Maintenance Therapy in Locally advanced stage III NSCLC

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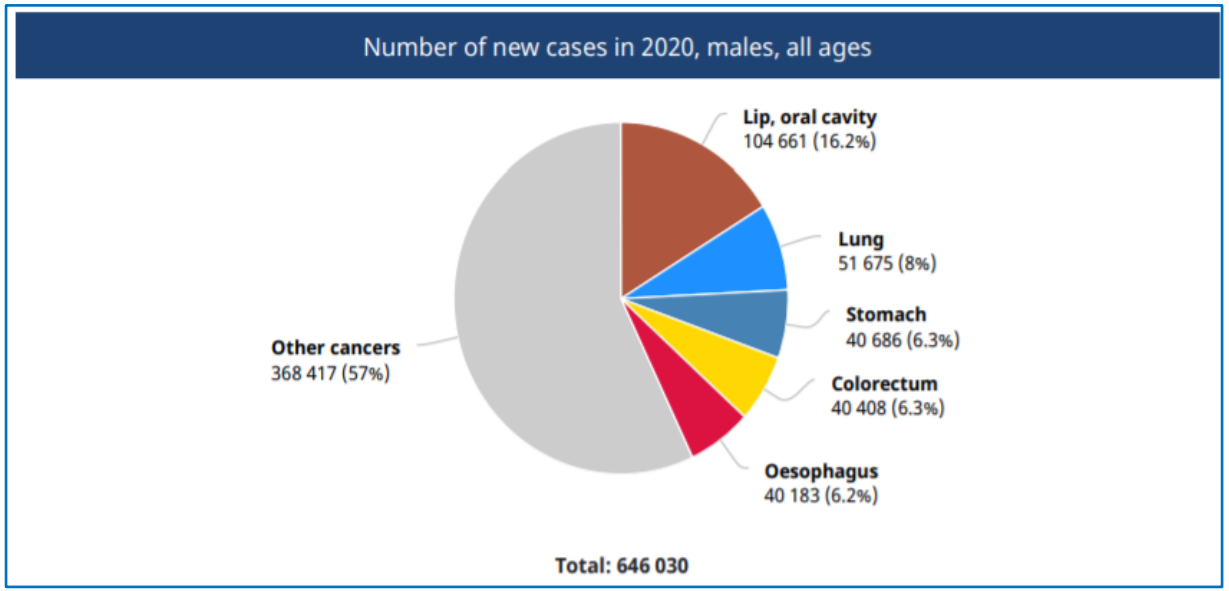
The burden of lung cancer in India

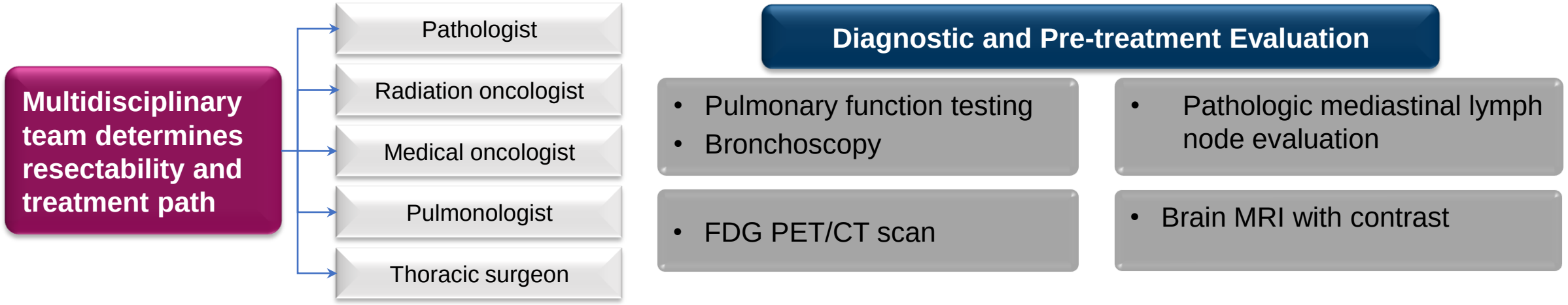
Incidence / death	
Total lung cancer incidence (N)	88,831*
Total lung cancer deaths (N)	80,523
Case fatality rate Incidence / death (%)	93%



2nd Most common cause in Males

* 2021 projection: https://gco.iarc.fr/today/data/factsheets/populations/356-india-fact-sheets.pdf

Management of unresectable Stage III NSCLC



Treatment

Definitive CRT is the standard of care for stage III unresectable NSCLC

Concurrent chemoradiation > **Sequential chemoradiation**

*According to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), determination of resectability, surgical staging, and pulmonary resection should be performed by board-certified thoracic surgeons who perform lung cancer surgery as a prominent part of their practice

Chemotherapy Regimens Used With Radiotherapy in NSCLC

Concurrent Regimens

Treatment	Study	Population	Radiation Dose, Gy	ORR, %	Median PFS, mo	Median OS, mo
Cisplatin, etoposide (two 4-week cycles)[1]	PROCLAIM	Nonsquamous stage IIIA/B NSCLC (n=297)	60-66	33	9.8	25.0
Cisplatin, vinblastine (5-week cycle)[2]	RTOG 9410	Untreated, inoperable stage II/III NSCLC (n=204)	63	70	NR	17.0
Cisplatin, pemetrexed (three 3-week cycles)[1]	PROCLAIM	Nonsquamous stage IIIA/B NSCLC (n=301)	60-66	35.9	11.4	26.8
Paclitaxel, carboplatin (weekly ± 2 cycles of consolidation)[3]	RTOG 0617	Stage IIIA/B NSCLC (n=228)	60	NR	10.7	24.0
Paclitaxel, carboplatin (7-week cycle)[4]	CALGB 39801	Untreated, inoperable stage III NSCLC (n=182)	66	67	NR	12.0
Cisplatin, etoposide (two 1-week cycles)[5]	HOG and US Oncology	Unresected stage III NSCLC (n=74)	59.4	NR	NR	23.2
Cisplatin, etoposide (four 1-week cycles)[6]	—	Stage IIIA NSCLC (n=194)	61	NR	10.5	22.2

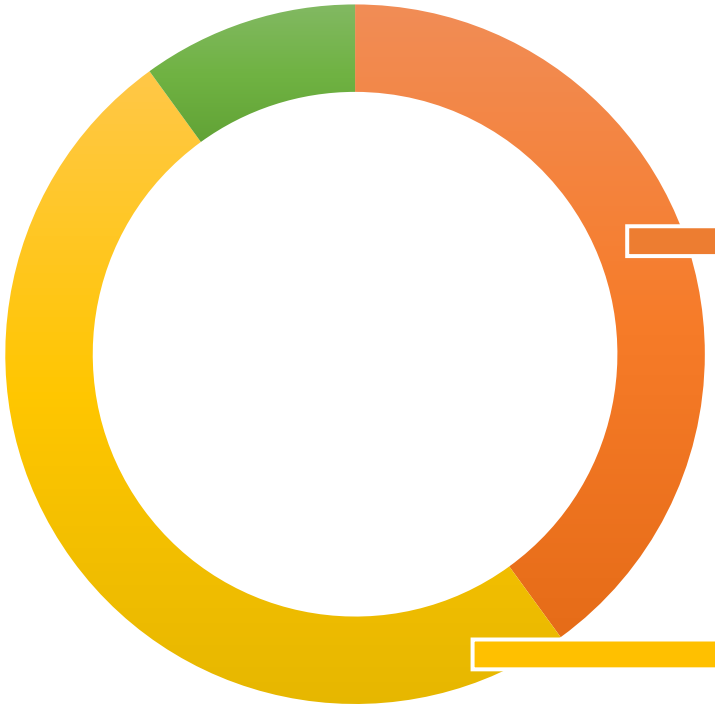
Sequential Regimens

Treatment		Population	Radiation Dose, Gy	ORR, %	Median PFS, mo	Median OS, mo
Cisplatin, vinblastine (5-week cycle)[2]	RTOG 9410	Untreated, inoperable stage II/III NSCLC (n=203)	45	61	NR	14.6
Paclitaxel, carboplatin (two 3-week cycles)[7]	LAMP	Unresectable stage IIIA/B NSCLC (n=91)	63	NR	9.0	13.0

- 1. Senan S, et al. J Clin Oncol. 2016;34:953-962. 2. Curran WJ Jr, et al. J Natl Cancer Inst. 2011;103:1452-1460. 3. Bradley JD, et al. Lancet Oncol. 2015;16:187-199.
  4. Vokes EE, et al. J Clin Oncol. 2007;25:1698-1704. 5. Hanna N, et al. J Clin Oncol. 2008;26:5755-5760. 6. Albain KS, et al. Lancet. 2009;374:379-386.
  7. Belani CP, et al. J Clin Oncol. 2005;23:5883-5891.

The Unmet need in Stage III NSCLC

CCRT given with Curative intent



40% Locoregional metastasis

50% Distant metastasis

Median PFS
8-12 months

5-year OS
15-25%

Perspectives on treatment advances for stage III locally advanced unresectable non-small-cell lung cancer; P.K. Cheema

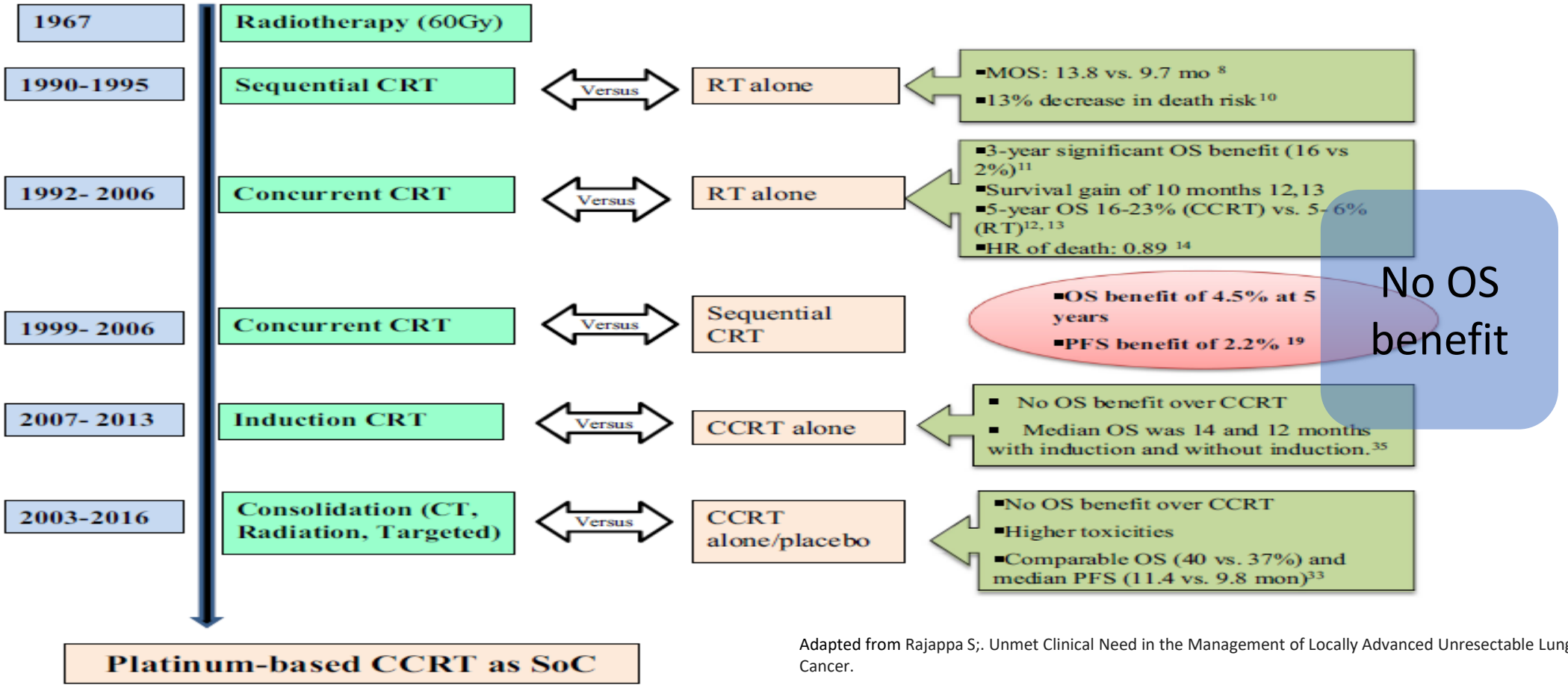
Various trials have been conducted to evaluate consolidation therapy

Study	Treatment groups	Survival (months)		Safety
		Progression-free	[illegible]	
Hanna *et al.*, 2008[17]	Docetaxel (75 mg/m²) every 3 weeks for 3 cycles vs. observation	Nonsignificant (p=0.960)	21.2 vs. 23.2 (p=0.883)	Higher rates of pneumonitis (9.6% vs. 1.4%, p<0.001) and infection (11.0% vs. 0%, p=0.003)
Kelly *et al.*, 2008[18] (SWOG S0023)	Gefitinib (250 mg daily) up to 5 years vs. observation	8.3 vs. 11.7 (p=0.17)	23 vs. 35 (p=0.013)	Toxicity-related deaths: 2% vs. 0%
Butts *et al.*, 2014[19] (START)	Tecemotide (806 µg) every 6 weeks until progression vs. placebo	10.0 vs. 8.4 (p=0.053)	25.6 vs. 22.3 (p=0.123)	Grade 3/4 adverse events not greater with tecemotide: ■ Dyspnea, 5% vs. 4% ■ Pneumonia, 2% vs. 3% Serious immune-related adverse events also did not differ
Ahn *et al.*, 2015[20]	Docetaxel–cisplatin (35 mg/m² and 35 mg/m²) every 3 weeks for 3 cycles vs. best standard of care	8.1 vs. 9.1 (p=0.36)	20.6 vs. 21.8 (p=0.44)	Higher rates of all-grade neutropenia (14.4% vs. 5.8%), esophagitis (35.3% vs. 26.9%) Treatment-related mortality: 3.6% vs. 0%
Giaccone *et al.*, 2015[21] (STOP)	Belagenpumatucel-L (2.5×10^7 cells per dose) for 20 cycles vs.	4.3 vs. 4.0 (p=0.947)	20.3 vs. 17.8 (p=0.594)	Grade 1/2 erythema: 35 vs. 7 events (p<0.001) Injection site reactions: 260 vs. 62 events (p<0.001)
Flentl (GI				

No phase III studies of consolidation with chemotherapy, targeted therapy, or vaccines have demonstrated a PFS or OS benefit in patients with unresectable locally advanced NSCLC

Perspectives on treatment advances for stage III locally advanced unresectable non-small-cell lung cancer; P.K. Cheema

Evolution of treatment approaches for unresectable stage III NSCLC



Adapted from Rajappa S;. Unmet Clinical Need in the Management of Locally Advanced Unresectable Lung Cancer.

Rajappa S, Sharma S, Prasad K. Unmet Clinical Need in the Management of Locally Advanced Unresectable Lung Cancer: Treatment Strategies to Improve Patient Outcomes. Adv Ther. 2019 Mar;36(3):563-578. doi: 10.1007/s12325-019-0876-4. Epub 2019 Jan 29. PMID: 30693419.

Improving outcomes in unresectable stage III NSCLC

- CCRT is considered the standard therapy for patients with good performance status while sequential CRT remains an option for patients with a marginal performance status.
- To improve prognosis further, strategies like increasing radiation doses, induction CT, and consolidation CT were evaluated in addition to CCRT. No significant improvement in OS was seen with these.
- Immunotherapy is increasingly being recognized as a safe and effective option as an adjunct to CCRT.

Rajappa S, Sharma S, Prasad K. Unmet Clinical Need in the Management of Locally Advanced Unresectable Lung Cancer: Treatment Strategies to Improve Patient Outcomes. Adv Ther. 2019 Mar;36(3):563-578. doi: 10.1007/s12325-019-0876-4. Epub 2019 Jan 29. PMID: 30693419.

PACIFIC: Study Design
Phase III, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study

- Patients with stage III, locally advanced, unresectable NSCLC who have not progressed following definitive platinum-based cCRT (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- Estimated life expectancy of ≥12 weeks
- Archived tissue was collected

All-comers population

1–42 days post-cCRT

R

Durvalumab
10 mg/kg IV q2w for up to 12 months
N=476

2:1 randomization, stratified by age, sex, and smoking history
N=713

Placebo
10 mg/kg IV q2w for up to 12 months
N=237

Co-primary endpoints

- PFS by BICR using RECIST v1.1*
- OS

Key secondary endpoints

- ORR (per BICR)
- DoR (per BICR)
- Safety and tolerability
- PROs

Reference: Antonia SJ et al. N Engl J Med 2017. DOI: 10.1056/NEJMoa1709937

PACIFIC Study: Patient Baseline Characteristics

Characteristic, n (%)	Durvalumab (n=476)	Placebo (n=237)	Total (N=713)
Age Median, years (range)	64 (31–84)	64 (23–90)	64 (23-90)
Sex, n (%) Male Female	 334 (70.2) 142 (29.8)	 166 (70.0) 71 (30.0)	 500 (70.1) 213 (29.9)
Race, n (%)[b] White Black or African-American Asian Other Not reported	 337 (70.8) 12 (2.5) 120 (25.2) 6 (1.3) 1 (0.2)	 157 (66.2) 2 (0.8) 72 (30.4) 6 (1.3) 0	 494 (69.3) 14 (2.0) 192 (26.9) 12 (1.68) 1 (0.1)
Disease stage IIIA IIIB Other[c]	 252 (52.9) 212 (44.5) 12 (2.5)	 125 (52.7) 107 (45.1) 5 (2.1)	 377 (52.9) 319 (44.7) 17 (2.4)
WHO performance status score, n (%)[d] 0 1 Not reported	 234 (49.2) 240 (50.4) 2 (0.4)	 114 (48.1) 122 (51.5) 1 (0.4)	 348 (48.8) 362 (50.8) 3 (0.4)
EGFR mutation status, n (%) Negative Positive Unknown	 317 (66.6) 29 (6.1) 130 (27.3)	 165 (69.6) 14 (5.9) 58 (24.5)	 482 (67.6) 43 (6.0) 188 (26.4)

- Antonia SJ et al. Article and supplementary appendix. N Engl J Med. 2018;379:2342-2350.

PACIFIC Study: Patient Baseline Characteristics

Characteristic, n (%)	Durvalumab (n=476)	Placebo (n=237)	Total (N=713)
PD-L1 expression level , n (%)			
TC <25%	187 (39.3)	105 (44.3)	292 (41.0)
TC ≥25%	115 (24.2)	44 (18.6)	159 (22.3)
Unknown	174 (36.6)	88 (37.1)	262 (36.7)
Histology, n (%)			
Squamous	224 (47.1)	102 (43.0)	326 (45.7)
Non-squamous	252 (52.9)	135 (57.0)	387 (54.3)
Smoking status, n (%)			
Current smoker	79 (16.6)	38 (16.0)	117 (16.4)
Former smoker	354 (74.4)	178 (75.1)	532 (74.6)
Never smoked	43 (9.0)	21 (8.9)	64 (9.0)
Prior radiotherapy, n (%)[e]			
<54 Gy	3 (0.6)	0	3 (0.6)
≥54–≤66 Gy	442 (92.9)	217 (91.6)	659 (92.4)
>66–≤74 Gy	30 (6.3)	19 (8.0)	49 (6.9)
Prior chemotherapy, n (%)[f]			
Induction chemotherapy	123 (25.8)	68 (28.7)	191 (26.8)
Concurrent with radiation therapy	475 (99.8)	236 (99.6)	711 (99.7)
Best response to previous CRT, n (%)			
Complete response	9 (1.9)	7 (3.0)	16 (2.2)
Partial response	237 (49.8)	112 (47.3)	349 (48.9)
Stable disease	223 (46.8)	115 (48.5)	338 (47.4)
Progression	2 (0.4)	0	2 (0.3)
Non-evaluable	5 (1.1)	2 (0.8)	7 (1.0)
Not applicable	0	1 (0.4)	1 (0.1)

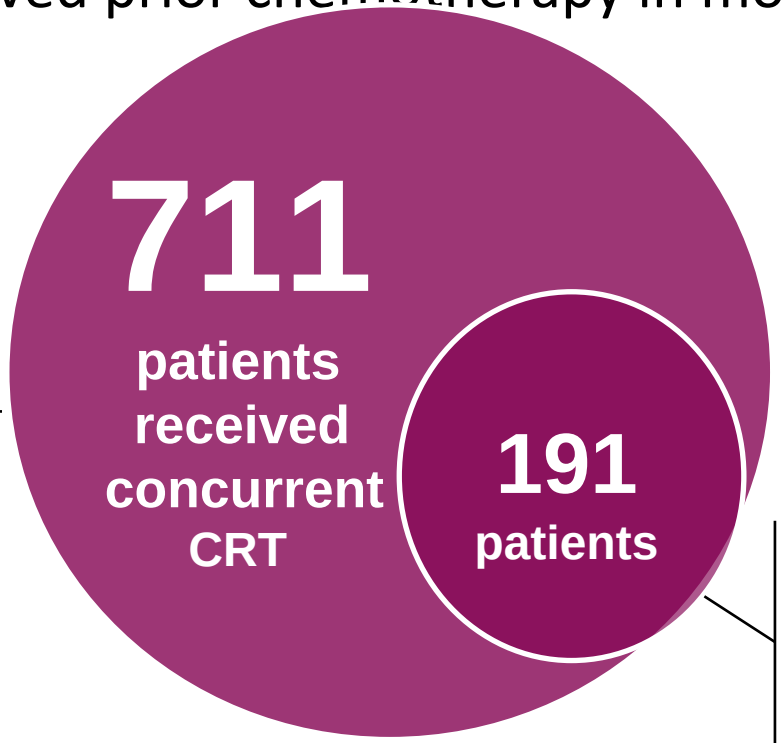
- Antonia SJ et al. Article and supplementary appendix. N Engl J Med. 2018;379:2342-2350.

Almost 27% patients received induction chemotherapy

PACIFIC Study: Prior CRT at baseline

- All patients received 2 or more overlapping cycles of platinum-based chemotherapy concurrent with RT.
  - Patients may have received prior chemotherapy in more than one context.

Most patients (99.7%) had received **concurrent chemotherapy + radiation** prior to study start



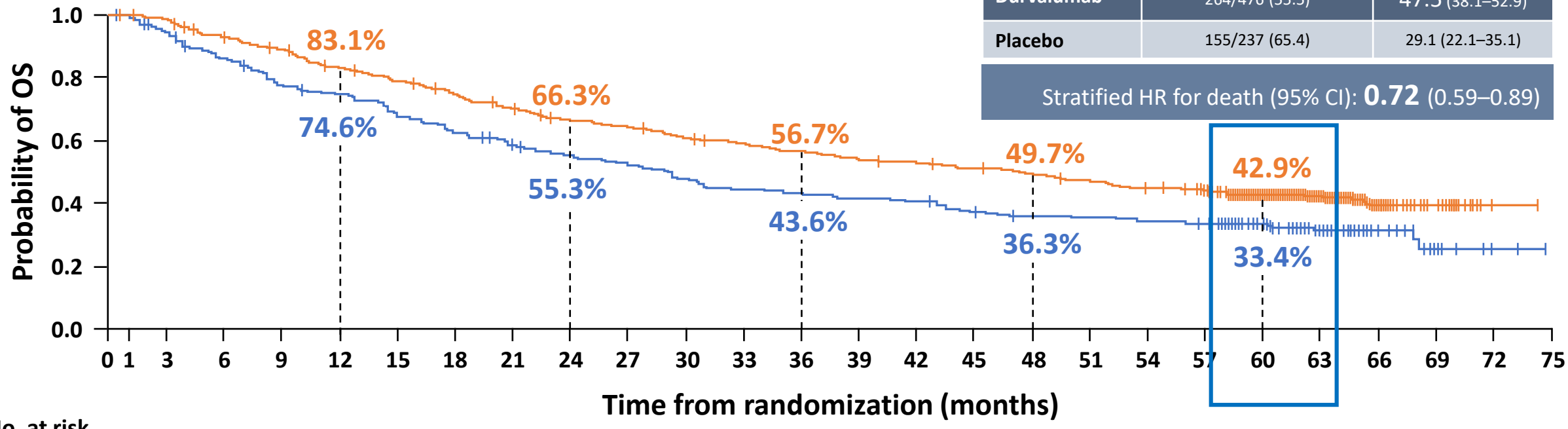
191 patients (26.8%) had received **induction chemotherapy** prior to study start

- CRT = chemoradiation therapy; RT = radiotherapy.
- Antonia SJ et al. Article and supplementary appendix. N Engl J Med. 2018;379:2342-2350.

Updated Five years Overall Survival (ITT)

	No. of events / No. of patients (%)	Median OS (95% CI) months
Durvalumab	264/476 (55.5)	47.5 (38.1–52.9)
Placebo	155/237 (65.4)	29.1 (22.1–35.1)

Stratified HR for death (95% CI): **0.72** (0.59–0.89)



No. at risk

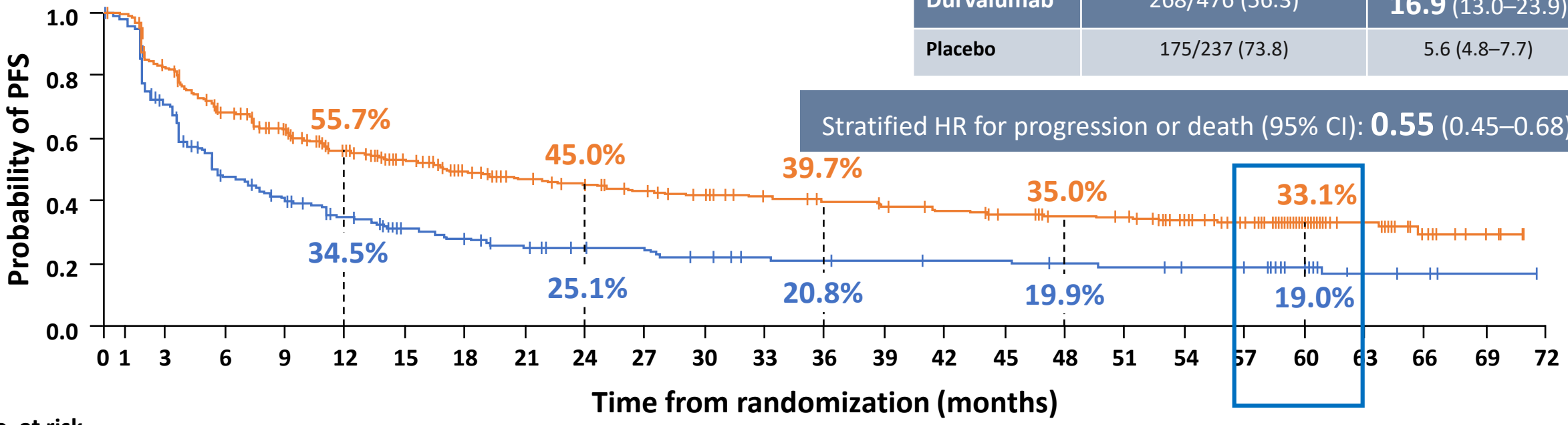
First and only approved IO to demonstrate 42.9% OS at 5 years

- CI = confidence interval; DCO = data cutoff; HR = hazard ratio; ITT = intention-to-treat; OS = overall survival.
- Spigel DR, et al. Poster presented at: ASCO Virtual Meeting; June 4-8, 2021.

Updated Progression-Free Survival (BICR;ITT)

	No. of events / No. of patients (%)	Median OS (95% CI) months
Durvalumab	268/476 (56.3)	**16.9** (13.0–23.9)
Placebo	175/237 (73.8)	5.6 (4.8–7.7)

Stratified HR for progression or death (95% CI): **0.55** (0.45–0.68)

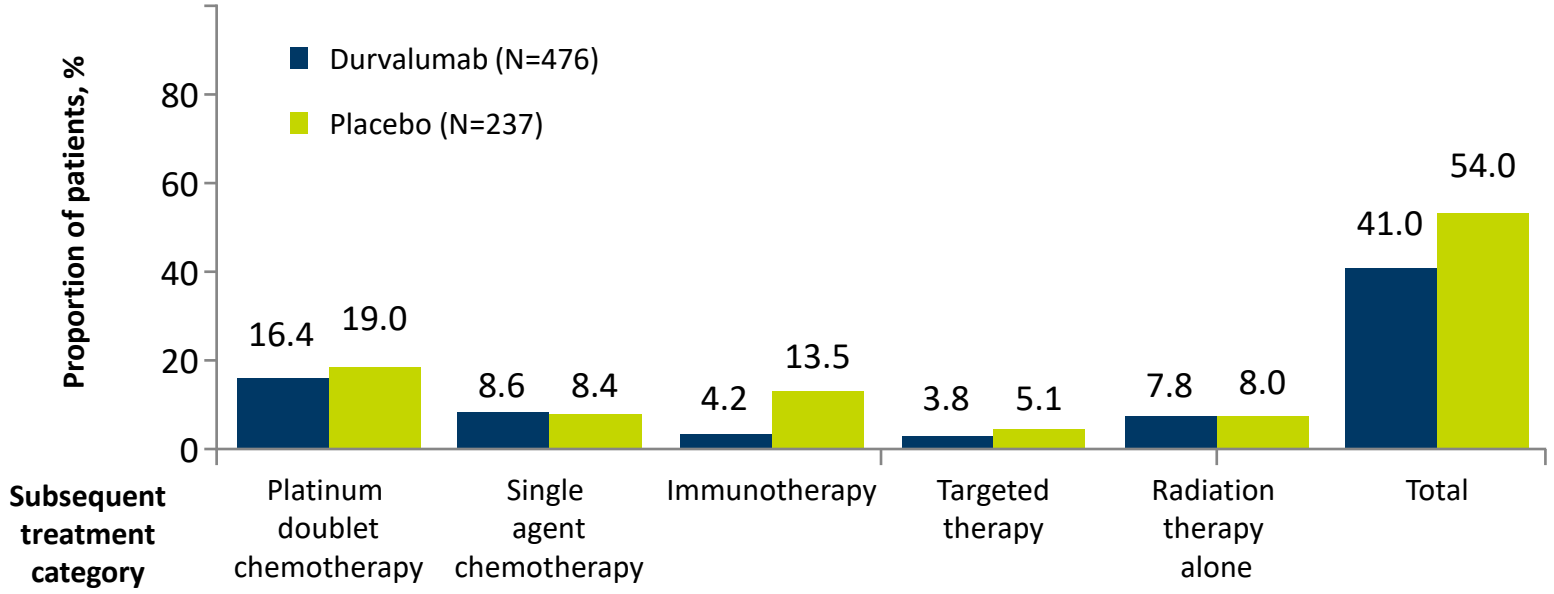


First and only approved IO to show sustained and durable PFS of 33.1% benefit at 5 years

- DCO5: January 11, 2021; median follow-up: all patients, 34.2 months [range, 0.2–74.7]; censored patients, 61.6 months [range, 0.4–74.7].
- BICR = blinded independent central review; CI = confidence interval; DCO = data cutoff; HR = hazard ratio; ITT = intent-to-treat; PFS = progression-free survival
- Spigel DR, et al. Poster presented at: ASCO Virtual Meeting; June 4-8, 2021.

First Subsequent Therapy After Discontinuation Of Durvalumab

- In durvalumab arm 41.0% of patients and 54.0% of patients in the placebo arm received a subsequent disease-related, anti-cancer therapy
- Systemic therapies (administered with or without radiation therapy) were the most common first subsequent anti-cancer treatments in both the durvalumab (33.2%) and placebo arms (46.0%)



DCO: March 22, 2018. Median follow-up was 25.2 months (range, 0.2–43.1). 216/476 (45.4%) and 153/237 (64.6%) patients in the durvalumab and placebo arms, respectively, had a RECIST-based PFS event per BICR (5.7% and 8.4% were due to death).

BICR = Blinded Independent Central Review; DCO = data cutoff; ITT = intention-to-treat; PFS = progression-free survival; RECIST = Response Evaluation Criteria in Solid Tumors.

Planchard D et al. Poster presented at: ASCO Annual Meeting. May 31-June 4, 2019; Chicago, IL.

Patterns of Disease Progression: First Progression by Location

- Reduced rates of first progression were seen in the durvalumab arm (45.4%) versus placebo (64.6%)
- Intrathoracic progression was the most common in durvalumab arm (80.6%) versus placebo (74.5%) in subpopulation with progression.

	ITT Population		Subpopulation with Progression	
	Durvalumab (n=476)	Placebo (n=237)	Durvalumab (n=216, 45.4% of ITT)	Placebo (n=153, 64.6% of ITT)
Any RECIST progression, n (%)	216 (45.4)	153 (64.6)	216 (100)	153 (100)
Intrathoracic only	174 (36.6)	114 (48.1)	174 (80.6)	114 (74.5)
Extrathoracic only	33 (6.9)	31 (13.1)	33 (15.3)	31 (20.3)
Intrathoracic and extrathoracic simultaneously	9 (1.9)	8 (3.4)	9 (4.2)	8 (5.2)

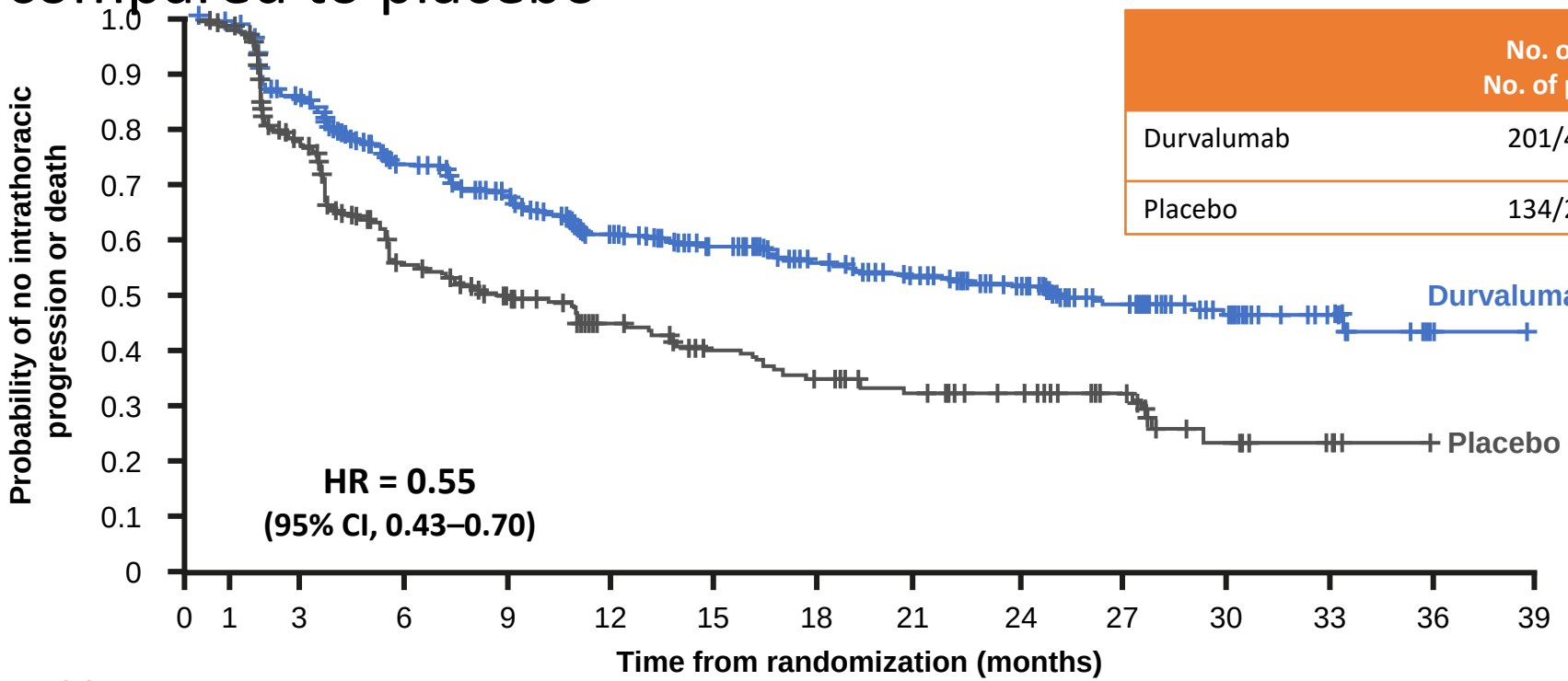
*New lesions identified within the lung parenchyma or chest wall, including the diaphragm, were categorized as intrathoracic, with all other lesions categorized as extra thoracic

Raben D et al. Presented at: American Society for Radiation Oncology Annual Meeting (ASTRO); September 15-18, 2019; Chicago, IL. Abs LBA6.

Patterns of Disease Progression: Time to Intrathoracic Progression Only or Death per BICR

- Durvalumab improved the time to intrathoracic progression when compared to placebo

	No. of events / No. of patients (%)	Median time (95% CI) months
Durvalumab	201/476 (42.2)	25.2 (19.2–NR)
Placebo	134/237 (56.5)	9.2 (5.6–13.6)



No. at risk

Durvalumab	476	377	302	268	213	188	163	143	116	83	43	23	1	0
Placebo	237	163	105	86	67	55	46	39	32	24	10	5	0	0

BICR = Blinded Independent Central Review;.

Raben D et al. Presented at: American Society for Radiation Oncology Annual Meeting (ASTRO); September 15-18, 2019; Chicago, IL. Abs LBA6.

Patterns of Progression: New Extrathoracic Lesions at First Progression (BICR)

- Reduction in new extrathoracic lesions was seen in durvalumab arm (8.8%) at first progression versus placebo (16.5%) for ITT population.
- Approximately 2/3rd of patients had 1 or 2 extrathoracic lesions at first progression in subpopulation with progression.

	ITT Population		Subpopulation with Progression and New Extrathoracic Lesions	
	Durvalumab (n=476)	Placebo (n=237)	Durvalumab (n=42, 8.8% of ITT)	Placebo (n=39, 16.5% of ITT)
Any new extrathoracic lesion, n (%)	42 (8.8)	39 (16.5)	42 (100)	39 (100)
1 lesion	19 (4.0)	15 (6.3)	19 (45.2)	15 (38.5)
2 lesions	9 (1.9)	13 (5.5)	9 (21.4)	13 (33.3)
3–5 lesions	9 (1.9)	8 (3.4)	9 (21.4)	8 (20.5)
>5 lesions	5 (1.1)	3 (1.3)	5 (11.9)	3 (7.7)

BICR = Blinded Independent Central Review, DCO = data cutoff, ITT = intention-to-treat.

Raben D et al. Presented at: American Society for Radiation Oncology Annual Meeting (ASTRO); September 15-18, 2019; Chicago, IL. Abs LBA6.

Safety Summary

	Durvalumab (n=475)	Placebo (n=234)
Any grade all-causality AEs, n (%)	460 (96.8)	222 (94.9)
Grade 3/4	145 (30.5)	61 (26.1)
Grade 5[a]	21 (4.4)	15 (6.4)
Leading to discontinuation	73 (15.4)	23 (9.8)
Serious AEs, n (%)	138 (29.1)	54 (23.1)
Any grade pneumonitis/radiation pneumonitis, n (%)	161 (33.9)	58 (24.8)
Grade 3/4	17 (3.6)	7 (3.0)
Grade 5	5 (1.1)	5 (2.1)
Leading to discontinuation	30 (6.3)	10 (4.3)
AESIs	317 (66.7)	114 (49.1)
AESI Grade 1/2	270 (56.8)	102 (43.6)

pneumonia, pneumococcal pneumonia, sepsis, septic shock, cardiomyopathy, cardiopulmonary failure, myocardial infarction, aortic dissection, dyspnea, emphysema, hemoptysis, respiratory distress, respiratory failure, radiation pneumonitis, right ventricular failure, increased level of brain natriuretic peptide, and unknown cause). Grade 5 AEs of any cause occurred in 14 patients (6.0%) who received placebo (3 each [1.3%] with pneumonitis and pneumonia and 1 each [0.4%] with the following: pneumonia streptococcal, West Nile virus infection, cardiac arrest, eosinophilic myocarditis, hemoptysis, interstitial lung disease, intestinal obstruction, radiation pneumonitis, and unknown cause). Each patient could have had >1 Grade 5 AE.

AE = adverse event; AESI = adverse event of special interest.

1. Antonia SJ et al. Article and supplementary appendix. N Engl J Med. 2018;379:2342-2350; 2. Antonia SJ et al. Presented at: IASLC 19th WCLC Annual Meeting; September 23-26, 2018; Toronto, Canada.

Safety Summary Based on Time from Radiation

	<14 days		≥14 days	
	Durvalumab (N=120)	Placebo (N=60)	Durvalumab (N=355)	Placebo (N=174)
Any-grade all-causality AEs, n (%)	**118 (98.3)**	**57 (95.0)**	**342 (96.3)**	**165 (94.8)**
Grade 3/4	37 (30.8)	18 (30.0)	108 (30.4)	43 (24.7)
Outcome of death	6 (5.0)	7 (11.7)	15 (4.2)	8 (4.6)
Leading to discontinuation	16 (13.3)	9 (15.0)	57 (16.1)	14 (8.0)
Serious AEs, n (%)	**36 (30.0)**	**20 (33.3)**	**102 (28.7)**	**34 (19.5)**
Any-grade pneumonitis/radiation pneumonitis, n (%)	**47 (39.2)**	**10 (16.7)**	**114 (32.1)**	**48 (27.6)**
Grade 3/4	5 (4.2)	1 (1.7)	12 (3.4)	5 (2.9)
Outcome of death	0	2 (3.3)	5 (1.4)	3 (1.7)
Leading to discontinuation	7 (5.8)	3 (5.0)	23 (6.5)	7 (4.0)

DCO: March 22, 2018

Note: Patients with multiple events in the same AE category are counted only once in that category and those with events in more than one category are counted once in each of those categories.

AE = adverse event CTCAE: ; DCO = data cutoff.

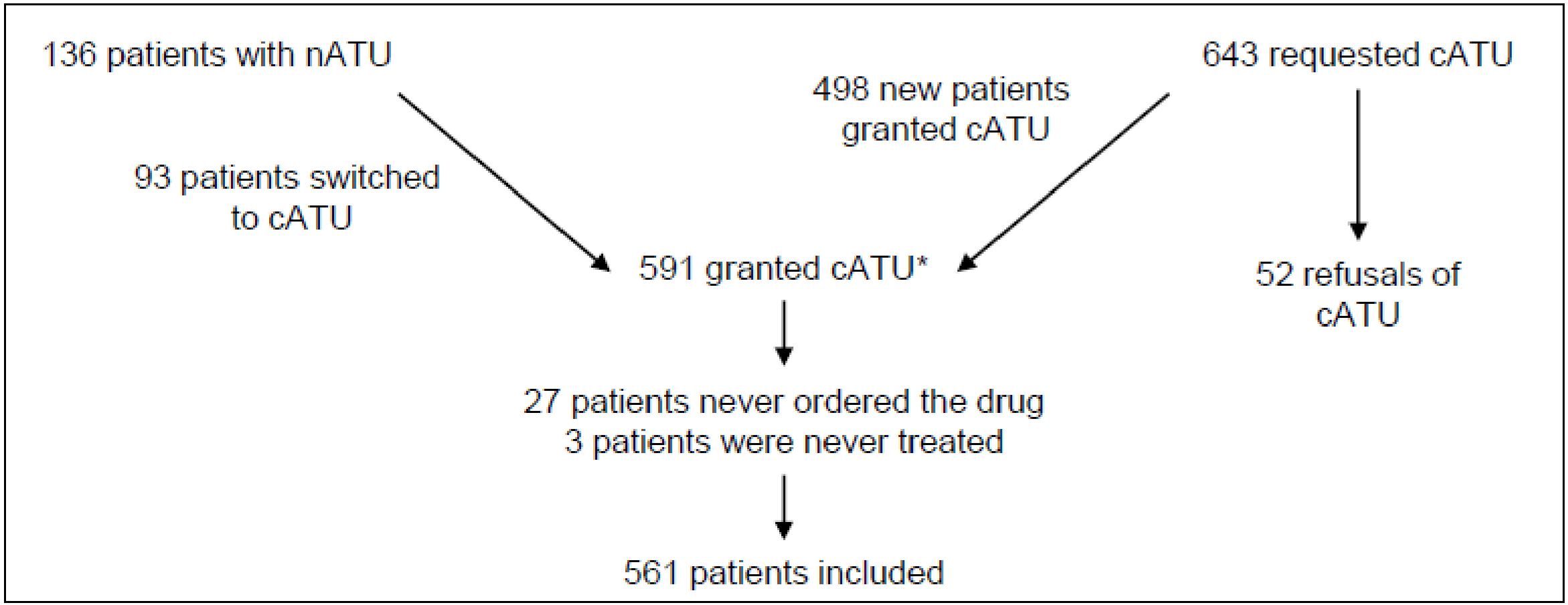
Faivre-Finn, C et al. Article and supplementary appendix. Lung Cancer. 2021;151:30-38.

The time to start Durvalumab after CCRT

First Real-life Data on Durvalumab After Definitive Concomitant Chemoradiotherapy(cCRT) in Unresectable Stage III Non-small Cell Lung Cancer (NSCLC) in France: Analysis of 591 Patients Enrolled in the French Cohort Temporary Authorisation for Use (cATU)

First real life data on durvalumab after definitive concomitant chemoradiotherapy (cCRT) in unresectable stage (St) III non-small cell lung cancer (NSCLC) in France: Analysis of 591 patients (pts) enrolled in the French cohort (c) temporary authorization of use (ATU), V. Avrillon

ATU program flow chart



ATU, Temporary Authorisation for Use; cATU, cohort ATU; nATU, nominative ATU. *Analysis set = 561 patients

First real life data on durvalumab after definitive concomitant chemoradiotherapy (cCRT) in unresectable stage (St) III non-small cell lung cancer (NSCLC) in France: Analysis of 591 patients (pts) enrolled in the French cohort (c) temporary authorization of use (ATU), V. Avrillon

Eligibility Criteria

- Patient with unresectable stage III NSCLC and with no possibility to enter an ongoing clinical trial.
- **No disease progression following 2 or more prior cycles of platinum-based cCRTwith total radiation dose of 60 Gy±10% (54–66 Gy).**
- **Performance status score of 0 or 1.**
- **Initiation of durvalumab treatment within 42 days after the end of radiation.**

- Major exclusion criteria were:
  - Unresolved grade 3 or 4 toxicity 6 weeks after cCRT
  - Or grade 2 pneumonitis 6 weeks after cCRT
  - Prior immunotherapy treatment
  - Prior immune syndrome history in the past 2 years.

First real life data on durvalumab after definitive concomitant chemoradiotherapy (cCRT) in unresectable stage (St) III non-small cell lung cancer (NSCLC) in France: Analysis of 591 patients (pts) enrolled in the French cohort (c) temporary authorization of use (ATU), V. Avrillon

Patient Characteristics

Characteristic	n=561
Median age, years (range)	62.4 ± 8.9 (36–85)
Gender M / F (%)	71.6 / 28.4
Mean weight after cCRT, kg (range)	71.2 ± 15.2 (37–144)
Histology, n (%)	
Adenocarcinoma	290 (51.7)
Squamous cell carcinoma	224 (39.9)
Large cell carcinoma	18 (3.2)
Other	29 (5.2)
Disease stage at diagnosis (IASLC 2017), n (%)	
IIB	2 (0.4)*
IIIA	227 (41.2)
IIIB	287 (52.1)
IIIC	35 (6.4)
Missing	10
EGFR mutation status, n (%)	561
EGFR+	10 (1.8)
EGFR–	259 (46.1)
Non-contributory	24 (4.3)
Not performed or missing	268 (47.8)
ALK mutation status, n (%)	561
ALK+	3 (0.5)
ALK–	273 (48.7)
Non-contributory	28 (5)
Not performed or missing	257 (45.8)

*IIB initial stage, both relapsed 6 months after initial diagnosis, and were finally at an unresectable stage and eligible for definitive cCRT

PACIFIC

Characteristic	Durvalumab (N=476)	Placebo (N=237)
Age		
Median (range), years	64 (31–84)	64 (23–90)
≥65 years, %	45.2	45.1
Sex, %		
Male	70.2	70.0
WHO performance status score, %*		
0	49.2	48.1
1	50.4	51.5
Smoking status, %		
Current	16.6	16.0
Former	74.4	75.1
Never	9.0	8.9
Disease stage, %†		
IIIA	52.9	52.7
IIIB	44.5	45.1
Histology, %		
Squamous	47.1	43.0
Non-squamous	52.9	57.0
PD-L1 status, %		
TC <25%	**39.3**	**44.3**
TC ≥25%	**24.2**	**18.6**
Unknown‡	**36.6**	**37.1**
Prior chemotherapy, %		
Induction	25.8	28.7
Definitive cCRT	99.8	99.6
Prior radiotherapy, %*		
<54 Gy	0.6	0
54 to ≤66 Gy	92.9	91.6
>66 to ≤74 Gy	6.3	8.0
Best response to previous cCRT, %		
Complete response	1.9	3.0
Partial response	48.7	46.8
Stable disease	46.6	48.1
Progressive disease¶	0.4	0

First real life data on durvalumab after definitive concomitant chemoradiotherapy (cCRT) in unresectable stage (St) III non-small cell lung cancer (NSCLC) in France: Analysis of 591 patients (pts) enrolled in the French cohort (c) temporary authorization of use (ATU), V. Avrillon

At the end of cCRT

- **RECIST response was evaluated**
  - 78.5% had PR
  - 15.2% had SD
  - 6.3% had CR

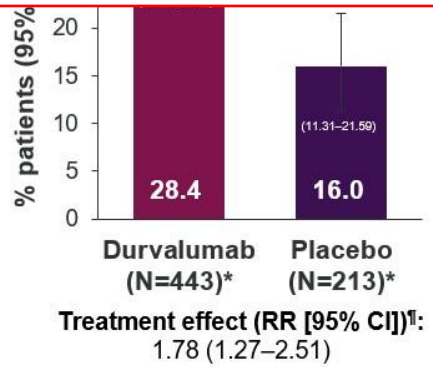
- **Median interval between the end of cCRT and effective initiation of Durvalumab was known for 161 patients**
  - <14 days for 4 (2.5%) patients
  - 14 to 42 days for 93 (57.8%) patients
  - **>42 days for 64 (39.7%) patients**

First real life data on durvalumab after definitive concomitant chemoradiotherapy (cCRT) in unresectable stage (St) III non-small cell lung cancer (NSCLC) in France: Analysis of 591 patients (pts) enrolled in the French cohort (c) temporary authorization of use (ATU), V. Avrillon

As of September 2019 – Data available for 360

DCR	267 (74.2%)
CR	38 (10.5%)
PR	74 (20.5%)
SD	155 (43%)

The responses were like what was observed in PACIFIC study despite almost 40% patients starting Durvalumab 42 days after CRT



Partial response	120 (27.1)	33 (15.5)
Stable disease	233 (52.6)	119 (55.9)
Progressive disease	73 (16.5)	59 (27.7)
Non-evaluable	10 (2.3)	1 (0.5)
Duration of response, months		
Median (95% CI)	NR	13.8 (6.0–NR)
Treatment effect, HR (95% CI)	0.43 (0.22-0.84)	
Ongoing response at data cutoff, %†		
At 12 months	72.8	56.1
At 18 months	72.8	46.8

*Patients with measurable disease at baseline. †Percentages calculated by Kaplan-Meier method.

BICR = blinded independent central review; NR = not reached; RR = relative risk.

PACIFIC

1. Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, et al. Durvalumab after Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer. New England Journal of Medicine [Internet]. 2017 Nov 16 [cited 2018 Mar 30];377(20):1919–29. Available from: https://doi.org/10.1056/NEJMoa1709937

First real life data on durvalumab after definitive concomitant chemoradiotherapy (cCRT) in unresectable stage (St) III non-small cell lung cancer (NSCLC) in France: Analysis of 591 patients (pts) enrolled in the French cohort (c) temporary authorization of use (ATU), V. Avrillon

Hope for Cure in Stage III NSCLC

- **5 yr Survival is Important end point**
- **Optimal CTRT -→ IO should be standard of care in all Stage III UR patients**
- **Converting Stage III lung cancer into never progressing disease* !**

Looking back and to the future: Are we improving 'cure' in non-small cell lung cancer?

David Walder [1], Mary O'Brien [2]

Affiliations

PMID: 28236771 DOI: 10.1016/j.ejca.2017.01.006

Abstract

In surgical series, cancer-free survival at 5 years is often referred to as a cure. In recent years, attempts to improve cure rates in non-small cell lung cancer (NSCLC) have focussed on earlier diagnosis through cost-effective screening programs. Systemic therapies have historically added only a small benefit to overall survival in both the adjuvant and palliative setting. However, in the last two decades, the development of new treatment options has added incremental improvements in NSCLC survival rates. Patients with a targetable sensitising mutation including epidermal growth factor receptor gene mutations and anaplastic lymphoma kinase rearrangements have significantly better prognosis, and many will survive beyond 5 years. Immunotherapy is an effective treatment in selected patients with NSCLC and is set to cause another leap in 5 year survival rates. Although these patients are not free from disease, survival at 5 years may become the more important end-point as NSCLC becomes seen as a chronic oncological disease.

*33% did not had progression and were alive at 5 yrs

- David Walder 1, Mary O'Brien 2 Eur J Cancer. 2017 Apr;75:192-194. doi: 10.1016/j.ejca.2017.01.006. Epub 2017 Feb 23. Looking back and to the future: Are we improving 'cure' in non-small cell lung cancer?

Key Takeaways

Durvalumab demonstrated a statistically significant and clinically meaningful improvement in OS and PFS versus placebo in the PACIFIC trial.

- **Median OS was 47.5 months** for durvalumab versus 29.1 months for placebo**,** HR 0.68**.**
- **Median PFS was 16.9 months** with durvalumab and 5.6 months with placebo, HR 0.51.
- OS and PFS improvement with durvalumab was demonstrated across all prespecified subgroups.
- **Five-year OS - 42.9%** of patients randomized to durvalumab remain alive at 5 years (vs. 33.4% randomized to placebo)
- A **third remain both alive and free of disease progression** (durvalumab, 33.1%; placebo, 19.0%), demonstrating OS benefit and PFS benefit with the PACIFIC regimen.

Key Takeaways

- Patients receiving durvalumab had a lower incidence of new lesions, including new brain metastases, compared with patients receiving placebo (22.5% in the durvalumab group vs 33.8% in the placebo group).

- Tolerability profile of Durvalumab was acceptable

- Low grade pneumonitis is not a deterrent to use of Durvalumab.

- In French EAP, Durvalumab was started >42 days after CRT and showed similar responses to the ones observed in PACIFIC.

Thank you