020.8.1)	ED

- 급여인정기간: 1년까지(단, 질병진행시 중단) 급여인정 하되, 1년 내에 최적의 투여기간에 대한 임상결과 미 발표 시 자동 연장하여 최대 2년으로 함.
- 투여대상: PD-L1 발현을 등의 biomarker를 활용하여 투여대상을 선정하되, 세부 암종별 특성에 따라 달리 적용할 수 있음.
- 사후관리: 요양기관에서 제출한 급여실시내역을 활용하여 효과 및 부작용에 대한 모니터링을 실시할 수 있음.

나. 투여단계: 2차 이상

연번	항암요법
1	cyclophosphamide + doxorubicin + vincristine (개정 제2021-46호: 2021.3.1)
	etoposide + platinum (개정 제2021-46호: 2021.3.1)
3	irinotecan + platinum
4	irinotecan
5	belotecan
6	topotecan(IV, PO) ※ 'PO 제제'는 식약처 허가사항에 따라 소세포폐암 성인 환자에게 사용 시 요양급여를 인정함 (개정 제2009-6호: 2009.10.1)
	paclitaxel (개정 제2017-21호: 2017.2.1)

Today's topic



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Clinical trials: ICI combined CTx in ES-SCLC

Trial	Year	Experimental arm (IO+CTx)	Control arm (CTx)	Phase	N	Primary endpoint
IMpower133	2016-2017	Atezolizumab	EPS+carbo	III	403	OS, Inv-ass PFS
CASPIAN*	2017-2018	Durvalumab	EPS+carbo/cis	III	537	OS
Keynote-604	2017-2018	Pembrolizumab	EPS+carbo/cis	III	453	PFS, OS in ITT
NCT01450761	2012-2014	Ipilimumab	EPS+carbo/cis	III	1132	OS
NCT00527735 [#]	2008-2009	Ipilimumab	Paclitaxel+carbo	II	130	PFS
ECOG-ACRIN 5161	2018-2022	Nivolumab	EPS+carbo/cis	II	160	PFS

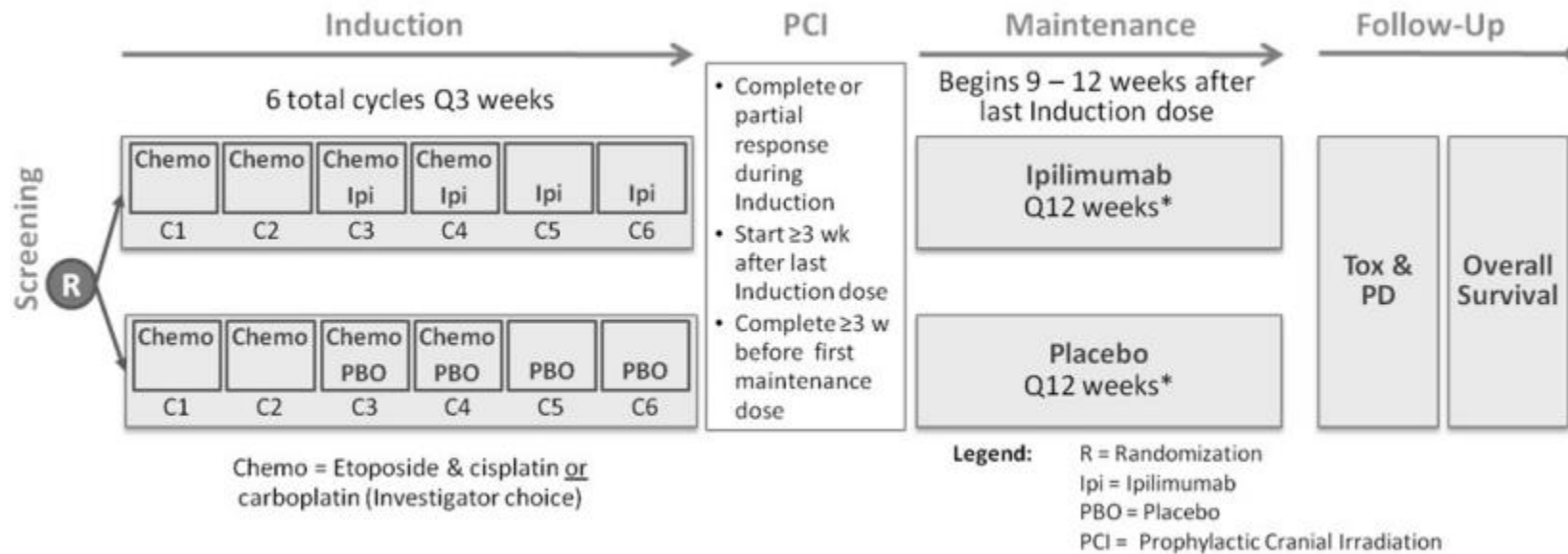
- CASPIAN*: Another experimental arm (EPS/plainum+ Durvalumab + Tremelimumab)
- NCT00527735[#]: three arms (A:concurrent/B:phased/C:control)

Arm A (concurrent): Ipi + CTx #4 --> CTx #2
 Arm B (phased): CTx #2 --> Ipi + CTx #4
 Control arm: CTx + placebo #4-6

Ipilimumab + Etoposide + Platinum

NCT01450761

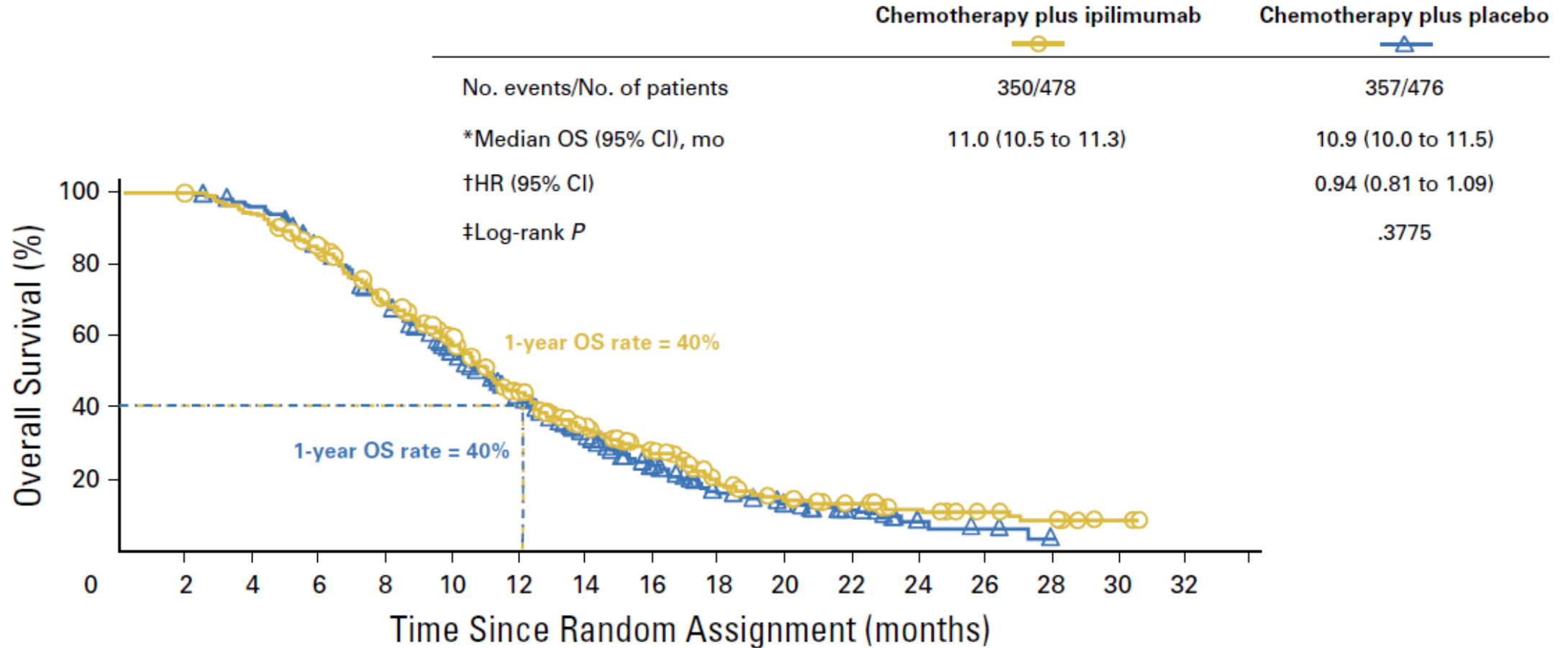
- Phase III RCT, EPS/platinum + Ipilimumab 10mg/kg or placebo every 3weeks (1:1)
- Primary endpoint : overall survival (OS)
- Of 1,132 patients randomly assigned, 478 chemotherapy+ ipilimumab: 476 chemotherapy plus placebo



*For a maximum duration of 3 years from the first dose of blinded study therapy

Characteristic	Chemotherapy Plus Ipilimumab (n = 478)	Chemotherapy Plus Placebo (n = 476)
Age, years		
Median	62	63
Range	39 to 85	36 to 81
Age categorization, years		
< 65	299 (63)	277 (58)
≥ 65	179 (37)	199 (42)
Sex		
Male	317 (66)	326 (68)
Female	161 (34)	150 (32)
Race		
White	365 (76)	359 (75)
Asian	108 (23)	107 (22)
Black/African American	3 (1)	5 (1)
Other	2 (< 1)	5 (1)
Region		
North America or Western Europe	186 (39)	197 (41)
Rest of world*	292 (61)	279 (59)
ECOG PS		
0	137 (29)	147 (31)
1	340 (71)	328 (69)
2	1 (< 1)	1 (< 1)
CNS metastasis at baseline	55 (12)	45 (10)
Smoking status		
Heavy smoker†	268 (56)	271 (57)
Light or nonsmoker‡	172 (36)	167 (35)
Unknown	9 (2)	11 (2)
Missing	29 (6)	27 (6)

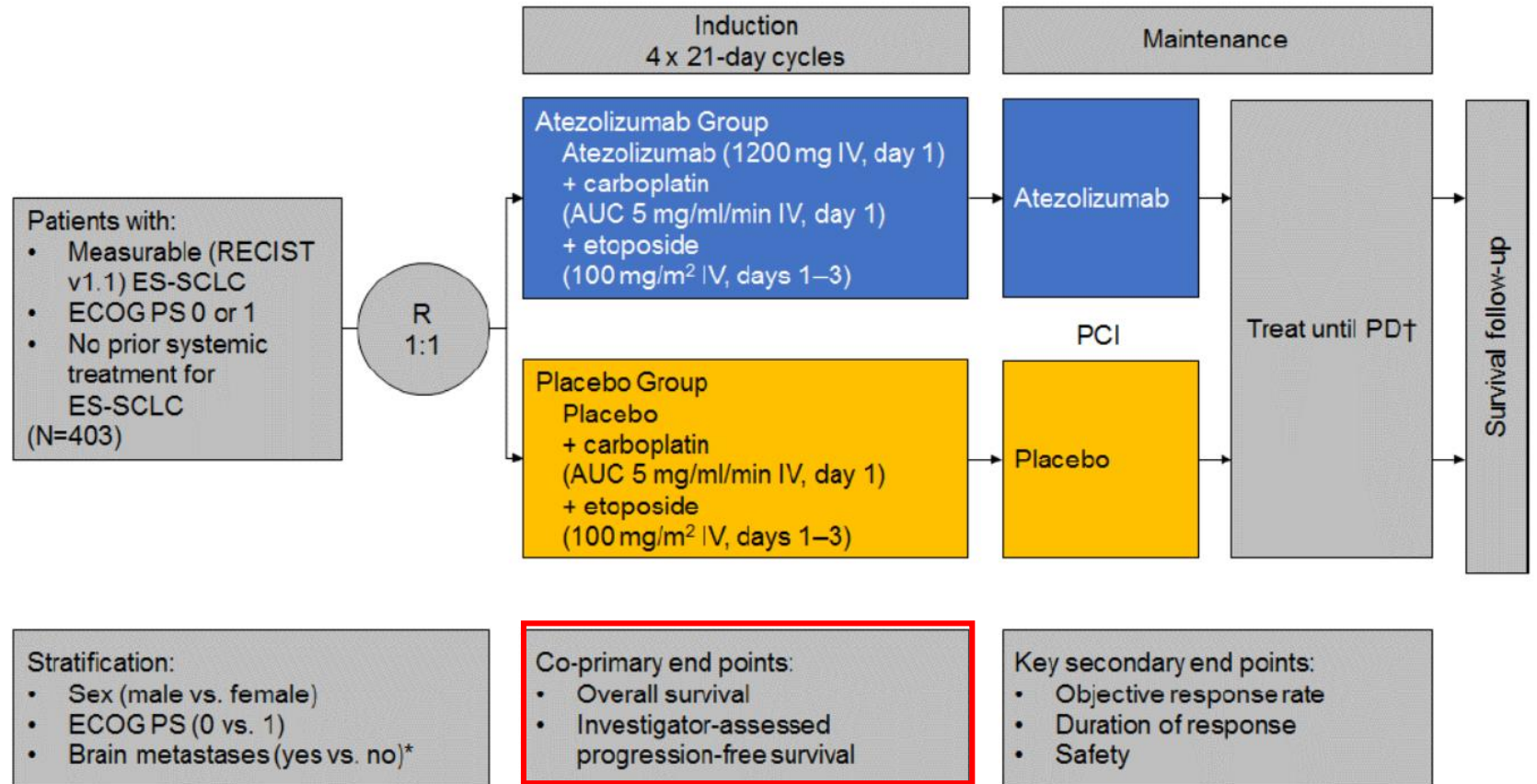
Addition of ipilimumab to chemotherapy did not prolong OS in ES-SCLC



IMpower133 (atezolizumab)

- Ph 3, RCT (2016-2017), including KOREA, 403 CTx naïve, extensive-stage SCLC
- Induction phase (EPS, 100mg/BSA + carboplatin, AUC 5 +/- atezolizumab/placebo 3wks cycles #4), followed by a maintenance phase → atezolizumab(1200mg)/placebo 3wks

- Induction CTx #4
- Until PD (no restriction)
- PCI permitted during maintenance
- Thoracic RTx, not permitted
- Only carboplatin



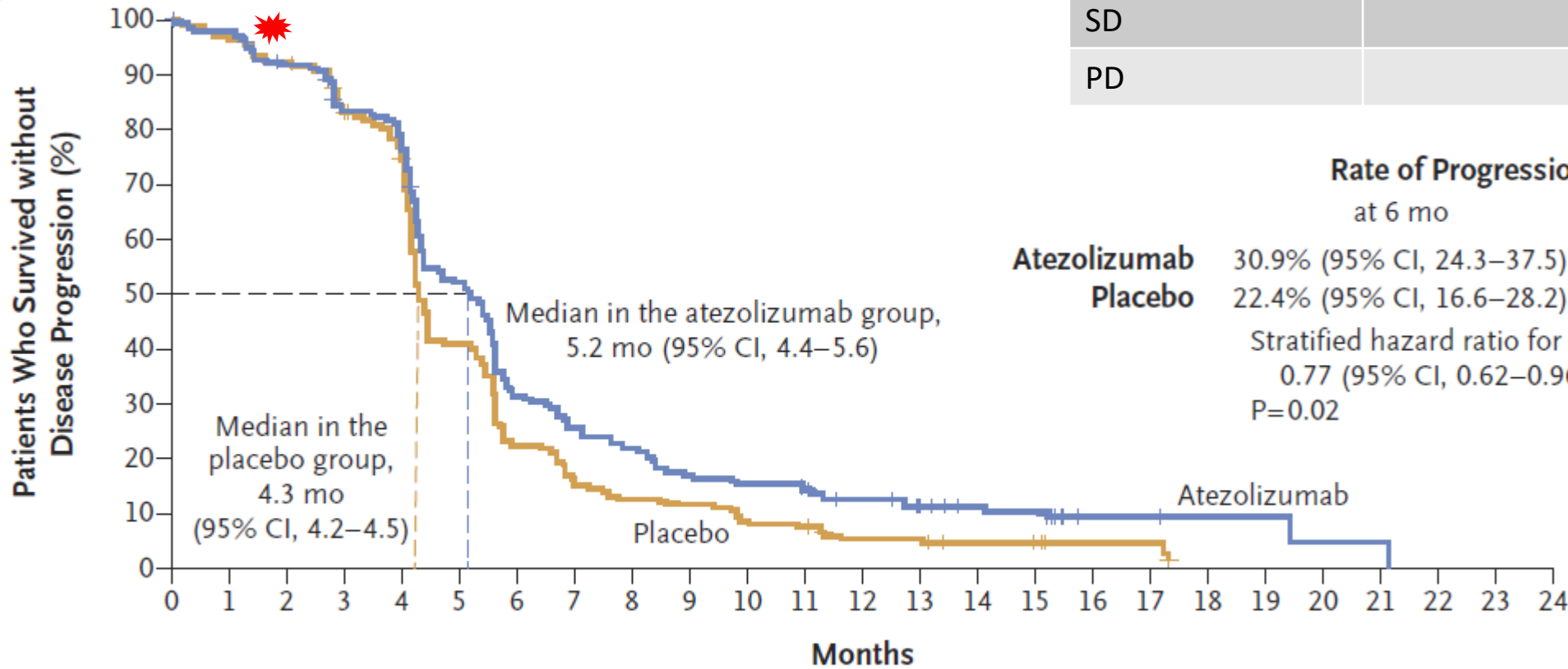
Baseline characteristics

Variable	Atezo + EC (n=201)	EC (n=202)
Median age, y	64	64
Age <65	55.2%	52.5%
Age ≥65	44.8%	47.5%
Gender		
Male	64.2%	65.3%
Smoking status		
Never	4.5%	1.5%
Current	36.8%	37.1%
Former	58.7%	61.4%
ECOG		
0/1	100%	100%
CNS metastasis		
Yes	8.5%	8.9%
PCI, yes	22 (10.9%)	22 (10.9%)

IMpower133 (atezolizumab)

Variable	Atezo + EC (n= 201)	EC (n=202)
ORR	60.2	64.4
CR	2.5	1.0
PR	57.7	63.4
Median DoR (m)	4.2 (1.4-19.5)	3.9 (2.0-16.1)
SD	20.9	21.3
PD	10.9	6.9

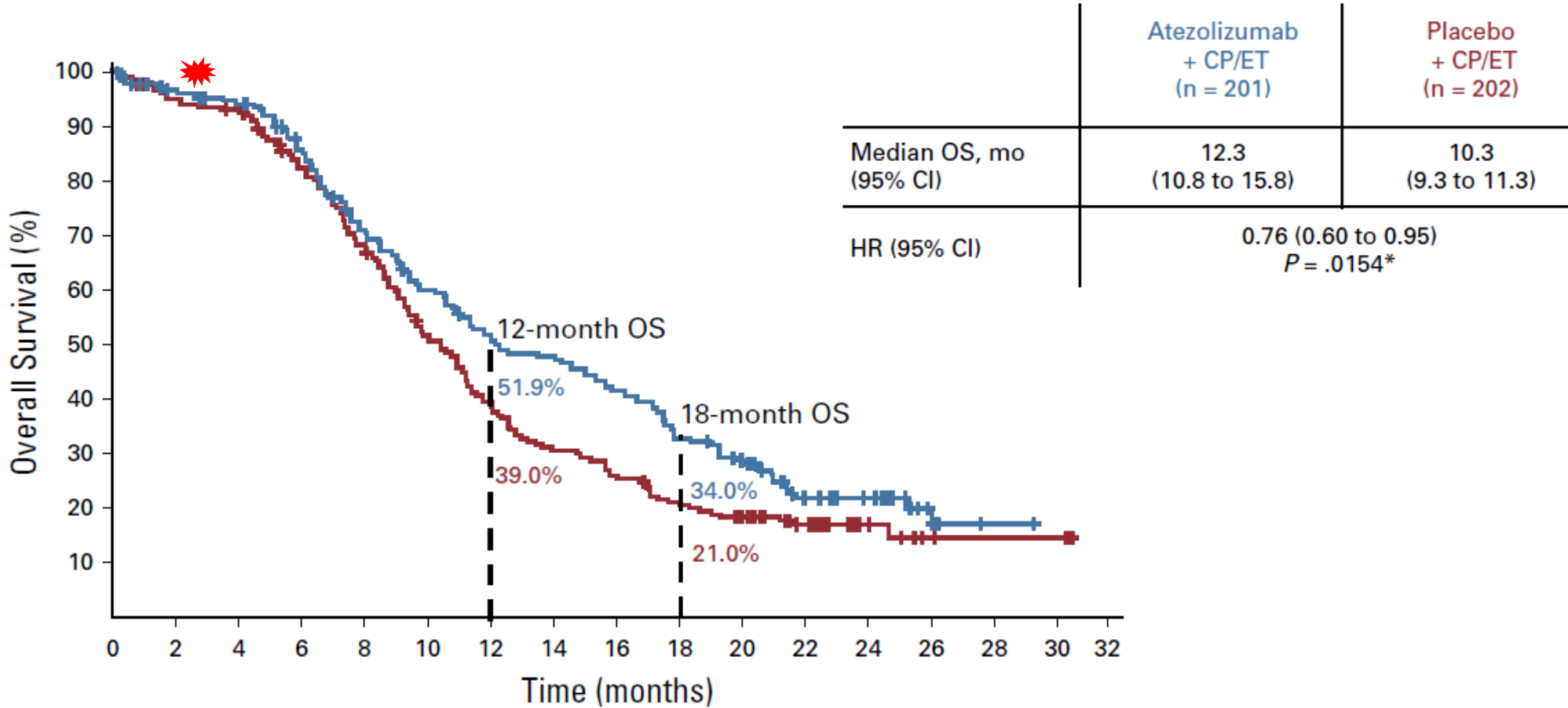
B Progression-free Survival



No. at Risk

Atezolizumab	201	190	178	158	147	98	58	48	41	32	29	26	21	15	12	11	3	3	2	2	1	1
Placebo	202	193	184	167	147	80	44	30	25	23	16	15	9	9	6	5	3	3				

IMpower133 (atezolizumab): updated OS



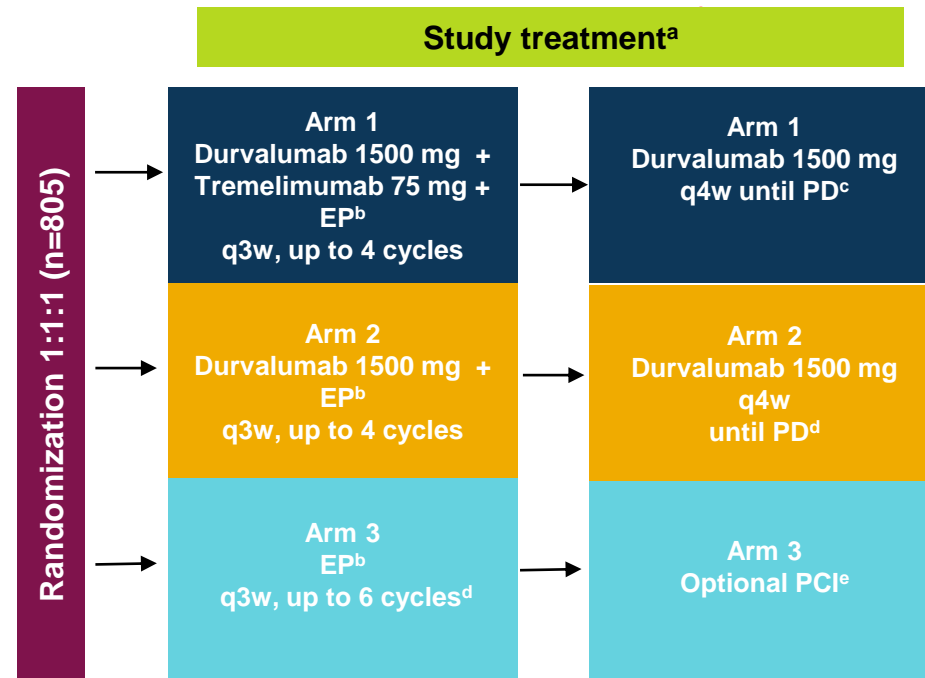
CASPIAN (Durvalumab)

- Ph 3, RCT (2017-2018), including KOREA, 805 CTx naïve, extensive-stage SCLC
- Three arms (EPS+platinum ± Durvalumab ± Tremelimumab)
- Primary endpoint: Overall survival
- Secondary endpoint: PFS, ORR, Safety & tolerability

- Induction q3wks, maintenance q4wks
- Until PD (no restriction)
- Platinum (cis/carbo)

**Treatment-naïve
ES-SCLC**
Actual Enrollment = 988

Stratification factor:
Planned platinum-based therapy
in Cycle 1 (carboplatin vs
cisplatin)



Primary Endpoint

- OS

Secondary Endpoints

- OS and OS18
- PFS^f, ORR^f, APF6^f, APF12^f
- PK
- Immunogenicity (durvalumab and tremelimumab)
- HRQoL
- Changes in WHO/ECOG PS
- Safety and tolerability

Exploratory Endpoint

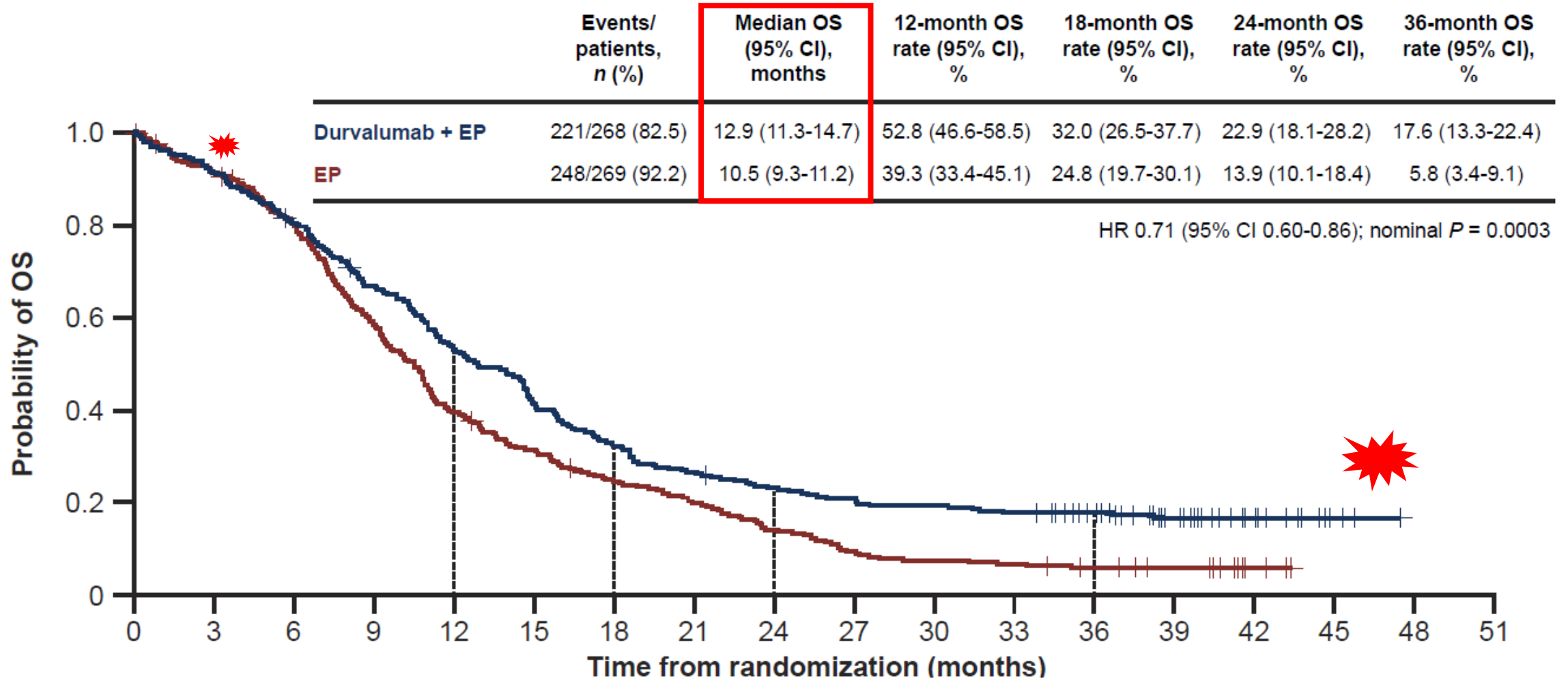
- Biomarker analysis (tTMB; PD-L1)^{3,5,g}
- OS and PFS analysis in patients with or without baseline brain metastases⁴ (prespecified subgroup analysis)

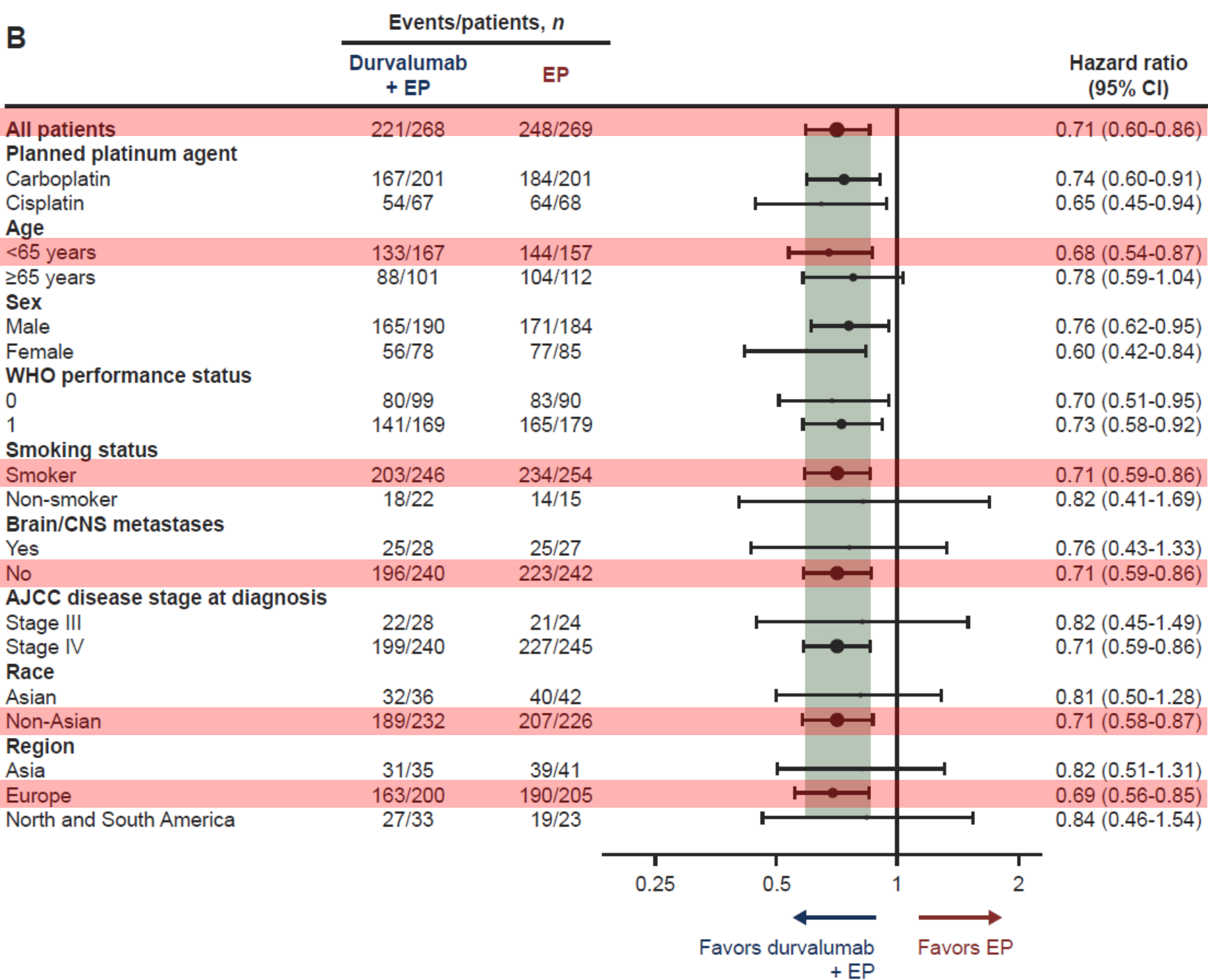
	Durvalumab plus platinum-etoposide (n=268)	Platinum-etoposide (n=269)
Median age, years	62 (58–68)	63 (57–68)
Age group, years		
<65	167 (62%)	157 (58%)
≥65	101 (38%)	112 (42%)
Sex		
Men	190 (71%)	184 (68%)
Women	78 (29%)	85 (32%)
Race		
White	229 (85%)	221 (82%)
Asian	36 (13%)	42 (16%)
Black or African American	2 (1%)	3 (1%)
Other or missing	1 (<1%)	3 (1%)
Disease stage		
III	28 (10%)	24 (9%)
IV	240 (90%)	245 (91%)
WHO performance status		
0	99 (37%)	90 (33%)
1	169 (63%)	179 (67%)
Smoking history		
Never smoker	22 (8%)	15 (6%)
Former smoker	126 (47%)	128 (48%)
Current smoker	120 (45%)	126 (47%)
Brain or CNS metastases		
Yes	28 (10%)	27 (10%)
No	240 (90%)	242 (90%)
Liver metastases		
Yes	108 (40%)	104 (39%)
No	160 (60%)	165 (61%)

Variable	Atezo + EC (n=201)	EC (n=202)
Median age, y	64	64
Age <65	55.2%	52.5%
Age ≥65	44.8%	47.5%
Gender		
Male	64.2%	65.3%
Smoking status		
Never	4.5%	1.5%
Current	36.8%	37.1%
Former	58.7%	61.4%
ECOG		
0/1	100%	100%
CNS metastasis		
Yes	8.5%	8.9%
PCI, yes	22 (10.9%)	22 (10.9%)

3-year OS update from CASPIAN

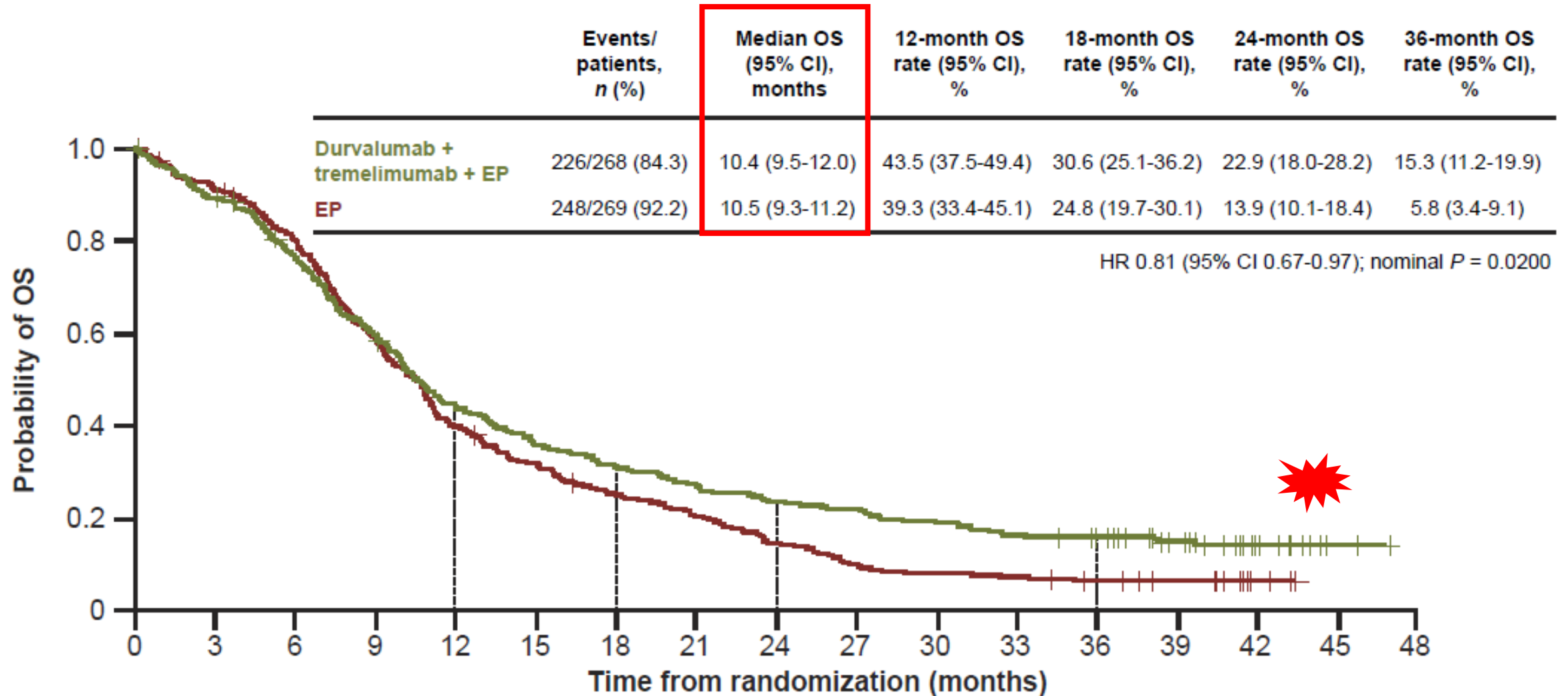
Arm 2 vs. Arm 3



B

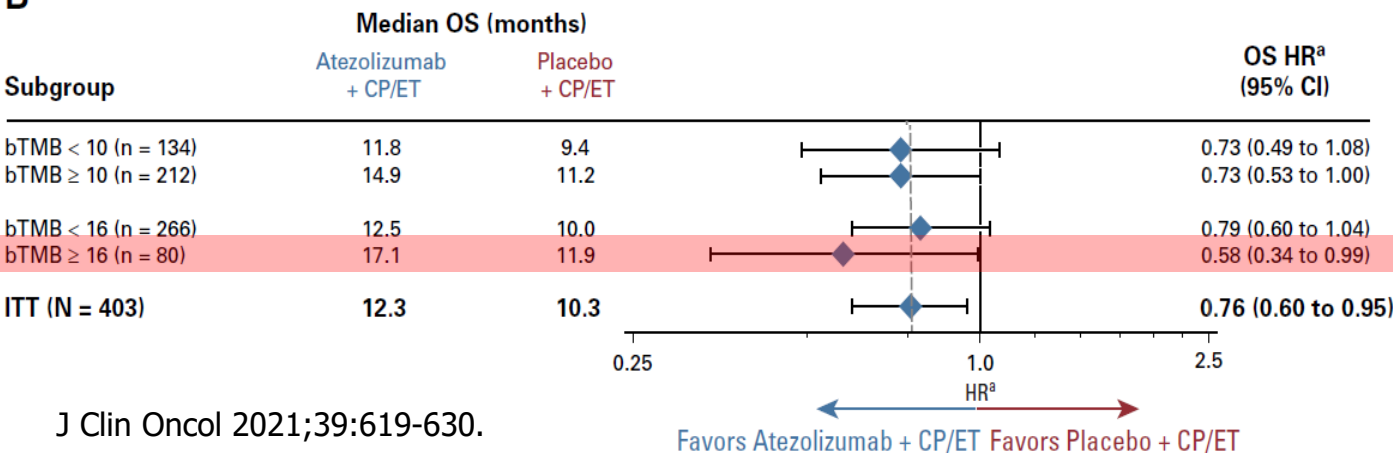
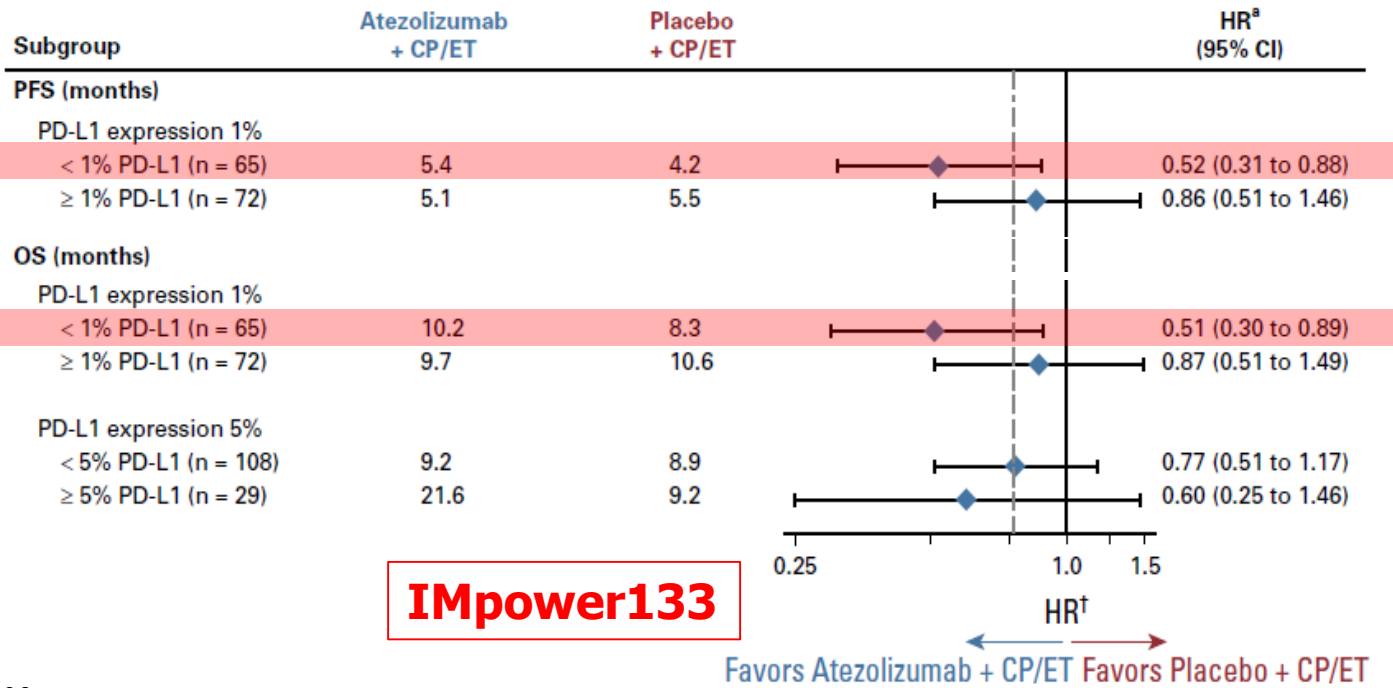
Adding tremelimumab (fully human monoclonal antibody against CTLA-4)

Arm 1 vs. Arm 3

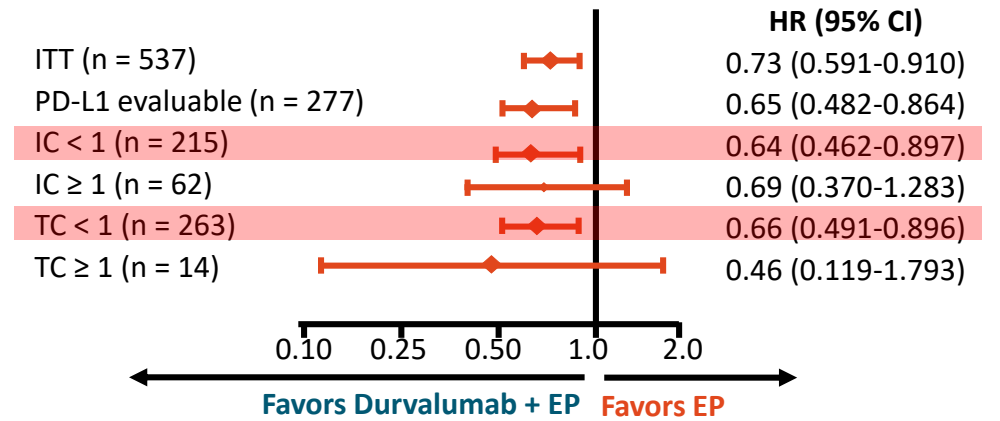


Variable	Atezo + EC (n= 201)	EC (n=202)	Durva + E/plat (n=268)	E/platinum (n=269)
ORR	60.2	64.4	68.0	58.0
CR	2.5	1.0	2.0	1.0
PR	57.7	63.4	66.0	57.0
Median DoR (m)	4.2 (1.4-19.5)	3.9 (2.0-16.1)	5.1 (3.4-10.4)	5.1 (3.7-6.8)
SD	20.9	21.3	7.0	16.0
PD	10.9	6.9	12.0	12.0
Median PFS (m)	5.2	4.3	5.1	5.4
HR (95% CI)	0.77 (0.62-0.96)		0.78 (0.65-0.94)	
6m PFS (%)	30.9	12.6	45.0	46.0
12m PFS (%)	22.4	5.4	18.0	5.0
Median OS (m)	12.3	10.3	12.9	10.5
HR (95% CI)	0.76 (0.60-0.90)		0.71 (0.60-0.86)	
12m OS (%)	51.9	39.0	52.8	39.3
18m OS (%)	34.0	21.0	32.0	24.8
24m OS (%)	-	-	22.9	13.9

Biomarker ? PDL1, TMB



CASPIAN OS by Subgroup^[5]



- PD-L1 and TMB are **NOT** Discriminant Biomarkers in Pts with ES-SCLC

Safety (1)

IMpower133

Table 3. Adverse Events Related to the Trial Regimen.*

Event	Atezolizumab Group (N = 198)			Placebo Group (N = 196)		
	Grade 1 or 2	Grade 3 or 4	Grade 5	Grade 1 or 2	Grade 3 or 4	Grade 5
	<i>number of patients (percent)</i>					
Any adverse event	73 (36.9)	112 (56.6)	3 (1.5)	68 (34.7)	110 (56.1)	3 (1.5)
Adverse events with an incidence of $\geq 10\%$ in any grade category or events of grade 3 or 4 with an incidence of $\geq 2\%$ in either group						
Neutropenia	26 (13.1)	45 (22.7)	1 (0.5)	20 (10.2)	48 (24.5)	0
Anemia	49 (24.7)	28 (14.1)	0	41 (20.9)	24 (12.2)	0
Alopecia	69 (34.8)	0	0	66 (33.7)	0	0
Nausea	62 (31.3)	1 (0.5)	0	58 (29.6)	1 (0.5)	0
Fatigue	39 (19.7)	3 (1.5)	0	37 (18.9)	1 (0.5)	0
Decreased neutrophil count	7 (3.5)	28 (14.1)	0	12 (6.1)	33 (16.8)	0
Decreased appetite	39 (19.7)	2 (1.0)	0	26 (13.3)	0	0
Thrombocytopenia	12 (6.1)	20 (10.1)	0	14 (7.1)	15 (7.7)	0
Decreased platelet count	17 (8.6)	7 (3.5)	0	21 (10.7)	7 (3.6)	0
Vomiting	25 (12.6)	2 (1.0)	0	19 (9.7)	3 (1.5)	0
Constipation	19 (9.6)	1 (0.5)	0	25 (12.8)	0	0
Leukopenia	15 (7.6)	10 (5.1)	0	10 (5.1)	8 (4.1)	0
Decreased white-cell count	10 (5.1)	6 (3.0)	0	16 (8.2)	9 (4.6)	0
Diarrhea	15 (7.6)	4 (2.0)	0	18 (9.2)	1 (0.5)	0
Febrile neutropenia	0	6 (3.0)	0	0	12 (6.1)	0
Infusion-related reaction	6 (3.0)	4 (2.0)	0	9 (4.6)	1 (0.5)	0

Safety (1) Caspian

	Durvalumab plus platinum- etoposide (n=265)		Platinum-etoposide (n=266)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Any event	260 (98%)	163 (62%)	258 (97%)	166 (62%)
Any serious event	82 (31%)	57 (22%)	96 (36%)	70 (26%)
Any event leading to discontinuation*	25 (9%)	7 (3%)	25 (9%)	7 (3%)
Any event leading to death†	13 (5%)	..	15 (6%)	..
Adverse events with an incidence of at least 10% in any grade category or events of grade 3 or 4 with an incidence of at least 2% in either group‡				
Neutropenia	111 (42%)	64 (24%)	124 (47%)	88 (33%)
Anaemia	102 (38%)	24 (9%)	125 (47%)	48 (18%)
Nausea	89 (34%)	1 (<1%)	89 (33%)	5 (2%)
Alopecia	83 (31%)	3 (1%)	91 (34%)	2 (1%)
Constipation	44 (17%)	2 (1%)	51 (19%)	0
Decreased appetite	48 (18%)	2 (1%)	46 (17%)	2 (1%)
Thrombocytopenia	41 (15%)	15 (6%)	53 (20%)	25 (9%)
Fatigue	48 (18%)	4 (2%)	45 (17%)	3 (1%)
Vomiting	39 (15%)	0	44 (17%)	3 (1%)
Asthenia	40 (15%)	5 (2%)	40 (15%)	3 (1%)
Leucopenia	40 (15%)	17 (6%)	32 (12%)	14 (5%)
Dyspnoea	31 (12%)	5 (2%)	28 (11%)	3 (1%)
Neutrophil count decreased	26 (10%)	17 (6%)	31 (12%)	17 (6%)
Diarrhoea	26 (10%)	3 (1%)	30 (11%)	3 (1%)
Cough	33 (12%)	2 (1%)	18 (7%)	0

Safety (2)

IMpower133

Table S10. Immune-Related Adverse Events.

Patients — no. (%)	Atezolizumab Group (N=198)	Placebo Group (N=196)
Rash		
All grades	37 (18.7)	20 (10.2)
Grade 3–4	4 (2.0)	0
Hypothyroidism		
All grades	25 (12.6)	1 (0.5)
Grade 3–4	0	0
Hepatitis (diagnosis)		
All grades	14 (7.1)	9 (4.6)
Grade 3–4	3 (1.5)	0
Hepatitis (laboratory abnormalities)		
All grades	14 (7.1)	9 (4.6)
Grade 3–4	3 (1.5)	0
Infusion-related reaction		
All grades	11 (5.6)	10 (5.1)
Grade 3–4	4 (2.0)	1 (0.5)
Hyperthyroidism		
All grades	11 (5.6)	5 (2.6)
Grade 3–4	0	0
Pneumonitis		
All grades	4 (2.0)	5 (2.6)
Grade 3–4	1 (0.5)	2 (1.0)
Colitis		
All grades	3 (1.5)	0
Grade 3–4	2 (1.0)	0
Pancreatitis		
All grades	1 (0.5)	2 (1.0)
Grade 3–4	1 (0.5)	2 (1.0)

Patients — no. (%)	Atezolizumab Group (N=198)	Placebo Group (N=196)
Severe cutaneous reaction		
All grades	2 (1.0)	0
Grade 3–4	0	0
Adrenal insufficiency		
All grades	0	2 (1.0)
Grade 3–4	0	0
Rhabdomyolysis		
All grades	2 (1.0)	0
Grade 3–4	1 (0.5)	0
Nephritis		
All grades	1 (0.5)	1 (0.5)
Grade 3–4	1 (0.5)	0
Hypophysitis		
All grades	1 (0.5)	0
Grade 3–4	0	0
Vasculitis		
All grades	0	1 (0.5)
Grade 3–4	0	0
Diabetes mellitus		
All grades	1 (0.5)	0
Grade 3–4	0	0
Guillain-Barre Syndrome		
All grades	1 (0.5)	0
Grade 3–4	1 (0.5)	0

Safety (2) Caspian

	Durvalumab + EP (n=265)		EP (n=266)	
	Any grade*	Grade 3 or 4	Any grade*	Grade 3 or 4
Any immune-mediated adverse event (grouped term), n (%) ^{†,‡}	52 (20%)	12 (5%)	7 (3%)	1 (<1%)
Hypothyroid events	24 (9%)	0	2 (1%)	0
Hyperthyroid events	14 (5%)	0	0	0
Pneumonitis	7 (3%)	2 (1%)	2 (1%)	1 (<1%)
Hepatic events	7 (3%)	5 (2%)	0	0
Dermatitis/rash	4 (2%)	0	2 (1%)	0
Diarrhoea/colitis	4 (2%)	1 (<1%)	1 (<1%)	0
Thyroiditis	4 (2%)	0	0	0
Type 1 diabetes mellitus	4 (2%)	4 (2%)	0	0
Adrenal insufficiency	1 (<1%)	0	0	0
Pancreatic events	1 (<1%)	1 (<1%)	0	0
Other rare/miscellaneous [§]	2 (1%)	0	0	0

Today's topic



- Standard treatment of ES-SCLC
- Clinical trials of ES-SCLC
- Real-world data of ES-SCLC
- Further clinical trials

RW data in US (1L setting)-01

- Retrospective study including ES-SCLC diagnosed 2018 Oct~2019 Dec, and follow-up through 2020 Mar
- The [US Oncology Network EHR](#) (electronic health records) data
- 408 patients enrolled, 267 (71.4%) received Atezo+EC vs. 80 (21.4%) received EC

Median follow-up 5.5m

Variable	US oncol network (n=267)	IMpower133 (n=201)
Median age, y	68	64
Gender		
Male	45%	64%
Female	55%	36%
Race, White	73%	81%
ECOG		
0/1	74%	100%
2/3	24%	0%
CNS metastasis		
Yes	23%	9%
No	77%	91%

Variable	US oncol network (n=267)	IMpower133 (n=201)
Median f/u	5.5m	13.9m
Median Duration of treatment	4.9m (Time to discontinuation)	4.7m
Treatment at 6M	35.1%	31.3%
Median PFS	6.9m (time to next treatment/death)	5.2m
PFS at 6M	64.5% (not initiated on 2L at 6M)	30.9%

RW data in US (1L setting)-02

- Retrospective study including ES-SCLC diagnosed 2018 Sep~2020 Apr
- Follow-up through 2020 Apr
- Nationwide Flatiron Health EHR database
- TO investigate clinical characteristics, treatment patterns, and early outcomes of the Atezo + CE
- Thoracic RTx, PCI permitted

Median follow-up 6.9m

The IMpower133 eligible like cohort
(subgroup of the main trial study cohort)

- ECOG 0/1
- Carboplatin, only
- Starting with Atezo+EC as 1st cycle
- No BM before start CTx

Table 1. Baseline characteristics of patients with ES-SCLC: Comparison of RW study and IMpower133¹

Variable	RW (N = 493)	RW IMpower133 trial eligible-like (n = 162)	IMpower133 study population (N = 201) ¹
Age group, y, n (%)			
<65	173 (35.1)	60 (37.0)	111 (55.2)
≥65	320 (64.9)	102 (63.0)	90 (44.8)
Gender, n (%)			
Female	234 (47.5)	73 (45.1)	72 (35.8)
Male	259 (52.5)	89 (54.9)	129 (64.2)
ECOG PS, n (%)			
0	97 (19.7)	66 (40.7)	73 (36.3)
1	178 (36.1)	96 (59.3)	128 (63.7)
2+	104 (21.1)	0 (0.0)	0 (0)
Not reported	114 (23.1)	0 (0.0)	0 (0)
Smoking status, n (%)			
History of smoking	481 (97.6)	158 (97.5)	192 (95.5)
No history	12 (2.4)	4 (2.5)	9 (4.5)
CNS metastasis, n (%)			
Yes	97 (19.7)	0 (0)	17 (8.5)
No	396 (80.3)	162 (100.0)	184 (91.5)
Liver metastasis, n (%)			
Yes	216 (43.8)	68 (42.0)	77 (38.3)
No	277 (56.2)	94 (58.0)	124 (61.7)
SCLC stage at diagnosis, n (%)			
Extensive disease	475 (96.3)	157 (96.9)	187 (93.0)
Limited disease	18 (3.7)	5 (3.1)	13 (6.5)

RW data in US (1L setting)-02

- 20% (97/493) : CNS metastasis at baseline
- 49% (48/97) received CNS treatment before commencing Atezo+ CE
- WBRT: 81% (n=39), SBRT: 10% (n=5)
 - Craniotomy/metastasectomy: 17% (n=8)
 - Surgery: 2% (n=1) Radiotherapy: 2% (n=1)
- Cumulative incidence of new CNS mets at 6M
 - 19% (no CNS mets at baseline)
 - vs. 38% (CNS mets at baseline)
- 13% (27/200): PCI done (in Pts without CNS mets at baseline)

Table 2. Comparison of clinical outcomes: RW study and IMpower133

Variable	RW (N = 493)	RW IMpower133 trial eligible-like (n = 162) ^a	IMpower133 study population (N = 201) ¹
Follow-up, median, mo	6.9	7.6	13.9
Tx duration, median (95% CI), mo	5.7 (5.1, 6.7)	6.2 (5.5, 7.8)	4.7 (range, 0-21) ^b
rwPFS, median (95% CI), mo	5.2 (5.0, 5.5)	5.8 (5.2, 6.7)	5.2 (4.4, 5.6) ^c
Sensitivity analysis	n=137	n=51	
Follow-up, median, mo ^d	14.4	14.1	
Tx duration, median (95% CI), mo ^d	4.8 (4.1, 5.5)	5.5 (4.8, 7.1)	
rwPFS, median (95% CI), mo ^c	4.8 (4.1, 5.4)	5.8 (4.7, 7.9)	

CI, confidence interval; mo, months; Tx, treatment.

^aA subgroup of RW patients comprising IMpower133 trial-eligible patients.

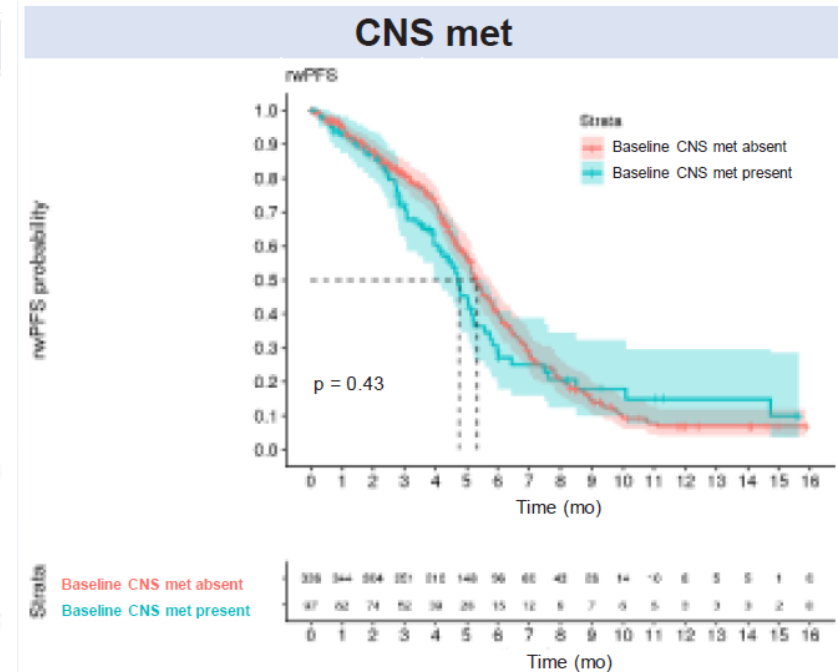
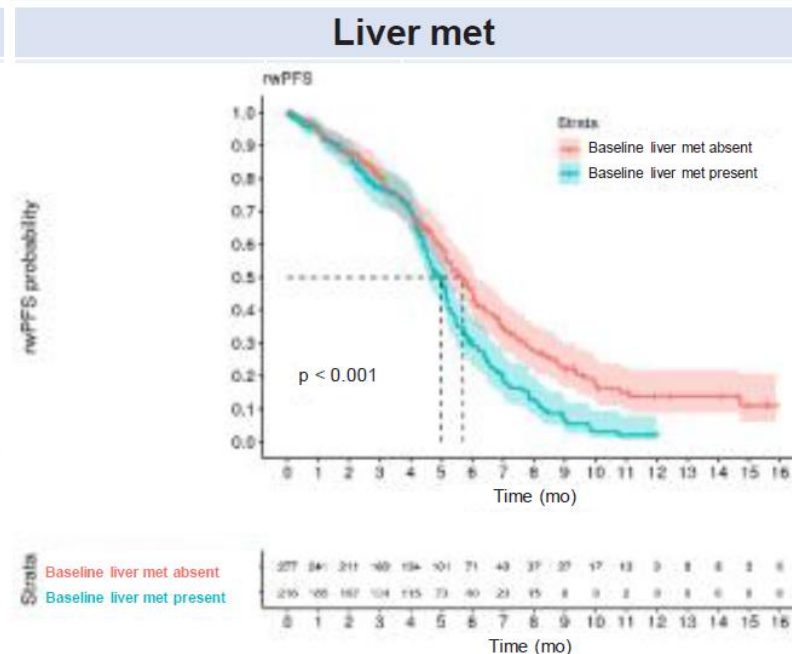
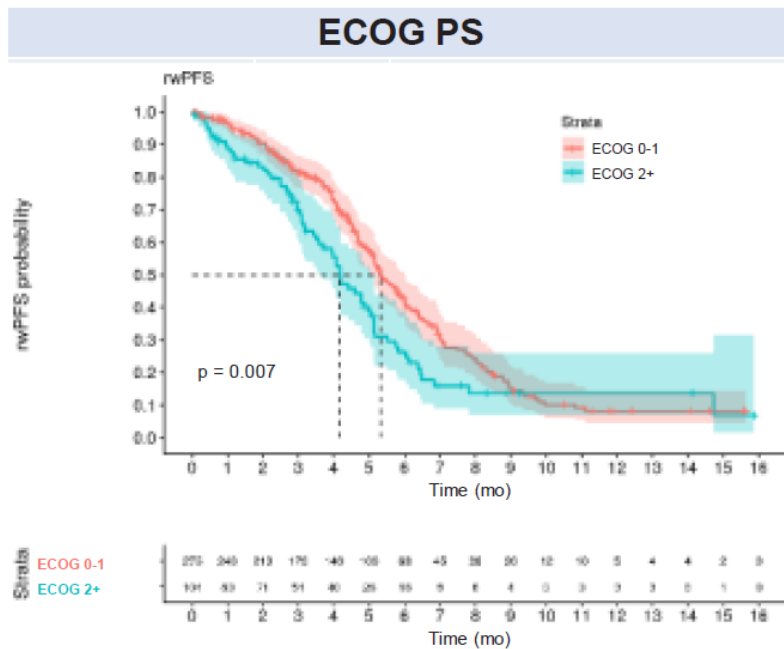
^bNot based on Kaplan-Meier methodology.

^cPFS was measured as a primary endpoint in IMpower133.

^dIncludes only patients initiating treatment at least 12 months before study end.

RW data in US (1L setting)-02

- rwPFS Stratifications in the RW cohort by baseline characteristics



ECOG PS	N	Median (95% CI), mo
ECOG 0-1	275	5.3 (5.1-6.0)
ECOG 2+	104	4.2 (3.6-5.1)

Liver met	N	Median (95% CI), mo
Absent	277	5.7 (5.1-6.1)
Present	216	5.0 (4.5-5.2)

CNS met	N	Median (95% CI), mo
Absent	396	5.3 (5.1-5.8)
Present	97	4.7 (4.1-5.6)

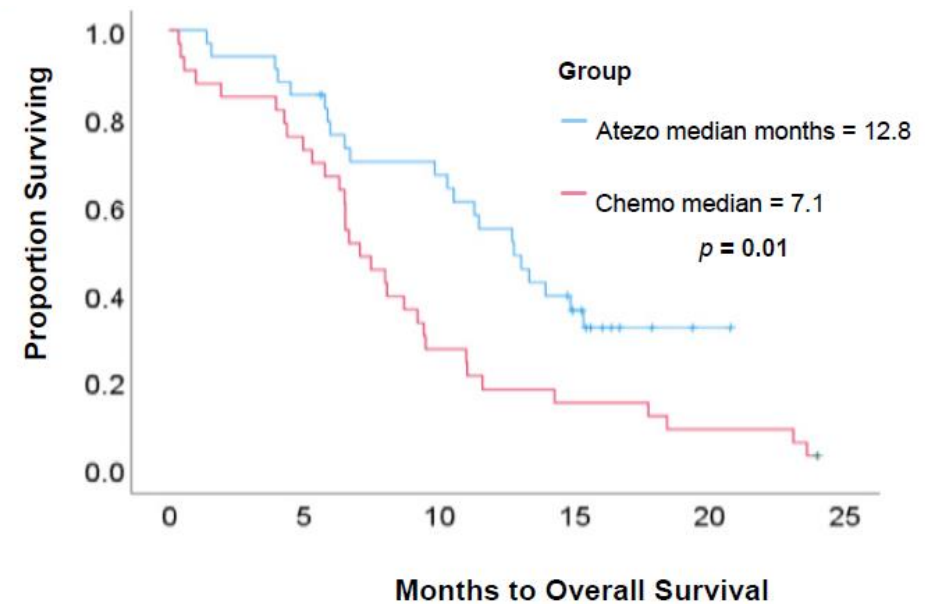
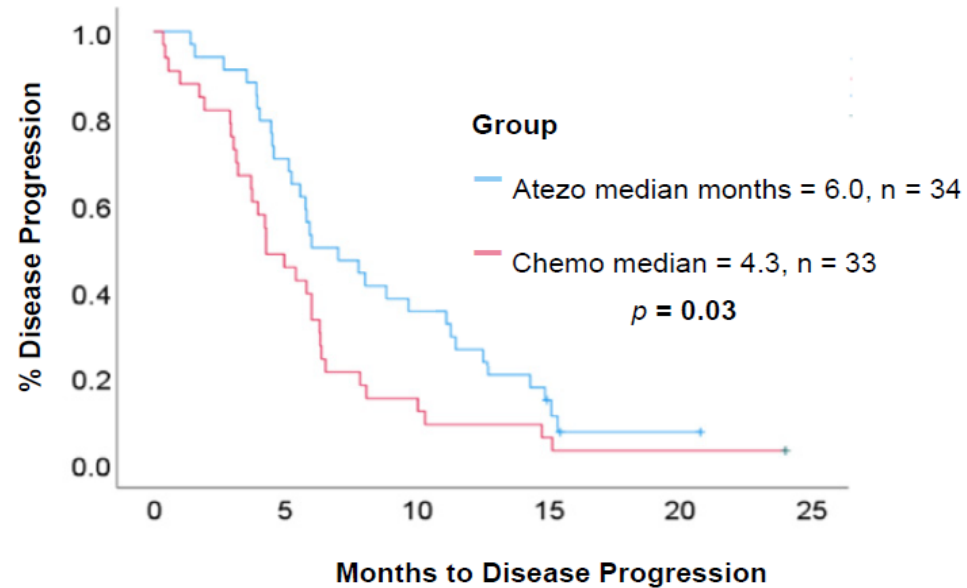
RW data in Canada

- Retrospective analysis (2017-2019)
- 67 CTx naïve, extensive-stage SCLC

Variable	Atezo + EC (n=201)	EC (n=202)
Median age, y	64	64
Age <65	55.2%	52.5%
Age ≥65	44.8%	47.5%
Gender		
Male	64.2%	65.3%
Smoking status		
Never	4.5%	1.5%
Current	36.8%	37.1%
Former	58.7%	61.4%
ECOG		
0/1	100%	100%
CNS metastasis		
Yes	8.5%	8.9%
PCI, yes	22 (10.9%)	22 (10.9%)

Variables	Atezolizumab	Chemotherapy	p Value
	n = 34	n = 33	
Median age (range), y	65 (54-78)	65 (45-85)	
≥65 y	17 (50)	17 (52)	1.0
ECOG performance status			1.0
0	2 (6)	1 (3)	
1	7 (21)	6 (18)	
2	5 (15)	4 (12)	
3	3 (9)	4 (12)	
4	0 (0)	1 (3)	
Unknown	17 (50)	17 (52)	
Male	18 (53)	15 (46)	0.63
Ever smoker ^a	30 (88)	30 (91)	1.0
TNM (AJCC eighth) M-status			0.65
M0	2 (6)	0 (0)	
M1a	5 (15)	4 (12)	
M1b	9 (27)	11 (33)	
M1c	18 (53)	18 (55)	
Had brain metastasis at diagnosis	8 (24)	5 (15)	0.54
Had any comorbidity at diagnosis	29 (85)	31 (94)	0.43
Treatment characteristic and outcomes			
Had adverse events	21 (62)	16 (49)	0.33
Median chemotherapy cycle# (range)	4 (1-6)	4 (1-6)	
RT—any site	22 (65)	19 (58)	0.62
Thoracic RT (frontline)	4 (12)	10 (30)	0.08
Prophylactic cranial irradiation	4 (12)	2 (6)	0.67
Reason for 1L discontinuation			0.02
Adverse events	11 (32)	5 (15)	
Disease progression (as per RECIST criteria)	15 (44)	20 (61)	
Health decline or patient's request	2 (6)	5 (15)	
Regimen completed and stable disease	0 (0)	1 (3)	
Unknown	1 (3)	3 (9)	
Received second line	9 (27)	5 (15)	0.37

RW data in Canada



Variable	Atezo + EC (n= 201)	EC (n=202)	Durva + E/plat (n=268)	E/platinum (n=269)	Atezo + CTx (RW, Canada)	CTx (RW, Canada)
Median PFS (m)	5.2	4.3	5.1	5.4	6.0	4.3
HR (95% CI)	0.77 (0.62-0.96)		0.78 (0.65-0.94)		0.53 (0.28-1.02)	
Median OS (m)	12.3	10.3	12.9	10.5	12.8	7.1
HR (95% CI)	0.76 (0.60-0.90)		0.71 (0.60-0.86)		0.42 (0.20-0.88)	

RW data in South Korea

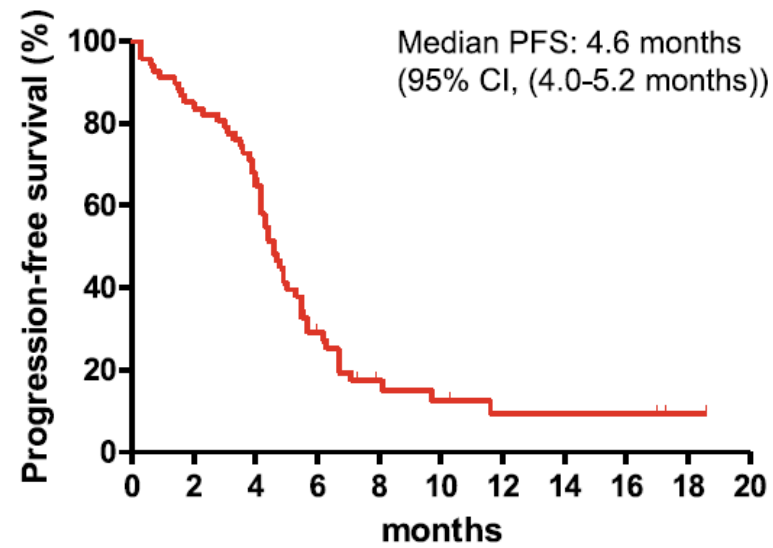
- Retrospective analysis (2019-2020), 68 CTx naïve, extensive-stage SCLC
- Yonsei Cancer Center
- The median follow-up was **11.6 months**

Variable	Atezo + EC (n=201)	EC (n=202)
Median age, y	64	64
Age <65	55.2%	52.5%
Age ≥65	44.8%	47.5%
Gender		
Male	64.2%	65.3%
Smoking status		
Never	4.5%	1.5%
Current	36.8%	37.1%
Former	58.7%	61.4%
ECOG		
0/1	100%	100%
CNS metastasis		
Yes	8.5%	8.9%
PCI, yes	22 (10.9%)	22 (10.9%)

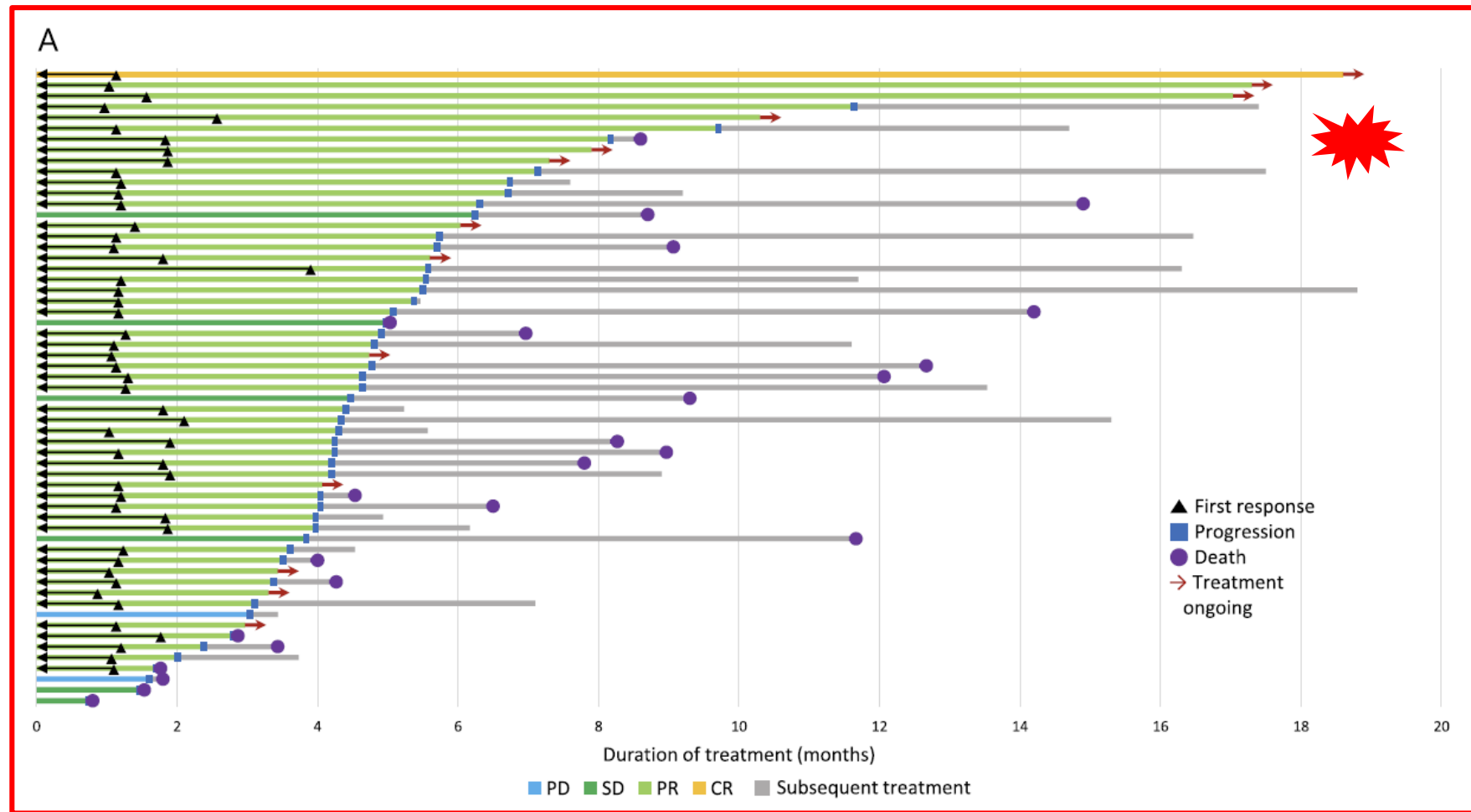
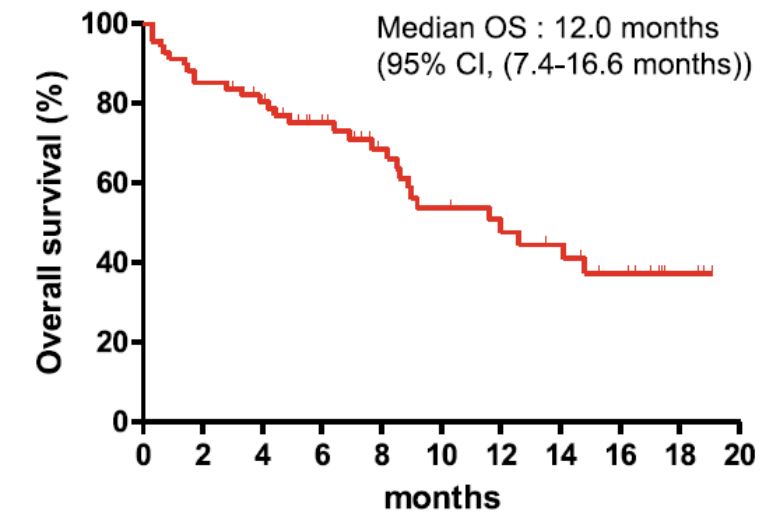
Baseline characteristics (N=68)

Median age (range)—year	68 (40–84)
Male sex, N (%)	61 (89.7%)
ECOG performance status score—N (%)	
0	14 (20.6%)
1	54 (79.4%)
Smoking status ^a —N (%)	
Never smoker	3 (4.4%)
Current smoker	38 (55.9%)
Former smoker	27 (39.7%)
Brain metastases at baseline—N (%)	17 (25.0%)
PCI	4 (6.0%)
Previous treatment for LS-SCLC	2 (3.0%)
PD-L1 status ^b	
≥ 1	2 (3.0%)
< 1	45 (66.2%)
Unknown	21 (30.9%)

A



B



RW data in Japan

- Retrospective analysis (2019-2020)
- 65 CTx naïve, ES-SCLC
- 1L Atezo+EPS+carbo
- The median follow-up was 13.3 months

Variable	Atezo + EC (n=201)	EC (n=202)
Median age, y	64	64
Age <65	55.2%	52.5%
Age ≥65	44.8%	47.5%
Gender		
Male	64.2%	65.3%
Smoking status		
Never	4.5%	1.5%
Current	36.8%	37.1%
Former	58.7%	61.4%
ECOG		
0/1	100%	100%
CNS metastasis		
Yes	8.5%	8.9%
PCI, yes	22 (10.9%)	22 (10.9%)

TABLE 1 Baseline patient characteristics

Characteristic	Total patients (n = 65)
Sex	
Male/female	54/11 83%
Age (years)	
Median	70
Range	43–89
PS	
0/1/2/3/4	13/45/5/2/0
Smoking status	
Yes/no	62/3
Histology	
Small-cell carcinoma/combined small-cell carcinoma	63/2
Disease stage	
3/4/recurrence	5/57/3
History of postoperative adjuvant chemotherapy	
Yes/no	1/64
Intracranial metastases	
Yes/no	19/46
Liver metastases	
Yes/no	14/51
Bone metastases	
Yes/no	22/43
Prior radiotherapy	
Yes/no	7/58

Variable	Atezo + EC (n= 201)	EC (n=202)	Durva + E/plat (n=268)	E/platinum (n=269)	Atezo + CTx (RW, Korea) (n=68)	Atezo + CTx (RW, Japan) (n=65)
ORR	60.2	64.4	68.0	58.0	51 (75%)	48 (73.8%)
CR	2.5	1.0	2.0	1.0	1 (1.5%)	5 (7.6%)
PR	57.7	63.4	66.0	57.0	50 (73.5%)	43 (66.2%)
Median DoR (m)	4.2 (1.4-19.5)	3.9 (2.0-16.1)	5.1 (3.4-10.4)	5.1 (3.7-6.8)	3.3 (0.6-17.5)	
SD	20.9	21.3	7.0	16.0	7 (10.3)	10
PD	10.9	6.9	12.0	12.0	2 (3.0)	6
Median PFS (m)	5.2	4.3	5.1	5.4	4.6	5.4
HR (95% CI)	0.77 (0.62-0.96)		0.78 (0.65-0.94)			
Median OS (m)	12.3	10.3	12.9	10.5	12.0	15.9
HR (95% CI)	0.76 (0.60-0.90)		0.71 (0.60-0.86)			
12m OS (%)	51.9	39.0	52.8	39.3	50.0	50.0
18m OS (%)	34.0	21.0	32.0	24.8	37.0	37.0

KOREA

Adverse events related to treatment			
Event	Grade 1 or 2	Grade 3 or 4	Grade 5
Treatment-related adverse events			
Number of patients (percent)			
Neutropenia	8 (11.7%)	29 (42.6%)	
Anemia	21 (30.9%)	15 (22.1%)	
Anorexia	4 (5.8%)		
Nausea/Vomiting	1 (1.5%)		
Alopecia	1 (1.5%)		
Fatigue	2 (2.9%)	1 (1.5%)	
Thrombocytopenia	14 (20.6%)	15 (22.1%)	
Constipation	5 (7.3%)	1 (1.5%)	
Creatinine elevation	2 (2.9%)		
Febrile neutropenia		6 (8.8%)	
Colitis			2 (2.9%)
Pneumonia		1 (1.5%)	2 (2.9%)
Immune-related adverse events			
Pruritus	6 (8.9%)		
Skin rash	9 (13.3%)		
Diarrhea	2 (2.9%)		
Adrenal insufficiency	3 (4.4%)		
Hypothyroidism	3 (4.4%)		
AST elevation	2 (2.9%)	1 (1.5%)	
ALT elevation	2 (2.9%)		
Hyperosmolar hyperglycemic state		1 (1.5%)	
Pneumonitis		3 (4.4%)	

JAPAN

Adverse event	All patients (n = 65)			
	Any grade	%	Grade ≥3	%
Led to discontinuation	6		5	
Led to death	–		1	
Treatment related^a				
White blood cell count decrease	42	64.6	21	32.3
Neutrophil count decrease	43	66.1	36	55.3
Anemia	35	53.8	1	1.5
Platelet count decrease	33	50.7	4	6.1
Febrile neutropenia	5	7.6	5	7.6
Nausea	16	24.6	1	1.5
Anorexia	19	29.2	1	1.5
Creatinine increase	4	6.1	1	1.5
ALT increase	13	20	2	3
Infection	5	7.6	5	7.6
Hyponatremia	2	3	1	1.5
Thromboembolic event	1	1.5	1	1.5
Immune-related^b				
Rash	3	4.6	1	1.5
Hypothyroidism	6	9.2	1	1.5
Pneumonitis	2	3	1	1.5
Adrenal insufficiency	1	1.5	1	1.5
Myositis	1	1.5	1	1.5
CPK increased	1	1.5	1	1.5

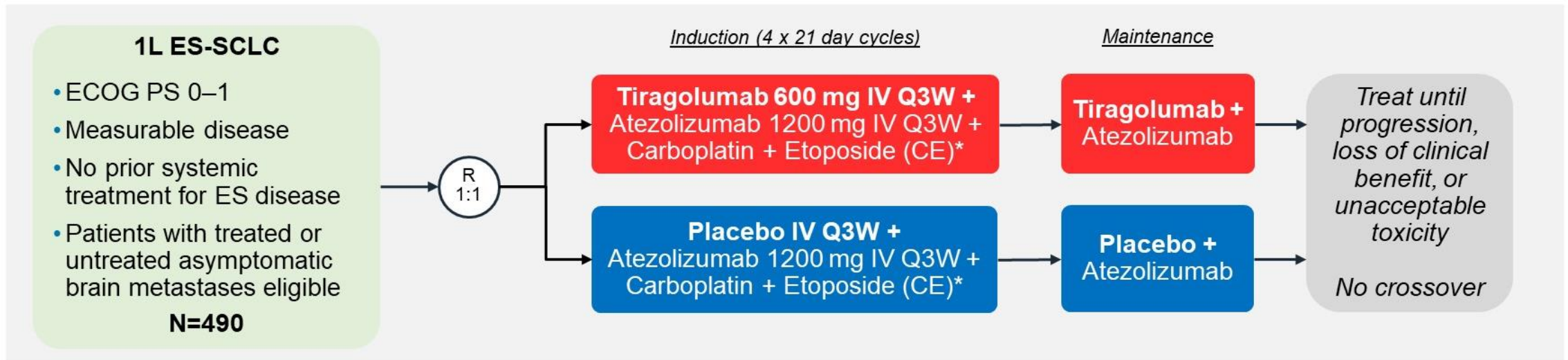
Today's topic



- Standard treatment of ES-SCLC
- Clinical trials of ES-SCLC
- Real-world data of ES-SCLC
- Further clinical trials

SKYSCRAPER-02

- Ph 3, RCT (2017-2018), 1L Atezolizumab + Carboplatin/Etoposide ± Tiragolumab for ES SCLC
- Tiragolumab: novel mAb targeting TIGIT



Stratification Factors:

- **ECOG PS** (0 vs. 1)
- **Brain metastases** (Yes vs. No)
- **LDH** (\leq ULN vs. $>$ ULN)

Co-Primary Endpoints:

- OS and investigator-assessed PFS in **Primary Analysis Set** (all randomized patients without presence or history of brain metastases at baseline)

Secondary Endpoints:

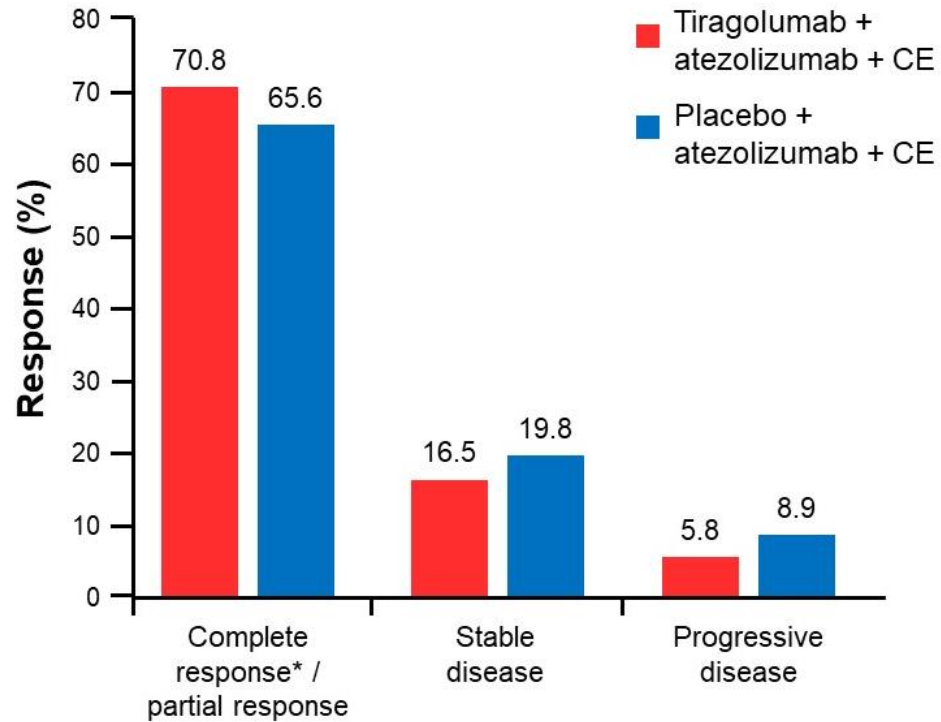
- PFS and OS in **Full Analysis Set** (all randomized patients)
- Confirmed objective response rate
- Duration of response
- Safety
- Pharmacokinetics
- PROs

Primary analysis

- Cut-off date of 6 February 2022
- Median follow-up of 14.3 months (Primary Analysis Set)

	Tiragolumab + atezolizumab + CE	Placebo + atezolizumab + CE	Total
Primary analysis set: All patients without presence or history of BM	196	201	397
Full analysis set: All patients including those BM	243	247	490

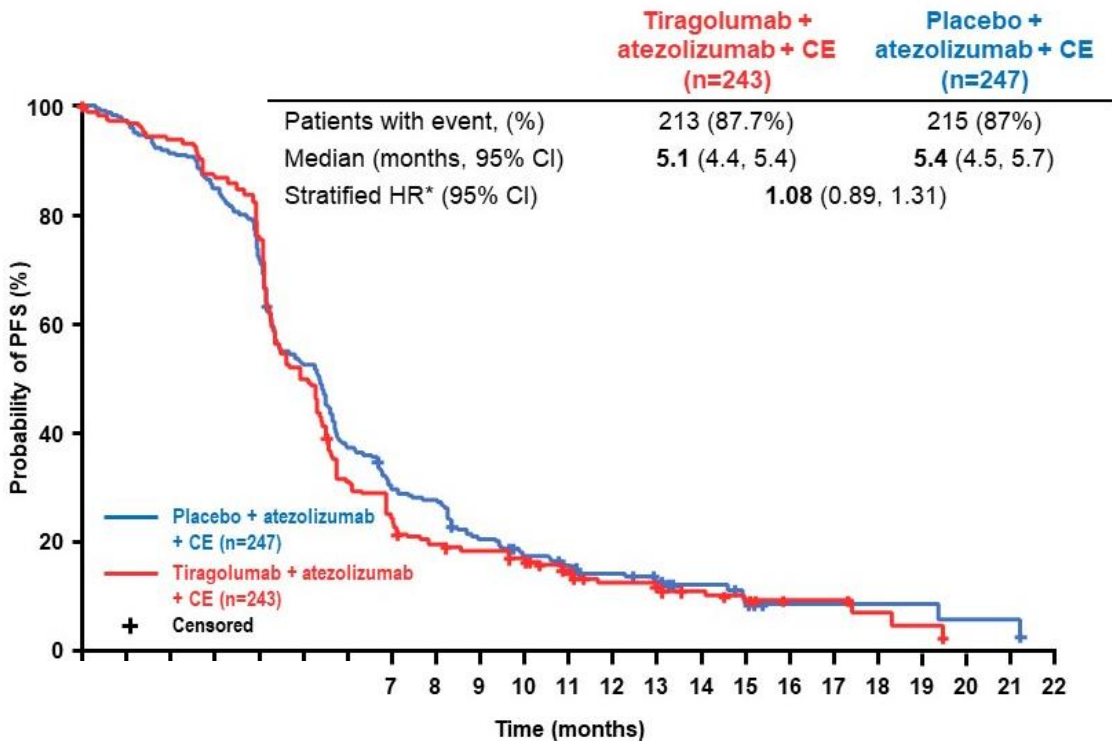
n (%)	Tiragolumab + atezolizumab + CE (n=243)	Placebo + atezolizumab + CE (n=247)
Age <65 years	117 (48.1)	116 (47.0)
Male	162 (66.7)	164 (66.4)
Race		
White	173 (71.2)	174 (70.4)
Asian	63 (25.9)	67 (27.1)
Other*	7 (2.9)	6 (2.4)
Tobacco Use		
Previous	153 (63.0)	161 (65.2)
Current	81 (33.3)	76 (30.8)
Never	9 (3.7)	10 (4)
Baseline ECOG PS†		
0	86 (35.4)	82 (33.2)
1	156 (64.2)	165 (66.8)
LDH ≤ULN	99 (40.7)	101 (40.9)
Brain metastases	47 (19.3)	46 (18.6)
Treated§	14 (5.8)	19 (7.7)
Untreated	33 (13.6)	27 (10.9)
Liver metastases	89 (36.6)	94 (38.1)



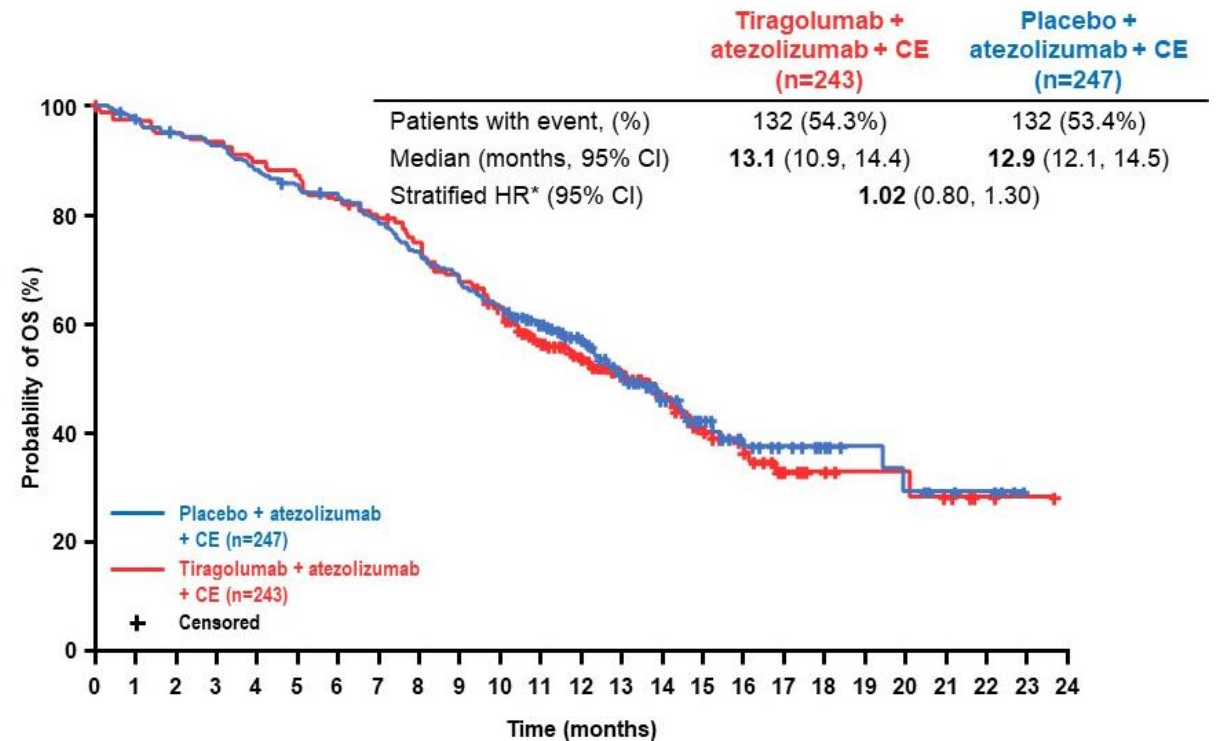
	Tiragolumab + atezolizumab + CE (n=243)	Placebo + atezolizumab + CE (n=247)
Objective response rate, % (95% CI)	70.8 (64.6, 76.3)	65.6 (59.3, 71.4)
Duration of response		
Responders, n	172	162
With subsequent event, n (%)	147 (85.5)	135 (83.3)
Median, months (95% CI)	4.2 (4.1, 4.4)	5.1 (4.4, 5.8)

Variable	Atezo + EC (n= 201)	EC (n=202)	Durva + E/plat (n=268)	E/platinum (n=269)	Tiragolumab Atezo+CE (n=243)	Placebo Atezo+CE (n=247)
ORR	60.2	64.4	68.0	58.0	70.8	65.6
SD	20.9	21.3	7.0	16.0	7 (10.3)	10
PD	10.9	6.9	12.0	12.0	2 (3.0)	6
Median PFS (m)	5.2	4.3	5.1	5.4	5.1	5.4
HR (95% CI)	0.77 (0.62-0.96)		0.78 (0.65-0.94)		1.08 (0.89-1.31)	
Median OS (m)	12.3	10.3	12.9	10.5	13.1	12.9
HR (95% CI)	0.76 (0.60-0.90)		0.71 (0.60-0.86)		1.02 (0.80-1.30)	

PFS in the Full Analysis Set



Interim OS in the Full Analysis Set

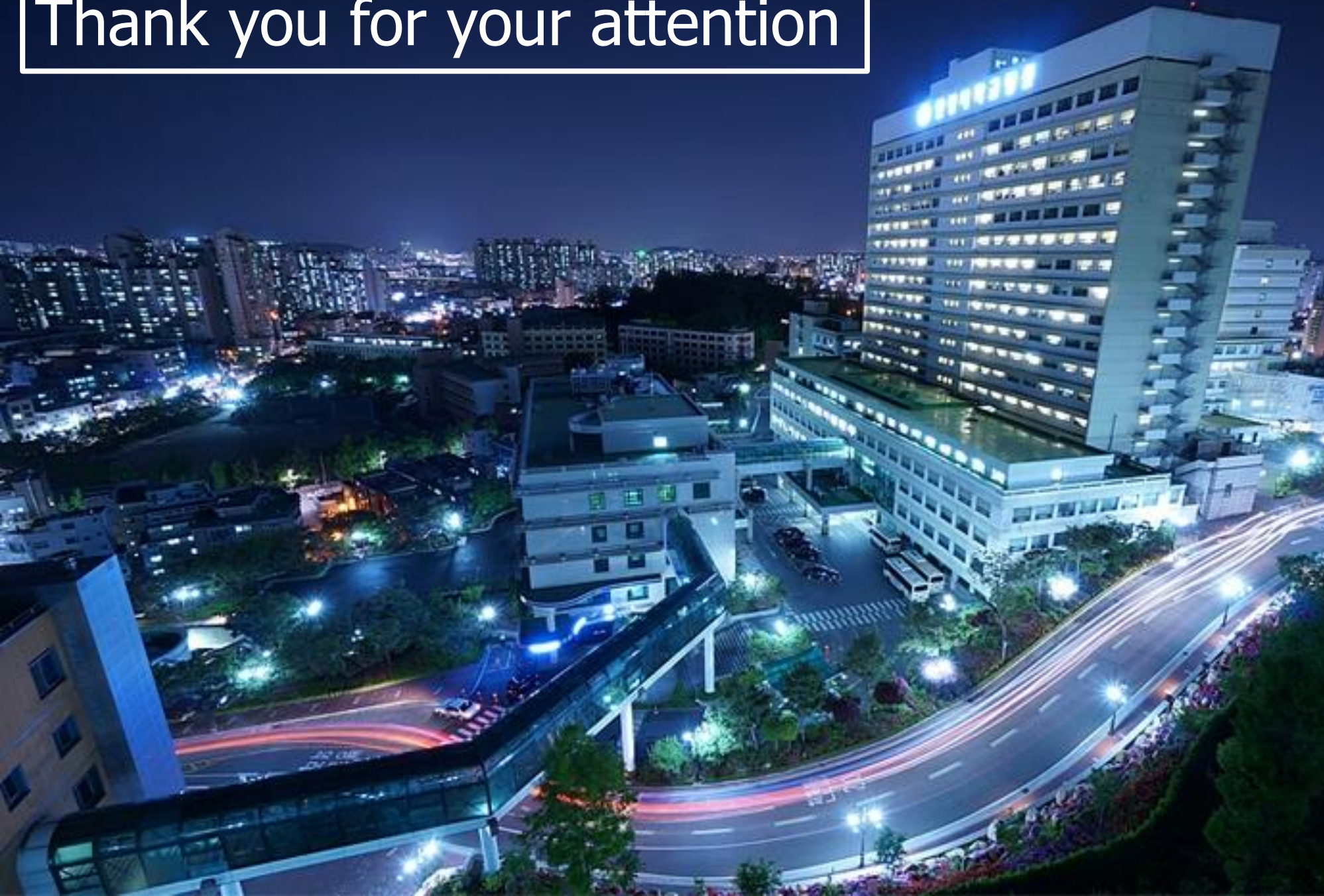


Summary



- Addition of PD-L1 inhibition to platinum/etoposide CTx significantly improves survival in ES SCLC
- Atezolizumab (IMpower133) in combination with carboplatin/etoposide and durvalumab (CASPIAN) in combination with carboplatin/etoposide or cisplatin/etoposide approved by FDA
- PD-L1 inhibition plus chemotherapy is standard of care for the first-line treatment of ES SCLC
- This trend would be valid, regardless of PD-L1 status
- Safety outcomes consistent with known safety profiles of each agent
- Further studies are needed to identify who might derive long term benefit.

Thank you for your attention



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