Dose Escalation of Radiation Therapy for Stage III Non-Small Cell Lung Cancer in the Era of Immunotherapy

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Disclosures

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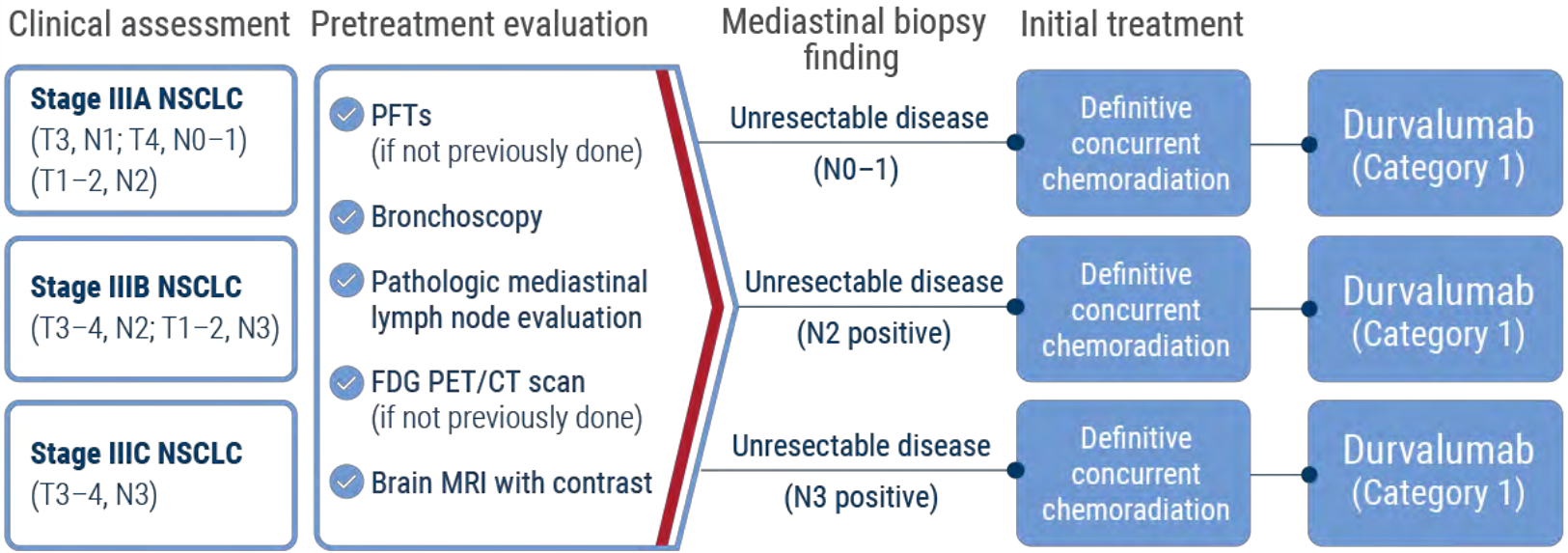
Overview

I. Review of current standard care of unresectable stage III NSCLC

I. Limitations of current standard care

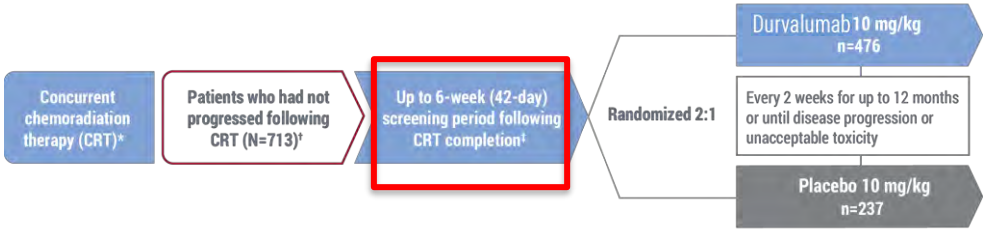
II. Discussion of dose escalation of radiotherapy in the era of immunotherapy for unresectable stage III NSCLC

dCRT→Durvalumab (Category 1) Recommended by NCCN for Unresectable Stage III NSCLC



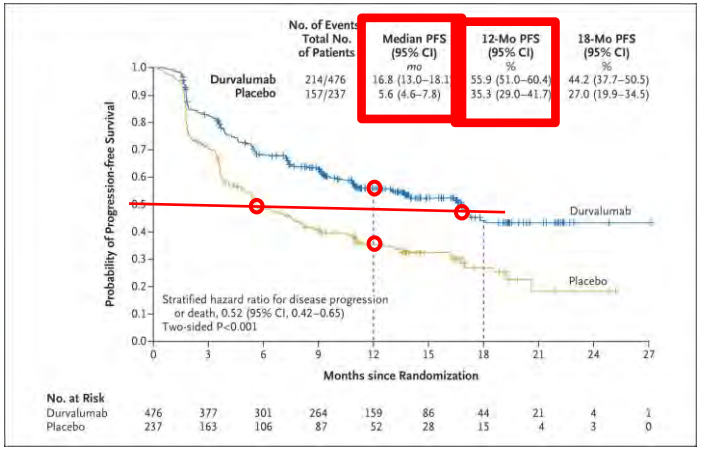
IO in Stage III NSCLC
PACIFIC Trial – Durvalumab after dCRT

Stage III NSCLC:

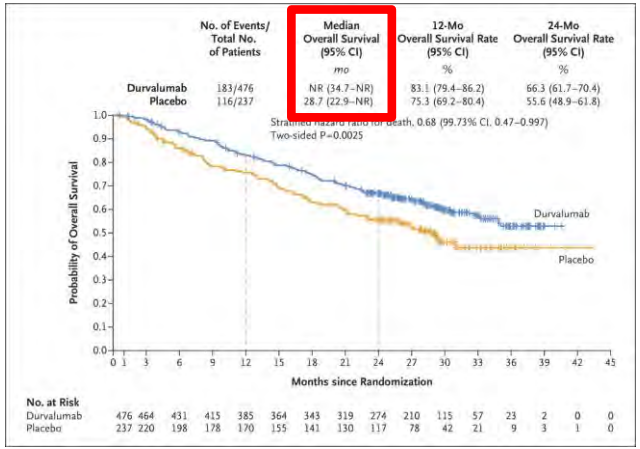


Coprimary endpoints:

- Progression-free survival (PFS)
- Overall survival (OS)



Progression-free Survival (ITT)

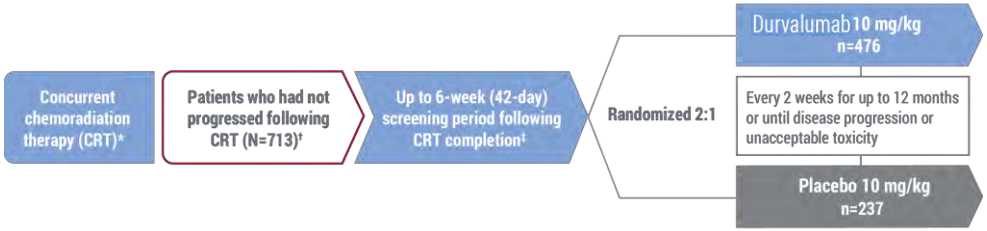


Overall Survival

Antonia et al., NEJM 2017, 2018

PACIFIC Trial – Durvalumab after dCRT

Stage III NSCLC:



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- Progression-free survival (PFS)
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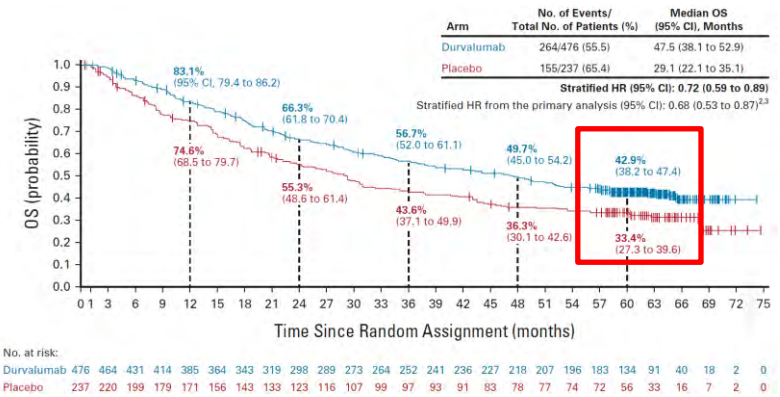
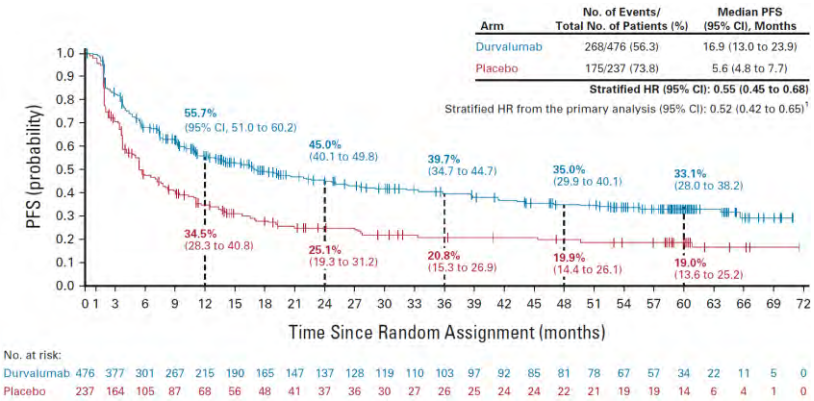




Spigel et al., JCO 2022

RT dose in PACIFIC Trial

Table 1. Baseline Characteristics, Stratification Factors, and Prior Therapy in the Intention-to-Treat Population.*

Characteristic	Durvalumab (N=476)	Placebo (N=237)	Total (N=713)
Age — yr			
Median	64	64	64
Range	31–84	23–90	23–90
Sex — no. (%)			
Male	334 (70.2)	166 (70.0)	500 (70.1)
Female	142 (29.8)	71 (30.0)	213 (29.9)
Race — no. (%)†			
White	337 (70.8)	157 (66.2)	494 (69.3)
Black	12 (2.5)	2 (0.8)	14 (2.0)
Asian	120 (25.2)	72 (30.4)	192 (26.9)
Disease stage — no. (%)			
IIIA	252 (52.9)	125 (52.7)	377 (52.9)
IIIB	212 (44.5)	107 (45.1)	319 (44.7)
Other‡	12 (2.5)	5 (2.1)	17 (2.4)
WHO performance-status score — no. (%)§			
0	234 (49.2)	114 (48.1)	348 (48.8)
1	240 (50.4)	122 (51.5)	362 (50.8)
Tumor histologic type — no. (%)			
Squamous	224 (47.1)	102 (43.0)	326 (45.7)
Nonsquamous	252 (52.9)	135 (57.0)	387 (54.3)
Smoking status — no. (%)			
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)
Previous radiotherapy — no. (%)¶			
<54 Gy	3 (0.6)	0	3 (0.4)
≥54 to ≤66 Gy	442 (92.9)	217 (91.6)	659 (92.4)
>66 to ≤74 Gy	30 (6.3)	19 (8.0)	49 (6.9)
Previous chemotherapy — no. (%)‖			
Induction	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 chemoradiotherapy — no. (%)			
Complete response	9 (1.9)	7 (3.0)	16 (2.2)
Partial response	232 (48.7)	111 (46.8)	343 (48.1)
Stable disease	222 (46.6)	114 (48.1)	336 (47.1)

Radiation Pneumonitis

PACIFIC Trial – Durvalumab after cCRT: Safety

Table 3. Adverse Events of Any Cause.

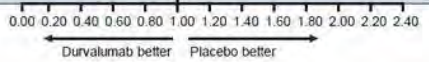
Event	Durvalumab (N=475)		Placebo (N=234)	
	Any Grade*	Grade 3 or 4	Any Grade*	Grade 3 or 4
	number of patients with event (percent)			
Any event	460 (96.8)	142 (29.9)	222 (94.9)	61 (26.1)
Cough	168 (35.4)	2 (0.4)	59 (25.2)	1 (0.4)
Pneumonitis or radiation pneumonitis†	161 (33.9)	16 (3.4)	58 (24.8)	6 (2.6)
Fatigue	113 (23.8)	1 (0.2)	48 (20.5)	3 (1.3)
Dyspnea	106 (22.3)	7 (1.5)	56 (23.9)	6 (2.6)
Diarrhea	87 (18.3)	3 (0.6)	44 (18.8)	3 (1.3)
Pyrexia	70 (14.7)	1 (0.2)	21 (9.0)	0
Decreased appetite	68 (14.3)	1 (0.2)	30 (12.8)	2 (0.9)
Nausea	66 (13.9)	0	31 (13.2)	0
Pneumonia	62 (13.1)	21 (4.4)	18 (7.7)	9 (3.8)
Arthralgia	59 (12.4)	0	26 (11.1)	0
Pruritus	58 (12.2)	0	11 (4.7)	0
Rash	58 (12.2)	1 (0.2)	17 (7.3)	0
Upper respiratory tract infection	58 (12.2)	1 (0.2)	23 (9.8)	0
Constipation	56 (11.8)	1 (0.2)	20 (8.5)	0
Hypothyroidism	55 (11.6)	1 (0.2)	4 (1.7)	0
Headache	52 (10.9)	1 (0.2)	21 (9.0)	2 (0.9)
Asthenia	51 (10.7)	3 (0.6)	31 (13.2)	1 (0.4)
Back pain	50 (10.5)	1 (0.2)	27 (11.5)	1 (0.4)
Musculoskeletal pain	39 (8.2)	3 (0.6)	24 (10.3)	1 (0.4)
Anemia	36 (7.6)	14 (2.9)	25 (10.7)	8 (3.4)

Antonia et al., NEJM 2017; NEJM 2018

Limitations of PACIFIC Trial Results

OS by Subgroup Analysis (ITT)

		Durvalumab No. of events / No. of patients (%)	Placebo No. of events / No. of patients (%)	Unstratified HR* (95% CI)
	All patients	183/476 (38.4)	116/237 (48.9)	0.68 (0.54–0.86)
Sex	Male	141/334 (42.2)	80/166 (48.2)	0.78 (0.59–1.03)
	Female	42/142 (29.6)	36/71 (50.7)	0.46 (0.30–0.73)
Age at randomization	<65 years	89/261 (34.1)	58/130 (44.6)	0.62 (0.44–0.86)
	≥65 years	94/215 (43.7)	58/107 (54.2)	0.76 (0.55–1.06)
Smoking status	Smoker	169/433 (39.0)	103/216 (47.7)	0.72 (0.56–0.92)
	Non-smoker	14/43 (32.6)	13/21 (61.9)	0.35 (0.16–0.76)
Disease stage	Stage IIIA	101/252 (40.1)	70/125 (56.0)	0.63 (0.46–0.85)
	Stage IIIB	79/212 (37.3)	44/107 (41.1)	0.77 (0.53–1.11)
Tumor histologic type	Squamous	103/224 (46.0)	56/102 (54.9)	0.72 (0.52–0.99)
	Non-squamous	80/252 (31.7)	60/135 (44.4)	0.61 (0.44–0.86)
Best response to prior treatment	CR	2/9 (22.2)	3/7 (42.9)	–
	PR	83/237 (35.0)	50/112 (44.6)	0.69 (0.49–0.99)
	SD	93/223 (41.7)	61/115 (53.0)	0.66 (0.48–0.91)
PD-L1 status	≥25%	37/115 (32.2)	23/44 (52.3)	0.46 (0.27–0.78)
	<25%	74/187 (39.6)	41/105 (39.0)	0.92 (0.63–1.34)
	Unknown	72/174 (41.4)	52/88 (59.1)	0.62 (0.43–0.89)
	≥1%†	70/212 (33.0)	45/91 (49.5)	0.53 (0.36–0.77)
	1–24%†	33/97 (34.0)	22/47 (46.8)	0.60 (0.35–1.03)
	<1%†	41/90 (45.6)	19/58 (32.8)	1.36 (0.79–2.34)
EGFR status	Positive	10/29 (34.5)	6/14 (42.9)	–
	Negative	117/317 (36.9)	80/165 (48.5)	0.64 (0.48–0.86)
	Unknown	56/130 (43.1)	30/58 (51.7)	0.77 (0.49–1.20)



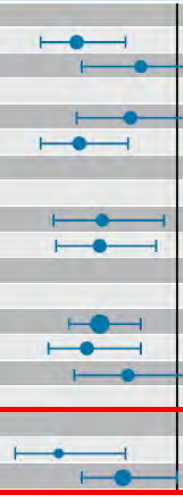
*Not calculated if the subgroup has less than 20 events
†Assessed as part of exploratory post-hoc analyses

Antonia et al., NEJM 2017, 2018

Limitations of PACIFIC Trial Results

OS by Subgroup Analysis (ITT)

Group	No. of Events / No. of Patients (%) Durvalumab	Placebo	Unstratified HR (95% CI)
NSCLC disease stage			
IIIA	136/252 (54.0)	91/125 (72.8)	0.61 (0.47 to 0.80)
IIIB	121/212 (57.1)	61/107 (57.0)	0.86 (0.63 to 1.17)
Tumor histologic type			
Squamous	138/224 (61.6)	67/102 (65.7)	0.82 (0.61 to 1.09)
All other	126/252 (50.0)	88/135 (65.2)	0.62 (0.47 to 0.81)
Best response to prior treatment			
Complete response	6/9 (66.7)	3/7 (42.9)	Not calculated[a]
Partial response	118/237 (49.8)	68/112 (60.7)	0.71 (0.52 to 0.95)
Stable disease	135/223 (60.5)	81/115 (70.4)	0.70 (0.53 to 0.92)
Prior chemotherapy type			
Gemcitabine-based	5/9 (55.6)	2/5 (40.0)	Not calculated[a]
Non–gemcitabine-based	259/467 (55.5)	153/232 (65.9)	0.70 (0.58 to 0.86)
Cisplatin	134/266 (50.4)	81/129 (62.8)	0.65 (0.50 to 0.86)
Carboplatin	121/199 (60.8)	69/102 (67.6)	0.81 (0.60 to 1.09)
Cisplatin and carboplatin	6/8 (75.0)	4/5 (80.0)	Not calculated[a]
Last radiation to random assignment			
< 14 days	64/120 (53.3)	43/62 (69.4)	0.54 (0.37 to 0.80)
≥ 14 days	200/356 (56.2)	112/175 (64.0)	0.79 (0.63 to 1.00)



Spigel et al., JCO 2022

Limitations of PACIFIC Results

Incidence of new lesions (%) in the ITT population at first planned PFS and OS analyses

New lesion site*	First planned PFS analysis[2]		First planned OS analysis[3]	
	Durvalumab (n=476)	Placebo (n=237)	Durvalumab (n=476)	Placebo (n=237)
Any site	20%	32%	23%	34%
Lung	12%	17%	13%	19%
Lymph nodes	6%	11%	7%	11%
Brain	6%	11%	6%	12%
Other	2%	2%	2%	2%

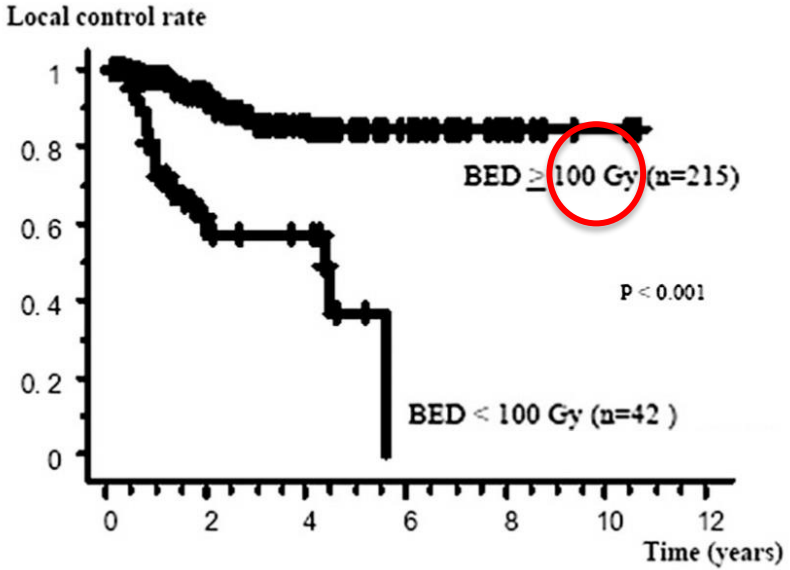
Which means: **60%** of all failure sites were in the lung even with durvalumab !

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

With longer follow-up (22 months)

Biological Effective Dose (BED) and Lung Tumor Control

- Onishi, Japan (*Cancer* October, 2004)
- Retrospective multi-institutional study
- 273 patients with Stage I tumors
- Dose was 18 – 75 Gy in 1 – 22 fractions
  - BED ranged from 57 – 180 Gy
- Complication rate 2.4%
- Local failure in 12.5%
  - Improved in good PS patients receiving > 100 Gy BED



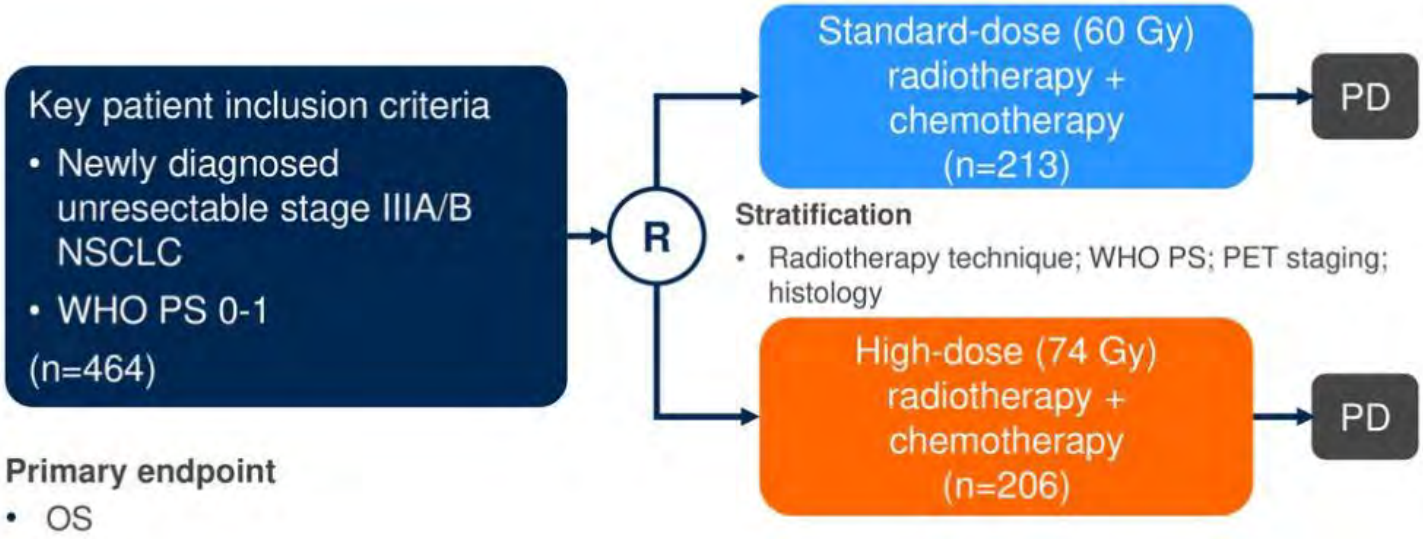
60Gy in 30 fractions (2Gy/fx): BED = 72Gy

Onishi, et al., *J Thor Onc*, 2007

RTOG 0617:

Dose escalation by conventional fractionated RT in the era of Pre-immunotherapy

Long-Term Results of NRG Oncology RTOG 0617:
Standard- Versus High-Dose Chemoradiotherapy With or Without Cetuximab for Unresectable Stage III Non–Small-Cell Lung Cancer



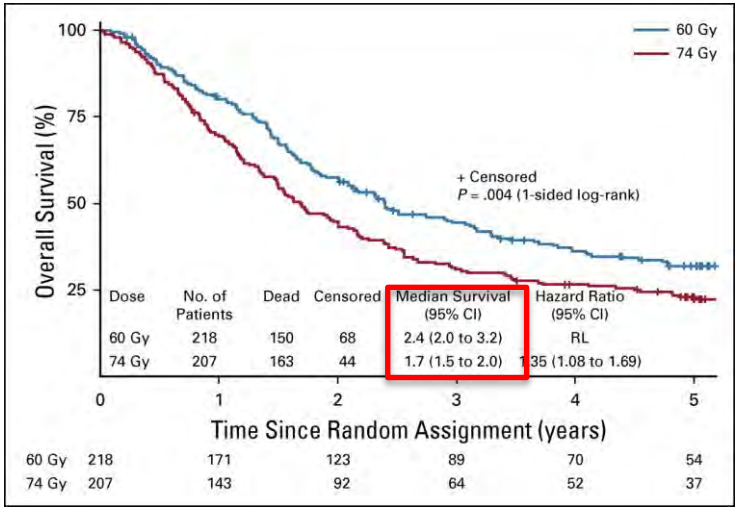
74Gy in 37 fractions (2Gy/fx): BED = 89Gy

Bradley et al., JCO 2020

RTOG 0617

Long-Term Results of NRG Oncology RTOG 0617:

Standard- Versus High-Dose Chemoradiotherapy With or Without Cetuximab for Unresectable Stage III Non–Small-Cell Lung Cancer



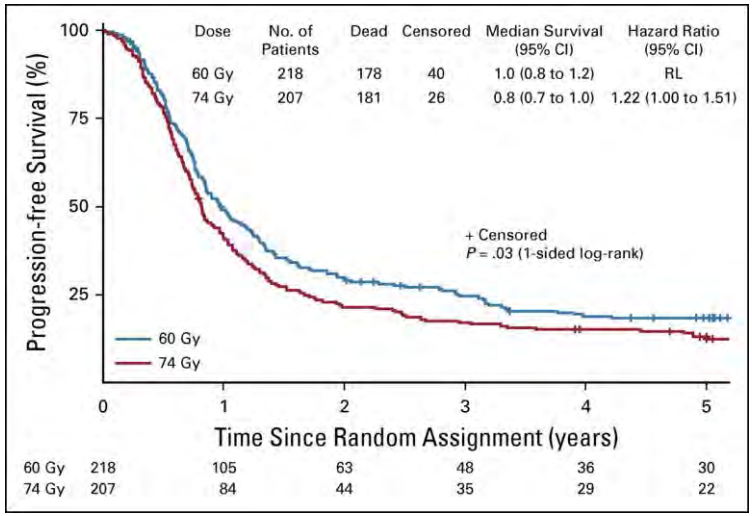


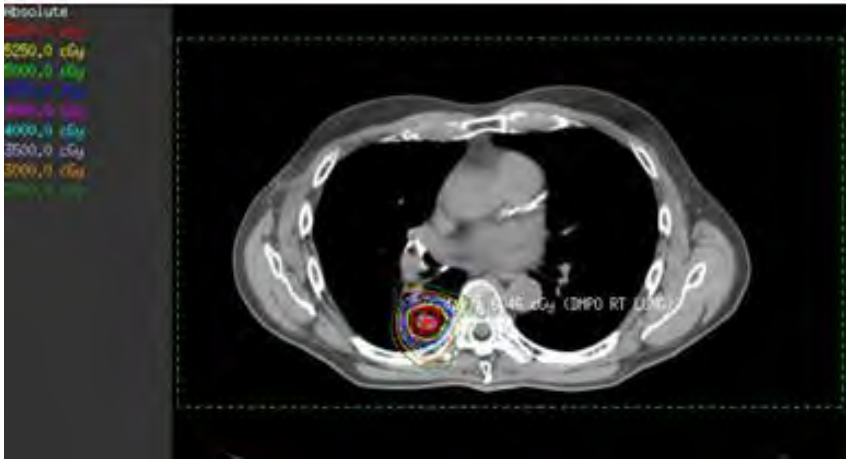
TABLE 3. Patterns of Failure at 5 Years

	Standard Dose (60 Gy)		High Dose (74 Gy)		
Failure Pattern	**Failed, % (95% CI)**	**No. at Risk**	**Failed, % (95% CI)**	**No. at Risk**	***P***
Local	38.2 (31.7 to 44.8)	40	45.7 (38.7 to 52.4)	27	.07
Regional	35.7 (29.3 to 42.2)	37	38.4 (31.7 to 45.0)	27	.54
Locoregional	49.7 (42.8 to 56.3)	34	55.4 (48.3 to 61.9)	25	.17
Distant	52.3 (45.3 to 58.8)	36	57.6 (50.4 to 64.1)	24	.32

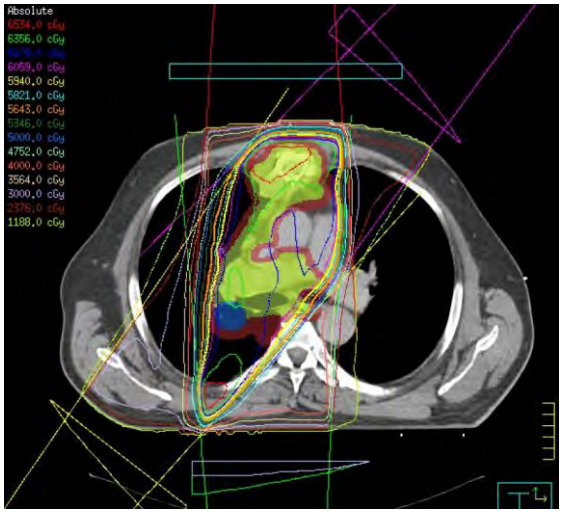
Bradley et al., JCO 2020

Volume of RT field

SBRT (stage I NSCLC)



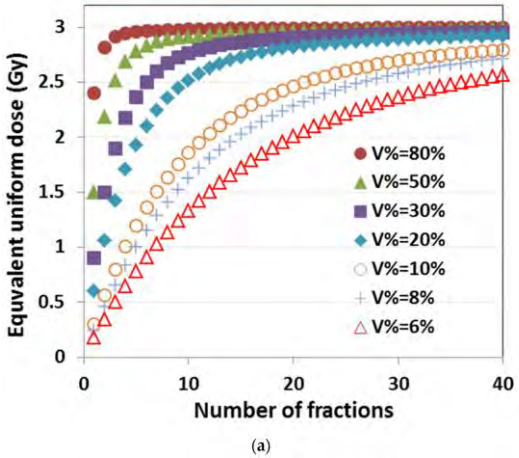
3DCRT (stage III NSCLC

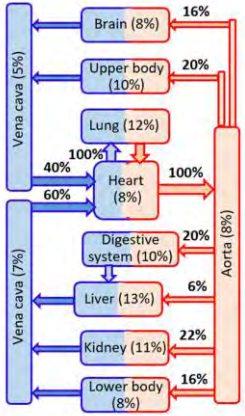


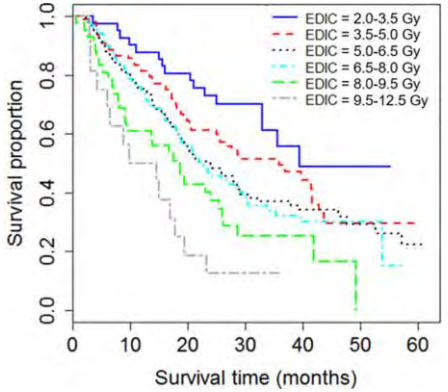
Effective radiation Dose to the Immune Cells (EDIC)

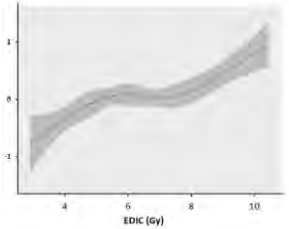
Higher Radiation Dose to the Immune Cells Correlates with Worse Tumor Control and Overall Survival, a secondary study of a phase III trial, NRG/RTOG 0617

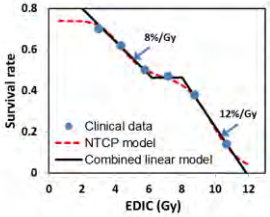
$$\boldsymbol{EDIC}=B_1\%*MLD+B_2\%*MHD+[B_3\%+B_4\%*k_1*(n\ /\ 45)^{0.5}]*ITDV/(61.8*10^3)$$











Jin et al., Cancers 2021

Effective radiation Dose to the Immune Cells (EDIC)

Higher Radiation Dose to the Immune Cells Correlates with Worse Tumor Control and Overall Survival, a secondary study of a phase III trial, NRG/RTOG 0617

Immune system should be considered as a critical organ at risk (OAR) for RT planning in practice !

Jin et al., Cancers 2021

Is It Safe to dose escalate of RT from 60Gy?

Only small scaled studies have looked into the safety of RT dose escalation when combined with IO.

Wass et al., 2022 (Europe): 78 patients; compared an RT dose of 73.5 Gy with 66 Gy followed by durvalumab and reported no difference in local control, regional control, and distant control. The authors concluded that RT dose escalation could safely be combined with durvalumab.

Landman et al., 2021 (Israel): 39 patients with stage III NSCLC who received RT dose >66 Gy followed by durvalumab, reported that this regimen is safe.

- Also possibly effective as thoracic failure was 21%, and 12-month OS was 79%.
- In contrast, in the PACIFIC trial, thoracic failure was 38%, and 12-months OS was 81%.

However, it remains inconclusive whether the safe intermediate escalated dose is beneficial in prolonging survival.

Table 4. Reported adverse events in 39 patients with stage III NSCLC during durvalumab therapy

Adverse event	Value
Fatigue	30 (77%)
Dyspnea	28 (72%)
Endocrine changes	18 (46%)
Hepatitis	14 (36%)
Diarrhea	5 (13%)
Nausea	4 (10%)
Patients with any grade 3–5 adverse event	14 (36%)
Immune related	
Pneumonitis	6 (15%)
Hepatitis	2 (5%)
Arthralgia	1 (3%)
Pericarditis	1 (3%)
Immune-related mortality – 1(3%) grade 5 pneumonitis	
Nonimmune related	
Pneumonia 2 – grade 3	
Anemia 1 – grade 3	
Acute myocardial infarction 1 – grade 5	
Massive hemoptysis 1 – grade 5	

Kumar et al., IJROBP 2017

Is it beneficial to dose escalate for dCRT → IO for stage III NSCLC?

- No prospective study!

- We thus conducted studies on NCDB.
  - The NCDB is a nationwide oncology outcomes database for more than 1500 Commission on Cancer-accredited cancer programs in the United States and Puerto Rico.
  - It is a multi-center hospital-based cancer registry, which collects >70% of cancer cases diagnosed in the U.S. annually from hospital cancer registries across the country. De-identified data were used

Is it beneficial to dose escalate for dCRT → IO for stage III NSCLC?

Study Population

Patients aged 18 and older who received definitive concurrent chemoradiation (within 30 days of each other) and were diagnosed with stage III NSCLC between 2004-2020 were included. All patients received multiagent chemotherapy. Patients with RT dose <57 Gy or >74 Gy were also excluded.

We divided the study population into two cohorts. The cohort before the era of immunotherapy included patients diagnosed between 2004 and 2016, while the cohort after the era of immunotherapy included patients diagnosed with unresectable stage III NSCLC between 2017 and 2020.

For the immunotherapy cohort, patients who started immunotherapy before the completion of RT or >180 days after RT completion or started chemotherapy and radiation non-concurrently (>30 apart) were excluded.

Is it beneficial to dose escalate for dCRT → IO for stage III NSCLC?

The sample size for the cohort before the era of immunotherapy included (47,315) patients, while the immunotherapy cohort included (4749) patients.

RT dose of 57-63 Gy were considered as standard dose (SD);

RT dose of 64-74 Gy were considered as intermediately dose escalation (IDE).

Amin et al., and Zhang, submitted

Dose escalate for dCRT for stage III NSCLC, pre-IO

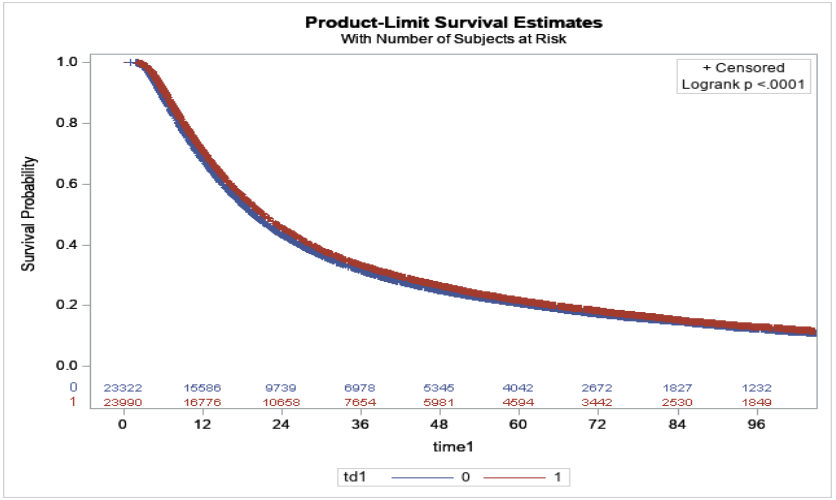
Statistically significant beneficial of dose escalate for dCRT for stage III NSCLC without immunotherapy

The median survival time:

19.7 (95% CI: 19.3-20.0) months for SD group **(57-63 Gy)** vs.

21.2 (95% CI: 20.8-21.5) months for IDE group **(64-74 Gy)**

($p < 0.0001$)



Amin et al., and Zhang, submitted

Dose escalate for dCRT for stage III NSCLC, with IO

Variable		The era of immunotherapy (2017-2020)			
		57-63 Gy N=3,210 (67.6%)	64-74 Gy N= 1,539 (32.4%)	Total N=4749	p
Age at diagnosis	(median and ranges)	67 (29-90)	66 (21-90)	67 (21-90)	0.22
Sex	Male	1,744 (54.3)	890 (57.8)	2,634 (55.5)	0.02
	Female	1,466 (45.7)	649 (42.2)	2,115 (44.5)	
Race	White	2,690 (84.2)	1,286 (83.8)	3976 (84.1)	0.12
	Black	387 (12.1)	206 (13.2)	593 (12.5)	
	Non-White non-Black	118 (3.7)	44 (3.0)	160 (3.4)	
Histology	Adenocarcinoma	1,446 (45.0)	703 (45.7)	2,149 (45.2)	0.98
	Squamous cell carcinoma	1,638 (51.0)	777 (50.5)	2,415 (50.8)	
	Large cell carcinoma	31 (1.0)	14 (0.9)	45 (1.0)	
	Undifferentiated	95 (3.0)	45 (2.9)	140 (3.0)	
Charlson/Deyo comorbidity score	0	1,841 (57.4)	867 (56.3)	2,708 (57.0)	0.14
	1	823 (25.6)	375 (24.4)	1,198 (25.2)	
	≥2	546 (17.0)	297 (19.3)	843 (17.8)	

Variable		The era of immunotherapy (2017-2020)			
		57-63 Gy N=3,210 (67.6%)	64-74 Gy N= 1,539 (32.4%)	Total N=4749	p
Neighborhood education level	≥10.9% NHD	1,333(49.3)	746 (58.3)	2,089 (52.2)	0.001
	<10.9% NHD	1,372 (50.7)	541 (41.7)	1,913 (47.8)	
Household income	<$50,353	1,251 (46.3)	706 (54.4)	1,957 (49.0)	0.001
	≥$50,353	1,449 (53.7)	591 (45.6)	2,040 (51.0)	
Treatment facility type	Academic	895 (28.0)	364 (23.8)	1,259 (26.6)	0.003
	Community	2,305 (72.0)	1,165 (76.2)	3,472 (73.4)	
Immunotherapy sequence with RT	≤ 42 days of RT completion	1,857 (57.9)	902 (58.6)	2,759 (58.0)	0.2
	43-70 days of RT completion	922 (28.7)	409 (26.6)	1,331 (33.8)	
	>70 days of RT completion	431 (13.4)	228 (14.8)	659 (8.2)	
Immunotherapy sequence with chemo	≤ 70 days after the start of chemo	778 (24.2)	283 (18.4)	1,061 (13.6)	0.001
	71-98 days after the start of chemo	1507 (47.0)	704 (35.9)	2,211 (50.0)	
	>98 days after the start of chemo	925 (28.8)	552 (41.9)	1,477 (36.4)	

Dose escalate for dCRT for stage III NSCLC, with IO

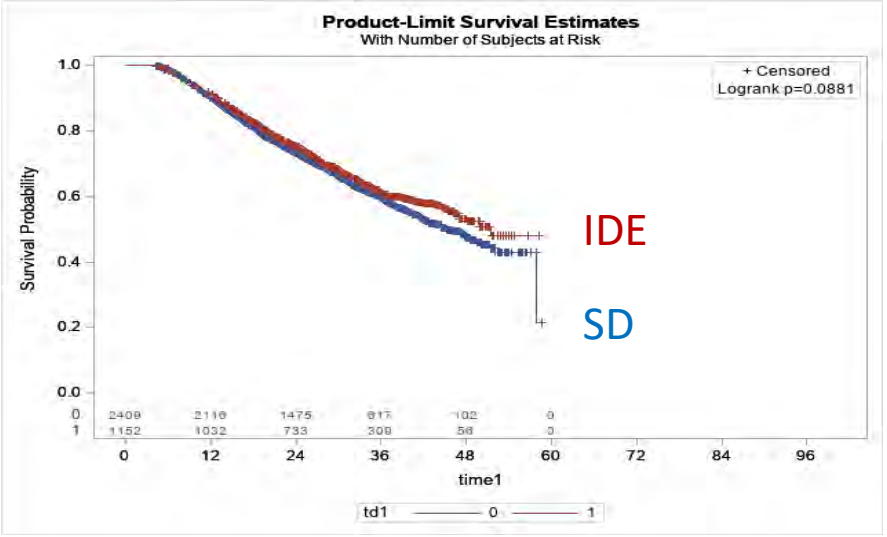
Stage III NSCLC (2017 and 2020) who received definitive CRT and adjuvant IO, the median follow-up time was 31 months.

Median survival time: 47.7 months.

45.2 (95% CI: 42.2-49.5) months for SD group **(57-63 Gy)** vs.

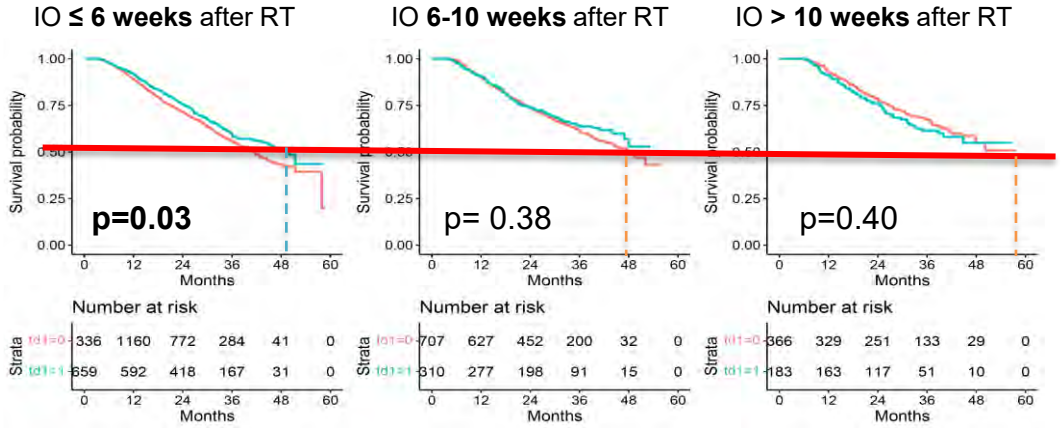
51.4 (95% CI: 46.9-NR) months for IDE group **(64-74 Gy)**

(p = 0.0881)



Amin et al., and Zhang, submitted

OS benefit of IDE for dCRT → IO is limited to early start of IO



Blue: IDE (64-74Gy)
Orange: SD (57-63Gy)

Median OS:

41.5 months (SD)	47.7 (SD)	Not reached (SD)
48.9 months (IDE)	Not reached (IDE)	Not reached (IDE)

Amin et al., and Zhang, submitted

OS benefit of IDE for dCRT → IO is limited to early start of IO

Hazard ratio of RT doses for all-cause mortality stratified by immunotherapy time after RT completion

Variable	Categories	HR 95% CI	P
Immunotherapy within 6 weeks of RT completion (42 days)			
RT dose	57-63 Gy	1.27 (1.08-1.51)	**0.005**
	64-74 Gy	Ref	
Immunotherapy between 7-10 weeks (43-70 days) after RT completion			
RT dose	57-63 Gy	1.13 (0.88-1.45)	0.35
	64-74 Gy	Ref	
Immunotherapy >10 weeks (70 days) after RT completion			
RT dose	57-63 Gy	0.82 (0.58-1.17)	0.28
	64-74 Gy	Ref	

The multivariable analysis was adjusted for age at diagnosis, gender, race, income, education, histology, comorbidity score, and treatment facility type.

Amin et al., and Zhang, submitted

Hypothesis #1

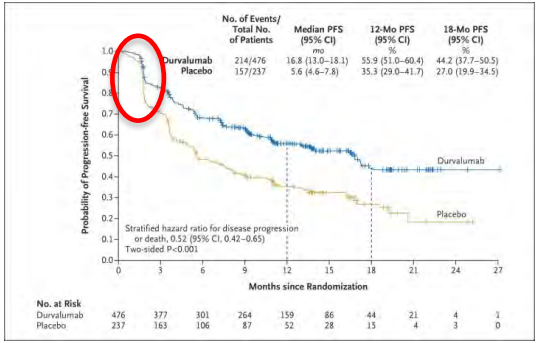
Early start of IO, i.e, IO ≤ 6 weeks after RT completion, is a surrogate for better performance status and favored by physicians to offer IDE.

Counter argument: it is less likely to be the case as the proportion of patients with a comorbidity score of zero, one, and two was similar between these two groups

Variable		The era of immunotherapy (2017-2020)			
		Dose 57-63 Gy N=3,210 (67.6%)	Dose 64-74 Gy N= 1,539 (32.4%)	Total N=4749	p
Charlson/Deyo comorbidity score	0	1,841 (57.4)	867 (56.3)	2,708 (57.0)	0.14
	1	823 (25.6)	375 (24.4)	1,198 (25.2)	
	≥2	546 (17.0)	297 (19.3)	843 (17.8)	

Amin et al., and Zhang, submitted

Hypothesis #2



Starting immunotherapy early or too soon after completing CRT may under counting those patients who develop early disease progression during or soon after CRT. IDE could have reduced these early failures thus provides an OS benefit.

Counter argument:

It is particularly uncommon these days with restaging imaging such as CT scans of the body becoming a routine practice before starting immunotherapy.

It is also interesting to point out that further analysis demonstrates that the survival benefits of IDE is limited to patients started immunotherapy within 2 weeks of completion of RT (HR: 2.19, 95% CI: 1.32-3.62, p=0.002 standard dose vs. IDE) with a 2-year survival rate of **65%** (95% CI: 57%-73%) and **84%** (95% CI: 76%-92%) for standard dose vs. IDE.

Hypothesis #3

dCRT may significantly affect the immune system which requires time (>4-6 weeks?) to recover before immunotherapy can take full effects.

This hypothesis fits our results the best with better OS observed when starting immunotherapy later with at least six weeks of interval from completion of RT in either standard or intermediate escalated dose of RT, and diminished OS benefit of IDE of RT when starting immunotherapy later than sooner.

Counter argument: PACIFIC trial

Group	No. of Events / No. of Patients (%) Durvalumab	Placebo	Unstratified HR (95% CI)
Last radiation to random assignment			
< 14 days	64/120 (53.3)	43/62 (69.4)	0.54 (0.37 to 0.80)
≥ 14 days	200/356 (56.2)	112/175 (64.0)	0.79 (0.63 to 1.00)

Spigel et al., JCO 2022

Summary

- Adjuvant IO after dCRT is now category 1 recommended therapy for unresectable stage III NSCLC.
- Local, regional and distant failure rate still high, close to 50% within the first two years.
- Majority of progression after dCRT and IO is still within lung/primary tumor.
- Dose escalation in the era of IO for unresectable stage III NSCLC is under studied. It may dampen immune system by over irradiating circulating immune cells.
- Our data from NCDB presented the largest cohort study which indicate the benefit of delayed started of IO (>6 weeks after completion of RT) after dCRT which may avoid the need of dose escalation.
- Prospective data!

Acknowledgement

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QUESTIONS?

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