Lung Cancer UPDATES
ASCO HIGHLIGTHS
04-08 JUNIO 2021

Iniciativa científica de:
GECP
lung cancer research

CPNCP precoz resecable

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ICO Hospitalet

Guión

- Tratamiento adyuvante o neoadyuvante:

✓ IMpower110: Primary results - DFS

✓ IMPACT: PFS and OS

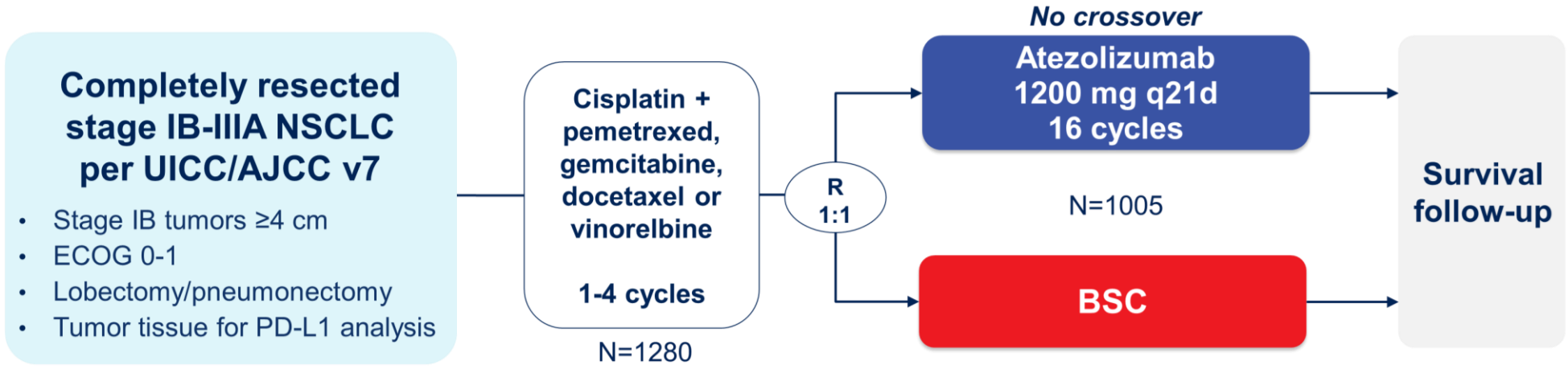
✓ EMERGING: Final analysis - OS

✓ CheckMate 816: surgical outcomes

✓ VIOLET: DFS, OS, QoL

IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs BSC After Adjuvant Chemo in Resected Stage IB-IIIA NSCLC

Study design



Stratification factors
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints
- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Key secondary endpoints
- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

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IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs BSC After Adjuvant Chemo in Resected Stage IB-IIIA NSCLC

Patients' characteristics

Characteristic	All patients (N=1005)	PD-L1 TC ≥1% (SP263) (stage II-IIIA)		All randomized (stage II-IIIA)		ITT (stage IB-IIIA)	
		Atezolizumab (n=248)	BSC (n=228)	Atezolizumab (n=442)	BSC (n=440)	Atezolizumab (n=507)	BSC (n=498)
Median (range) age, y	**62 (26-84)**	61 (34–82)	62 (26–84)	62 (33–82)	62 (26–84)	62 (33–83)	62 (26–84)
Age ≥65 y, n (%)	**382 (38.0)**	92 (37.1)	97 (42.5)	161 (36.4)	177 (40.2)	184 (36.3)	198 (39.8)
Sex, male, n (%)	**672 (66.9)**	171 (69.0)	147 (64.5)	295 (66.7)	294 (66.8)	337 (66.5)	335 (67.3)
Race, n (%)							
White	**738 (73.4)**	162 (65.3)	166 (72.8)	307 (69.5)	324 (73.6)	362 (71.4)	376 (75.5)
Asian	**242 (24.1)**	78 (31.5)	56 (24.6)	121 (27.4)	106 (24.1)	130 (25.6)	112 (22.5)
Other	**25 (2.5)**	8 (3.2)	6 (2.6)	14 (3.2)	10 (2.3)	15 (3.0)	10 (2.0)
ECOG PS, n (%)							
0	**556 (55.3)**	140 (56.5)	125 (54.8)	239 (54.1)	252 (57.3)	273 (53.8)	283 (56.8)
1	**446 (44.4)**	107 (43.1)	102 (44.7)	201 (45.5)	187 (42.5)	232 (45.8)	214 (43.0)
Histology, non-squamous, n (%)	**659 (65.6)**	152 (61.3)	143 (62.7)	292 (66.1)	296 (67.3)	328 (64.7)	331 (66.5)
Stage, n (%)							
IB	**123 (12.2)**	–	–	–	–	65 (12.8)	58 (11.6)
IIA	**295 (29.4)**	85 (34.3)	76 (33.3)	147 (33.3)	148 (33.6)	147 (29.0)	148 (29.7)
IIB	**174 (17.3)**	46 (18.5)	37 (16.2)	90 (20.4)	84 (19.1)	90 (17.8)	84 (16.9)
IIIA	**413 (41.1)**	117 (47.2)	115 (50.4)	205 (46.4)	208 (47.3)	205 (40.4)	208 (41.8)
Tobacco use history, n (%)							
Never	**222 (22.1)**	51 (20.6)	41 (18.0)	100 (22.6)	96 (21.8)	114 (22.5)	108 (21.7)
Current/previous	**783 (77.9)**	197 (79.4)	187 (82.0)	342 (77.4)	344 (78.2)	393 (77.5)	390 (78.3)
PD-L1 by SP263, TC≥1%, n (%)[a]	**535 (54.6)**	248 (100)	228 (100)	248 (57.8)	228 (53.0)	283 (57.4)	252 (51.9)
EGFR mutation status, n (%)[b]							
Positive	**117 (11.6)**	23 (9.3)	20 (8.8)	49 (11.1)	60 (13.6)	53 (10.5)	64 (12.9)
Negative	**527 (52.4)**	123 (49.6)	125 (54.8)	229 (51.8)	234 (53.2)	261 (51.5)	266 (53.4)
Unknown[c]	**361 (35.9)**	102 (41.1)	83 (36.4)	164 (37.1)	146 (33.2)	193 (38.1)	168 (33.7)
ALK rearrangement status, n (%)[b]							
Positive	**33 (3.3)**	12 (4.8)	11 (4.8)	14 (3.2)	17 (3.9)	15 (3.0)	18 (3.6)
Negative	**574 (57.1)**	133 (53.6)	121 (53.1)	251 (56.8)	256 (58.2)	280 (55.2)	294 (59.0)
Unknown[c]	**398 (39.6)**	103 (41.5)	96 (42.1)	177 (40.0)	167 (38.0)	212 (41.8)	186 (37.3)

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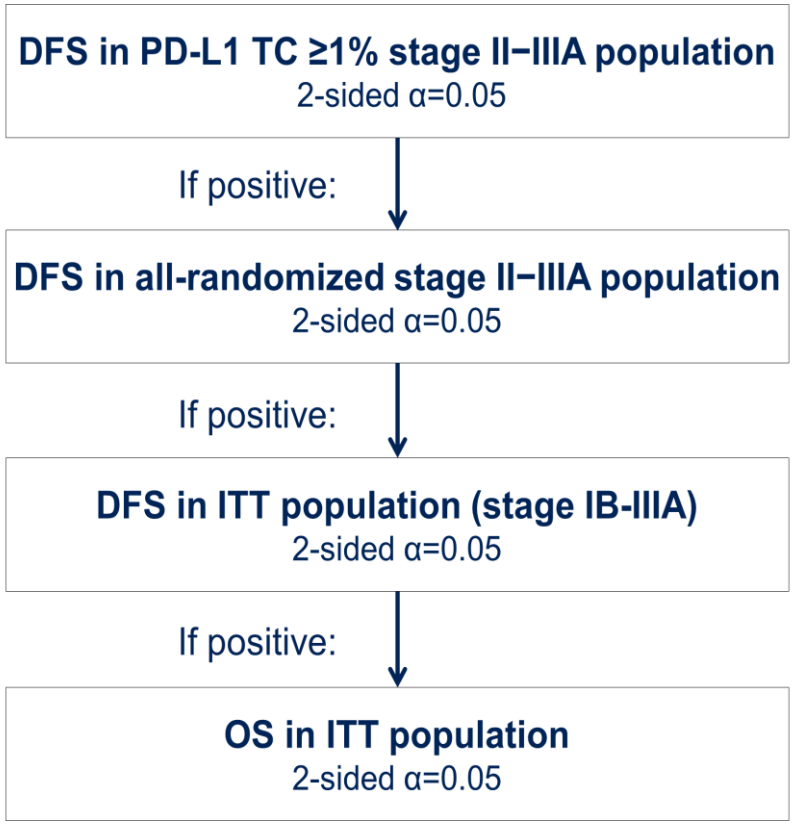
IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs BSC After Adjuvant Chemo in Resected Stage IB-IIIA NSCLC

The primary DFS endpoint was tested hierarchically in 3 primary analysis populations



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IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs BSC After Adjuvant Chemo in Resected Stage IB-IIIA NSCLC

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DFS in PD-L1 TC ≥1% stage II−IIIA population
2-sided α=0.05

If positive:

DFS in all-randomized stage II−IIIA population
2-sided α=0.05

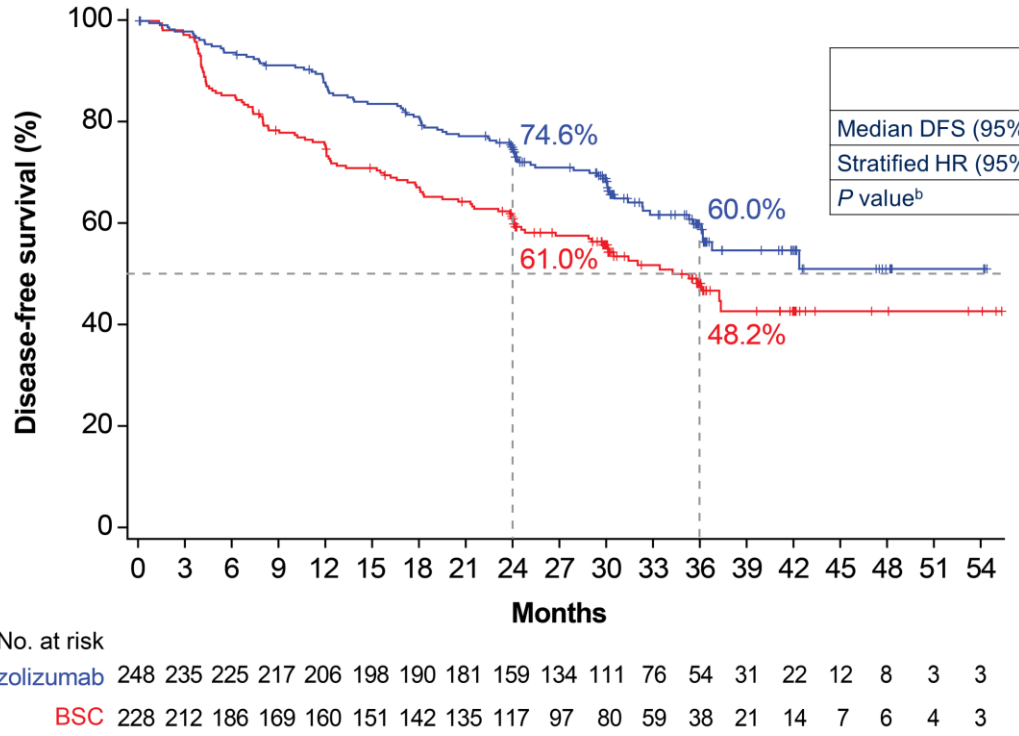
If positive:

DFS in ITT population (stage IB-IIIA)
2-sided α=0.05

If positive:

OS in ITT population
2-sided α=0.05

DFS in the PD-L1 TC ≥1%[a] stage II-IIIA population



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

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DFS in PD-L1 TC ≥1% stage II–IIIA population
2-sided α=0.05

If positive:

DFS in all-randomized stage II–IIIA population
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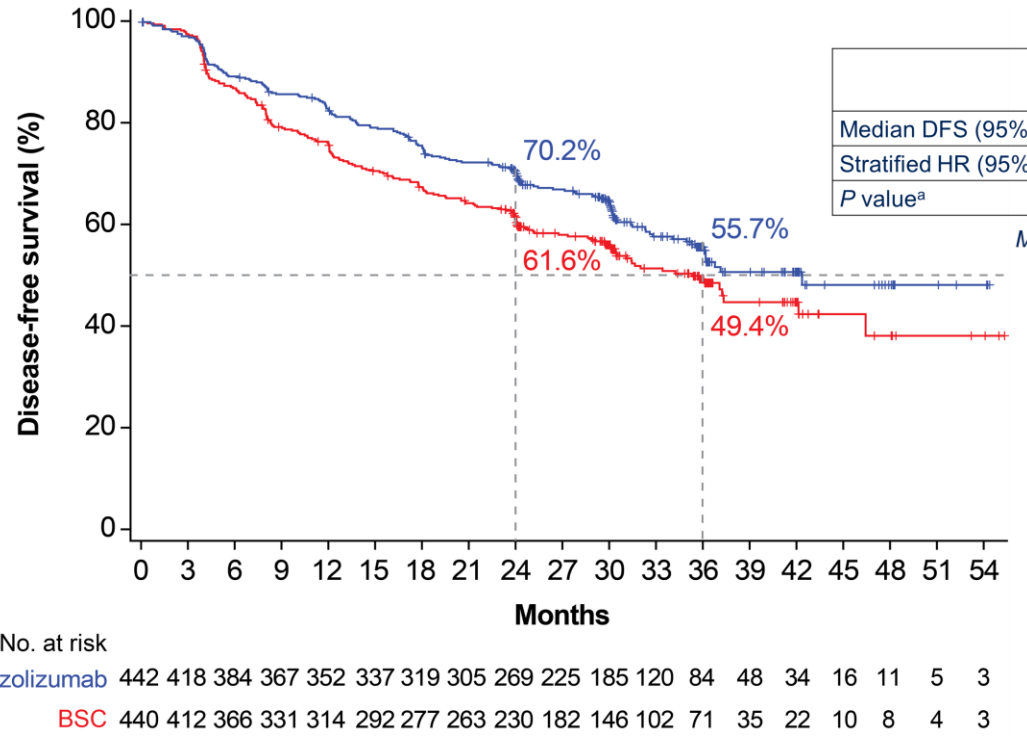
If positive:

DFS in ITT population (stage IB-IIIA)
2-sided α=0.05

If positive:

OS in ITT population
2-sided α=0.05

DFS in the all-randomized stage II-IIIA population



	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[a]	0.02[b]	

Median follow-up: 32.2 mo (range, 0-57.5)

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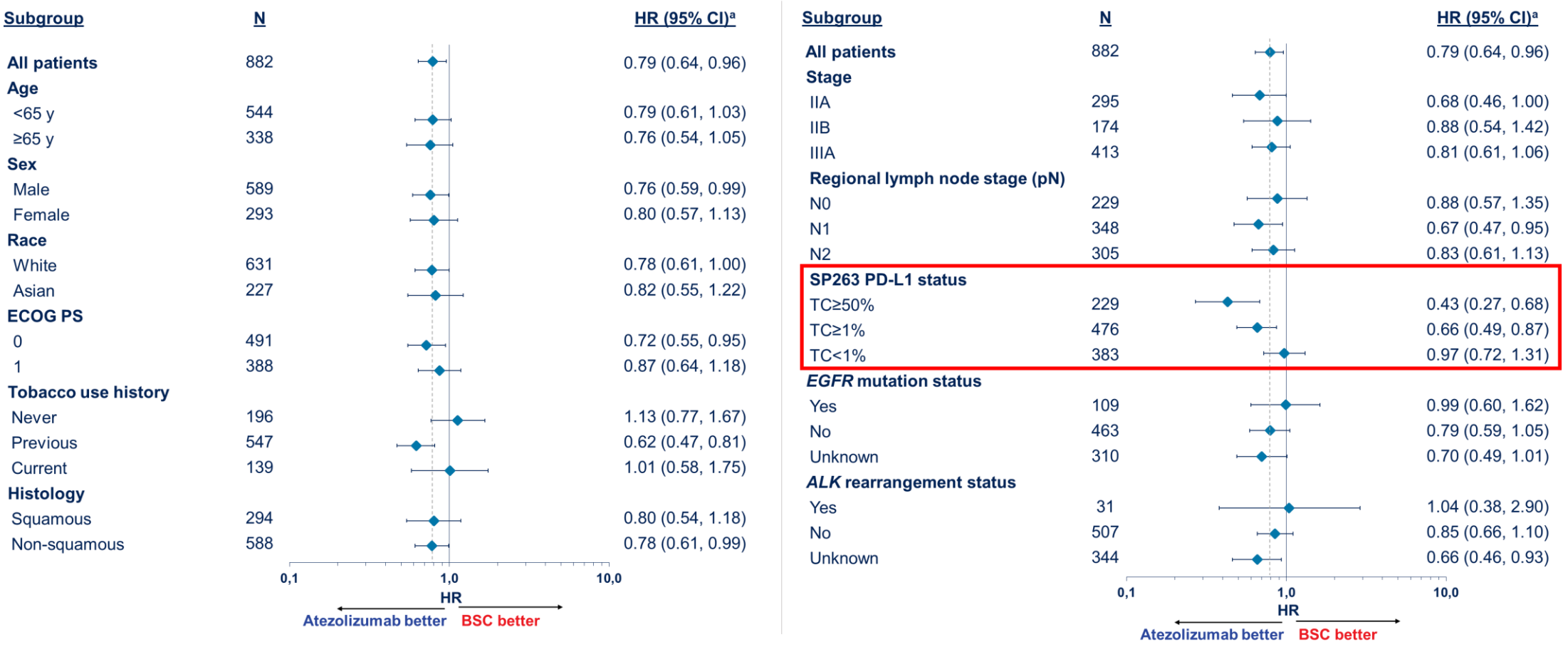
IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs BSC After Adjuvant Chemo in Resected Stage IB-IIIA NSCLC

Subgroup analysis for DFS in stage II-IIIA (any PD-L1): correlation DFS with PD-L1 expression



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IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs BSC After Adjuvant Chemo in Resected Stage IB-IIIA NSCLC

The primary DFS endpoint was tested hierarchically in 3 primary analysis populations

DFS in PD-L1 TC ≥1% stage II–IIIA population
2-sided α=0.05

If positive:

DFS in all-randomized stage II–IIIA population
2-sided α=0.05

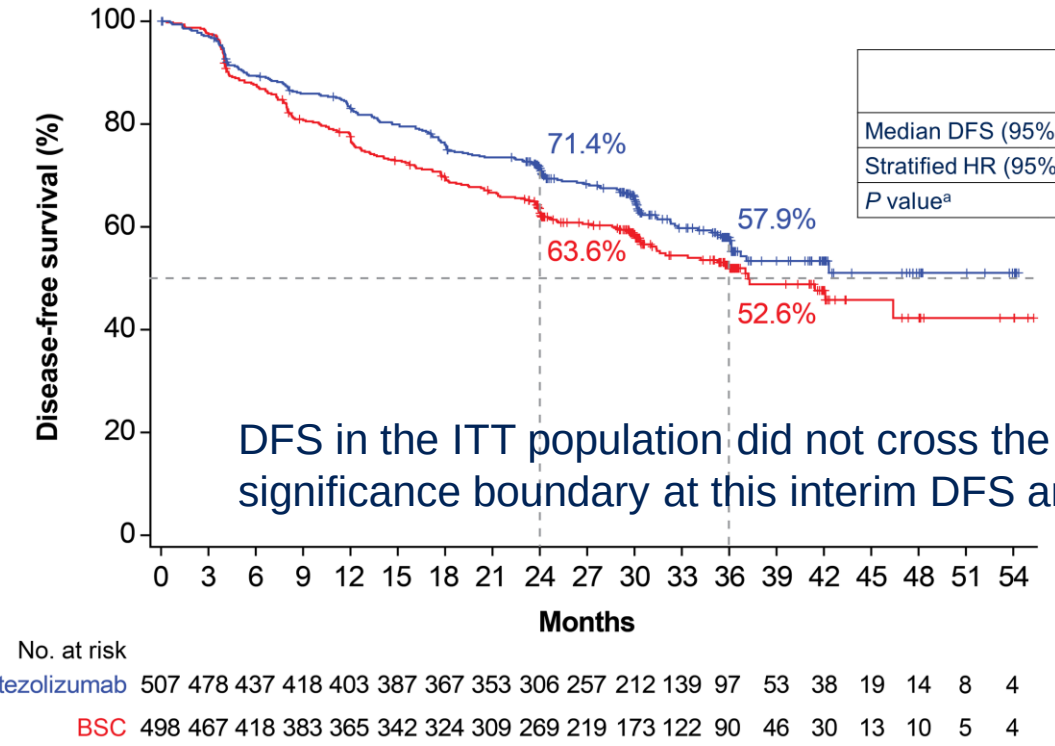
If positive:

DFS in ITT population (stage IB-IIIA)
2-sided α=0.05

If positive:

OS in ITT population
2-sided α=0.05

DFS in the ITT population (stage IB-IIIA)



	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[a]	0.04[b]	

DFS in the ITT population did not cross the significance boundary at this interim DFS analysis

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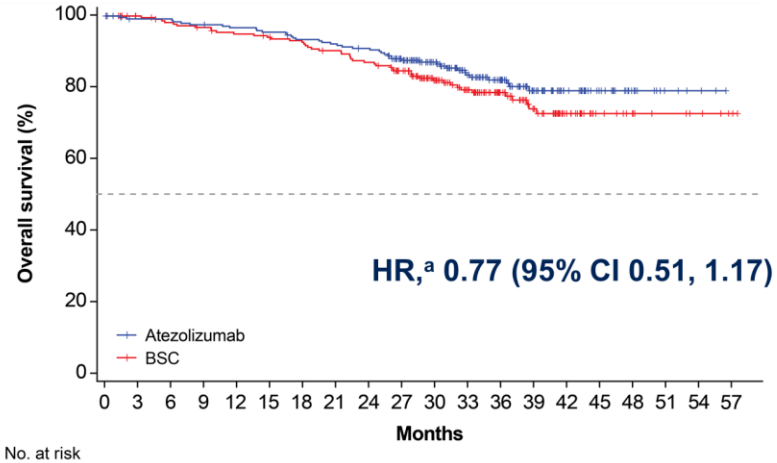
OS data were immature at this interim analysis

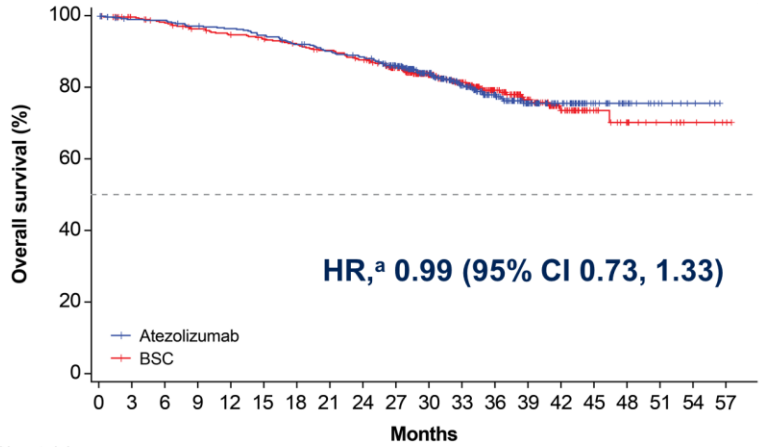
PD-L1 TC ≥ 1% stage II-IIIA



No. at risk

Atezolizumab	248	241	241	237	234	231	225	222	218	196	164	126	99	62	40	26	13	5	3	NE
BSC	228	220	214	210	205	201	198	192	185	172	135	110	80	57	32	17	10	7	5	2

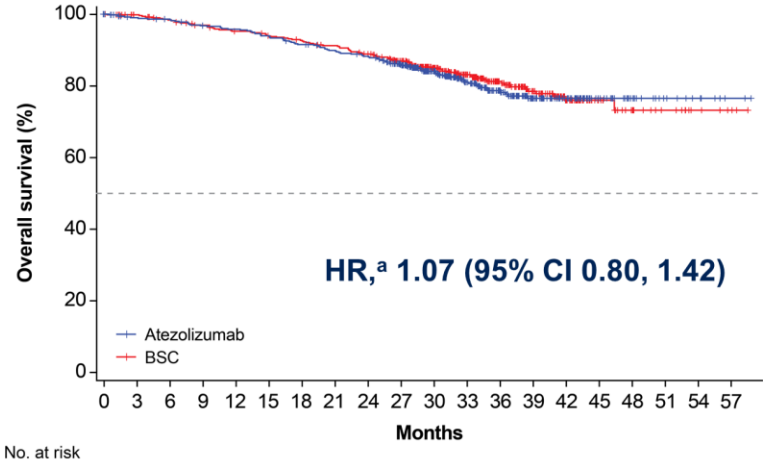
All-randomized stage II-IIIA



No. at risk

Atezolizumab	442	429	428	420	416	408	396	386	378	344	279	203	152	97	66	32	17	8	4	NE
BSC	440	426	416	405	396	389	382	373	361	331	258	204	143	100	55	26	16	10	5	2

ITT



No. at risk

Atezolizumab	507	492	488	478	472	463	450	439	430	392	315	227	170	108	71	36	20	11	7	2
BSC	498	484	473	462	452	444	437	428	415	384	304	236	169	121	71	31	19	12	6	3

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IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs BSC After Adjuvant Chemo in Resected Stage IB-IIIA NSCLC

Despiste no new safety signals, there were 52% of irAEs (only 8% G3-4) and 4 toxic deaths

n (%)	Atezolizumab (n=495)	BSC (n=495)
Any-cause AE	459 (92.7)	350 (70.7)
Treatment-related AE	335 (67.7)	–
Grade 3-4 AE	108 (21.8)	57 (11.5)
Treatment-related grade 3-4 AE	53 (10.7)	–
Serious AE	87 (17.6)	42 (8.5)
Treatment-related serious AE	37 (7.5)	–
Grade 5 AE	8 (1.6)[b]	3 (0.6)[c]
Treatment-related grade 5 AE	4 (0.8)	–
AE leading to dose interruption of atezolizumab	142 (28.7)	–
AE leading to atezolizumab discontinuation	90 (18.2)	–
Immune-mediated AEs	256 (51.7)	47 (9.5)
Grade 3-4 immune-mediated AEs	39 (7.9)	3 (0.6)
Immune-mediated AEs requiring the use of systemic corticosteroids	60 (12.1)	4 (0.8)

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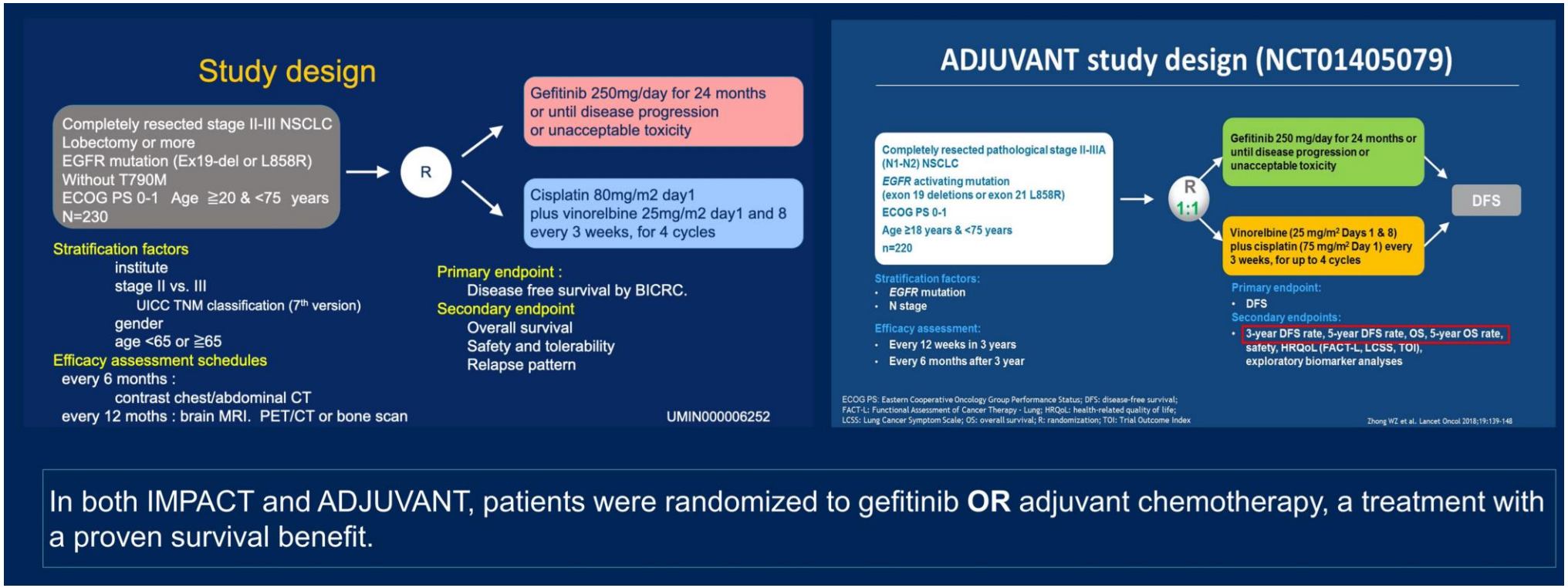
IMPACT (WJOG6419L): A randomized phase III trial comparing adjuvant gefitinib vs CDDP-VNR in Japanese patients with completely resected, EGFR mutated, stage II-III NSCLC

IMPACT vs ADJUVANT (CTONG-1104)



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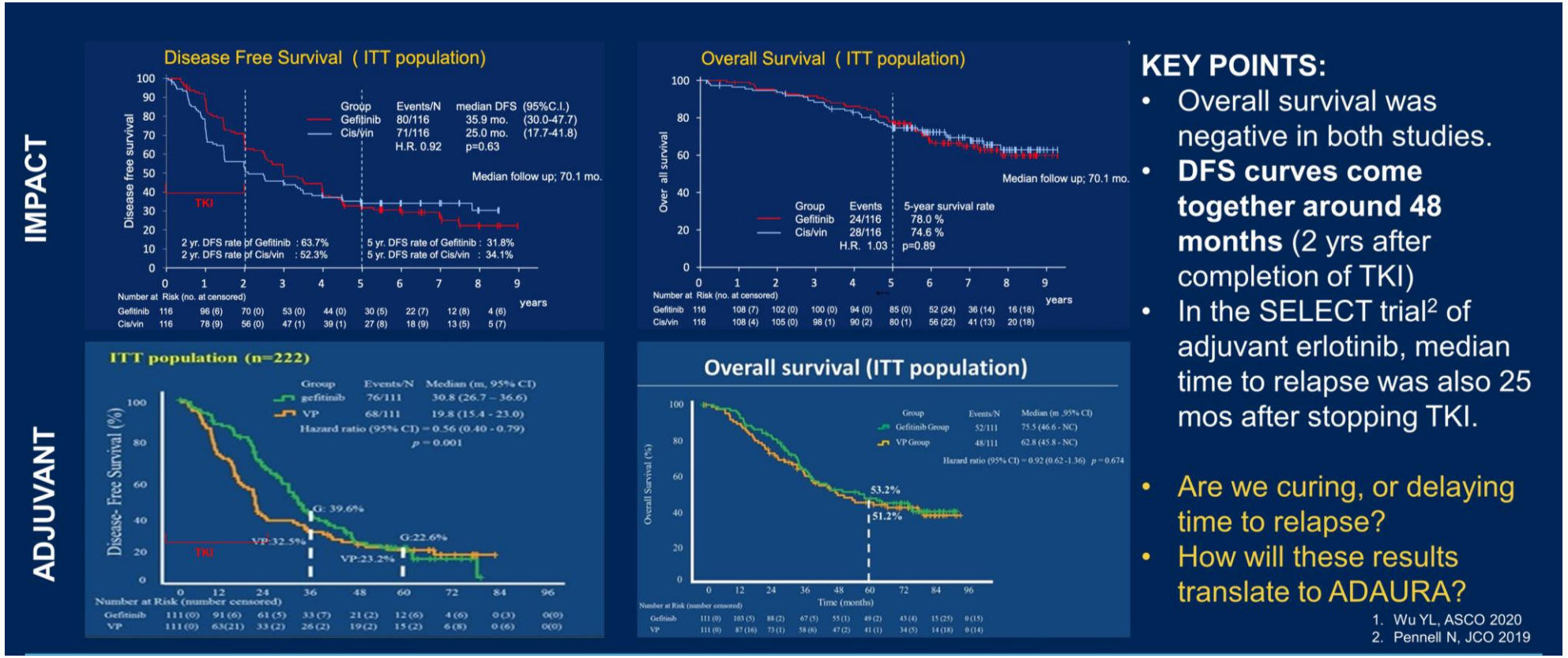
IMPACT (WJOG6419L): A randomized phase III trial comparing adjuvant gefitinib vs CDDP-VNR in Japanese patients with completely resected, EGFR mutated, stage II-III NSCLC

Outcomes of the IMPACT consistent with ADJUVANT (CTONG-1104)



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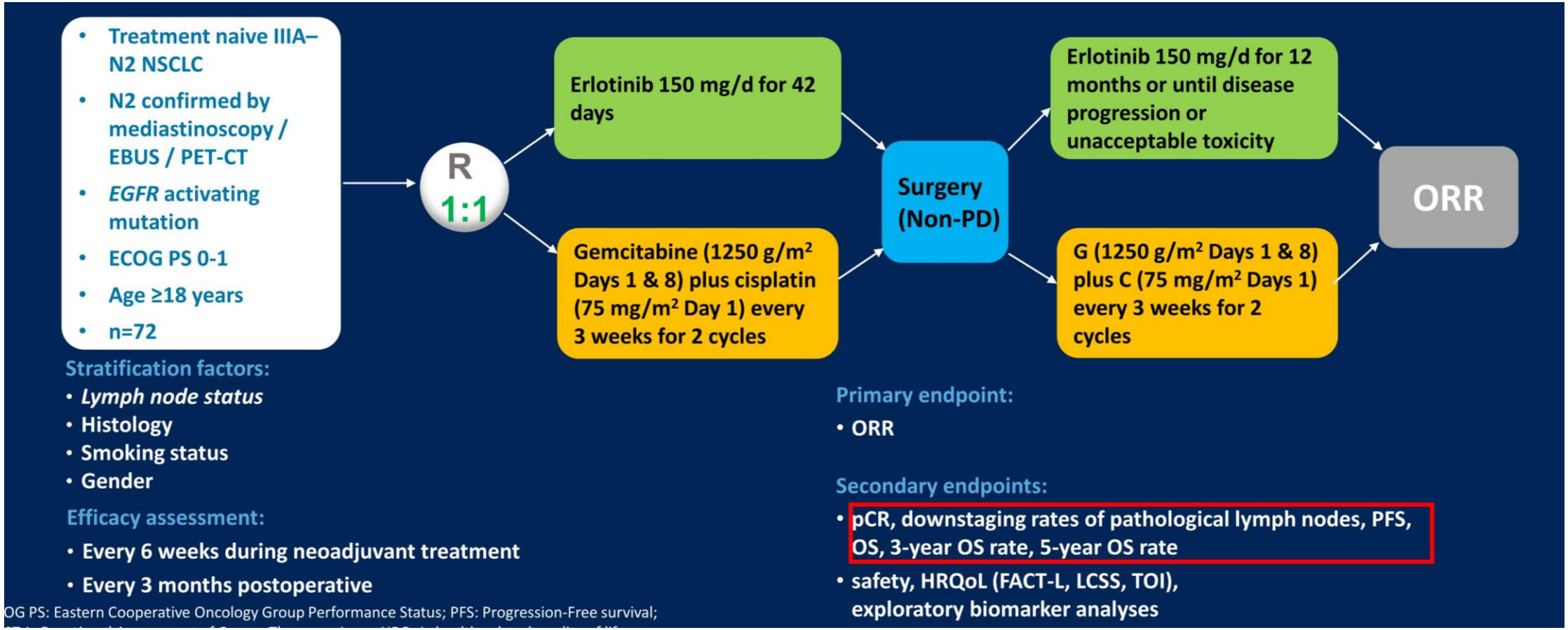
EMERGING (CTONG-1103): Neoadjuvant erlotinib vs chemotherapy for stage IIIA-N2 EGFR mutant NSCLC – Final OS analysis of the randomized phase II trial

Study design



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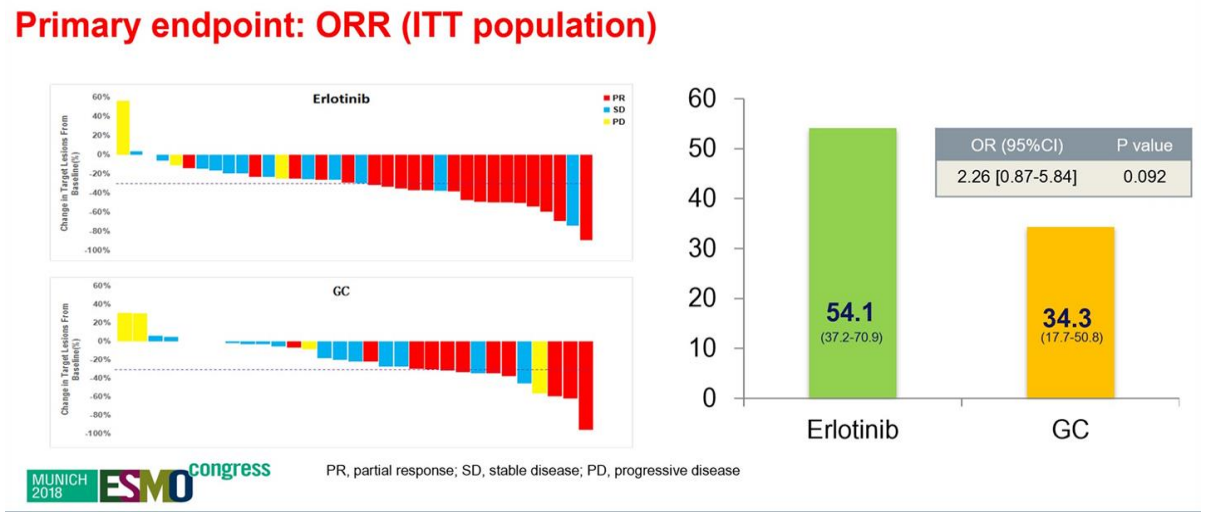
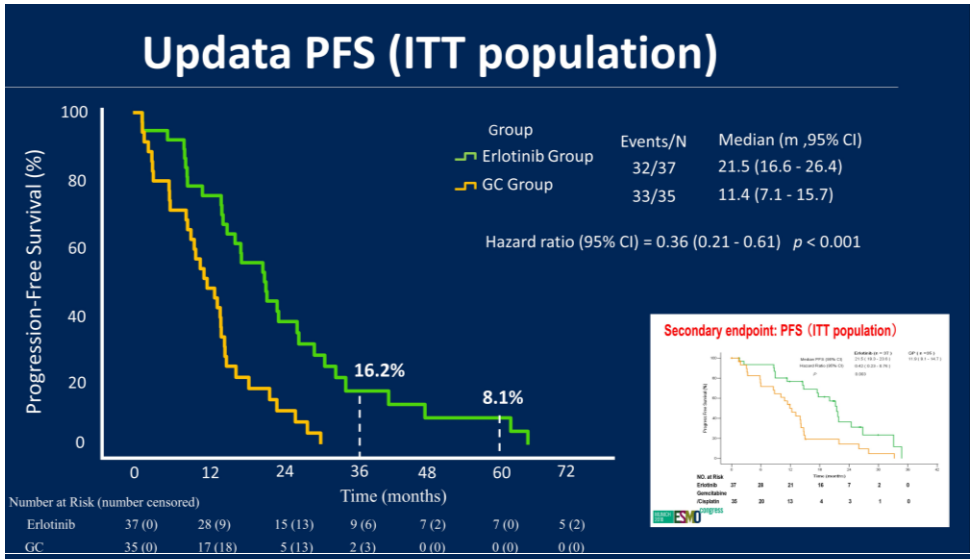
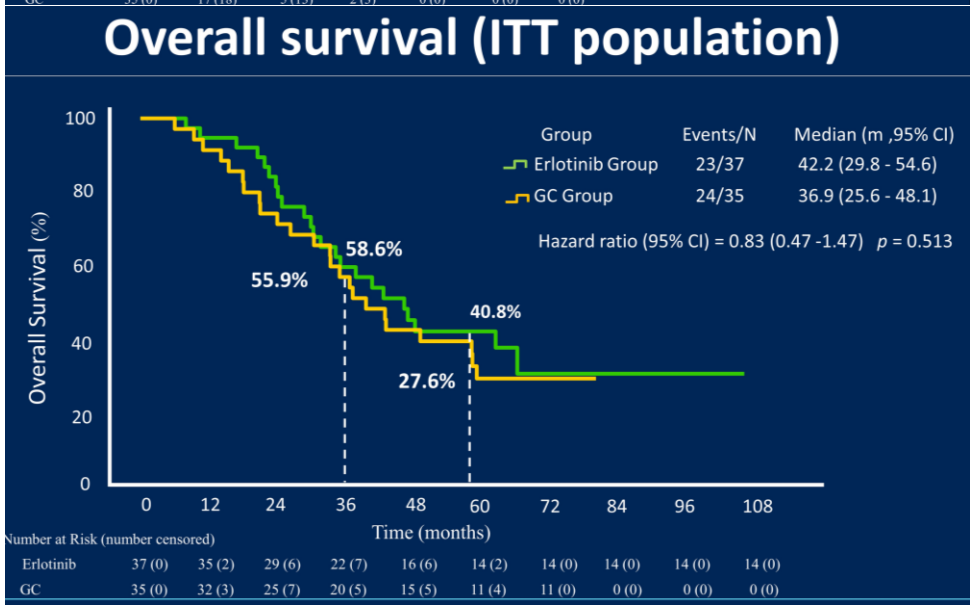
EMERGING (CTONG-1103): Neoadjuvant erlotinib vs chemotherapy for stage IIIA-N2 EGFR mutant NSCLC - Final OS analysis of the randomized phase II trial

DFS Benefit does not always translate into OS (particularly with EGFR TKI)



At ESMO 2018: ORR = 54.1 vs 34.3% (p=0.092)





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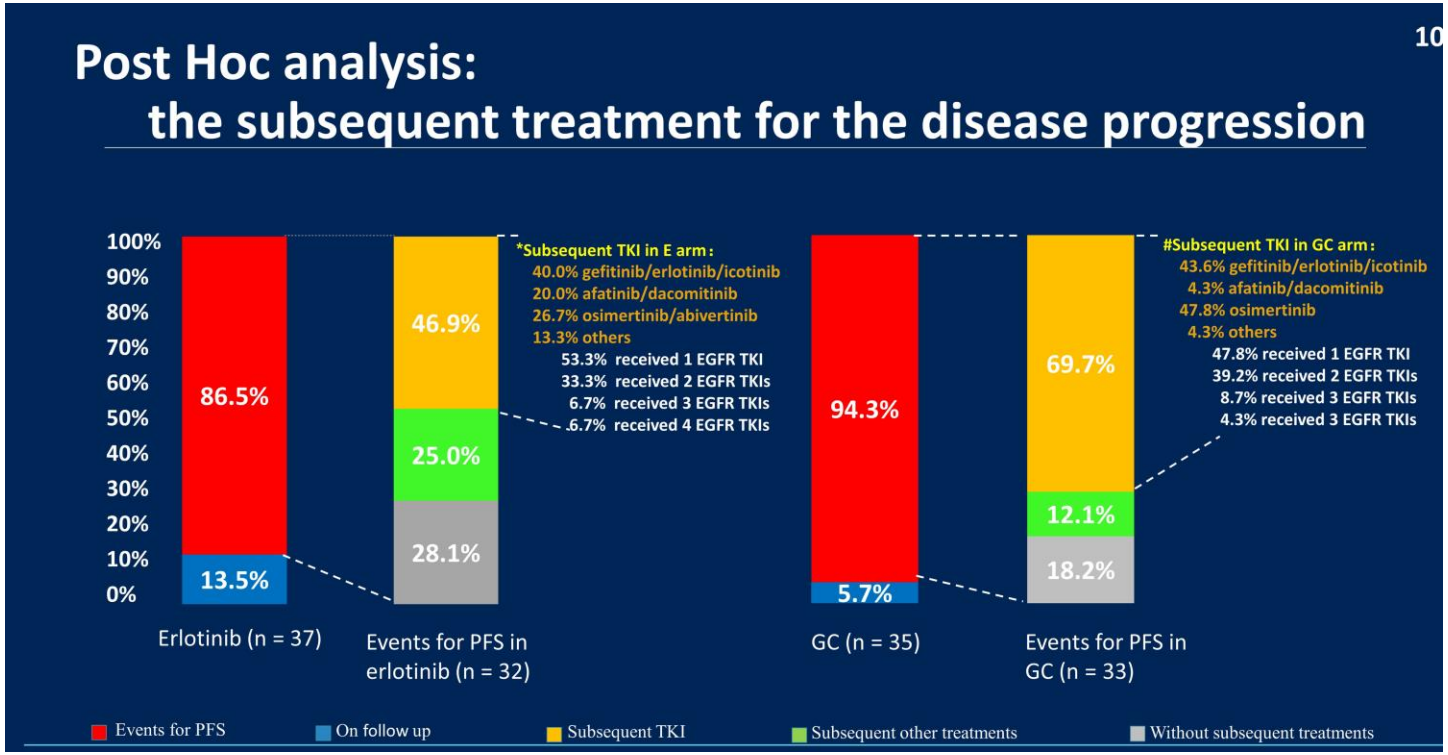
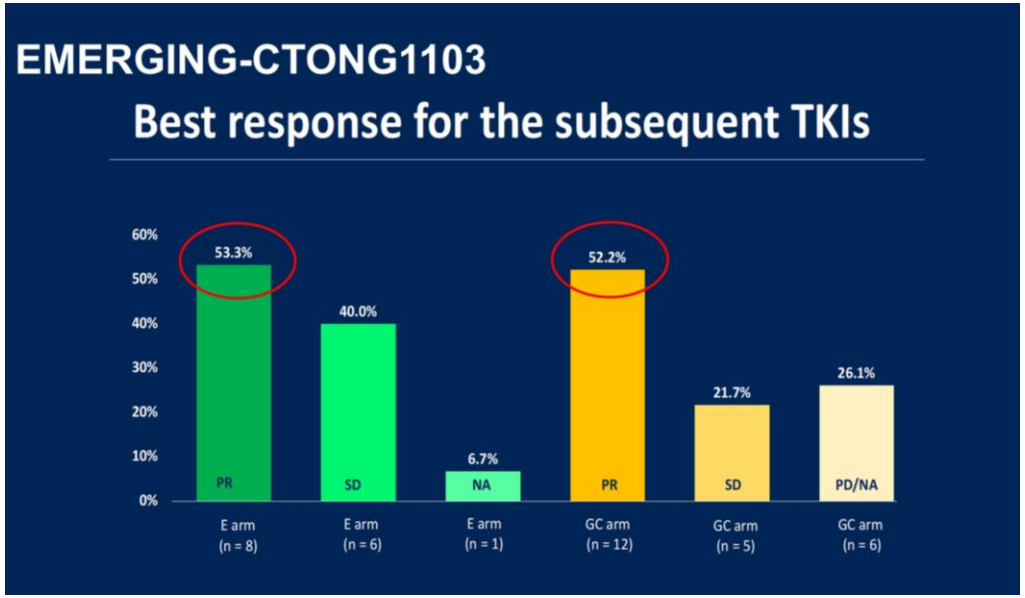
EMERGING (CTONG-1103): Neoadjuvant erlotinib vs chemotherapy for stage IIIA-N2 EGFR mutant NSCLC - Final OS analysis of the randomized phase II trial

Efficacy of subsequent EGFR TKIs





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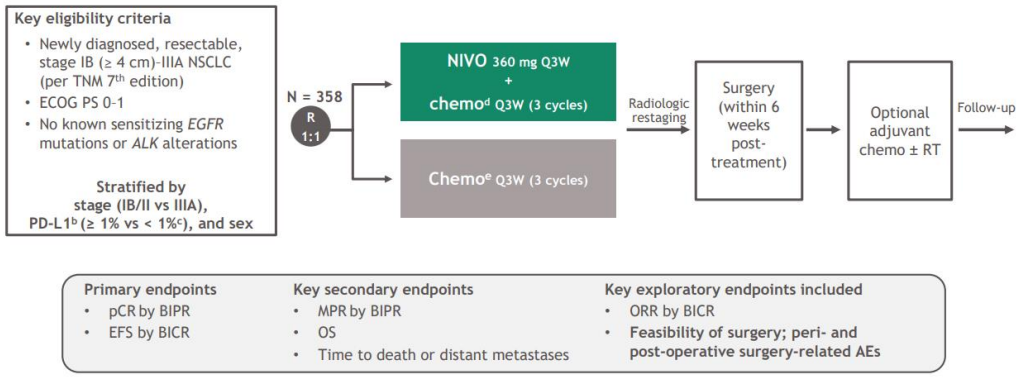
Surgical outcomes from the CheckMate 816

Most patients in both arms had surgery within the pre-specified time window and length of hospitalización was comparable among arm.



Hospital stay summary

	NIVO + chemo (n = 135)	Chemo (n = 124)
Length of hospital stay, median (IQR), days	10.0 (7.0-14.0)	10.0 (7.0-14.5)
Length of hospital stay by surgery type,[a] median (IQR), days		
Lobectomy	10.0 (7.0-15.0)	9.0 (6.0-14.0)
Pneumonectomy	10.0 (8.0-13.0)	11.0 (9.0-16.0)
Other[b]	8.5 (4.0-13.0)	9.0 (7.0-14.0)
Length of hospital stay per region,[c,d] median (IQR), days		
North America	4.0 (4.0-7.0)	6.0 (4.0-8.0)
Europe	9.5 (8.0-14.0)	13.0 (7.0-18.0)
Asia	11.0 (9.0-16.0)	13.0 (10.0-16.0)

- Length of hospital stay was similar regardless of baseline stage of disease in both the NIVO + chemo and chemo arms

Surgery delay summary[a]

	All stages		Stage IB/II		Stage IIIA	
	NIVO + chemo (n = 149)	Chemo (n = 135)	NIVO + chemo (n = 55)	Chemo (n = 52)	NIVO + chemo (n = 94)	Chemo (n = 83)
Patients with delayed surgery,[b,c] n (%)	31 (21)	24 (18)	9 (16)	13 (25)	22 (23)	11 (13)
AE	6 (4)	9 (7)	2 (4)	7 (13)	4 (4)	2 (2)
Length of delay in surgery, weeks						
Median (IQR)	2.0 (0.6-3.0)	2.4 (1.0-3.7)	2.1 (0.9-2.9)	2.1 (1.3-3.6)	1.9 (0.6-3.0)	2.6 (0.6-4.9)
Of patients with delayed surgery, proportion n (%) with delay of[d]						
≤ 2 weeks	17 (55)	11 (46)	4 (44)	6 (46)	13 (59)	5 (46)
> 2 and ≤ 4 weeks	8 (26)	8 (33)	4 (44)	5 (38)	4 (18)	3 (27)
> 4 and ≤ 6 weeks	3 (10)	2 (8)	0	0	3 (14)	2 (18)
> 6 weeks	3 (10)	3 (12)	1 (11)	2 (15)	2 (9)	1 (9)

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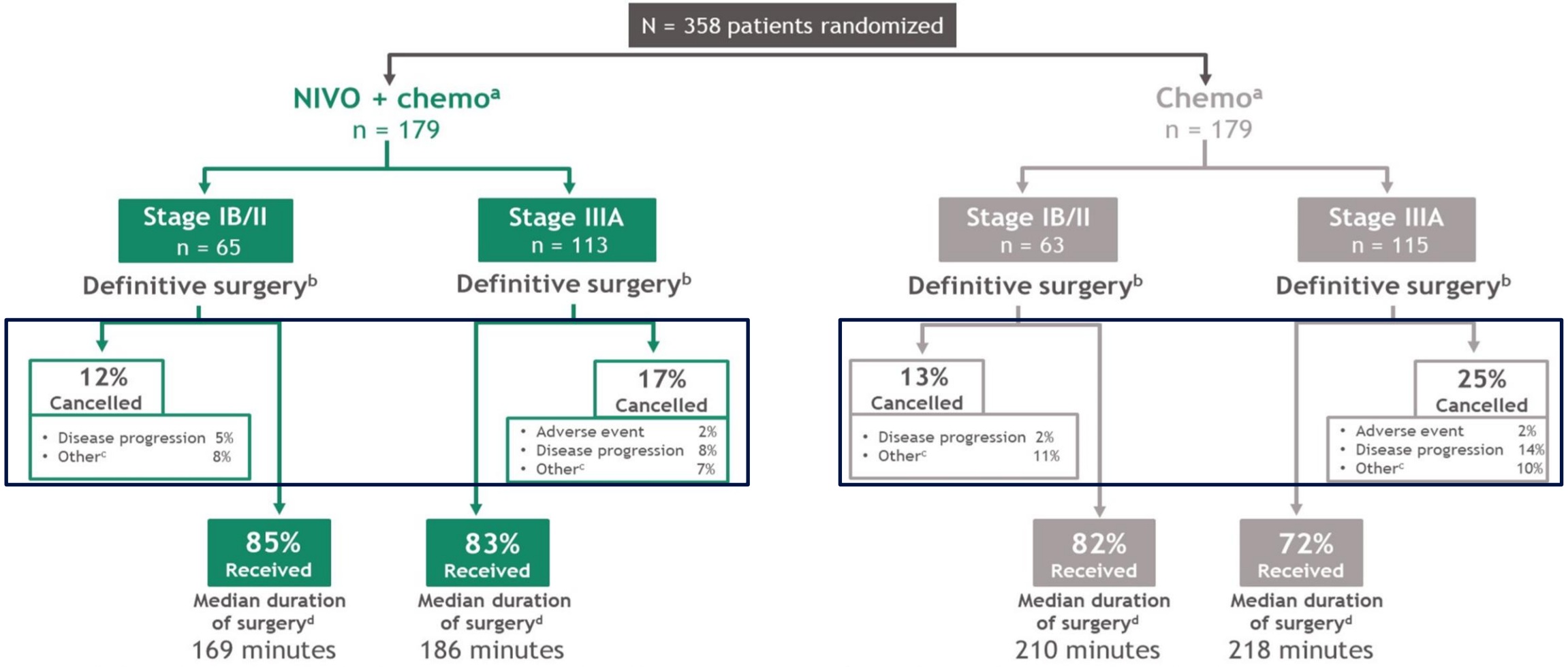
Surgical outcomes from the CheckMate 816

A subset of patients in the nivo-chemo arm were not resected (12% IB/II; 17% IIIA) mainly due to PD or AE, no significant differences in the control arm (13% & 25% respectively)



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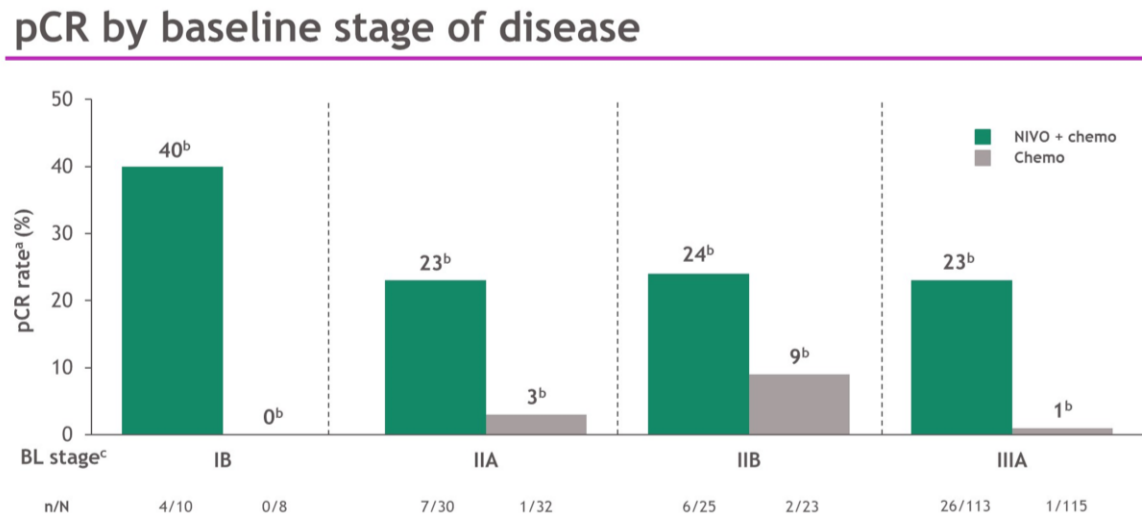
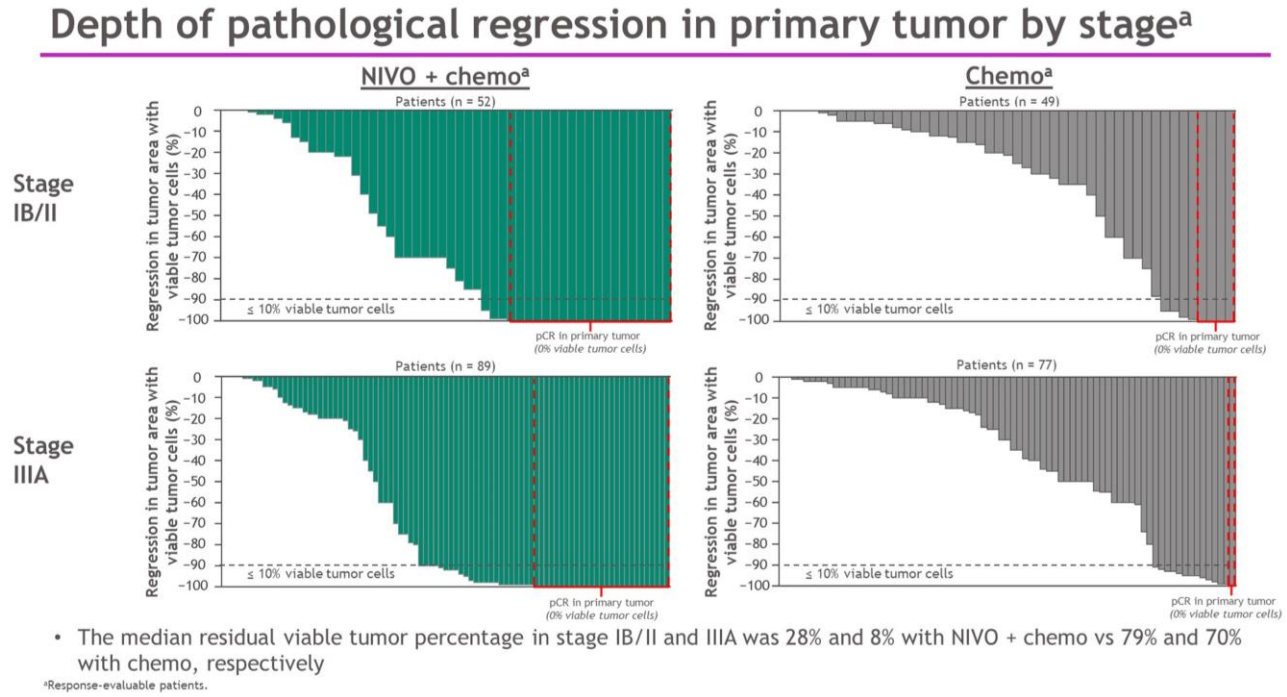
Surgical outcomes from the CheckMate 816

Median residual viable tumor percentage in chemo +nivo was 28% in IB/II and 8% in IIIA, while in the control arm was 79% and 70% respectively





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Surgical outcomes from the CheckMate 816

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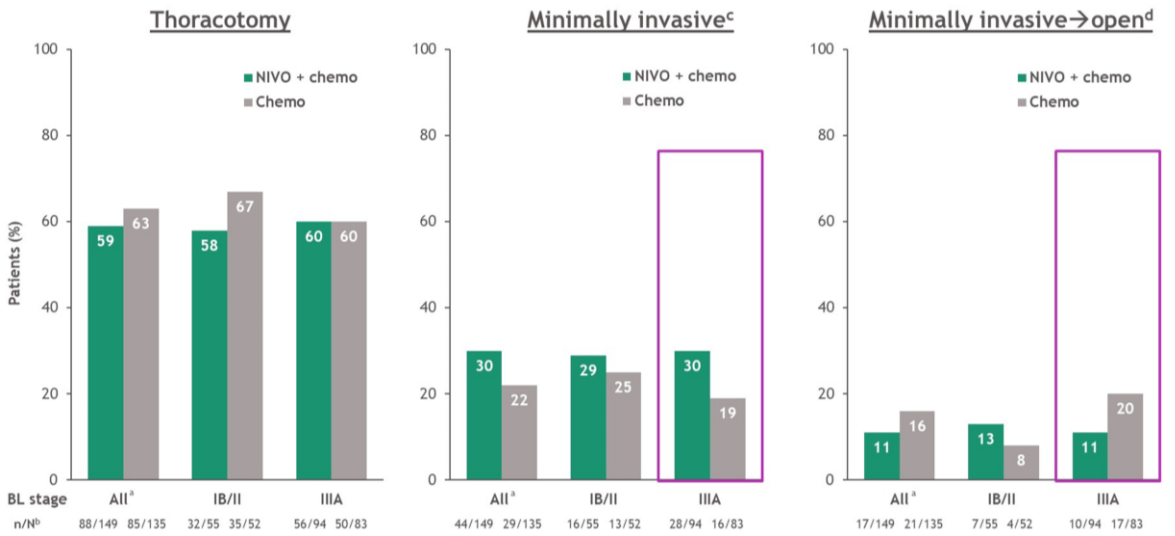
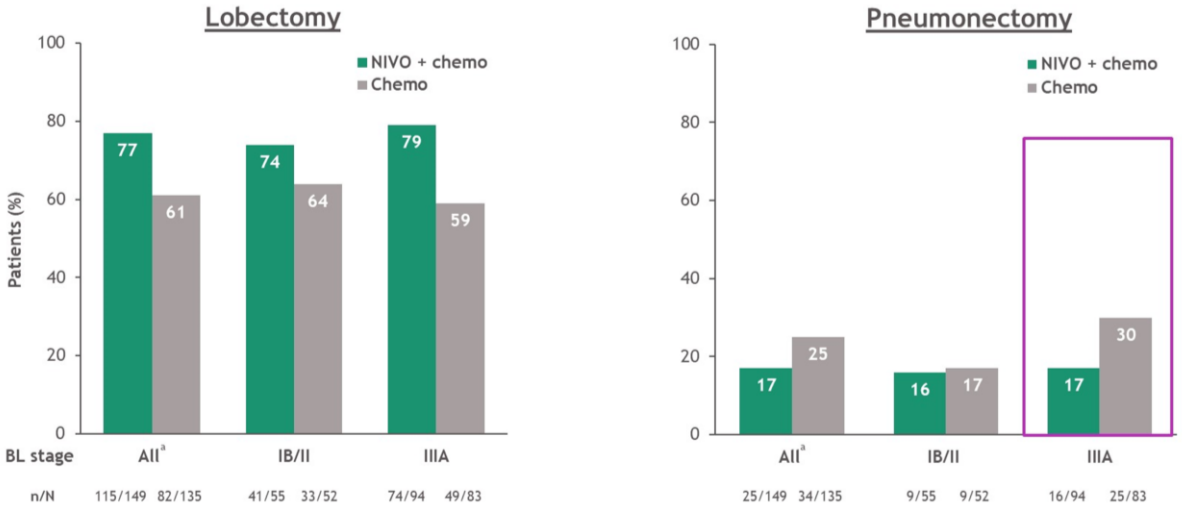
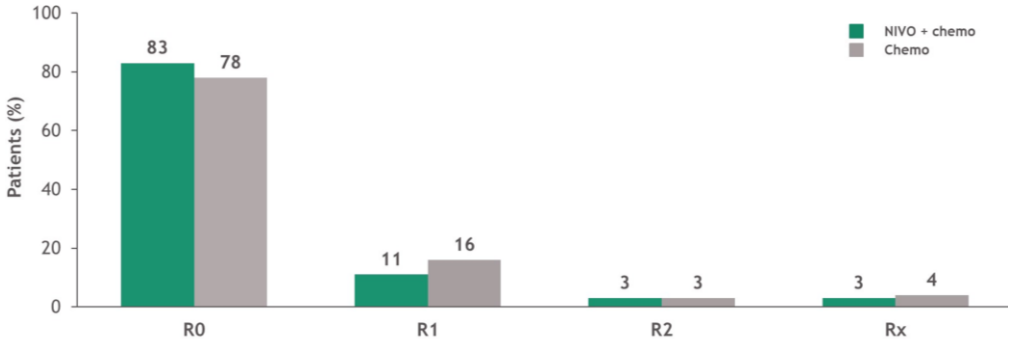
Surgical approach by baseline stage of disease



Type of surgery by baseline stage of disease



Completeness of resection: all randomized population



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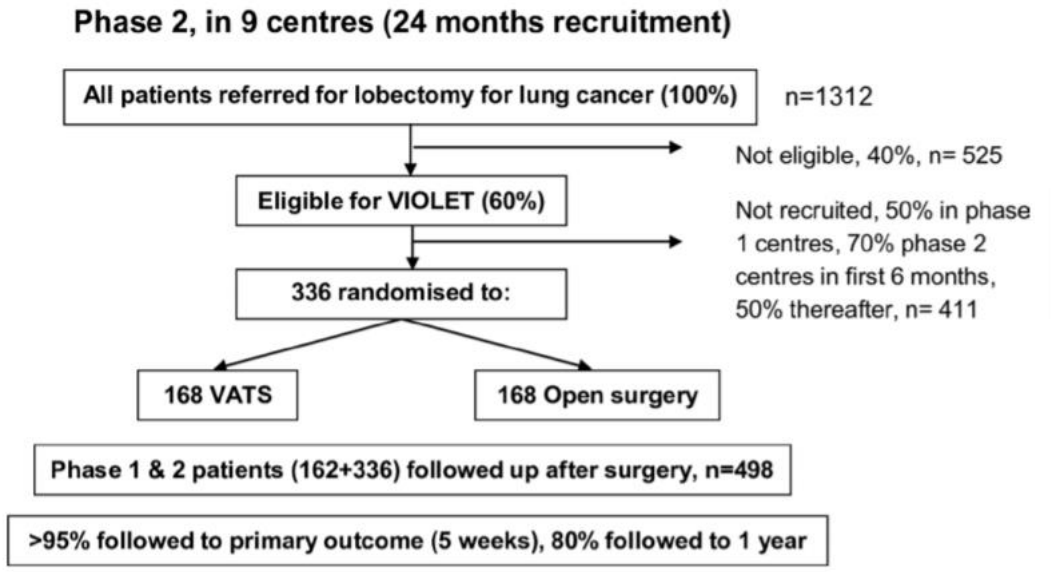
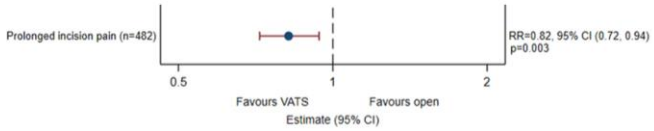
VIOLET: VATS vs open lobectomy in patients with early-stage lung cancer

VATS lobectomy associated with les pain and lower complications rate



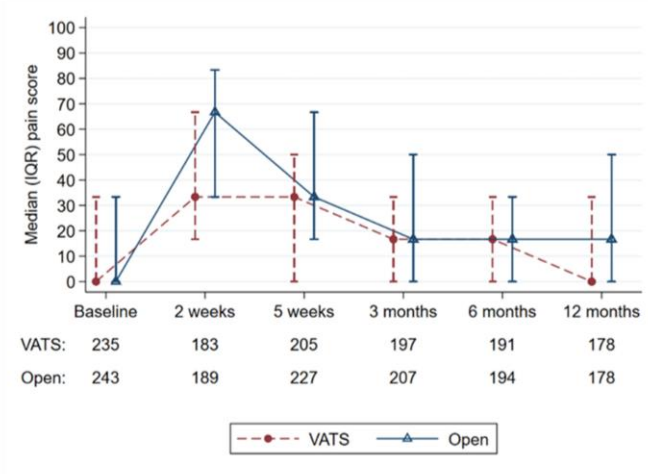
Clinical efficacy (pain to one year)



Outcome	Randomised to VATS (n=247)	Randomised to open surgery (n=255)
Prolonged incision pain [a]	143/240 (59.6%)	175/242 (72.3%)

Data are n/N (%). Analyses are adjusted for operating surgeon.

a need for analgesia after 5 weeks post-randomisation



Higher scores indicate more symptoms.

Procedural safety (complications & readmissions)

Outcome	Randomised to VATS (n=247)	Randomised to open surgery (n=255)	RR (95% CI)	p value
In-hospital before discharge				
Any in-hospital AE	81/247 (32.8%)	113/255 (44.3%)	RR=0.74 (0.66, 0.84)	<0.001
Any in-hospital SAE	20/247 (8.1%)	21/255 (8.2%)	RR=0.98 (0.59, 1.63)	0.948

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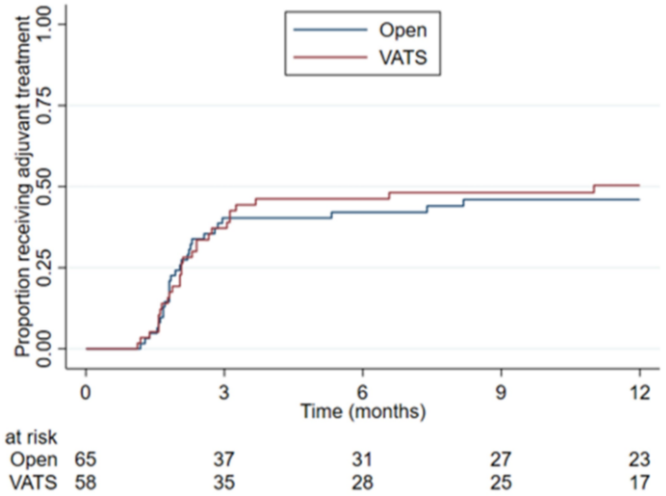
VATS lobectomy associated with shorter length of stay, no compromise of oncologic outcomes and no differences in DFS or OS

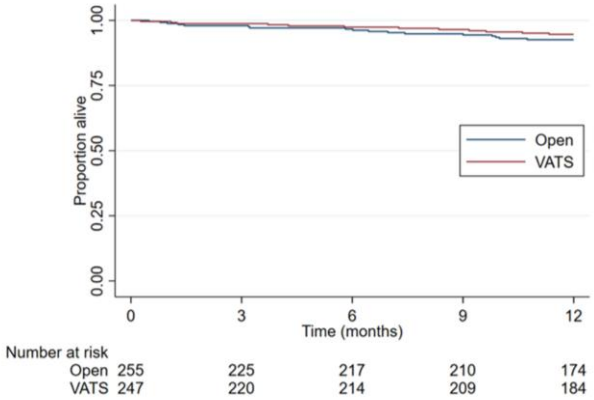
Outcome	Randomised to VATS (n=247)	Randomised to open surgery (n=255)
Total number of lymph node stations harvested	5 (4.0, 6.0)	5 (4.0, 6.0)
Mediastinal nodes harvested (stations 2 to 9)	3 (3.0, 4.0)	3 (3.0, 4.0)
Complete (R0) resection	210/215 (97.7%)	219/224 (97.8%)
Site of residual (R1) disease		
Bronchial margin	2/5 (40.0%)	3/5 (60.0%)
Vascular margin	0/5 (0.0%)	1/5 (20.0%)
Lung parenchymal margin	2/5 (40.0%)	0/5 (0.0%)
Other	1/5 (20.0%)	0/5 (0.0%)
No data	0/5 (0.0%)	1/5 (20.0%)

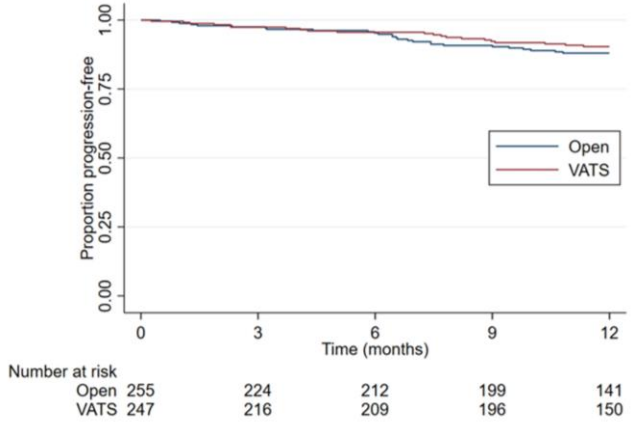
ıal tumour.

Outcome	Randomised to VATS (n=247)	Randomised to open surgery (n=255)
cN0 to pN1		
Yes	15/244 (6.2%)	13/252 (5.2%)
No	211/244 (86.5%)	219/252 (86.9%)
Not cancer	18/244 (7.4%)	20/252 (7.9%)
cN0/1 to pN2		
Yes	15/244 (6.2%)	12/252 (4.8%)
No	211/244 (86.5%)	220/252 (87.3%)
Not cancer	18/244 (7.4%)	20/252 (7.9%)

Data are presented as n/N (%).







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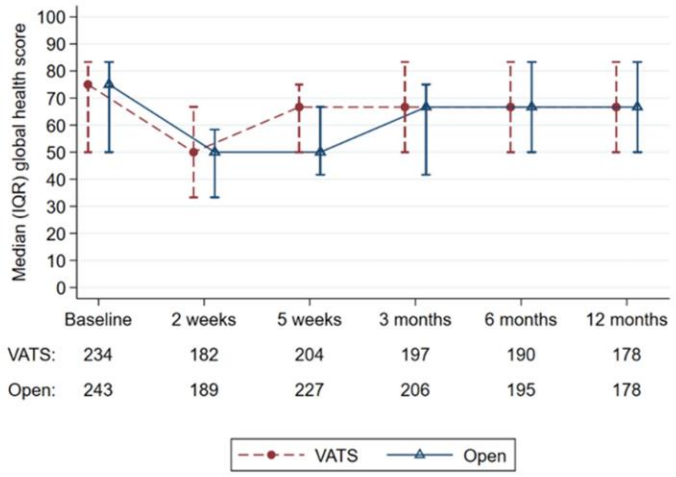
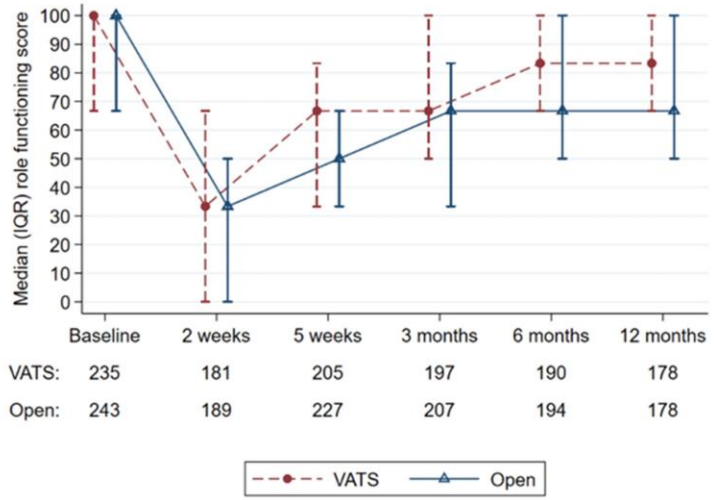
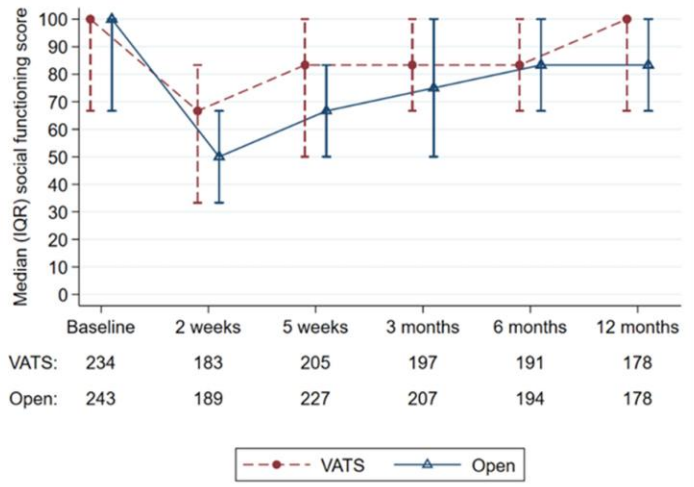
VIOLET: VATS vs open lobectomy in patients with early-stage lung cancer

VATS lobectomy associated with improved QoL and more cost-effective

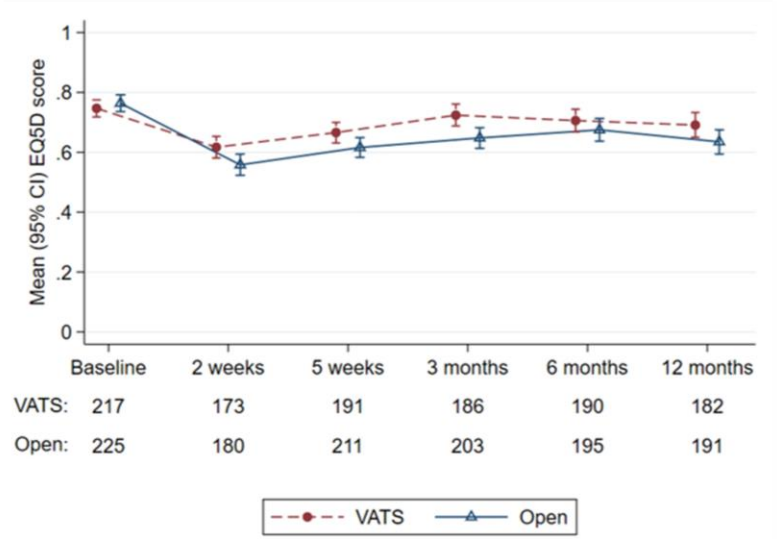


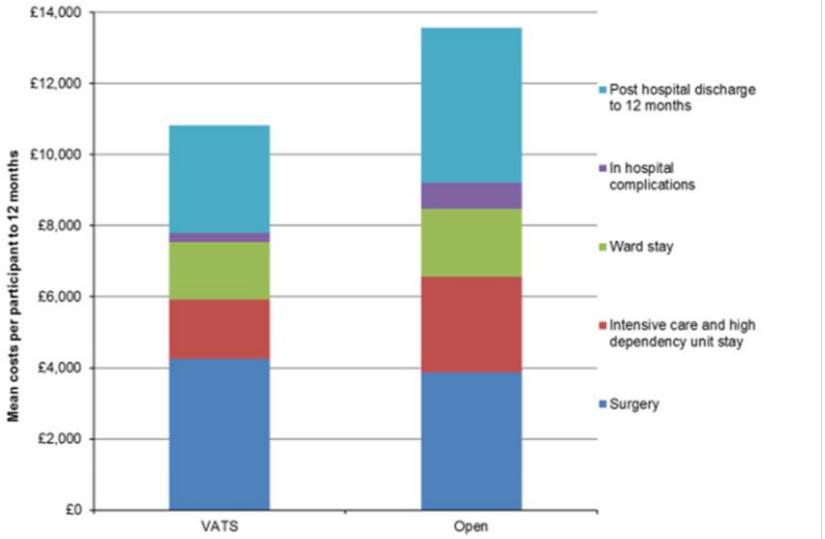
Higher scores indicate better health.





Higher scores indicate better health.





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Muchas gracias por vuestra atención