AstraZeneca

Optimizing treatment decisions in Unresectable Stage III NSCLC : A Case Study

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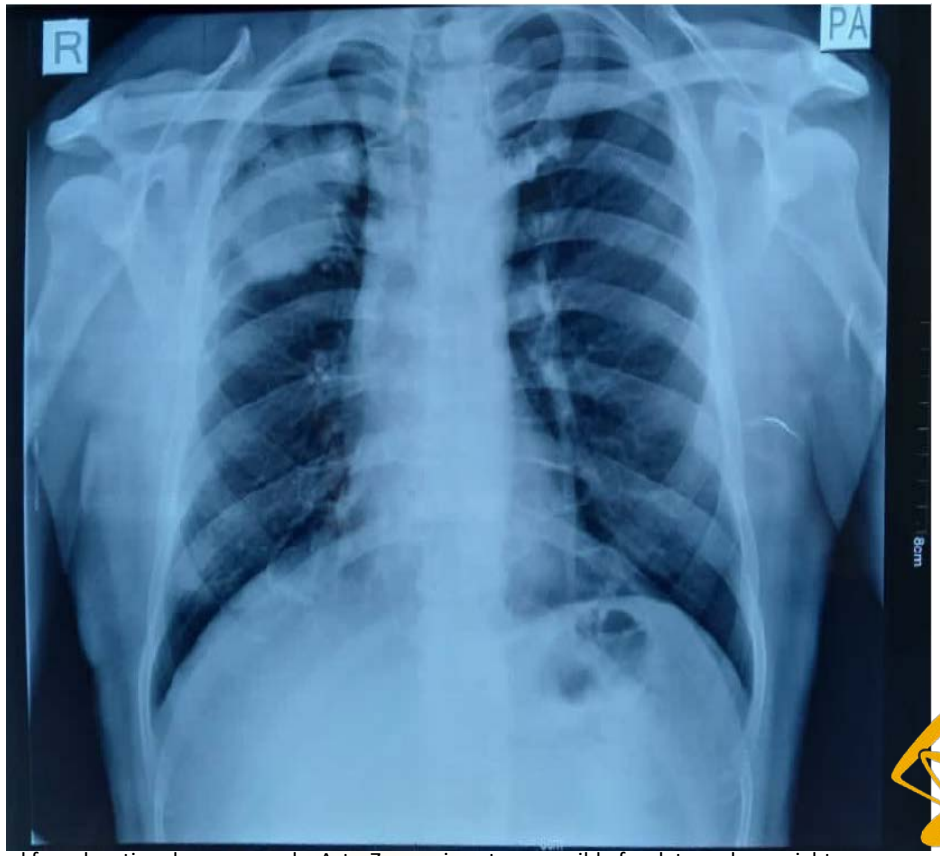
Case

- Mr. X, a 59 years old gentleman presented on 17th July 2021 with cough and weight loss, for past 3 months.
- No history of any co-morbidities.
- Patient came with Chest Xray



On CT Scan

- 03/07/2021
- Well-defined mass in Rt. Upper lobe (5.4 x 5.3cm)
- Few Lymphadenopathy- Rt. Paratracheal, Rt. Hilar region.

On PET Scan

- 11/07/2021
- Posterior segment of upper lobe- metabolically active enhancing soft tissue density mass lesion.
- Mediastinal and right hilar lymph nodes – metabolically active.

Other investigations

- **On histopathology**

  Moderately differentiated adenocarcinoma lung

- **MRI Brain**

  No significant abnormality was detected.

- **Molecular testing**

  PDL-1 testing- Positive (20%)

  EGFR – Negative in tumor cells.

Staging

- Lung T3N2M0, IIIB

TABLE 4] N Subclassification

Category	Subclass	Description
Nx		Regional lymph nodes cannot be assessed
N0		No regional lymph node involvement
N1	N1a	Single-station N1 involvement
	N1b	Multiple-station N1 involvement
N2	N2a1	Single-station N2 without N1 involvement (skip)
	N2a2	Single-station N2 with N1 involvement
	N2b	Multiple-station N2 involvement
N3		N3 lymph node involvement

TABLE 5] Lung Cancer Stage Grouping (Eighth Edition)

T/M	Label	N0	N1	N2	N3
T1	T1a ≤1	IA1	IIB	IIIA	IIIB
	T1b >1-2	IA2	IIB	IIIA	IIIB
	T1c >2-3	IA3	IIB	IIIA	IIIB
T2	T2a *Cent, Visc Pl*	IB	IIB	IIIA	IIIB
	T2a >3-4	IB	IIB	IIIA	IIIB
	T2b >4-5	IIA	IIB	IIIA	IIIB
T3	T3 >5-7	IIB	IIIA	IIIB	IIIC
	T3 *Inv*	IIB	IIIA	IIIB	IIIC
	T3 *Satell*	IIB	IIIA	IIIB	IIIC
T4	T4 >7	IIIA	IIIA	IIIB	IIIC
	T4 *Inv*	IIIA	IIIA	IIIB	IIIC
	T4 *Ipsi Nod*	IIIA	IIIA	IIIB	IIIC
M1	M1a *Contr Nod*	IVA	IVA	IVA	IVA
	M1a *Pl Dissem*	IVA	IVA	IVA	IVA
	M1b *Single*	IVA	IVA	IVA	IVA
	M1c *Multi*	IVB	IVB	IVB	IVB

See Table 3 text and legend for expansion of abbreviations.

Heineman DJ, Daniels JM, Schreurs WH. Clinical staging of NSCLC: current evidence and implications for adjuvant chemotherapy. Ther Adv Med Oncol. 2017 Sep;9(9):599-609. doi: 10.1177/1758834017722746. Epub 2017 Aug 2. PMID: 29081843; PMCID: PMC5564882.

Final Diagnosis

Rt. Lung NSCLC
Stage III B

Adenocarcinoma
EGFR- Negative
PDL1- Positive(20%)

Treatment options

- Chemotherapy and Radiotherapy
  - Concurrent vs Sequential
  - Induction / Definitive
- Consolidation therapy or Maintenance therapy

Outcomes of definitive chemotherapy in unresectable Stage III B

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

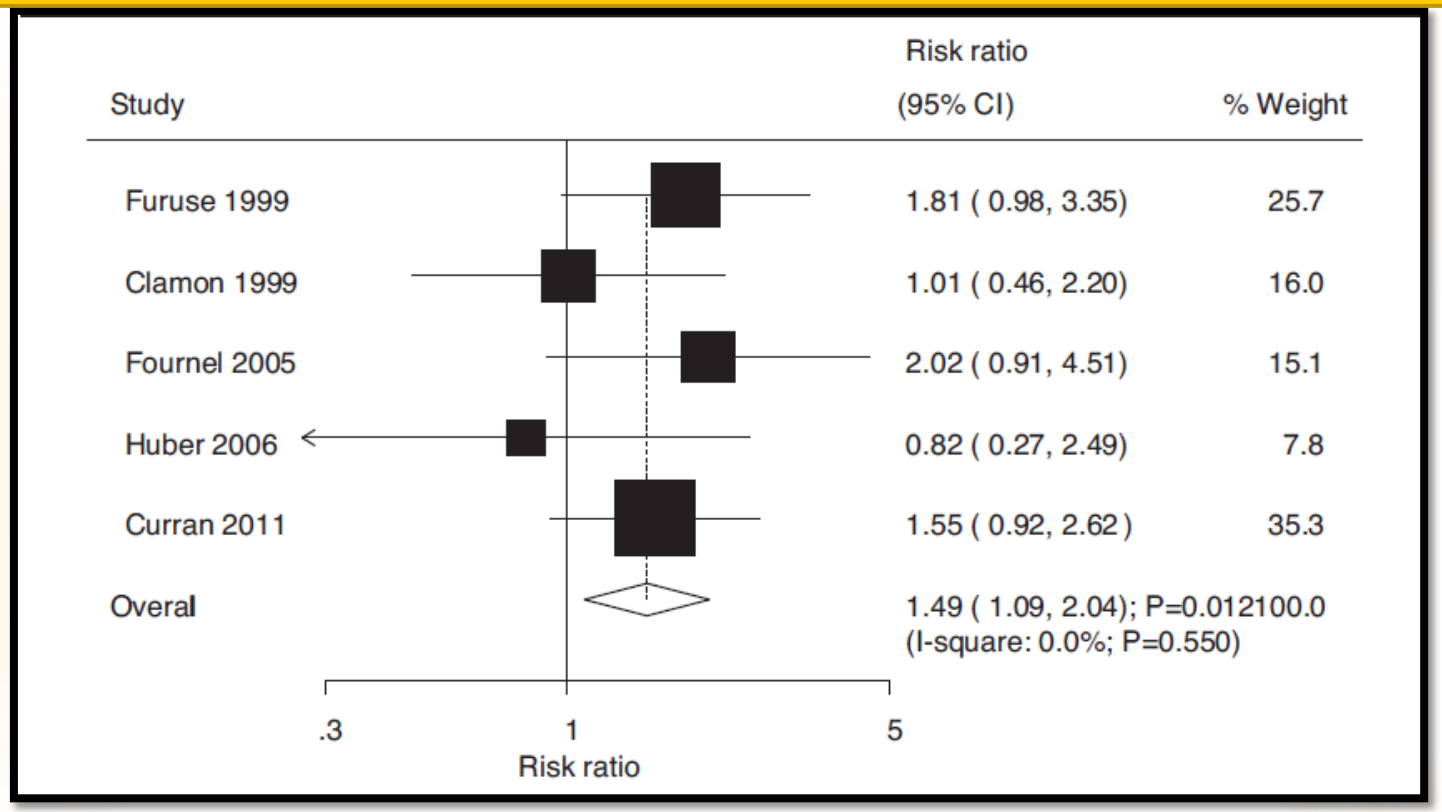
Treatment		Population	Radiation Dose, Gy	ORR, %	Median PFS, mo	Median OS, mo
Cisplatin, vinblastine (5-week cycle)[2]	RTOG 9410	Untreated, inoperable stage II/III NSCLC (n=203)	45	61	NR	14.6
Paclitaxel, carboplatin (two 3-week cycles)[7]	LAMP	Unresectable stage IIIA/B NSCLC (n=91)	63	NR	9.0	13.0

- 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.

CCRT vs SCRT

Impact on 5-yr survival rates

Concurrent chemoradiotherapy significantly increased the 5-year survival rates (RR: 1.49; 95% CI: 1.09–2.04; P=.012)

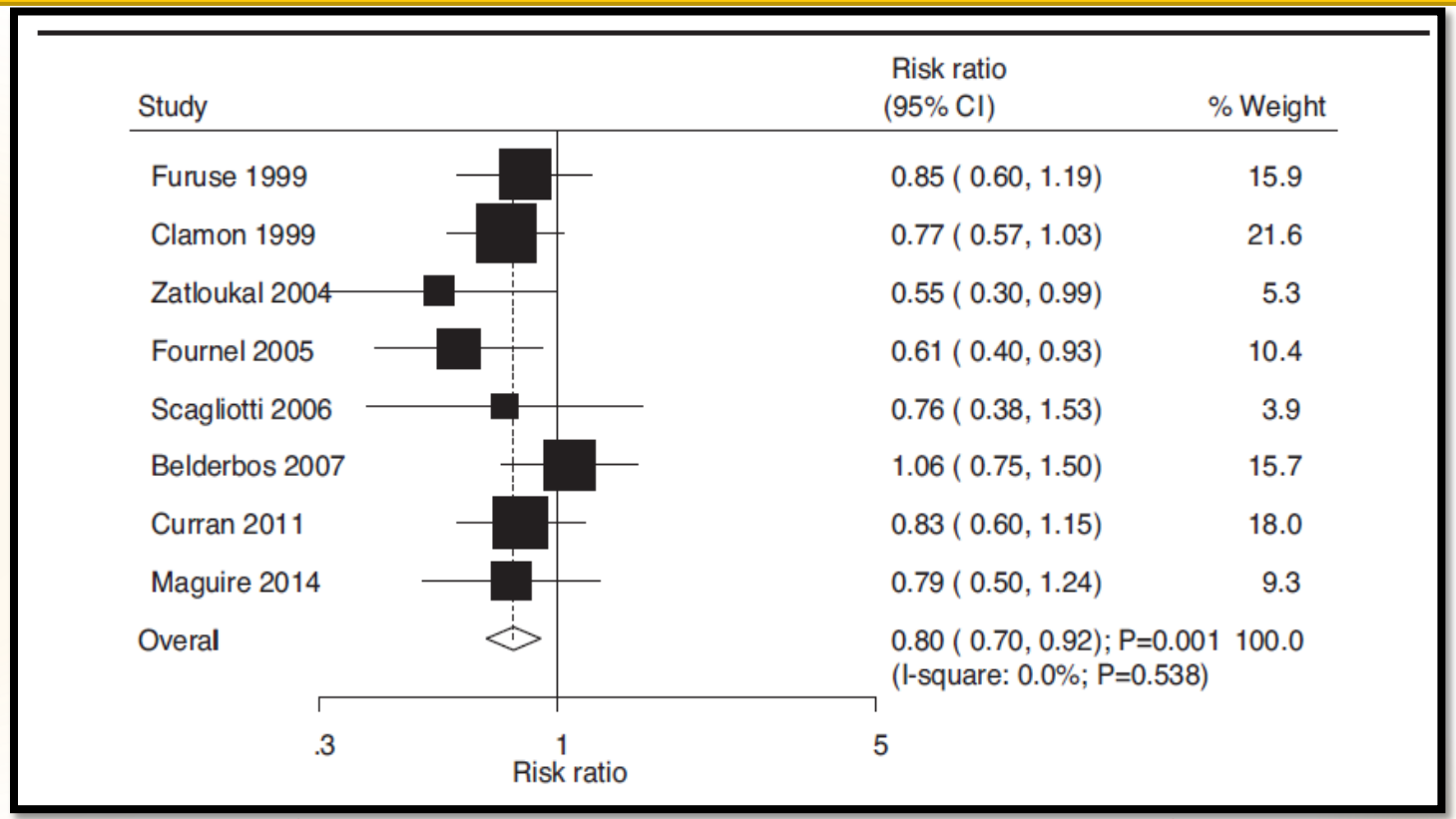


Xiao W, Hong M. Concurrent vs sequential chemoradiotherapy for patients with advanced non-small-cell lung cancer: A meta-analysis of randomized controlled trials. Medicine (Baltimore). 2021 Mar 19;100(11):e21455.

CCRT vs SCRT

Effect on locoregional relapse

Concurrent chemoradiotherapy significantly reduced the risk of locoregional relapse (RR: 0.80; 95% CI: 0.70–0.92; P=.001)



Xiao W, Hong M. Concurrent vs sequential chemoradiotherapy for patients with advanced non-small-cell lung cancer: A meta-analysis of randomized controlled trials. Medicine (Baltimore). 2021 Mar 19;100(11):e21455.

Patient was initially given chemoradiotherapy

- Started on 29/07/2021
- Radiation:

  External Beam radiotherapy, IGRT to the lung with 6Mv photons;

  Dose -60 Gy-30 cycles.

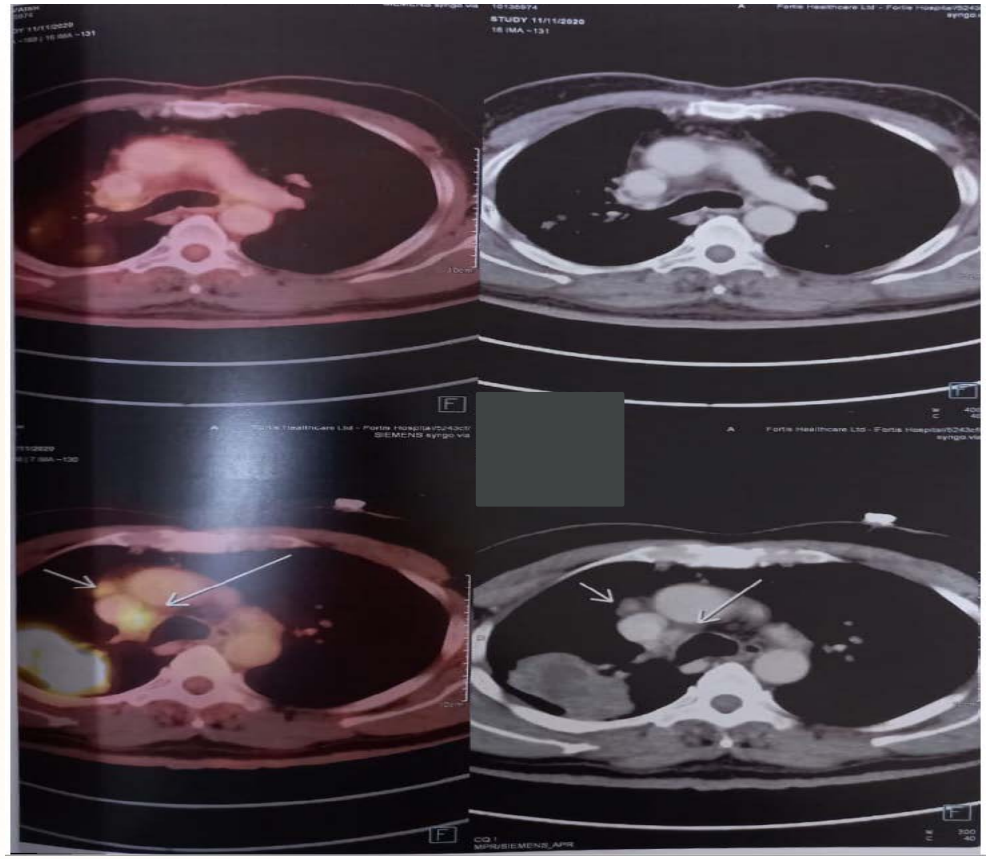
- Concomitant weekly chemotherapy;

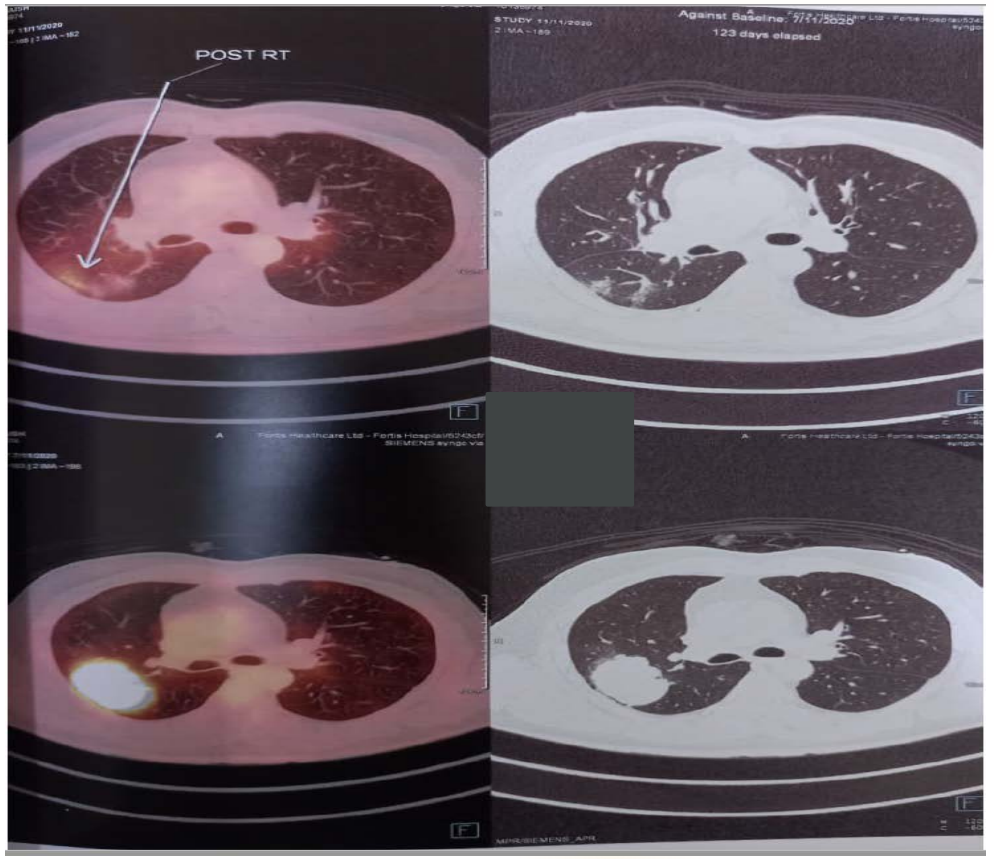
  Paclitaxel and carboplatin – 4 cycles (completed on 10/9/2021)

  (Chemotherapy was stopped due to raised SGPT)

CASE:
Post CRT follow up Scan

- 11/09/2021





Consolidation therapy has not demonstrated any benefit in Stage III patients

Chemotherapy Regimens Used With Radiotherapy in NSCLC

Concurrent Regimens

Treatment	Study	Po
Cisplatin, etoposide (two 4-week cycles)[1]	PROCLAIM	Nonsquamous stag
Cisplatin, vinblastine (5-week cycle)[2]	RTOG 9410	Untreated, inoperable
Cisplatin, pemetrexed (three 3-week cycles)[1]	PROCLAIM	Nonsquamous stag
Paclitaxel, carboplatin (weekly ± 2 cycles of consolidation)[3]	RTOG 0617	Stage IIIA/B
Paclitaxel, carboplatin (7-week cycle)[4]	CALGB 39801	Untreated, inoperable
Cisplatin, etoposide (two 1-week cycles)[5]	HOG and US Oncology	Unresected sta
Cisplatin, etoposide (four 1-week cycles)[6]	—	Stage IIIA

Sequential Regimens

Treatment		Po
Cisplatin, vinblastine (5-week cycle)[2]	RTOG 9410	Untreated, inoperable
Paclitaxel, carboplatin (two 3-week cycles)[7]	LAMP	Unresectable stag

CALGB=Cancer and Leukemia Group B; HOG=Hoosier Oncology Group; LAMP=locally advanced multim
ORR=overall response rate; PFS=progression-free survival; RTOG=Radiation Therapy Oncology Group.
1. Senan S, et al. *J Clin Oncol*. 2016;34:953-962. **2.** Curran WJ Jr, et al. *J Natl Cancer Inst*. 2011;103:145
4. Vokes EE, et al. *J Clin Oncol*. 2007;25:1698-1704. **5.** Hanna N, et al. *J Clin Oncol*. 2008;26:5755-5760.
7. Belani CP, et al. *J Clin Oncol*. 2005;23:5883-5891.

Outcomes from Consolidation trials in locally advanced unresectable NSCLC

Trial	Description	PFS		OS	
		HR	p-value	HR	p-value
Chemotherapy					
HOG[1]	Consolidation docetaxel	NR	NR	NR	0.81
KCSG[2]	Consolidation docetaxel / cisplatin	0.91	0.36	0.91	0.44
PROCLAIM[3]	Pemetrexed/cis vs etoposide/cis with XRT	0.86	0.13	0.98	0.83
Radiation therapy					
RTOG 0617[4]	60 vs 74 Gy of XRT	1.19	0.12	1.38	0.004
Targeted therapy					
SWOG S0023[5]	Consolidation Placebo vs Gefitinib	0.80*	0.17	0.63*	0.013
RTOG 0617[4]	Consolidation Cetuximab vs Placebo	0.99	0.89	1.07	0.29

* = Placebo vs Treatment; 1) Hanna, N. et al. *J Clin Oncol* 2008 26:5755-5760; 2) Ahn, JS et al. J Clin Oncol 2015 33:2660-2666;
3) Senan, S. et al. J Clin Oncol 2016 34:953; 4) Bradley, J. et al. Lancet Oncol. 2015 February ; 16(2): 187–199; 5) Kelly, K et al. J Clin Oncol 2008 26:2450-2456.

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.

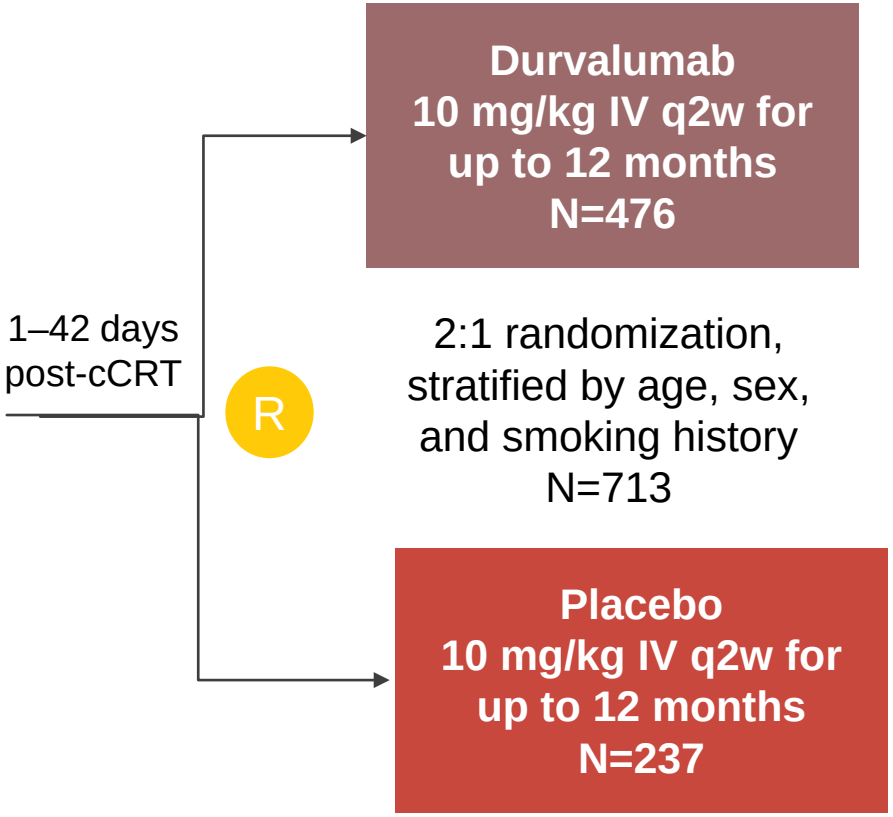
Rajappa S, Sharma S, Prasad K. Unmet Clinical Need in the Management of Locally Advanced Unresectable Lung Cancer: Treatment Strategies to Improve Patient Outcomes. Adv Ther. 2019 Mar;36(3):563-578. doi: 10.1007/s12325-019-0876-4. Epub 2019 Jan 29. PMID: 30693419.

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



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

*Defined as the time from randomization (which occurred up to 6 weeks post-cCRT) to the first documented event of tumor progression or death in the absence of progression.
ClinicalTrials.gov number: NCT02125461 BICR, blinded independent central review; cCRT, concurrent chemoradiation therapy; DoR, duration of response; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PROs, patient-reported outcomes; PS, performance status; q2w, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; WHO, World Health Organization

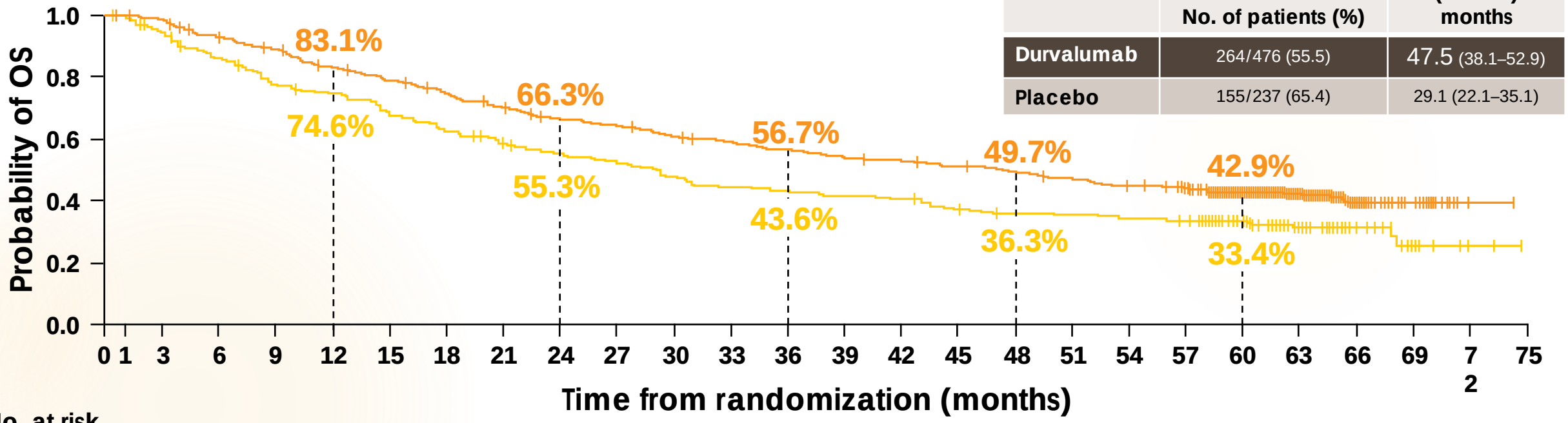
PACIFIC Study
Patient Baseline Characteristics

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

PACIFIC trial did include EGFR mutation positive patients

Updated Five years Overall Survival

	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)

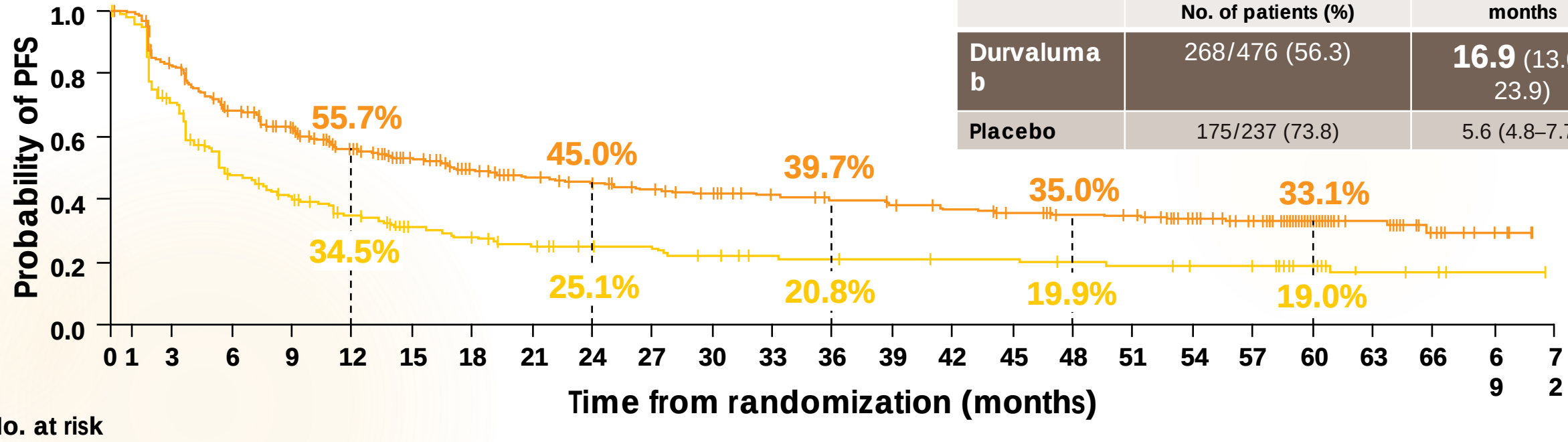


First and only approved IO to demonstrate 42.9% OS at 5 years

- 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 5 Year Progression-Free Survival

	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)



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

- 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.

Real-world outcomes with durvalumab after chemoradiotherapy in patients with unresectable stage III NSCLC (SPOTLIGHT)

Meghan J Mooradian,[1] Allison Allen,[2] Ling Cai,[2] Yang Xiao,[2] Pratibha Chander[2]

[1]Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA;
[2]AstraZeneca, Gaithersburg, MD, USA

- SPOTLIGHT is a retrospective, observational cohort study using de-identified, patient-level data from a US oncology medical record database (Flatiron Health).

Patients and treatment

- Total of 332 patients who received durvalumab were analyzed
- Approximately 50% of patients started durvalumab within the suggested period of 42 days after the end of CRT, and 40.5% received durvalumab for ≥11 months (recommended DoT is 12 months or until PD/unacceptable toxicity6,7).5
- Median follow-up was 17.5 months (range, 0.2–32.0).

M. Mooradian1 , A. Allen2 , L. Cai2 , Y. Xiao2 , P. Chander2 . Real-world outcomes with durvalumab (durva) after chemoradiotherapy (CRT) in patients with unresectable stage III NSCLC (SPOTLIGHT). Annals of Oncology .Volume 33 , Issue S2, 2022

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[1]Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA;
[2]AstraZeneca, Gaithersburg, MD, USA

Endpoints and assessments

- The primary endpoints evaluating real-world effectiveness included TFST and TTM, defined as follows:

–TFST: time from durvalumab initiation until the start of first subsequent anticancer therapy or death.

–TTM: time from durvalumab initiation until the first date of metastasis or death in the absence of metastasis.

- Exploratory endpoints included rwPFS and OS, defined as follows:

–rwPFS : time from durvalumab initiation until progression or death due to any cause.

–OS: time from durvalumab initiation until death due to any cause.

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Primary Endpoints – TFST & TTM

Figure 2: TFST

No. of events/ total no. of patients (%)	Median TFST (95% CI), Months	12-mo TFST rate (95% CI), %	24-mo TFST rate (95% CI), %
134/332 (40.4)	Not reached	70.0 (64.5–74.8)	52.9 (46.4–59.0)

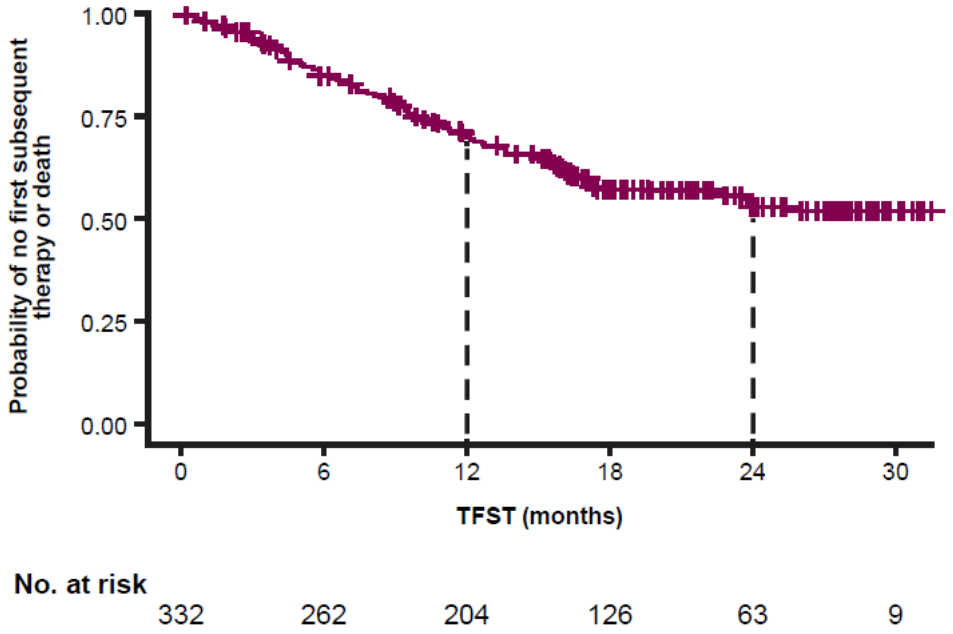
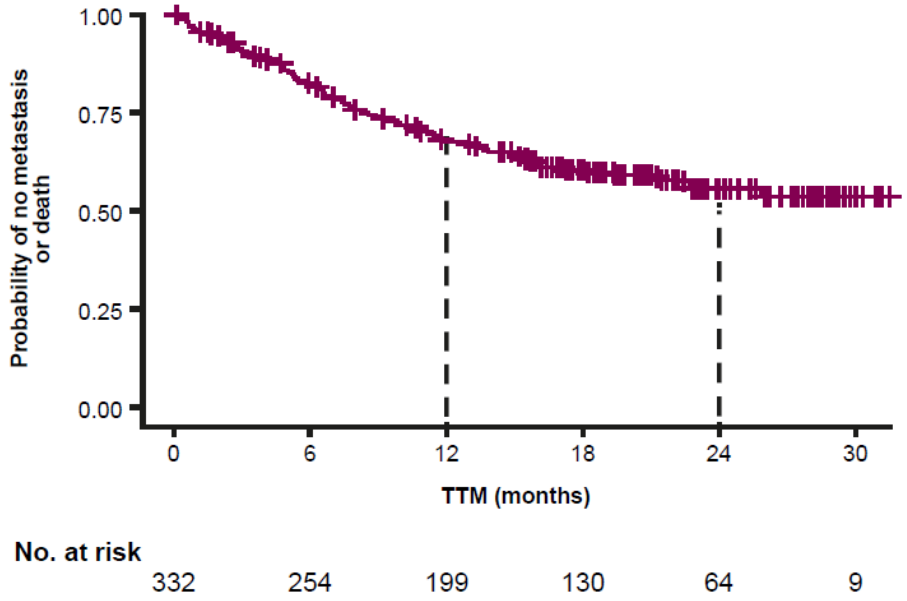


Figure 3: TTM

No. of events/ total no. of patients (%)	Median TTM (95% CI), Months	12-mo TTM rate (95% CI), %	24-mo TTM rate (95% CI), %
131/332 (39.5)	Not reached	67.4 (61.9–72.3)	55.7 (49.4–61.5)



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Secondary Endpoint – rPFS & OS

Figure 4: rwPFS

No. of events/ total no. of patients (%)	Median rwPFS (95% CI), Months	12-mo rwPFS rate (95% CI), %	24-mo rwPFS rate (95% CI), %
166/332 (50.0)	17.5 (14.2–24.8)	58.1 (52.4–63.4)	44.6 (38.6–50.5)

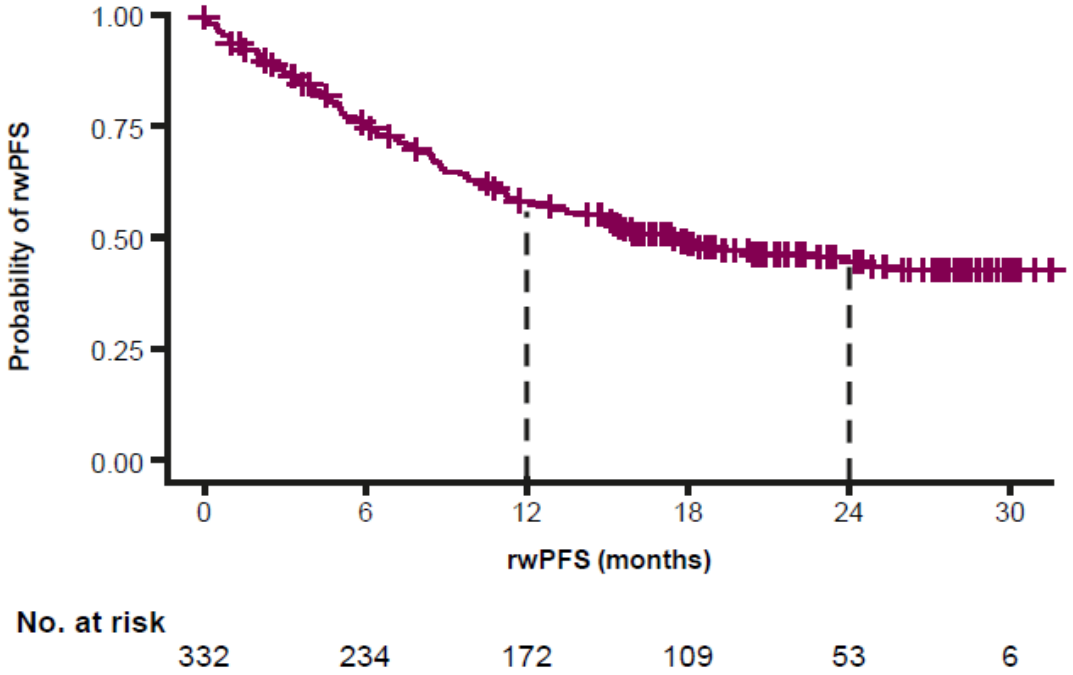
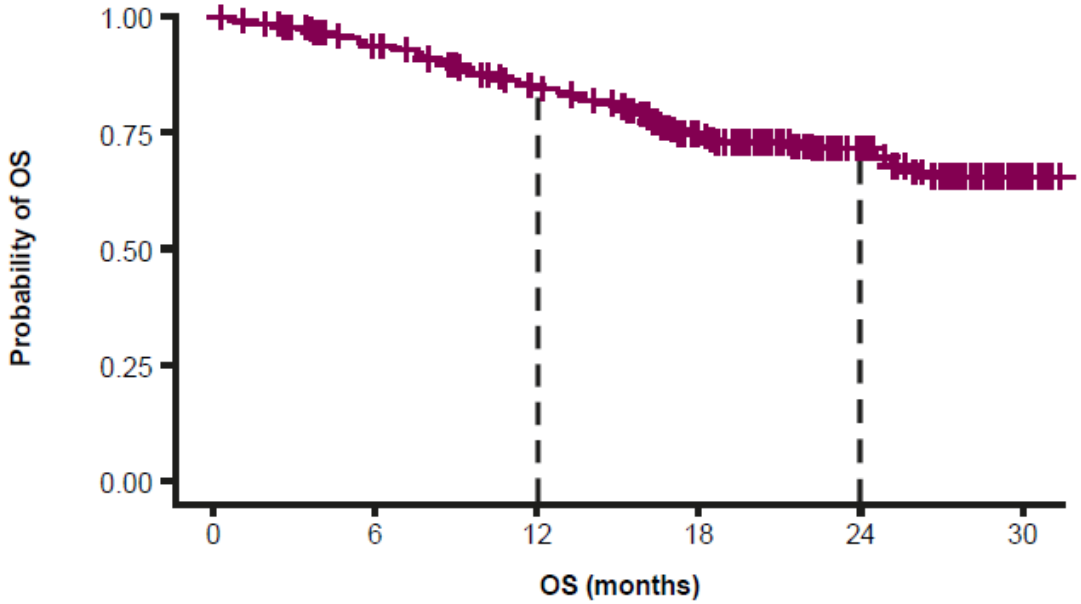


Figure 5: OS

No. of events/ total no. of patients (%)	Median OS (95% CI), Months	12-mo OS rate (95% CI), %	24-mo OS rate (95% CI), %
86/332 (25.9)	Not reached	84.5 (79.9–88.1)	71.6 (65.7–76.7)



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Conclusion

- Data from our retrospective, observational study are consistent with results from PACIFIC1–3and indicate that durvalumab is effective in real-world patients.

–Median rwPFS reported here was 17.5 months, which is in alignment with the 16.9-month median PFS in PACIFIC seen after ~5 years' follow up.3

–TFST, TTM, and OS data remain immature (medians not reached), due to the short median follow-up time (17.5 months). However, landmark rates appear consistent with those in PACIFIC.

- The SPOTLIGHT study shows that durvalumab after CRT is effective and well tolerated in patients with unresectable stage III NSCLC, suggesting that the treatment benefit observed in PACIFIC can be translated to everyday clinical practice in the USA.

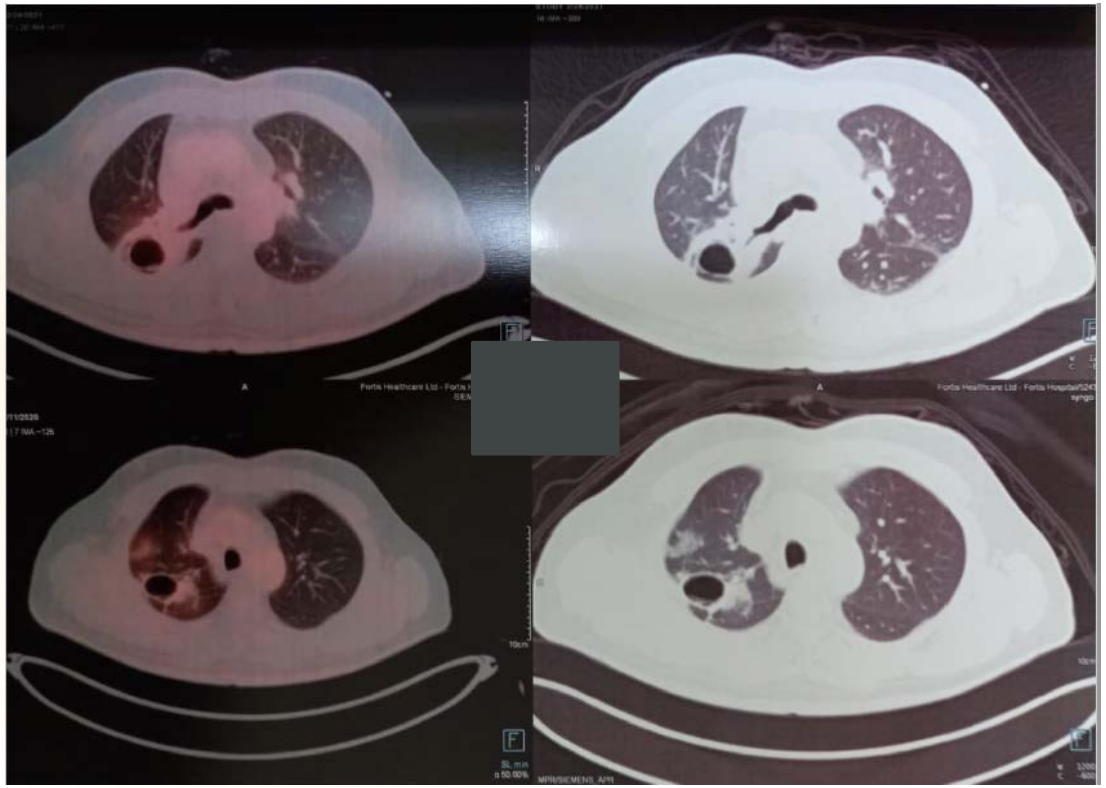
CASE:
Patient was started on Durvalumab therapy

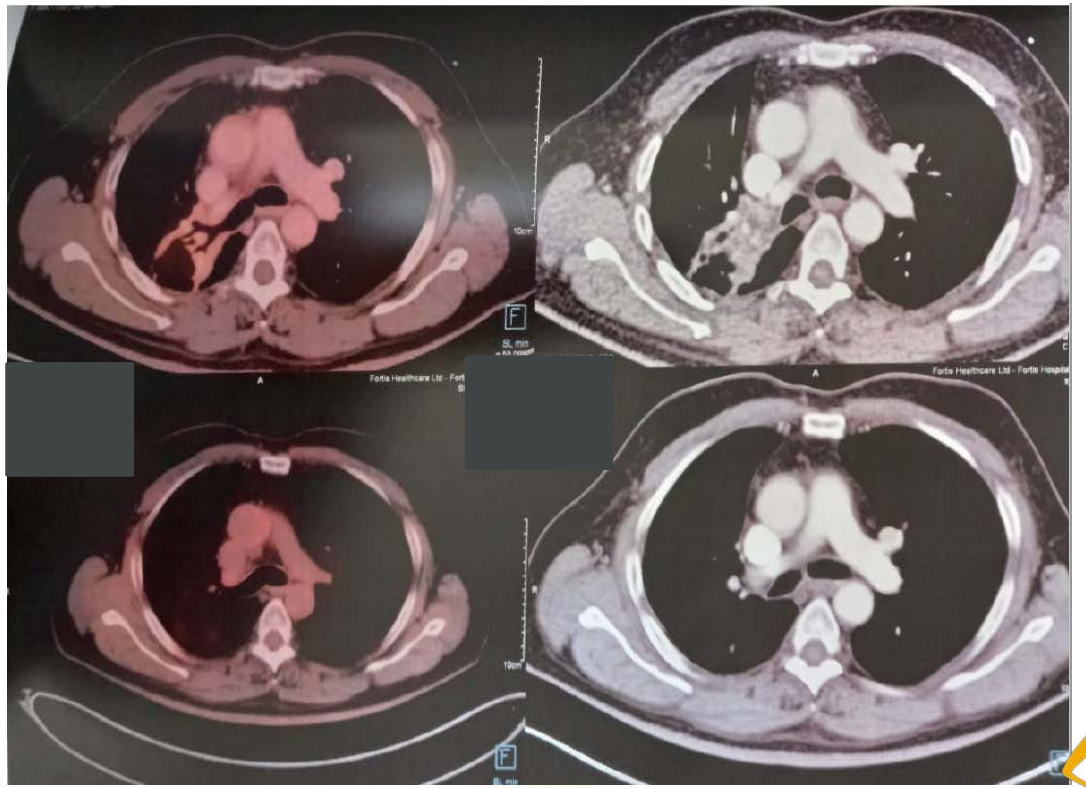
- Started on- 30/09/2021 (20 days after CCRT)
- 3 cycles completed on– 03/11/2021

- Follow-up PET Scan (11/11/2021)

CASE:
Follow-up PET Scan

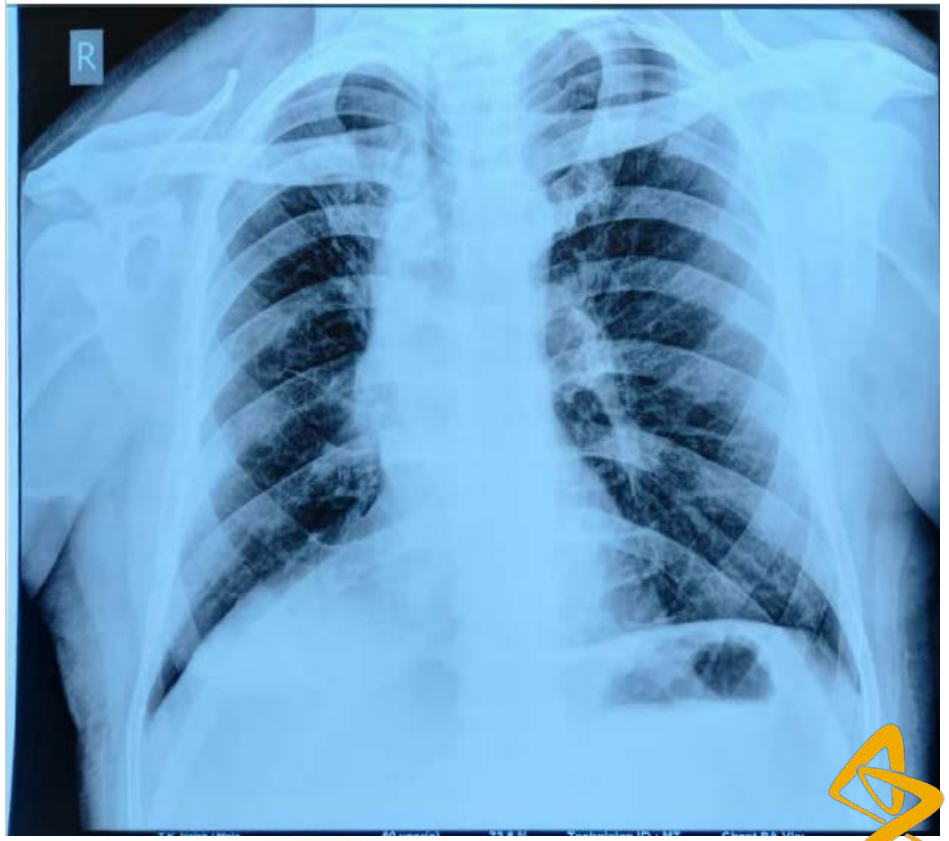
- 11/11/2021





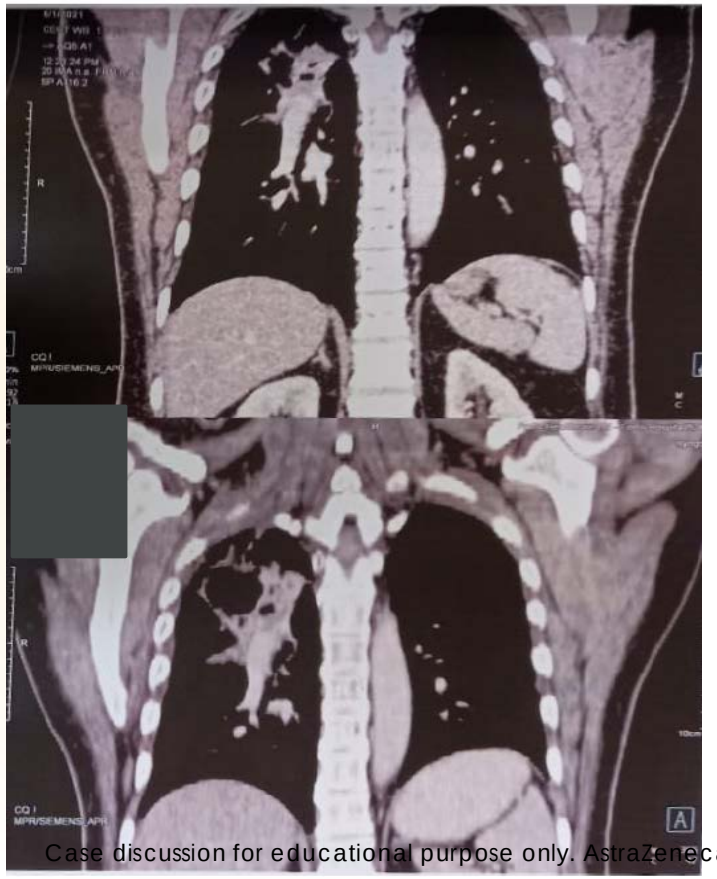
CASE:
Patient continued to receive durvalumab

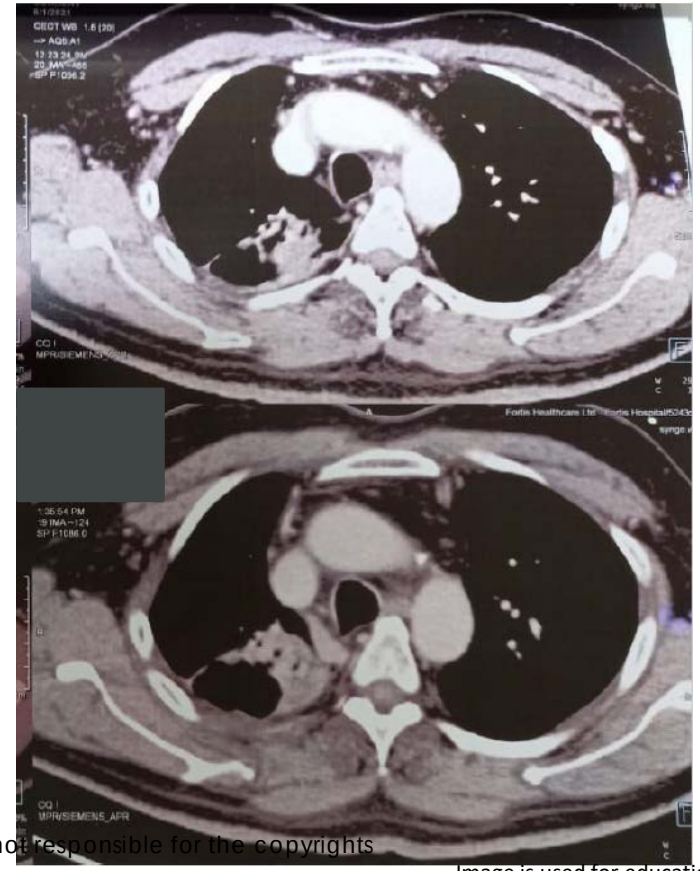
- There was a good response to Durvalumab, hence patient continued to receive the therapy.
- Chest Xray

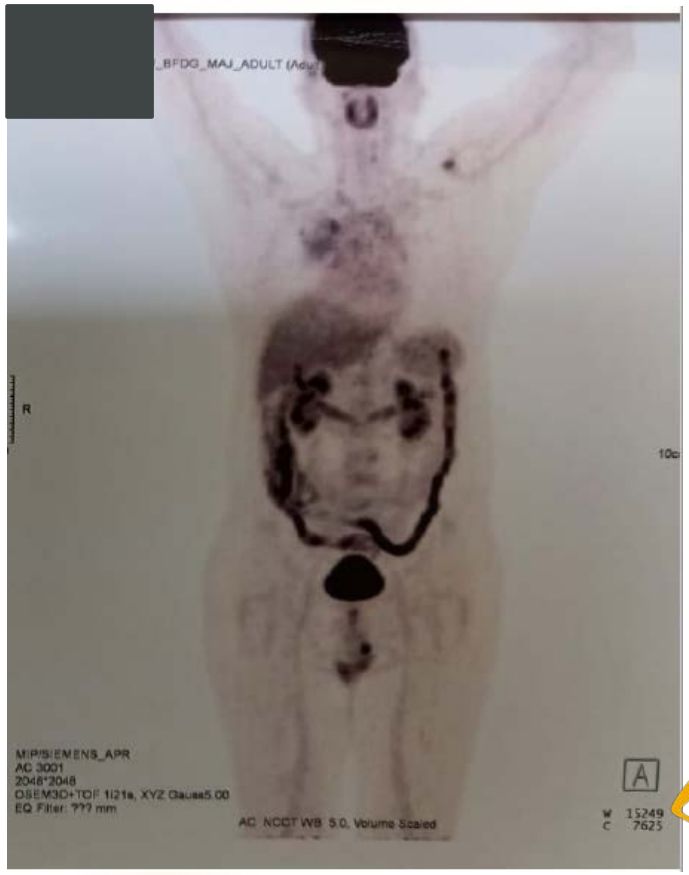


CASE:
Follow up PET Scan

- **24/02/2022**





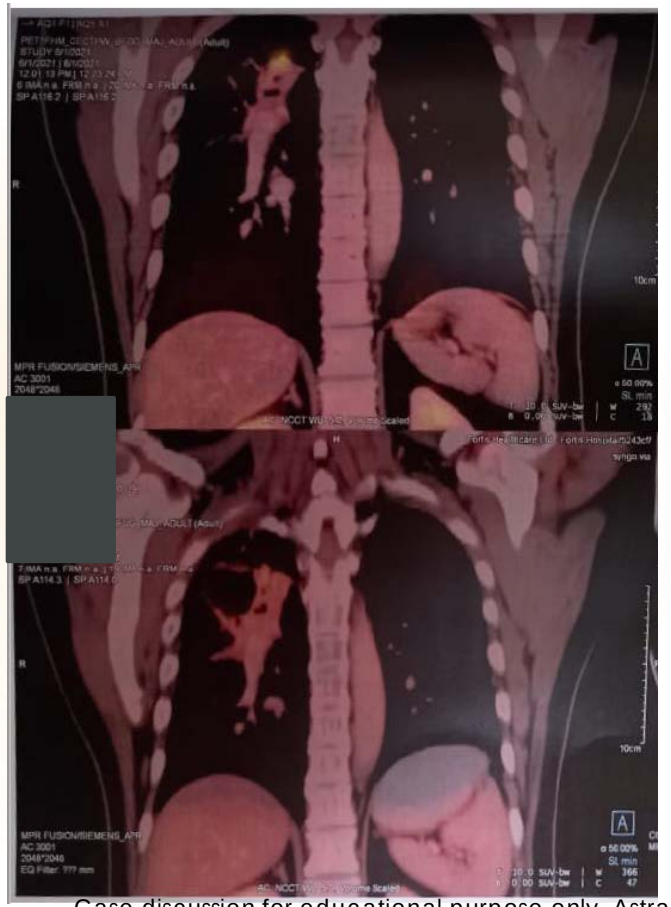


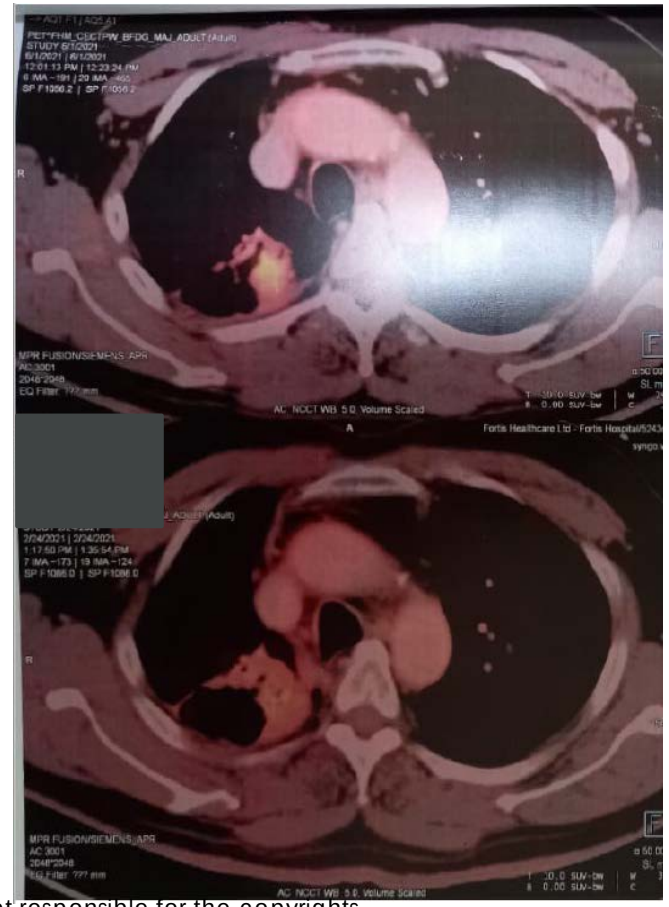
CASE:
Patient continued to receive durvalumab

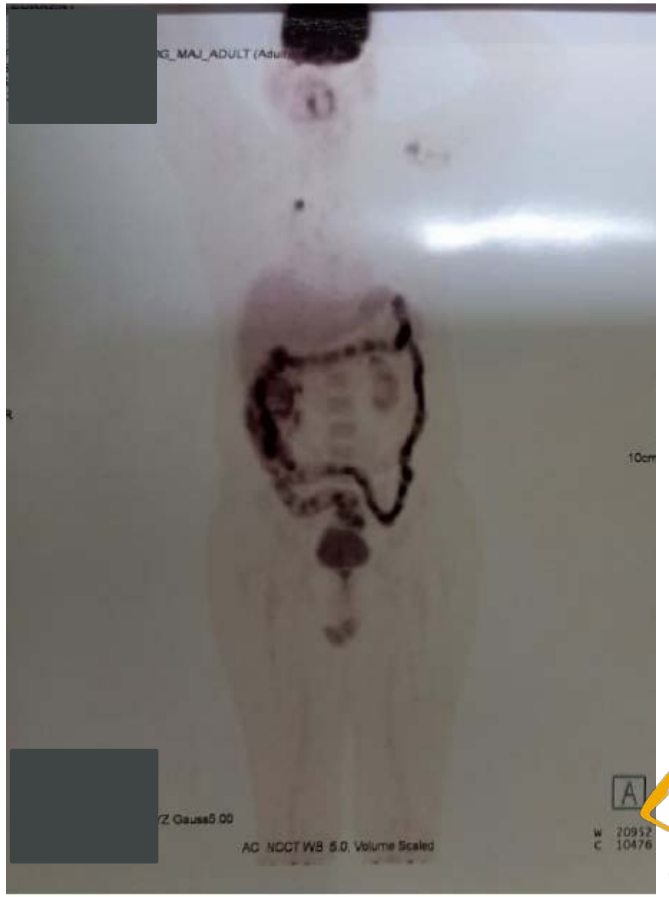
- Total 15 cycles of durvalumab received.
- Patient came with complain of- chest pain
- PET Scan (1/06/2022)

CASE:
Follow up PET Scan

- 1/06/2022







CASE:
Patient likely progressed

- The likely next steps in management-
  - Chemotherapy
  - Chemoradiotherapy
  - Radiotherapy
  - Immunotherapy

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)

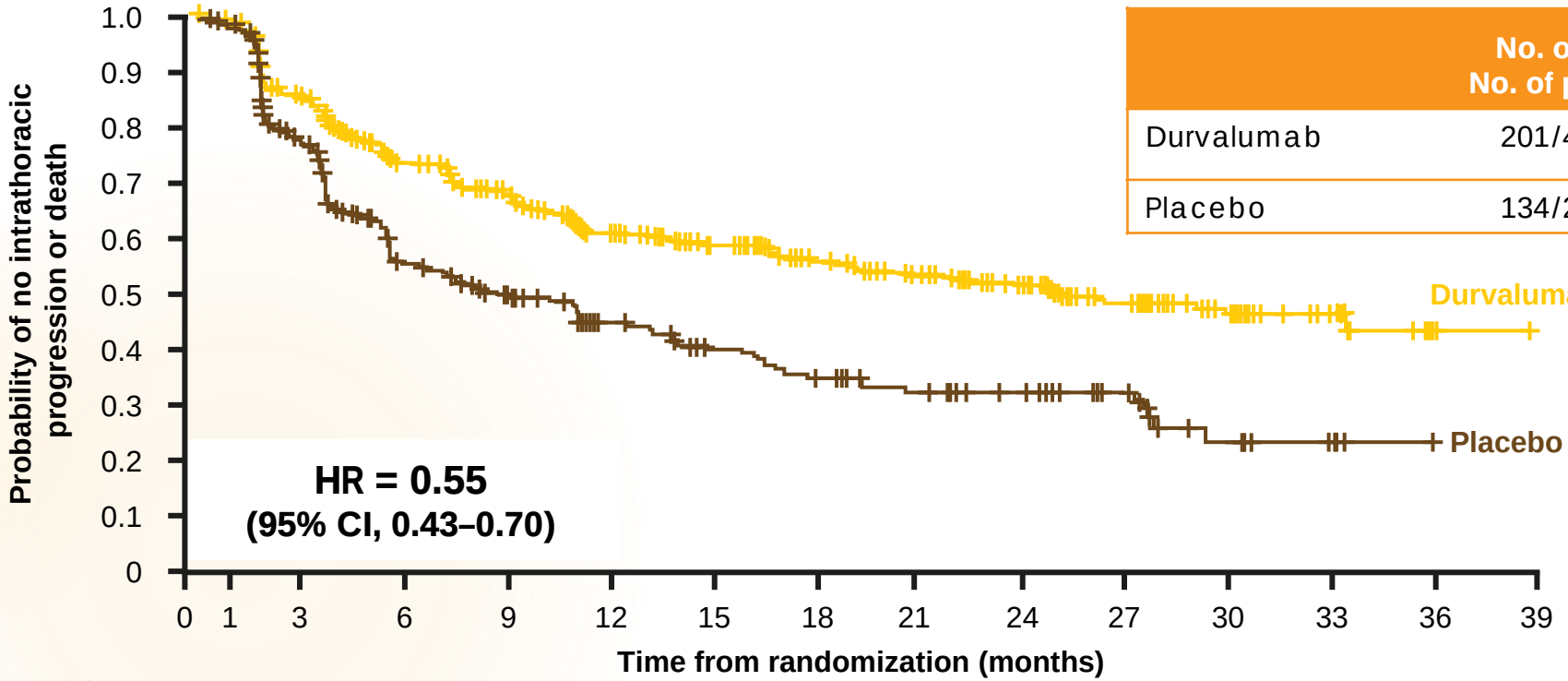
*New lesions identified within the lung parenchyma or chest wall, including the diaphragm, were categorized as intrathoracic, with all other lesions categorized as extra thoracic

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

	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

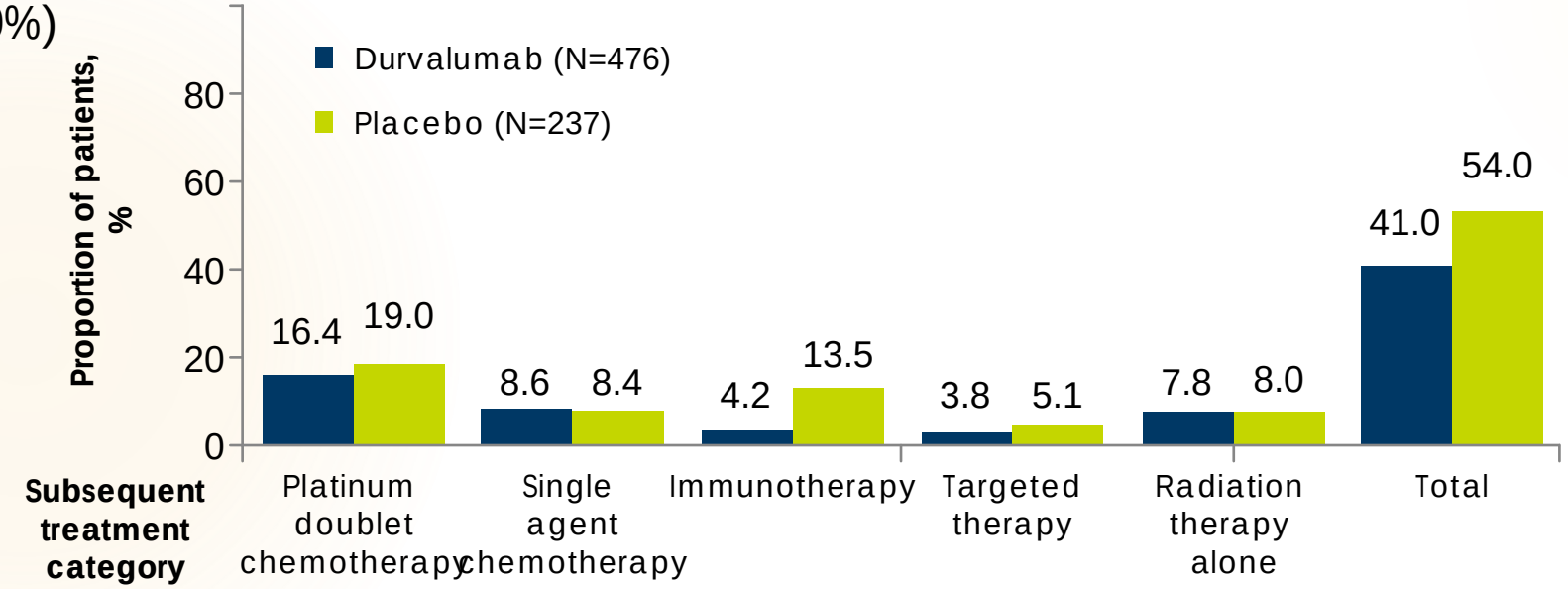
Durvalumab	476	377	302	268	213	188	163	143	116	83	43	23	1	0
Placebo	237	163	105	86	67	55	46	39	32	24	10	5	0	0

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.

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.

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)

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.

Key Takeaways

Durvalumab is the new Standard of Care in Stage III unresectable NSCLC post CRT

- MDT approach gives best outcomes for patients of Stage III NSCLC
- CCRT gives better outcomes than RT alone or CT alone
- Consolidation CT doesn't improve outcomes
- First and only approved immunotherapy to demonstrate a 5- year OS and PFS benefit
- Durvalumab should be considered as a treatment option in all unresectable stage III patients not progressed on CTRT
- Durvalumab improves outcomes all subgroups irrespective of PD-L1 status or EGFR status.

Abbreviated Prescribing Information
Durvalumab intravenous solution

For the use of a registered oncologist only DURVALUMAB Solution for INFUSIONIMFINZI™ Vial 500 mg (500mg/10mL) and 120 mg (120 mg/2.4mL) in 10 mL Abbreviated Prescribing Information QUALITATIVE AND QUANTITATIVE COMPOSITION Each mL contains 50 mg of IMFINZI. Each vial of 2.4 mL contains 120 mg of durvalumab. Each vial of 10 mL contains 500 mg of durvalumab. IMFINZI is a human immunoglobulin (IgG1κ) monoclonal antibody. **THERAPEUTIC INDICATIONS:** Locally Advanced Non-small Cell Lung Cancer (NSCLC)IMFINZI is indicated for the treatment of patients with locally advanced, unresectable NSCLC whose disease has not progressed following platinum-based chemoradiation therapy.Small Cell Lung Cancer (SCLC)IMFINZI in combination with etoposide and either carboplatin or cisplatin is indicated for the first-line treatment of patients with extensive-stage small cell lung cancer (ES-SCLC).**POSOLOGY AND METHOD OF ADMINISTRATION:** ***Locally Advanced NSCLC*** The recommended dose of IMFINZI is 10 mg/kg administered as an intravenous infusion over 60 minutes every 2 weeks or 1500 mg every 4 weeks, until disease progression orunacceptable toxicity. Dose escalation or reduction is not recommended. Dose withholding or discontinuation may be required based on individual safety and tolerability. ES-SCLC1500 mg in combination with chemotherapy, every 3 weeks (21 days) for 4 cycles, followed by 1500 mg every 4 weeks as monotherapy Until disease progression or unacceptable toxicity.**CONTRAINDICATIONS:** None. **WARNINGS & PRECAUTIONS** Given the mechanism of action of IMFINZI®, potential immune-mediated adverse reactions may occur. Patients should be monitored for signs and symptoms and managed as recommended in full prescribing information. For suspected immune-mediated adverse reactions, adequate evaluation should be performed to confirm aetiology or exclude alternate aetiologies. Withholding of IMFINZI should be considered for Grade 3 immune-mediated adverse reactions, unless clinical judgment indicates discontinuation. Systemic corticosteroids should be considered. ***Special patient populations*** **Paediatric and adolescents** The safety and effectiveness of IMFINZI have not been established in children and adolescents aged less than 18 years. **Elderly (≥65 years)** No dose adjustment is required for elderly patients (≥65 years of age) **Renal Impairment** Based on a population pharmacokinetic analysis, no dose adjustment of IMFINZI is recommended in patients with renal impairment. **Hepatic Impairment** Based on a population pharmacokinetic analysis, no dose adjustment of IMFINZI is recommended for patients with mild hepatic impairment. IMFINZI has not been studied in patients with moderate or severe hepatic impairment ***Fertility, Pregnancy and Lactation*** **Pregnancy** Durvalumab is not recommended during pregnancy and in women of childbearing potential not using effective contraception during treatment and for at least 3 months after the last dose. **Breast-feeding** Because of the potential for adverse reactions in breastfed infants from durvalumab, advise lactating women not to breastfeed during treatment and for at least 3 months after the last dose. **Fertility** There are no data on the potential effects of durvalumab on fertility in humans. In repeat-dose toxicology studies with durvalumab in sexually mature cynomolgus monkeys of up to 3 months duration, there were no notable effects on the male and female reproductive organs. **Interaction with other medicinal products and other forms of interaction** Durvalumab is an immunoglobulin, therefore no formal pharmacokinetic drug-drug interaction studies have been conducted with durvalumab. **PHARMACOLOGICAL PROPERTIES** ***Pharmacodynamic properties*** **Mechanism of Action** Durvalumab is a fully human, high affinity, immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that selectively blocks the interaction of PD-L1 with PD-1 and CD80 (B7.1) while leaving PD-1/PD-L2 interaction intact. Durvalumab does not induce antibody dependent cell mediated cytotoxicity (ADCC). Selective blockade of PD-L1/PD-1 and PD-L1/CD80 interactions enhances anti-tumour immune responses. These anti-tumour responses may result in tumour elimination. In preclinical studies, PD-L1 blockade led to increased T-cell activation and decreased tumour size. **Pharmacokinetic properties** Pharmacokinetic (PK) exposure increased more than dose-proportionally (non-linear PK) at doses <3 mg/kg and dose proportionally (linear PK) at doses ≥ 3 mg/kg. Steady state was achieved at approximately 16 weeks. Based on population PK analysis, the geometric mean steady state volume of distribution (Vss) was 5.64 L. The terminal half-life (t1/2), based on baseline CL, was approximately 18 days. ***PHARMACEUTICAL PARTICULARS*** **List of excipients** L-histidineL-histidine hydrochloride monohydrateα,α-Trehalose dihydratePolysorbate 80Water for Injection **Incompatibilities** *Durvalumab* No incompatibilities between IMFINZI and 9 g/L (0.9%) sodium chloride or 50 g/L (5%) dextrose in polyvinylchloride or polyolefin IV bags have been observed. IMFINZI infusion solution must not be mixed with other drug products. Do not co-administer other drugs through the same intravenous line. **Instructions for use, handling and disposal** Preparation of solution IMFINZI is supplied as a single-dose vial and does not contain any preservatives, aseptic technique must be observed. Visually inspect drug product for particulate matter and discoloration. IMFINZI is clearto opalescent, colorless to slightly yellow solution. Discard the vial if the solution iscloudy, discolored or visible particles are observed. Do not shake the vial.Administration Administer infusion solution intravenously over 60 minutes through an intravenous line containing a sterile, low-protein binding 0.2 or 0.22 micron in-line filter. **For full prescribing information, please contact: AstraZeneca Pharma India Limited Block N1, 12th Floor Manyata Embassy Business Park Rachenahalli, Outer Ring Road Bangalore – 560045** www.astrazenecaindia.com Based on prescribing information Version 7, dated 17 July 2022


Thank
You