# Durvalumab in Stage III NSCLC Panel Discussion

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NARAYANA HEALTH, GURUGRAM



### **PANELIST**

- Dr Bharat Chauhan
- Dr Shashank Das
- Dr Prahlad Elamarthi
- Dr Dipalee Borade
- Dr Biren
- Dr Vipul Doshi

#### ESMO IMMUNO-ONCOLOGY

**Annual Congress** 

580 - REAL-WORLD OVERALL SURVIVAL WITH DURVALUMAB AFTER CHEMORADIOTHERAPY IN PATIENTS WITH UNRESECTABLE STAGE III NON-SMALL-CELL LUNG CANCER (NSCLC): INTERIM ANALYSIS FROM THE PACIFIC-R STUDY

Nicolas Girard, Daniel C. Christoph, Marina C. Garassino, Fiona McDonald, Françoise Mornex, John K. Field, Rainer Fietkau,





Original Investigation | Oncology

Association of Driver Oncogene Variations With Outcomes in Patients With Locally Advanced Non-Small Cell Lung Cancer Treated With Chemoradiation and Consolidative Durvalumab

Yufei Liu, MD, PhD; Zhe Zhang, PhD; Waree Rinsurongkawong, MS; Carl M. Gay, MD, PhD; Xiuning Le, MD, PhD; Matthew S. Ning, MD, MPH; Jeff Lewis, BS;

Poster 118P

Impact of grade ≥2 pneumonitis on patient-reported outcomes (PROs) with durvalumab after chemoradiotherapy (CRT) in unresectable stage III NSCLC



Proton-therapy and concurrent chemotherapy in stage III NSCLC:





Peeters<sup>2</sup>, Antonio Angrisani<sup>2</sup>, Djoya Hattu<sup>2</sup> and Lizza Hendriks<sup>3</sup>





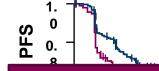
Concurrent versus sequential immune checkpoint inhibition in stage III NSCLC patients treated with



Lukas Kāsmann<sup>128</sup>, Julian Taugner<sup>1</sup>, Chukwuka Eze<sup>1</sup>, Julian Guggenberger<sup>1</sup>, Benedikt Flörsch<sup>1</sup>, Saskia Kenndoff<sup>1</sup>, Amanda Tufman<sup>1</sup>, Niels Reinmuth<sup>5</sup>, Claus Belka<sup>123</sup>, Farkhad Manap

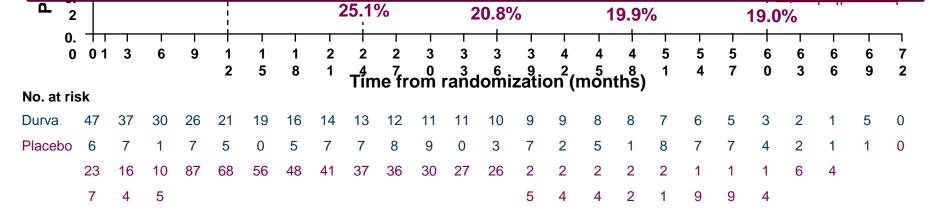
### Primary Endpoints: Progression-Free Survival by BICR (ITT)

	No. of events / No. of patients (%)	Median PFS (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 benefit at 5-years

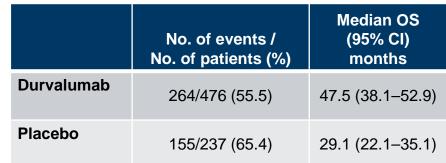


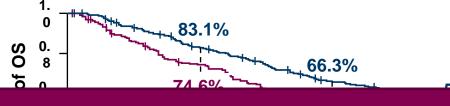
- DCO5: January 11, 2021; median follow-up: all patients, 34.2 months [range, 0.2–74.7]; censored patients, 61.6 months [range, 0.4–74.7].
- BICR = blinded independent central review; CI = confidence interval; DCO = data cutoff; HR = hazard ratio; ITT = intent-to-treat; PFS = progression-free survival



Spigel DR, et al. Poster presented at: ASCO Virtual Meeting; June 4-8, 2021.

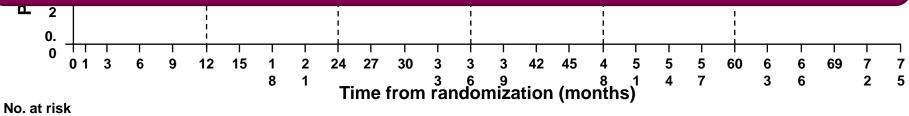
### First and only approved IO to show 5 year OS





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

### Almost 43% patients taking Durvalumab were alive at 5-years



Durva. Placebo 9 56 0 99 97 10 93 3

- 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].
- 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.

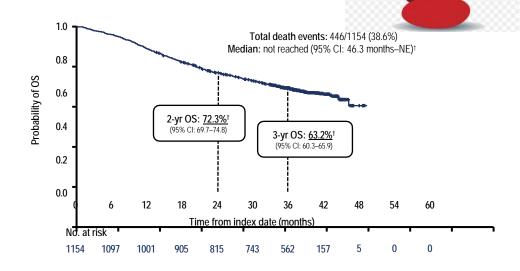


## Do you still wish to see RWE??

### **OVERALL SURVIVAL\***

- Median OS had not matured at the time of this analysis
  - More than 60% of patients were estimated to be alive at 3 years
- OS outcomes were numerically better among patients who received durvalumab within 42 days of finishing RT

	cCRT						
Outcome	PACIFIC-R* (N=900)	PACIFIC <sup>1†</sup> (N=476)					
2-yr OS rate, %	73.8	66.3					
(95% CI)	(70.8–76.6)	(61.8–70.4)					
3-yr OS rate, %	64.8	56.7					
(95% CI)	(61.5–67.9)	(52.0–61.1)					



	Time from end of RT to durva. initiation					
Outcome	<b>≤42</b> days (N=398)	>42 days (N=732)				
<b>2-yr OS rat</b> e, % (95% CI)†	<b>74.8</b> (70.2–78.8)	<b>71.2</b> (67.8–74.4)				
<b>3-yr OS rat</b> e, <b>%</b> (95% Cl) <sup>†</sup>	<b>66.0</b> (61.1–70.5)	<b>61.8</b> (58.1–65.2)				

<sup>\*</sup>Analyses are based on the 3<sup>rd</sup> chart extraction from PACIFIC-R (end date: 30 Nov 2021). 
†Calculated using the Kaplan–Meier method.



### PROGRESSION-FREE SURVIVAL\*

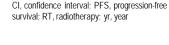
- Median PFS was 24.1 months (95% CI: 20.2–27.8)
  - More than 40% of patients were estimated to be alive and free of progression at 3 years
- PFS outcomes were numerically better among patients who received durvalumab within 42 days of finishing RT

* -												
S	1.0						tal PFS e an: 24.1 n UPD:	nonths (9			ı	
ty of PF	0.6											
Probability of PFS	0.4			0 050	50.404			_	_			
Δ.	0.2			(95% CI:	5: <u>50.1%</u> † 47.2–53.0)	) (		S: <u>42.2%</u> 39.2–45.1)	†			
	0.0	6	12	18	24	30	36	42	48	54	60	
	No. at	risk		Tir	ne from i	ndex da	te (month	s)				
	1154	902	723	627	547	462	225	37	0	0	0	

	cCRT						
Outcome	PACIFIC-R* PACIFIC <sup>1†</sup> (N=476)						
mPFS, months	25.6	16.9					
(95% CI)	(20.7–31.1)	(13.0–23.9)					

	Time from end of RT to durva. initiation				
Outcome	≤ <b>42</b> days (N=398)	>42 days (N=732)			
<b>2-yr PFS rat</b> e, <b>%</b> (95% CI)†	<i>52.3</i> (47.3–57.1)	<b>48.9</b> (45.3–52.5)			
<b>3-yr PFS rat</b> e, <b>%</b> (95% CI) <sup>†</sup>	<b>45.5</b> (40.4–50.4)	<b>40.3</b> (36.5–44.0)			

\*Analyses are based on the 3<sup>rd</sup> chart extraction from PACIFIC-R (end date: 30 Nov 2021). ¹Calculated using the Kaplan–Meier method. ¹The original PFS analysis was based on the 2<sup>rd</sup> chart extraction (end date: 30 Nov 2020) and is published elsewhere.¹² ¹Girard N et al., Ann Oncol 2021;32(suppl\_5):S939–48; ²Girard N et al., J Thorac Oncol; doi: <a href="https://doi.org/10.1016/j.jtho.2022.10.003">https://doi.org/10.1016/j.jtho.2022.10.003</a> (ePub ahead of print)





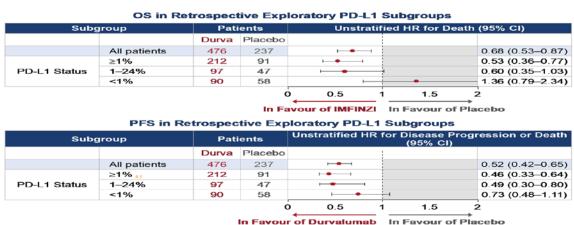
### COMPARISON WITH CLINICAL TRIAL DATA - PD-L1 STATUS

Outcomes in PD-L1 subgroups from PACIFIC-R were numerically better than those observed in the PACIFIC trial<sup>1</sup>

	PD-L1 TC ≥1%						
Outcome	PACIFIC-R* (N=573)	PACIFIC <sup>1†</sup> (N=212)					
<b>2-yr OS rate, %</b> (95% CI)	<b>76.0</b> (72.3–79.3)	<b>72.9</b> (66.2–78.4)					
<b>3-yr OS rate, %</b> (95% CI)	<b>67.0</b> (63.0–70.8)	<b>61.9</b> (54.8–68.2)					
mPFS, months (95% CI)	<b>25.3</b> (19.1–31.6)	<b>24.9</b> (16.9–38.7)					

	PD-L1 1	「C <1%
Outcome	PACIFIC-R* (N=138)	PACIFIC <sup>1†</sup> (N=90)
<b>2-yr OS rate, %</b> (95% CI)	<b>64.3</b> (55.6–71.7)	<b>56.1</b> (45.0–65.8)
<b>3-yr OS rate, %</b> (95% CI)	<b>54.4</b> (45.7–62.4)	<b>47.5</b> (36.5–57.6)
mPFS, months (95% CI)	<b>16.3</b> (10.7–28.1)	<b>10.7</b> (7.3–20.6)

 Outcomes from RWE studies and clinical trials should be compared with caution owing to differences in study design and methods of data collection/analysis



Antonia S, et al. N Eng J Med 2018



### Would you consider Durva for EGFR mNSCLC Stage III

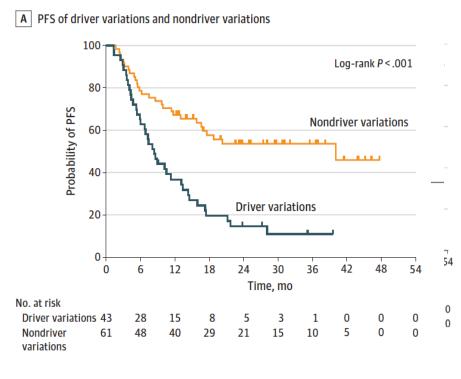
### Imfinzi has shown efficacy across all sub-groups

		os		
	No. of events / No	. of patients (%)		
	Durvalumab	Placebo		Unstratified HR (95% C
All patients	264/476 (55.5%)	155/237 (65.4%)	+●	0.72 (0.59-0.87)
Sex				
Male	192/334 (57.5%)	112/166 (67.5%)	⊢●	0.75 (0.59-0.95)
Female	72/142 (50.7%)	43/71 (60.6%)		0.64 (0.44-0.94)
Age at randomization				
<65 years	130/261 (49.8%)	79/130 (60.8%)	<b>⊢</b> •	0.66 (0.50-0.87)
≥65 years	134/215 (62.3%)	76/107 (71.0%)	<b>⊢•</b>	0.79 (0.60-1.05)
Smoking status				
Smoker	244/433 (56.4%)	140/216 (64.8%)		0.75 (0.61-0.93)
Non-smoker	20/43 (46.5%)	15/21 (71.4%)		0.42 (0.21-0.82)
Disease stage				
IIIA	136/252 (54.0%)	91/125 (72.8%)	⊢•	0.61 (0.47-0.80)
IIIB	121/212 (57.1%)	61/107 (57.0%)	<b>⊢•</b>	0.86 (0.63-1.17)
Tumor histologic type				
^- caroopiauri	177271481003/4	~~UNTO 2 FUTO 10/10/		^020 (~0.00±0.00±0.00±
EGFR mutation status				
Positive	17/29 (58.6%)	8/14 (57.1%)	1	0.85 (0.37-1.97)
	400.000.000.000			
Negative	166/317 (52.4%)	109/165 (66.1%)	+•	0.66 (0.52-0.84)
Unknown	81/130 (62.3%)	38/58 (65.5%)		0.85 (0.57-1.24)
PD-I 1 everession level				
PD-L1 expression level	01/130 (02.376)	30/30 (00.576)		0.55 (5.57 1.21)
>25%	51/115 (44.3%)	27/44 (61.4%)	<b>—</b>	0.52 (0.32-0.82)
<25%	111/187 (59.4%)	64/105 (61.0%)		0.90 (0.67-1.23)
Unknown	102/174 (58.6%)	64/88 (72.7%)		0.68 (0.50-0.93)
1–24% (post-hoc analysis)	52/97 (53.6%)	29/47 (61.7%)	-	0.73 (0.46–1.14)
≥1% (post-hoc analysis)	103/212 (48.6%)	56/91 (61.5%)		0.61 (0.44-0.85)
<1% (post-hoc analysis)	59/90 (65.6%)	35/58 (60.3%)		1.15 (0.75–1.75)
- 1 70 (prost-froe alialysis)	36/60 (03.076)	0.3		
		U.,	1 1.	

		PFS		
No. of events / N	o. of patients (%)			
Durvalumab	Placebo			Unstratified HR (95% C
268/476 (56.3%)	175/237 (73.8%)	₩H		0.58 (0.48-0.70)
192/334 (57.5%)	122/166 (73.5%)			0.61 (0.48-0.76)
76/142 (53.5%)	53/71 (74.6%)			0.52 (0.36-0.74)
140/261 (53.6%)	100/130 (76.9%)	<b>⊢</b>		0.46 (0.36-0.60)
128/215 (59.5%)	75/107 (70.1%)	-		0.76 (0.57-1.01)
246/433 (56.8%)	158/216 (73.1%)	₩		0.61 (0.50-0.75)
22/43 (51.2%)	17/21 (81.0%)	←—		0.33 (0.17-0.63)
132/252 (52.4%)	95/125 (76.0%)	⊷		0.53 (0.40-0.69)
130/212 (61.3%)	77/107 (72.0%)	<b>⊢</b>		0.64 (0.48-0.85)
12847786 (51,55%)	76/102 (79.5%)	<del></del>		VVI/0314V391,
21/29 (72.4%)	11/14 (78.6%)	-	-	0.82 (0.39–1.71)
169/317 (53.3%)	124/165 (75.2%)	₩		0.52 (0.41-0.65)
78/130 (60.0%)	40/58 (69.0%)		-	0.74 (0.51-1.09)
10/100 (00.076)	T0100 (00.070)			0.17 (0.01-1.00)
61/115 (53.0%)	33/44 (75.0%)			0.44 (0.29-0.67)
105/187 (56.1%)	77/105 (73.3%)	⊢•—		0.64 (0.48-0.86)
102/174 (58.6%)	65/88 (73.9%)	⊢•─		0.60 (0.44-0.82)
50/97 (51.5)	38/47 (76.6%)			0.51 (0.33-0.78)
111/212 (52.4%) 55/90 (61.1%)	69/91 (75.8%) 41/58 (70.7%)	<b>⊢</b>		0.47 (0.35–0.64)
(31.176)	11100 (10.176)	0.2 0.6 1	1.4 1.8 Placebo better	0.80 (0.53–1.20)



<sup>\*</sup>HRs and 95% CIs were not calculated if the subgroup had <20 events

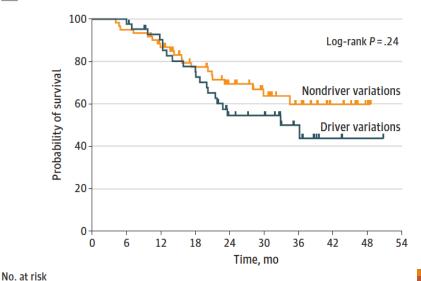




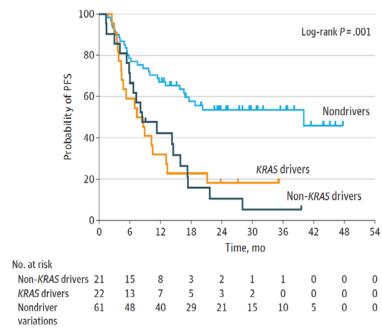
Driver variations 43

Nondriver

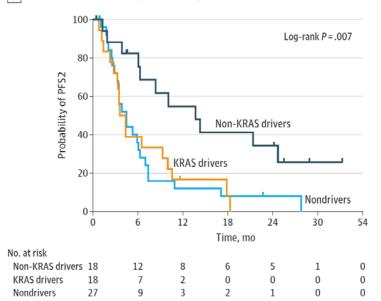
variations



B PFS of nondriver variations, KRAS drivers, and non-KRAS drivers



B PFS2 for non-KRAS drivers, KRAS drivers, and nondrivers





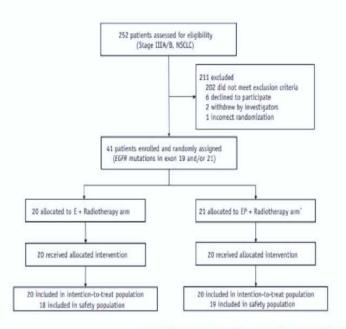
## Stage III NSCLC: Driver +

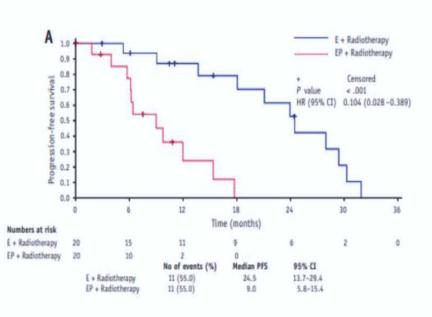
		Author	Туре	Time	Pathol	N	Regimen	%0RR	2- yrPFS	LRR	DMR	BMR	2-yr0S
	ر	Tanaka	Retrosp	06-13	ADK	28	P-based CTRT	72.4		14	76	35	
	population	Yagishita	Retrosp	01-10	Non Squam	34	P-based CTRT	79		4	80	16	
		Nakamura	Retrosp	06-16	Non Squam	34	P-based CTRT	-	10-25	53	85	29	~80
	EGFR+	Akamatsu	Retrosp	02-09	ADK	13	P-based CTRT	76.9		15	69	46	
		Hotta	Phase 2	11-17	NSCLC	20	Gefitinib+CTRT	85	36.9	10	65	30	90
þ		OLCSG0007	Phase 3	00-05	NSCLC	101	DPccTRT	78.8		38	37	35	60.3
EGFR unselected population	ation	Proclaim	Phase 3	08-12	Non Squam	301	PP or EPccTRT	35.9	20-30	58	50	19	52
		WJTOG0105	Phase 3	01-05	NSCLC	156	PCccTRT	63					*45
	рс	Pacific	Phase 3	14-16	NSCLC	473	CTRT_Durval	30	45	-	-	5	66.3
Ш						236	CTRT_Placebo	17.8	20	-	-	12	55.6



Erlotinib Versus Etoposide/Cisplatin With Radiation Therapy in Unresectable Stage III Epidermal Growth Factor Receptor Mutation-Positive Non-Small Cell Lung Cancer: A Multicenter, Randomized, Open-Label, Phase 2 Trial

Ligang Xing, MD, PhD • Gang Wu, MD, PhD • Luhua Wang, MD • ... Baolin Qu, MD • Wanqi Zhu, MD •







Median PFS of E + RT significantly > EP+RT (24.5 vs 9.0 mo) [hazard ratio, 0.104; 95% confidence interval, 0.028-0.389; P < .001]).

Xing, Red J, 2021





## **TOXICITY DATA**

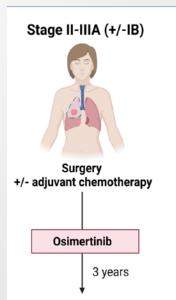
Table 3. Treatment Toxic Effects by Variation Status

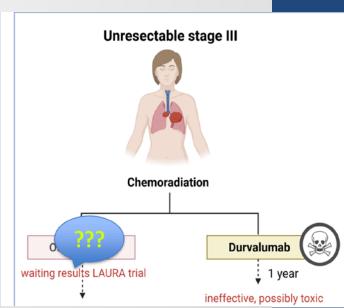
	No. (%)								
Toxic Effects	All patients (n = 104)	Non- $KRAS$ driver variations (n = 21)	KRAS driver variations (n = 22)	Nondriver variations (n = 61)	P value				
All toxicities									
Grade 2 or higher	78 (75.0)	17 (81.0)	17 (77.3)	44 (72.1)	.78				
Grade 3 or higher	24 (23.1)	6 (28.6)	5 (22.7)	13 (21.3)	.77				
Pneumonitis									
Grade 2 or higher	44 (42.3)	13 (61.9)	10 (45.5)	21 (34.4)	.09				
Grade 3 or higher	17 (16.3)	4 (19.0)	3 (13.6)	10 (16.4)	.87				
Dysphagia									
Grade 2 or higher	30 (28.8)	4 (19.0)	6 (27.3)	20 (32.8)	.53				
Grade 3 or higher	0	0	0	0	> .99				
Esophagitis									
Grade 2 or higher	48 (46.2)	9 (42.9)	9 (40.9)	30 (49.2)	.80				
Grade 3 or higher	2 (1.9)	0	0	2 (3.3)	> .99				
Pain									
Grade 2 or higher	25 (24.0)	4 (19.0)	3 (13.6)	18 (29.5)	.30				
Grade 3 or higher	3 (2.9)	0	0	3 (4.9)	.57				
Dermatitis									
Grade 2 or higher	12 (11.5)	2 (9.5)	2 (9.1)	8 (13.1)	> .99				
Grade 3 or higher	2 (1.9)	1 (4.8)	0	1 (1.6)	.41				
Arthritis									
Grade 2 or higher	1 (1.0)	1 (4.8)	0	0	.202				
Grade 3 or higher	0	0	0	0	> .99				
Diarrhea									
Grade 2 or higher	2 (1.9)	1 (4.8)	1 (4.5)	0	.169				
Grade 3 or higher	2 (1.9)	1 (4.8)	1 (4.5)	0	.17				
Anorexia									
Grade 2 or higher	6 (5.8)	0	1 (4.5)	5 (8.2)	.62				
Grade 3 or higher	1 (1.0)	0	0	1 (1.6)	> .99				
Dehydration									
Grade 2 or higher	3 (2.9)	0	0	3 (4.9)	.57				
Grade 3 or higher	1 (1.0)	0	0	1 (1.6)	> .99				
Fatigue									
Grade 2 or higher	9 (8.7)	0	2 (9.1)	7 (11.5)	.38				
Grade 3 or higher	0	0	0	0	> .99				



## Would you consider Durva for Driver positive mNSCLC Stage III

- Would you consider NGS for all driver mutation before considering consolidation Durva or only EGFR/ALK/ROS
- Would you consider mEGFR positive and other mutations separately for DURVA consolidation.
- Toxicity of Durva in Driver mut + mNSCLC ??
- FOR EGFR + mNSCLC
  - Observation after CTRT
  - Durva for 1 year
  - Osimertinib /Targeted after
     CTRT for 2 yrs (Laura Trial)





### Impact of grade ≥2 pneumonitis on patientreported outcomes (PROs) with durvalumab after chemoradiotherapy (CRT) in unresectable stage III NSCLC

Rina Hui,¹ Jarushka Naidoo,²-⁴ Marina C. Garassino,⁵.⁶ Helen Broadhurst,² Nikunj Patel,⁶ Michael Newton,⁶ Piruntha Thiyagarajah,⁶ Johan F. Vansteenkiste¹⁰

Figure 3. Changes in Scores for Prespecified PROs at Weeks 16 and 24 (from Baseline)



Figure 4. Confirmed TTD for PROs of Interest Adjusted for Time-dependent Grade ≥2 Pneumonitis

N	No. of events / No. of patients (%)			Hazard ratio		
	Durvalumab	Placebo			(95% CI)	
Global health status/QoL (C30)	208/470 (44.3)	118/232 (50.9)			0.74 (0.59–0.94) 0.72 (0.57–0.91) 0.70 (0.56–0.89)	
Physical functioning (C30)	190/472 (40.3)	94/232 (40.5)	<b>⊢</b>	—   -   -	0.95 (0.75–1.23) 0.91 (0.71–1.17) 0.91 (0.71–1.18)	
Cough symptom (LC13)	203/442 (45.9)	108/216 (50.0)	-	- <b>-</b>   -  	0.84 (0.66–1.07) 0.82 (0.65–1.04) 0.80 (0.63–1.03)	
Dyspnoea symptom (LC13)	276/467 (59.1)	134/230 (58.3)	<b>⊢</b> •		0.93 (0.75–1.14) 0.90 (0.73–1.11) 0.89 (0.72–1.10)	
Chest pain symptom (LC13)	162/463 (35.0)	94/229 (41.0)			0.75 (0.58–0.97) 0.74 (0.57–0.95) 0.74 (0.56–0.96)	
Haemoptysis symptom (LC13)	95/472 (20.1)	63/232 (27.2)		ı	0.65 (0.47–0.90) 0.62 (0.45–0.86) 0.59 (0.43–0.83)	
● ITT ● I	Model 1 • M	0.2 <b>←</b> lodel 2 <b>Durvalun</b>	0.6 1 nab better	1.4 Placebo	1.8 → better	

Model 1 (the base model) is a multivariable Cox model accounting for trial stratification factors (as used for the ITT analyses) and the time-dependent occurrence of grade ≥2 pneumonitis.

Model 2 is the base model plus additional factors :

stage
histology
best response to prior
therapy
PS
region
race





## PACIFIC Study – IO Pneumonitis or Radiation Pneumonitis

Pneumonitis (grouped terms)/radiation pneumonitis, n (%)*	Durvalumab (N=475)	Placebo (N=234)
Any grade	161 (33.9)	58 (24.8)
Grade 3/4	16 (3.4)	6 (2.6)
Grade 5	5 (1.1)	4 (1.7)
Leading to discontinuation	30 (6.3)	10 (4.3)

Safety analysis set (all-causality). \*Pneumonitis/radiation pneumonitis was assessed by investigators with subsequent review and adjudication by the study sponsor. In addition, pneumonitis, as reported in the table, is a grouped term, which includes acute interstitial pneumonitis, interstitial lung disease, pneumonitis, and pulmonary fibrosis.

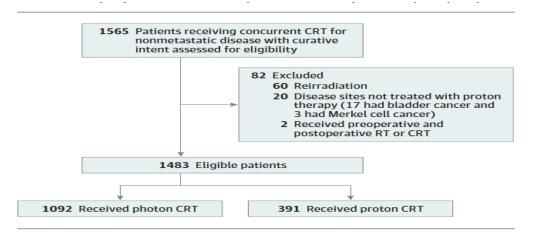
1. Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, et al. Durvalumab after Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer. New England Journal of Medicine [Internet]. 2017 Nov 16 [cited 2018 Mar 30];377(20):1919–29. Available from: <a href="https://doi.org/10.1056/NEJMoa1709937">https://doi.org/10.1056/NEJMoa1709937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

## How do you diagnose and manage pneumonitis on Durva maintenance



## Comparative Effectiveness of Proton vs Photon Therapy as Part of Concurrent Chemoradiotherapy for Locally Advanced Cancer

Brian C. Baumann, MD; Nandita Mitra, PhD; Joanna G. Harton, MS; Ying Xiao, PhD; Andrzej P. Wojcieszynski, MD;



Retrospective nonrandomized comparative effectiveness study

PRIMARY END PT

Figure 3. Adverse Events and Decline in Eastern Cooperative Oncology Group (ECOG) Performance Status for Proton vs Photon Chemoradiotherapy (CRT) and Propensity Analysis Results

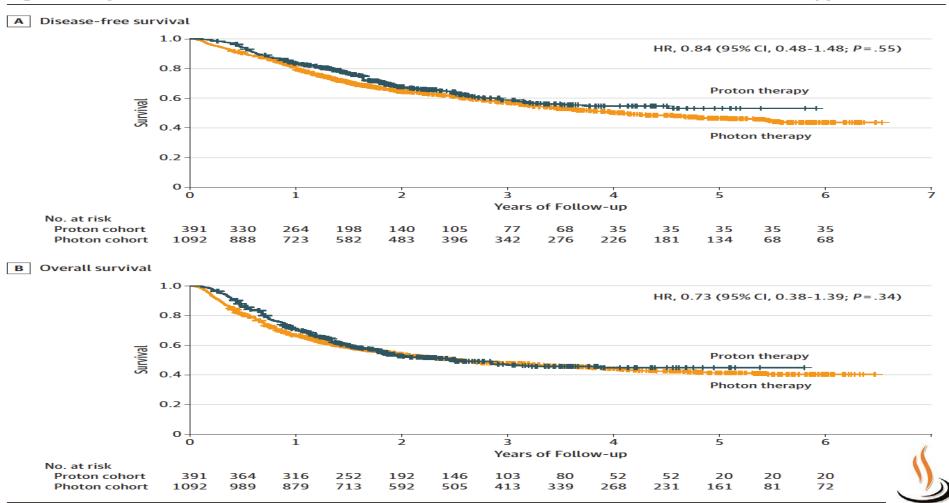
	Proton	CRT Group (n=391)	Photon	CRT Group (n = 1092)		Favors	Favors
Outcome	No. of Events	Percentage (95% CI)	No. of Events	Percentage (95% CI)	Relative Risk (95% CI)	i	Photon Therapy PVa
90-day Grade ≥3 adverse events	45	11.5% (8.3%-14.7%)	301	27.6% (24.9%-30.2%)	0.31 (0.15-0.66)		.002
90-day Grade ≥2 adverse events	290	74.2% (69.8%-78.5%)	926	84.8% (82.7%-86.9%)	0.78 (0.65-0.93)		.006
ECOG performance status decline	145	37.1% (32.3%-41.9%)	434	42.4% (39.4%-45.4%)	0.51 (0.37-0.71)		<.00
					0.1	0.5 1	1 2.0
					0.1	0. Relative Risk	

#### JAMA Oncology | Original Investigation

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Figure 4. Adjusted Disease-Free and Overall Survival for the Proton vs Photon Chemoradiotherapy Cohorts





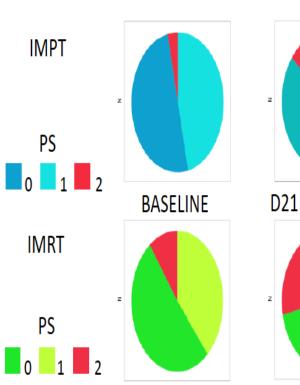
### Disclaimer: "This Document has been supplied under an AstraZeneca License. It is protected by copyright and it may not be further copied without permission, except as may be permitted by law". Proton-therapy and concurrent chemotherapy in stage III NSCLC: Effects on Durvalumab eligibility and safety profile

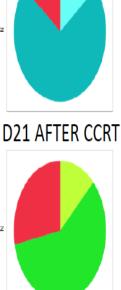


Francesco Cortiula<sup>1</sup>, Dirk De Ruysscher<sup>2</sup>, Safiye Dursun<sup>3</sup>, Michelle Steens<sup>4</sup>, Gerben Bootsma<sup>4</sup>, Richard Canters<sup>2</sup>, Ilaria Rinaldi<sup>2</sup>, Vicki Taasti<sup>2</sup>, Ruud Houben<sup>2</sup>, Kobe Reynders<sup>2</sup>, Stéphanie Peeters<sup>2</sup>, Antonio Angrisani<sup>2</sup>, Djoya Hattu<sup>2</sup> and Lizza Hendriks<sup>3</sup>

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Variable	Overall (n=67)	Protons (n= 28)	Photons (n=39)	p. value
Age – years Median (Range)	66 (35-79)	66 (35-77)	67 (49-79)	0.9
Male (%)	52.2	57.1	48.7	0.49
Tumor Stage - no. (%) IIIA IIIB IIIC	25 (37.3) 38 (56.7) 4 (6)	10 (35.7) 17 (60.7) 1 (3.6)	15 (38.5) 21 (53.8) 3 (7.7)	0.7
PD-L1 % 0-49 ≥ 50% Unknown	31 (46) 20 (30) 16 (24)	10 (35.7) 8 (28.8) 10 (35.7)	21 (53) 13 (33) 5 (12)	0.2
WHO PS after CCRT At day 21 (0-1/≥2)	80.6%/ 19.4%	92.9%/ 7.1%	71.8%/ 28.2%	0.032
Immune related adverse events - no. (%) Any grade Grade ≥ 3	18 (26.9) 5 (7.4)	6 (21.4) 3 (10)	12 (30.8) 2 (5)	0.062
Pneumonitis rate during Durvalumab - no. (%) Any grade Grade ≥ 3	16 (26) 4 (6)	7 (25) 2 (7)	9 (23) 2 (5.1)	0.8
Median FU - months	14	9.5	19.5	<0.001







## IMPT Vs IMRT : Stage III NSCLC

- Any experience ?
- Any particular scenario : Old age , large mass ,
   bulky mediastinum etc ?
- Prime time or would like more data to mature ?



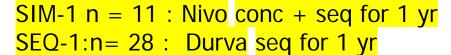


### Concurrent versus sequential immune checkpoint inhibition in stage III NSCLC patients treated with chemoradiation

Poster: #115

Author

Lukas Käsmann<sup>1,2,3</sup>, Julian Taugner<sup>1</sup>, Chukwuka Eze<sup>1</sup>, Julian Guggenberger<sup>1</sup>, Benedikt Flörsch<sup>1</sup>, Saskia Kenndoff<sup>1</sup>, Amanda Tufman<sup>4</sup>, Niels Reinmuth<sup>5</sup>, Claus Belka<sup>1,2,3</sup>, Farkhad Manapov<sup>1,2,3</sup>



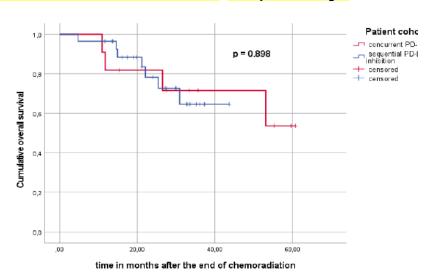


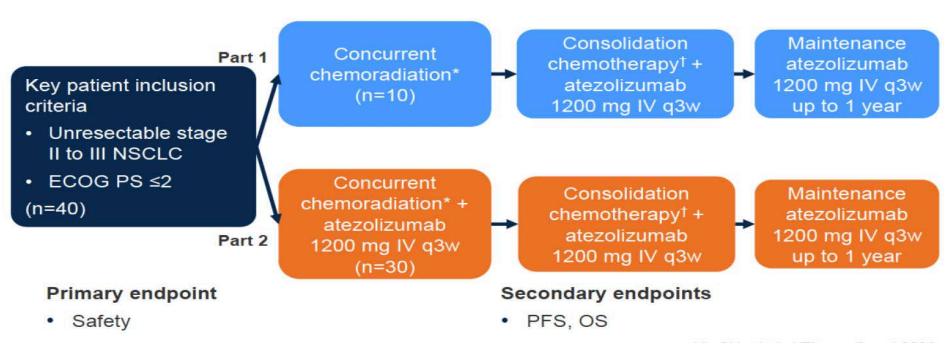
Figure I: Kaplan-Meier curves for overall survival according to concurrent versus sequential checkpoint in

Figure II: Kaplan-Meier curves for progression free survival according to concurrent versus sequential checkpoint inhibitio

In the SIM-I cohort, 18.2% of patients showed grade III radiogenic pneumonitis and in the SEQ-I cohort 14.3% (p=0.765). Grade 4 and 5 toxicities did not occur.

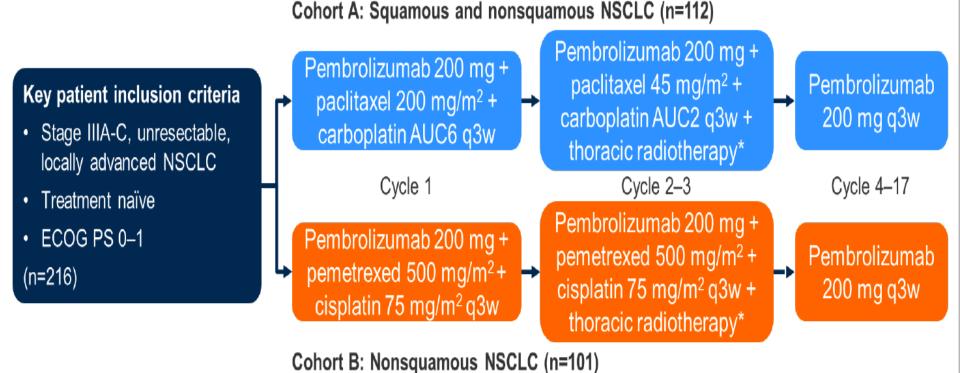
PFS at 12/24 months was 82 and 44% in the SIM-I cohort, respectively, and 63 and 59% in the SEQ-I cohort (p=0.583)

### ATEZO /CTRT IN STAGE III NSCLC



Grade ≥3 AEs, n (%)					
Part 1 (n=10)		Part 2 (n=30)			
Dyspnea (G3) Arthralgia (G3)	1 (10) 1 (10)	Diarrhea (G3); radiation pneumonitis (G3)	1 (3)		
Lung infection (G5);	1 (10)	Nephritis (G3), fatigue (G3)	1 (3)		
tracheoesophageal fistula (G5)		Fatigue (G3)	2(7)		
		Heart failure (G3)	1 (3)		
		Respiratory failure NOS (G4)	1 (3)		

### PEMBRO /CTRT IN STAGE III NSCLC



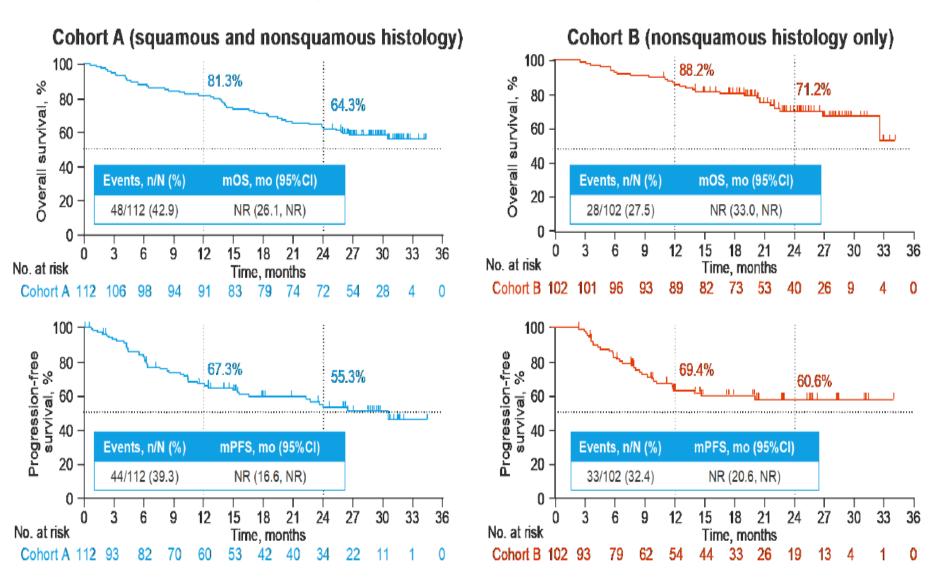
### **Primary endpoints**

- ORR (BICR, RECIST v1.1)
- Proportion developing grade ≥3 pneumonitis

### Secondary endpoints

PFS, OS, safety

## PEMBRO /CTRT IN STAGE III NSCLC



Reck M, et al. J Thorac Oncol 2021;16(suppl):Abstr OA02.03; update at 2 years, ASCO 2022

## PEMBRO /CTRT IN STAGE III NSCLC

AEs, n (%)	Cohort A (n=112)	Cohort B (n=102)
Grade ≥3 pneumonitis	9 (8.0)	7 (6.9)
TRAEs	105 (93.8)	99 (97.1)
Grade 3-5	72 (64.3)	52 (51.0)
Occurring in >10% Neutropenia Anemia	18 (16.1) 12 (10.7)	10 (9.8) 4 (3.9)
Led to death	4 (3.6)	1 (1.0)
Led to discontinuation	38 (33.9)	21 (20.6)
irAEs	58 (51.8)	46 (45.1)
Grade 3-5	18 (16.1)	9 (8.8)
Occurring in >10% Pneumonitis	7 (6.3)	6 (5.9)
Led to death	4 (3.6)	1 (1.0)
Led to discontinuation	21 (18.8)	12 (11.8)

## TAKE HOME MESSAGE: MONDAY MORNING STAGE 3 CTRT WITH IO

1: For Driver mutated mNSCLC: DURVA Yes or no, what all mutations would you consider for or against Durva

2: Would you continue Durva maintenance for GARDE I/II pneumonitis

3: Will you consider IMPT in any patient of yours with CTRT

4: Any concerns regarding Durva maintenance for patients undergoing

IMPT based CTRT

5:What will be the best way to combine IO with CTRT for the future



## International Journal of Molecular & ImmunoOncology

Online ISSN: 2456-3994

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