Incontournables en oncologie thoracique en 2019

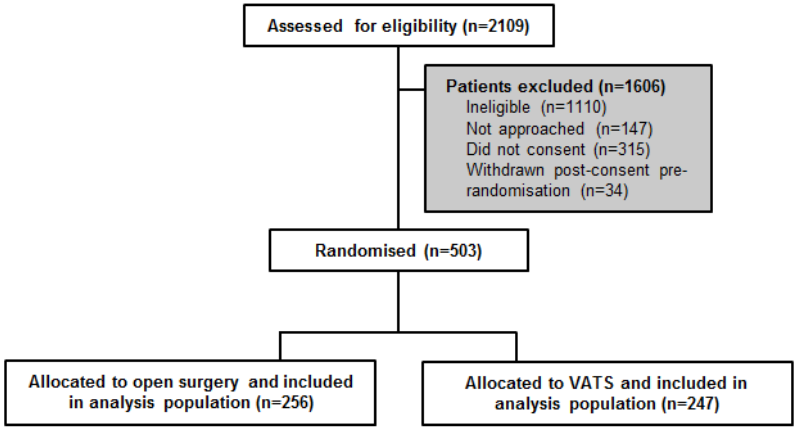
Anne-Claire Toffart

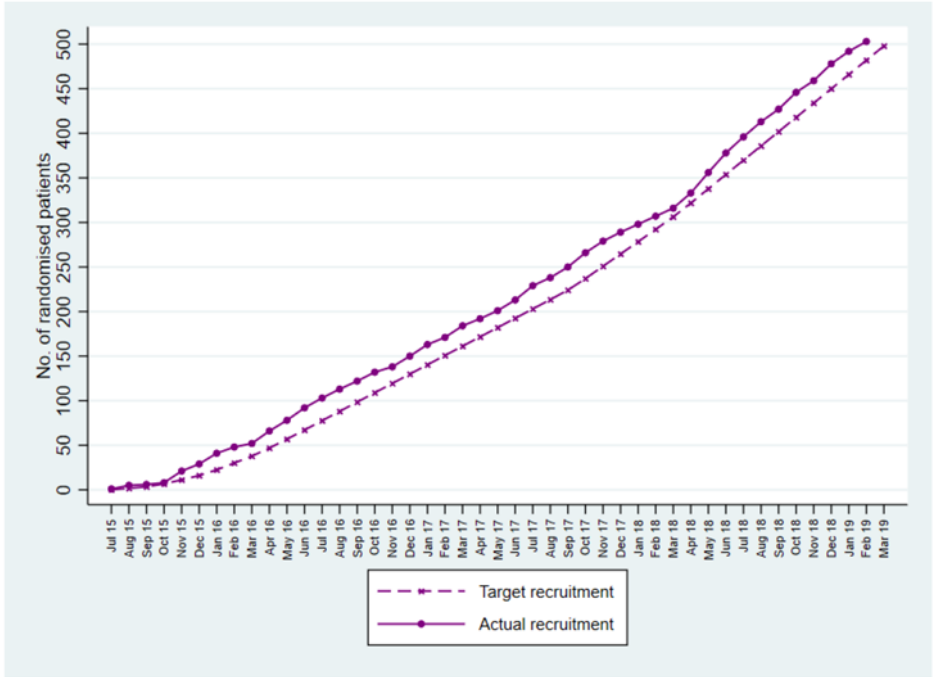
15/10/2019

- VATS
- EGFR mutés: FLAURA, RELAY
- Immunothérapie
  - CBNPC: CheckMate 227
  - CBPC: Impower 133, CASPIAN

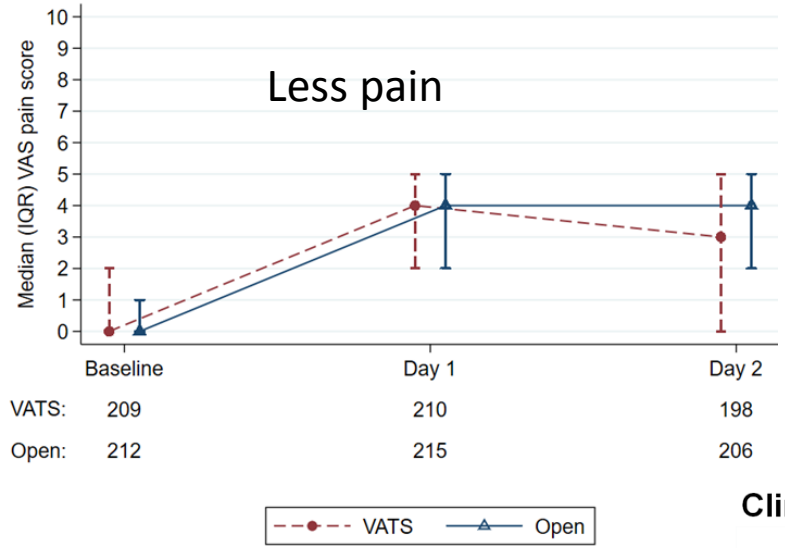
- VATS

VIOLET
A UK Multi-Centre RCT of VATS Versus Open Lobectomy for Lung Cancer





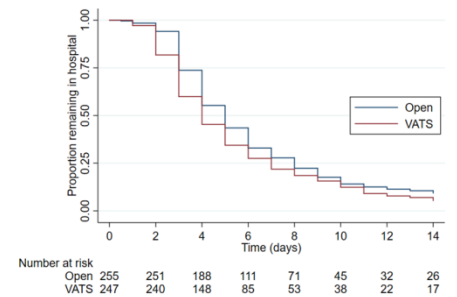
VIOLET



Safety – in-hospital adverse events

	VATS (n=247)	Open (n=256)	Relative risk (95% CI)	P value
Any adverse event	81/247 (32.8%)	113/255 (44.3%)	0.74 (0.66, 0.84)	<0.001
Any serious adverse event	20/247 (8.1%)	20/255 (7.8%)	1.03 (0.64, 1.68)	0.897

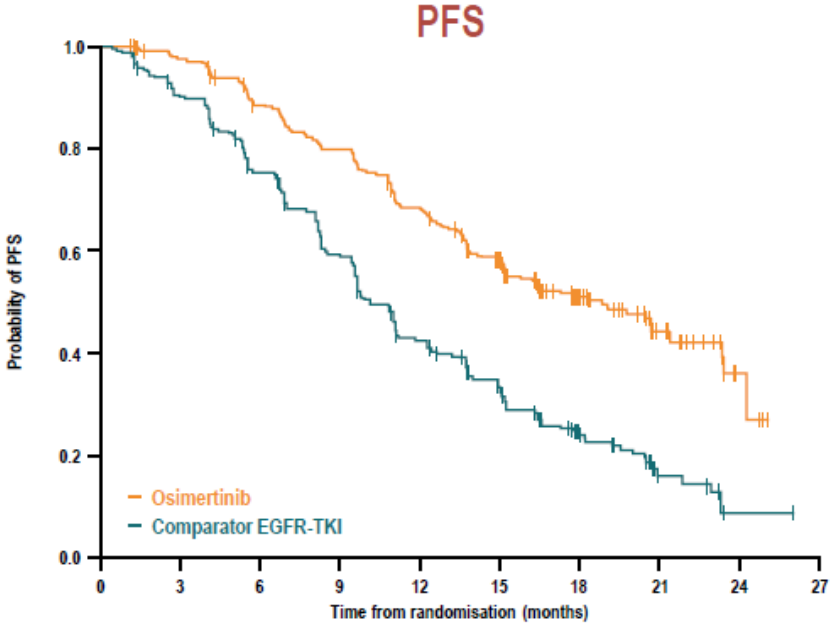
Clinical efficacy – length of stay



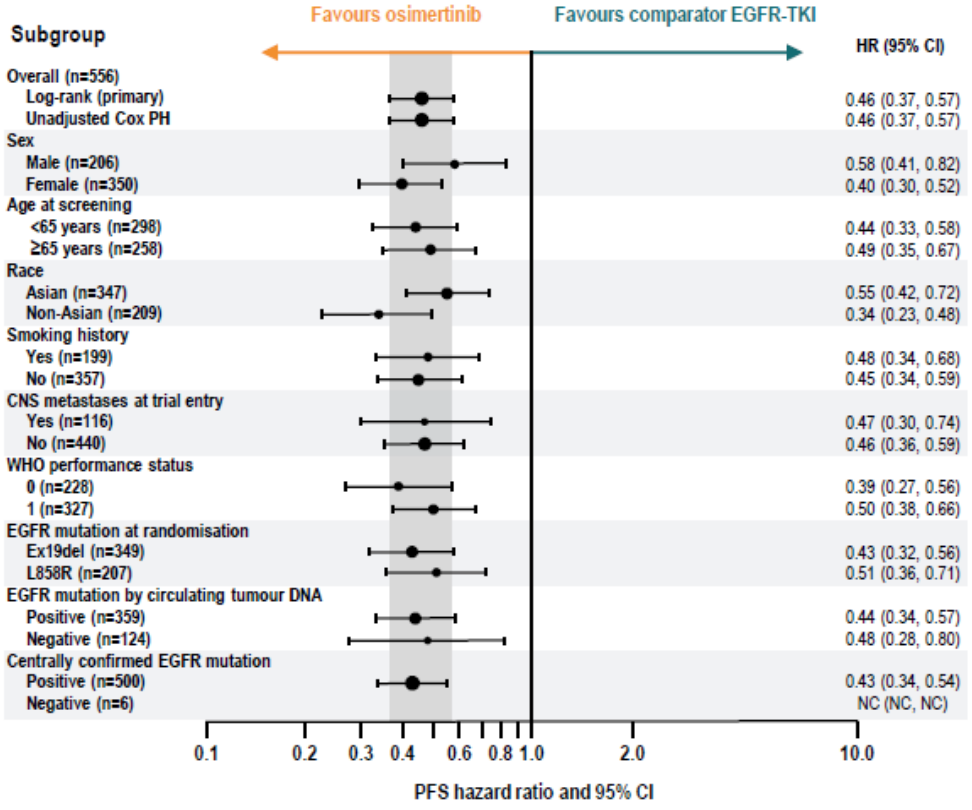
	VATS (n=247)	Open (n=256)	HR (95% CI)	P value
Median (IQR) length of stay (days)	4 (3, 7)	5 (3, 8)	1.34 (1.09, 1.65)	0.006

- VATS
- EGFR mutés: FLAURA, RELAY

FLAURA - Primary analysis: progression-free survival



	Median PFS, months (95% CI)	HR (95% CI)
Osimertinib	18.9 (15.2, 21.4)	0.46 (0.37, 0.57); p<0.001
Comparator EGFR-TKI	10.2 (9.6, 11.1)	

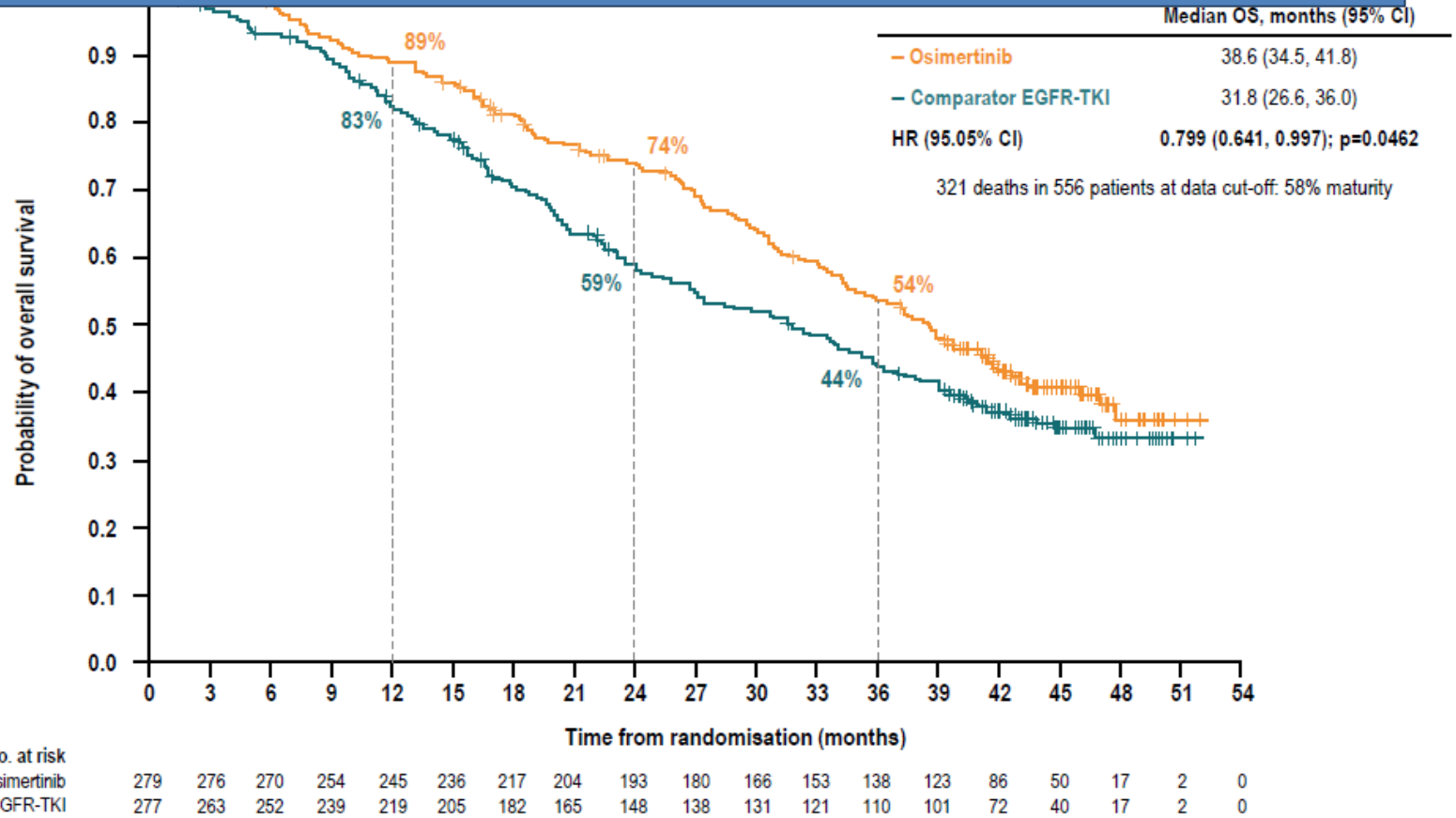


Data cut-off: 12 June 2017

Soria et al. N Engl J Med 2018;378:113-25

CI, confidence interval; ctDNA, circulating tumour DNA; NC, not calculable; PH, proportional-hazards

FLAURA - Final analysis: overall survival



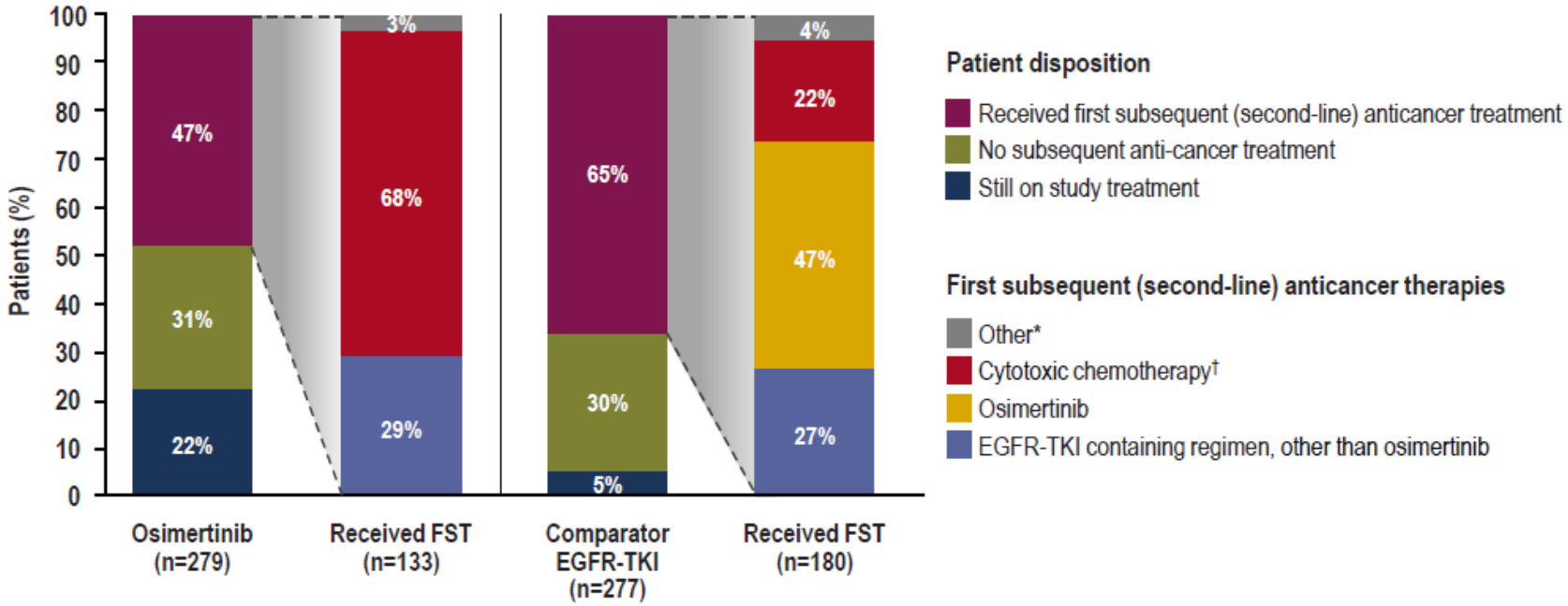
BARCELONA 2019 ESMO congress

Data cut-off: 25 June 2019

For statistical significance, a p-value of less than 0.0495, determined by O'Brien-Fleming approach, was required

FLAURA – Second-line treatment following progression

- Of the 180 patients in the comparator EGFR-TKI arm who received a first subsequent treatment, **85 patients (47%) crossed over to osimertinib** (31% of all patients randomised from the comparator EGFR-TKI arm)



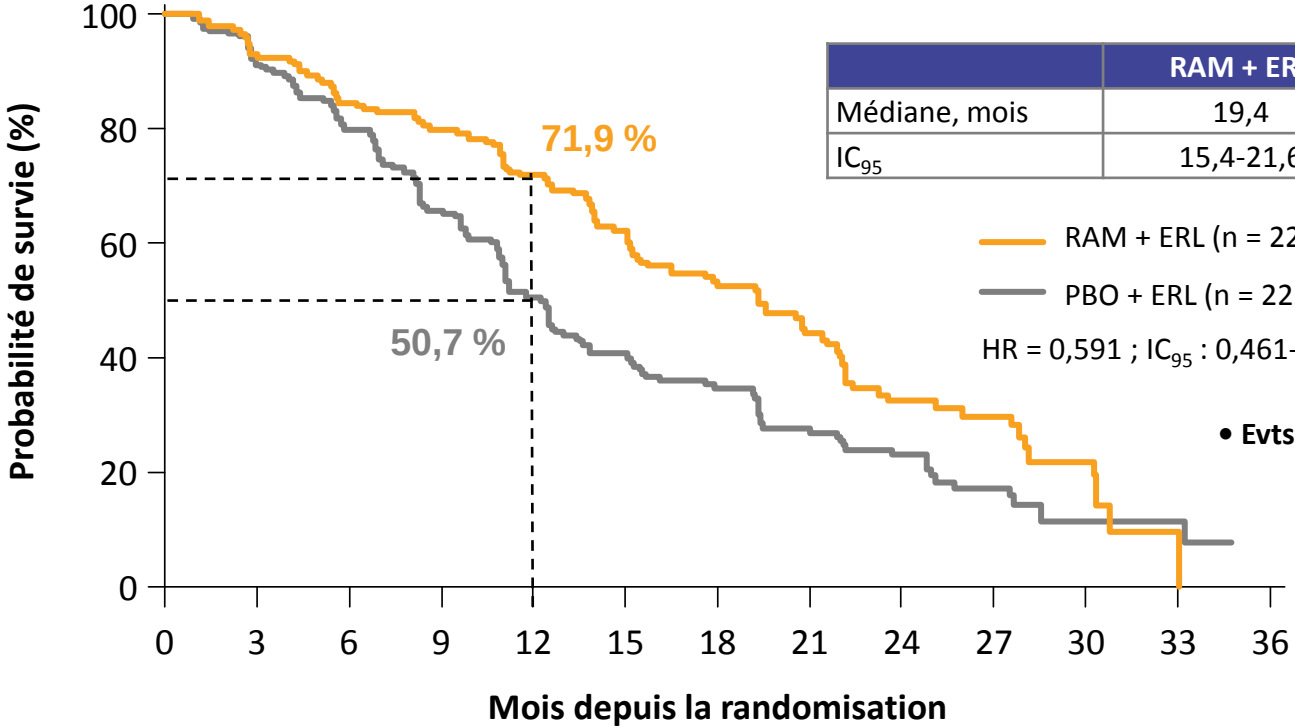
*Refers to those patients who did not receive either chemotherapy or an EGFR-TKI; †The majority of patients who received cytotoxic chemotherapy received a platinum-based chemotherapy regimen

Data cut-off: 25 June 2019

FST, first subsequent treatment

CBNPC EGFR – Etude RELAY

Objectif principal : SSP (évaluée par les investigateurs)



	RAM + ERL	PBO + ERL
Médiane, mois	19,4	12,4
IC_{95}	15,4-21,6	11,0-13,5

RAM + ERL (n = 224)

PBO + ERL (n = 225)

HR = 0,591 ; IC_{95} : 0,461-0,760 ; p < 0,0001

- **Evts** : 122 versus 158

SSP par revue indépendante (HR = 0,671 ; IC_{95} : 0,518-0,869 ; p = 0,0022)

D'après Nakagawa et al. Abstract 9000

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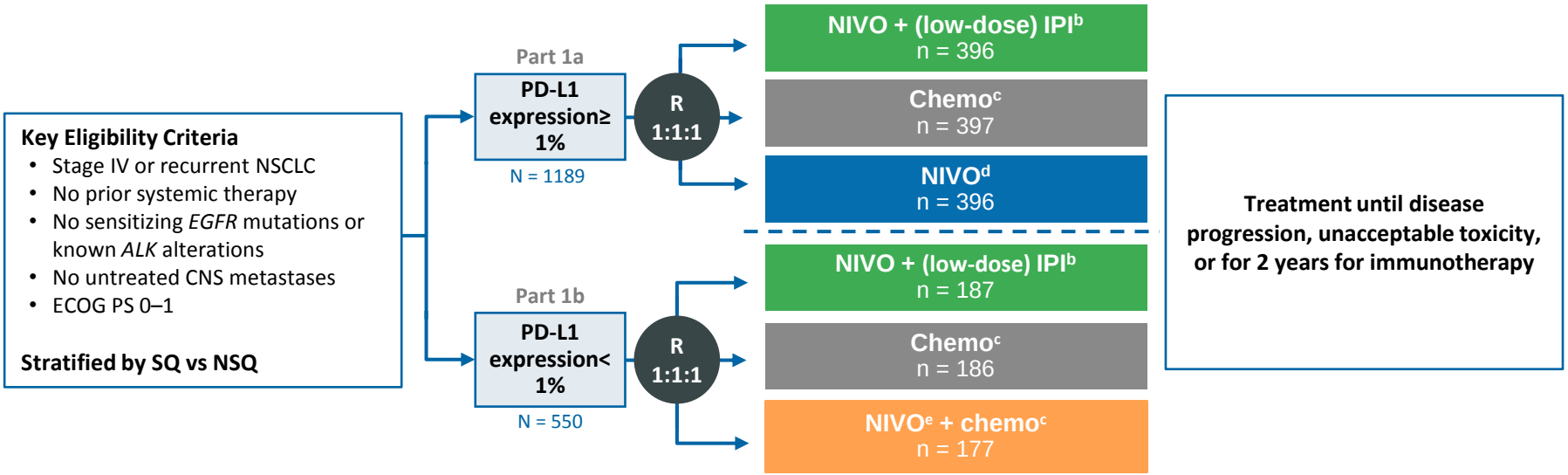
  - CBNPC: CheckMate 227

CheckMate 227 Part 1 Study Design[a]



Independent co-primary endpoints: NIVO + IPI vs chemo
- PFS in high TMB (≥10 mut/Mb) population[f]
- OS in PD-L1 ≥ 1% population[g]

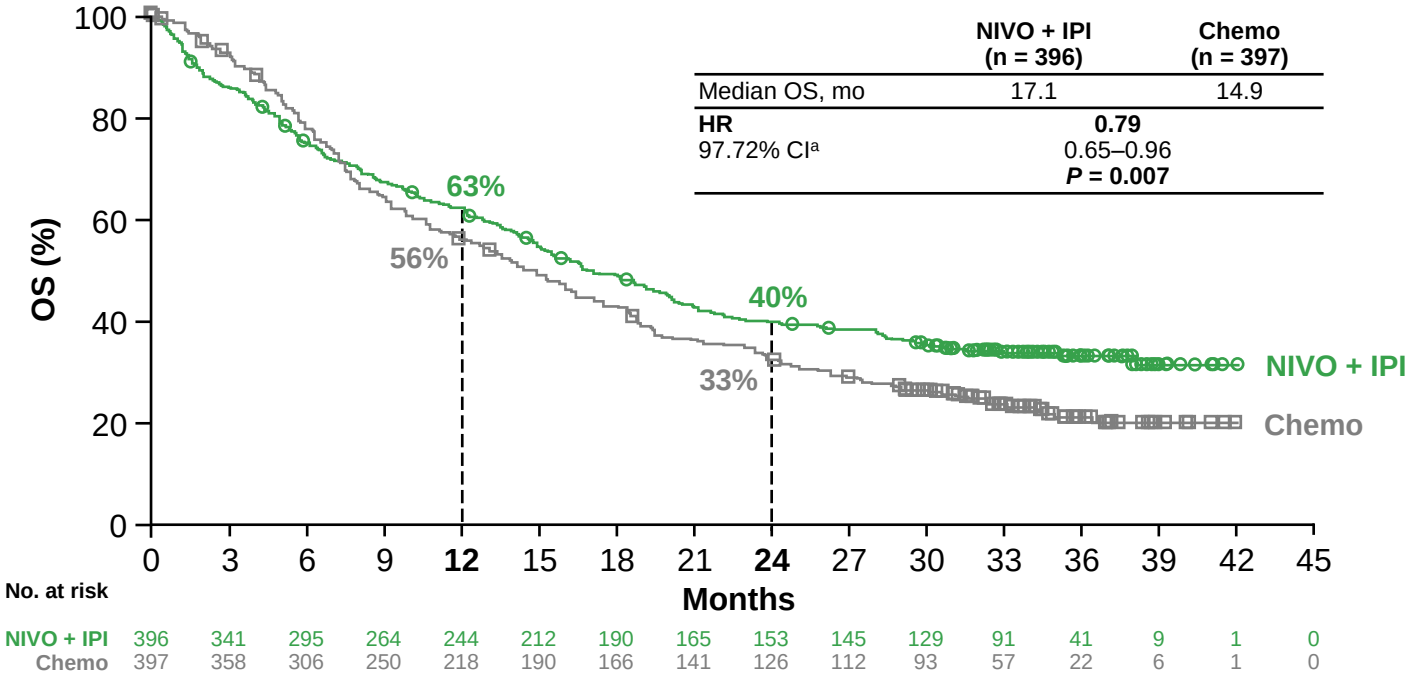
Secondary endpoints (PD-L1 hierarchy):
- PFS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO vs chemo** in PD-L1 ≥ 50%

Database lock: July 2, 2019; **minimum follow-up for primary endpoint: 29.3 months**

[a]NCT02477826; [b]NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W); [c]**NSQ:** pemetrexed + cisplatin or carboplatin, Q3W for ≤ 4 cycles, with optional pemetrexed maintenance following chemo or NIVO + pemetrexed maintenance following NIVO + chemo; **SQ:** gemcitabine + cisplatin, or gemcitabine + carboplatin, Q3W for ≤ 4 cycles; [d]NIVO (240 mg Q2W); [e]NIVO (360 mg Q3W); [f]TMB primary endpoint analysis conducted at January 24, 2018 database lock in subset of patients randomized to NIVO + IPI or chemo; alpha allocated was 0.025; [g]Alpha allocated was 0.025 overall (0.023 for final analysis)

Primary Endpoint: OS With NIVO + IPI vs Chemo in Patients With Tumor PD-L1 Expression ≥ 1%

Part 1a
NIVO + IPI
Chemo
NIVO

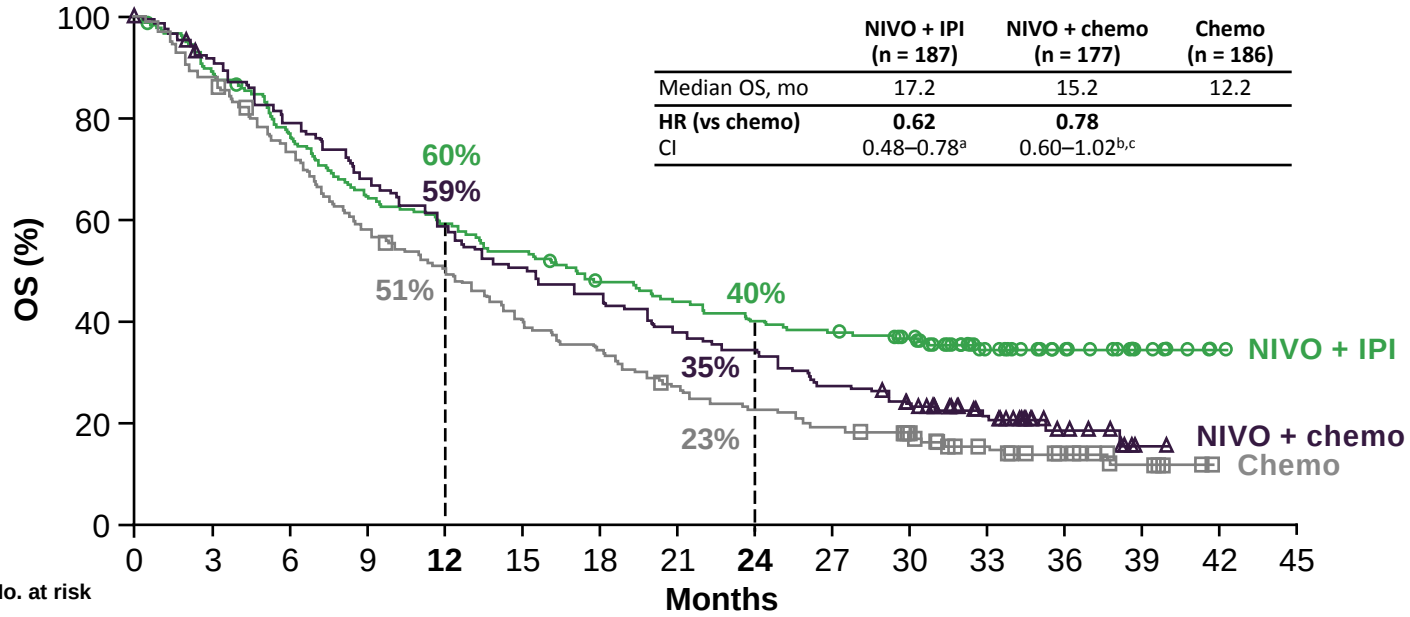


	NIVO + IPI (n = 396)	Chemo (n = 397)
Median OS, mo	17.1	14.9
HR	**0.79**	
97.72% CI[a]	0.65–0.96	
	***P* = 0.007**	

Minimum follow-up for primary endpoint: 29.3 months.
NIVO + IPI dosage was NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W). Subsequent systemic therapy was received by 35% of patients in the NIVO + IPI arm and 54% of patients in the chemo arm; subsequent immunotherapy was received by 6% and 43%, respectively.
[a]95% CI, 0.67–0.94.

OS With NIVO + IPI and NIVO + Chemo vs Chemo in Patients With Tumor PD-L1 Expression < 1%

Part 1b
NIVO + IPI
Chemo
NIVO + chemo



	NIVO + IPI (n = 187)	NIVO + chemo (n = 177)	Chemo (n = 186)
Median OS, mo	17.2	15.2	12.2
HR (vs chemo)	**0.62**	**0.78**	
CI	0.48–0.78[a]	0.60–1.02[b,c]	

No. at risk

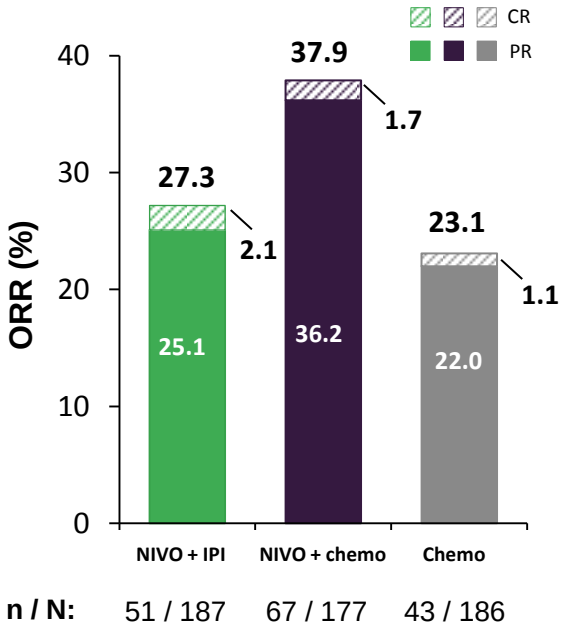
NIVO + IPI	187	165	142	120	110	100	87	80	73	69	59	34	19	8	2	0
NIVO + chemo	177	159	139	119	102	88	78	67	60	48	40	23	9	1	0	0
Chemo	186	164	135	107	92	74	62	49	41	35	29	19	12	5	0	0

Dosages were NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W), and NIVO (360 mg Q3W) plus chemo. Subsequent systemic therapy was received by 44% of patients in the NIVO + IPI arm, 41% of patients in the NIVO + chemo arm, and 53% of patients in the chemo arm; subsequent immunotherapy was received by 4%, 4%, and 36%, respectively.
[a]95% CI; [b]97.72% CI; [c]*P* = 0.0352.

ORR and DOR for NIVO + IPI and NIVO + Chemo vs Chemo in Patients With Tumor PD-L1 Expression < 1%

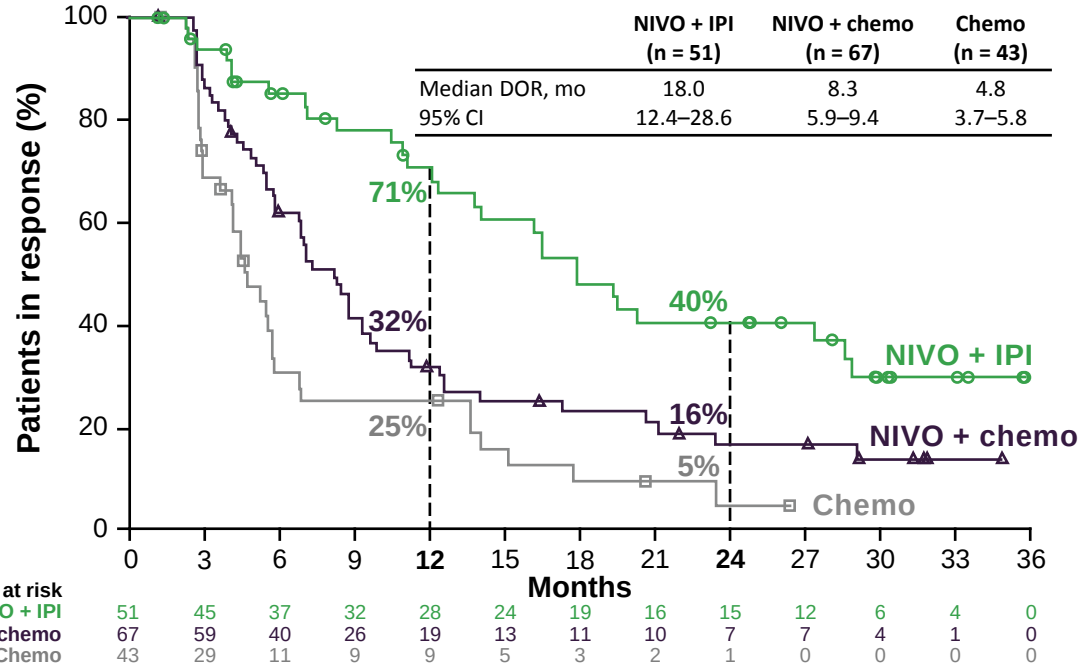
Part 1b
NIVO + IPI
Chemo
NIVO + chemo

ORR by BICR



n / N:	51 / 187	67 / 177	43 / 186

DOR by BICR[a]



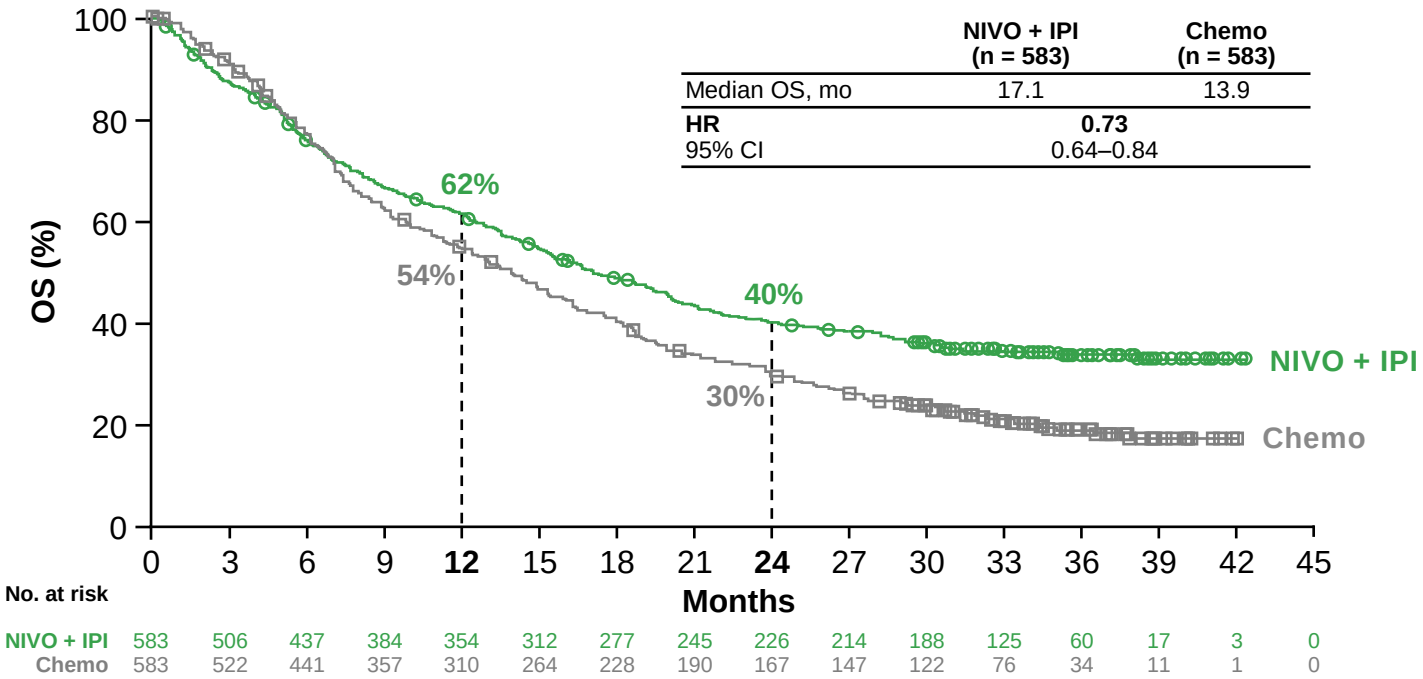
	NIVO + IPI (n = 51)	NIVO + chemo (n = 67)	Chemo (n = 43)
Median DOR, mo	18.0	8.3	4.8
95% CI	12.4–28.6	5.9–9.4	3.7–5.8

No. at risk													
NIVO + IPI	51	45	37	32	28	24	19	16	15	12	6	4	0
NIVO + chemo	67	59	40	26	19	13	11	10	7	7	4	1	0
Chemo	43	29	11	9	9	5	3	2	1	0	0	0	0

Dosages were NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W), and NIVO (360 mg Q3W) plus chemo.
[a]Median time to response was 2.8 mo with NIVO + IPI, 1.7 mo with NIVO + chemo, and 1.5 mo with chemo.

OS With NIVO + IPI vs Chemo in All Randomized Patients (Regardless of PD-L1)

Part 1 (1a and 1b)
NIVO + IPI
Chemo



NIVO + IPI dosage was NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W). Subsequent systemic therapy was received by 38% of patients in the NIVO + IPI arm and 54% of patients in the chemo arm; subsequent immunotherapy was received by 5% and 41%, respectively.

- VATS
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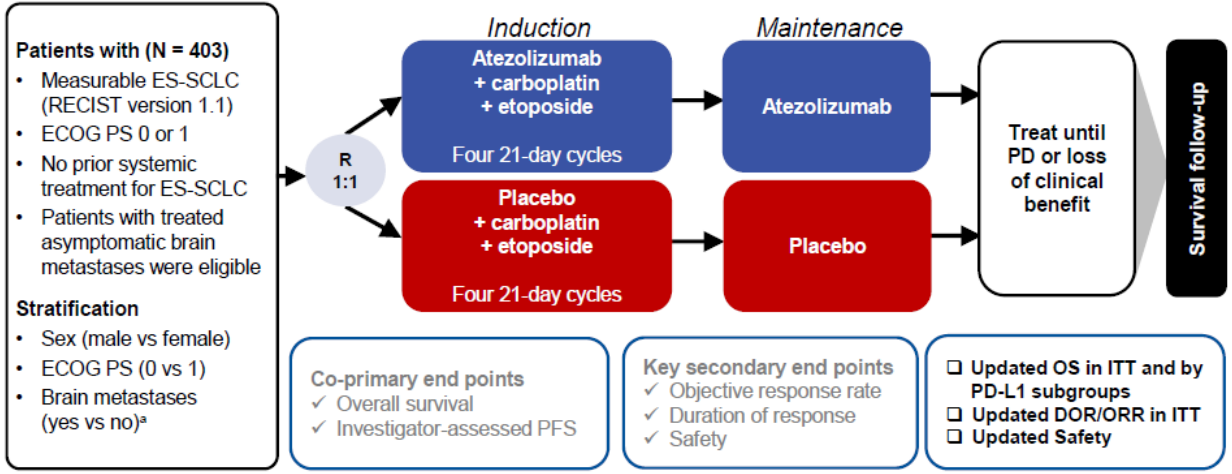
  - CBPC: Impower 133, CASPIAN

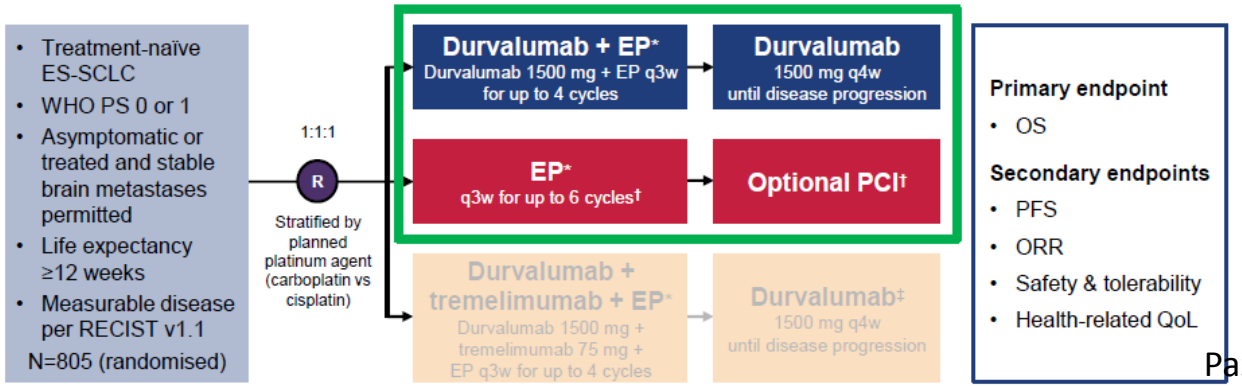
IMpower133 study design



Reck, *IASLC* 2019

CASPIAN Study Design

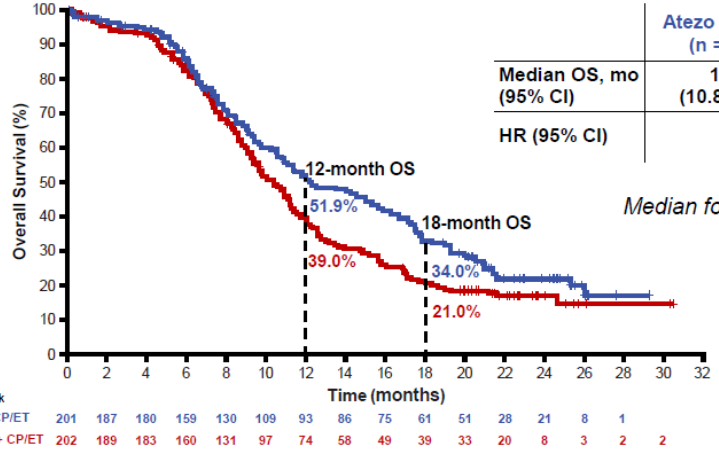
Phase 3, global, randomised, open-label, sponsor-blind multicentre study



Paz Ares L, *IASLC* 2019

IMPOWER 133

Updated OS in ITT



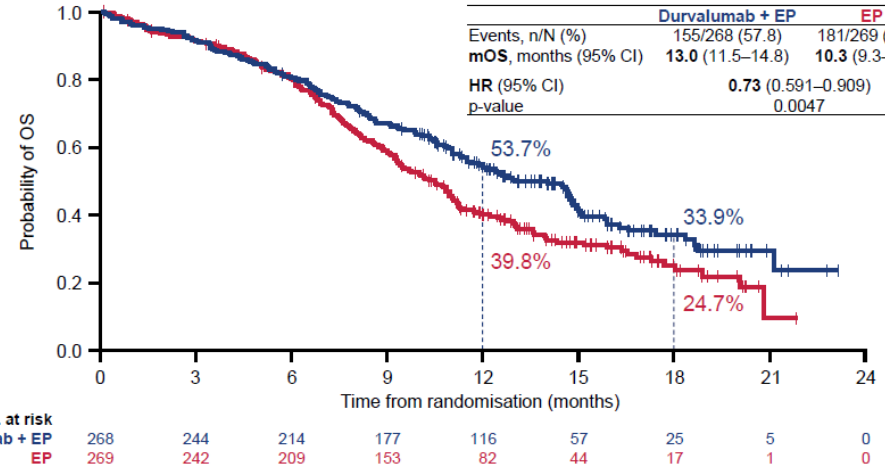
	Atezo + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8, 15.8)	10.3 (9.3, 11.3)
HR (95% CI)	0.76 (0.60, 0.95) p = 0.0154[a]	

Median follow-up, 22.9 months

Reck, *IASLC* 2019

CASPIAN

Overall Survival (Primary Endpoint)

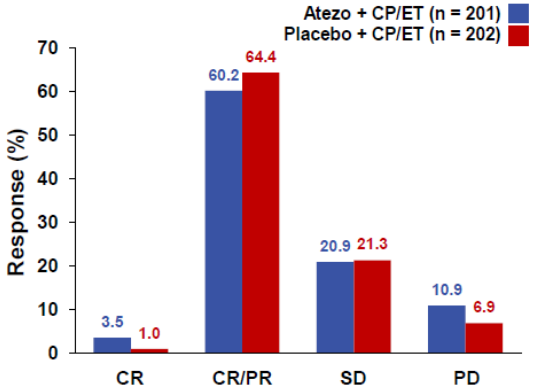


	Durvalumab + EP	EP
Events, n/N (%)	155/268 (57.8)	181/269 (67.3)
mOS, months (95% CI)	**13.0** (11.5–14.8)	**10.3** (9.3–11.2)
HR (95% CI)	**0.73** (0.591–0.909)	
p-value	0.0047	

Paz Ares L, *IASLC* 2019

IMPOWER 133

Updated ORR and DOR in ITT

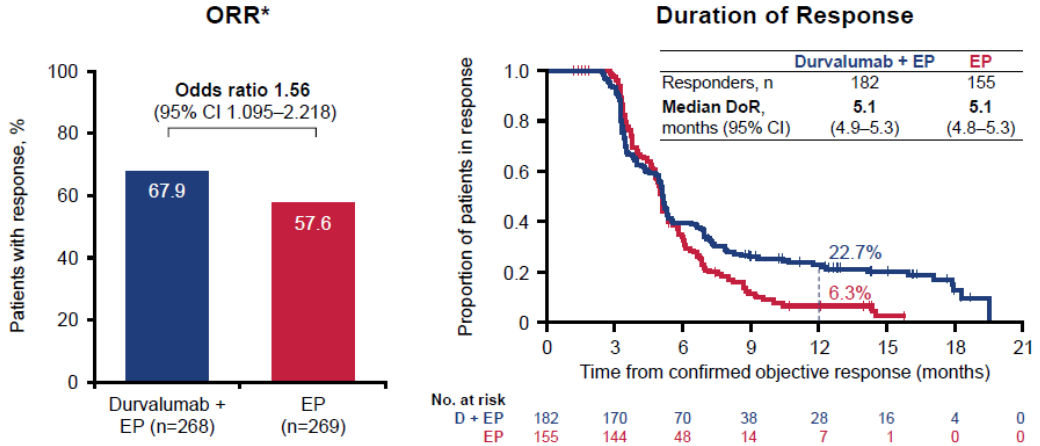


Duration of response	Atezo + CP/ET (n = 121)	Placebo + CP/ET (n = 130)
mDOR, months (range)	4.2 (1.4+ to 24.3+)	3.9 (2.0 to 24.2+)
Patients with ongoing response, n (%)[a]	11 (9.1)	3 (2.3)

Reck, *IASLC* 2019

CASPIAN

Confirmed Objective Response



Paz Ares L, *IASLC* 2019