Supplemental Online Content

Jabbour SK, Lee KH, Frost N, et al. Pembrolizumab plus concurrent chemoradiation therapy in patients with unresectable, locally advanced, stage III non–small cell lung cancer: the phase 2 KEYNOTE-799 nonrandomized trial. *JAMA Oncol*. Published online June 4, 2021. doi:10.1001/jamaoncol.2021.2301

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods. Additional thoracic radiotherapy details.

Patients in both cohorts A and B received concurrent thoracic radiotherapy (TRT) using a standardized 3-dimensional conformal radiotherapy (3DCRT) or intensity modulated radiation therapy (IMRT) technique on a linear accelerator operating at beam energy of ≥6 MV. While 6 MV photons were preferred, 10 MV photons were also permitted. Use of photon energies >10 MV was allowed but discouraged. The target total dose of TRT was 60 Gy in 30 daily fractions of 2 Gy, to the planning target volume (PTV), as detailed in the study protocol section 8.1.9.2 (online-only supplement). Proton treatment was not allowed. The treatment plan was normalized such that 95% of the prescription dose covered ≥99% of the PTV (V57 >99%). All radiation doses were calculated with inhomogeneity corrections that took into account the density differences within the irradiated volume (that is, air in the lung and bone). No more than 0.03 cc of the PTV received >120% of the prescription dose (maximum dose constraint). A summary of protocol constraints and compliance criteria is provided below. This study required a pretreatment review of the treatment plan for each patient that was evaluated by the central vendor, QARC (who performed a posttreatment review also).

Table. Summary of protocol constraints and compliance criteria for thoracic radiotherapy

Structure	Metric	Per protocol	Variation acceptable	Deviation acceptable
PTV	V60Gy	≥95%	≥90%	<90%
	Minimum dose (D99%)	≥55.8 Gy (93%) ≥57 Gy (95%)	≥54 Gy (90%)	<54 Gy
	Maximum dose (0.03 cc)	≤72 Gy (120%)	≤75 Gy (125%)	>75 Gy
Spinal cord	Maximum dose (0.03 cc)	≤50.0 Gy	≤52 Gy	>52 Gy
Lungs (minus GTV)	V20Gy	≤31%	None	>31
	V5Gy	≤60%	≤65%	>65%
	Mean dose	≤20 Gy	≤22 Gy	>22 Gy
Heart	Mean dose	≤20 Gy	≤26 Gy	>26 Gy
Esophagus	Maximum dose (0.03 cc)	≤63 Gy	≤66 Gy	>66 Gy
	Mean dose	≤34 Gy	≤35 Gy	>35 Gy
	V60Gy	Not circumferential	Circumferential for ≤0.5 cm contiguous length	Circumferential for >0.5 cm contiguous length
Brachial plexus	Maximum dose (0.03 cc)	≤63 Gy	≤66 Gy	>66 Gy

GTV, gross tumor volume; PTV, planning target volume.

The use of 4-dimensional computed tomography (4DCT) scans and 4-dimensional radiation treatment planning was permitted. The PTV could be treated with any combination of coplanar or noncoplanar 3-dimensional conformal fields shaped to deliver the specified dose while restricting the dose to the normal tissues. The use of IMRT was also permitted at institutions that had been credentialed by the central vendor (QARC) for intrathoracic IMRT treatments. For additional TRT-related details, please refer to section 8.1.9.2 of the study protocol (online-only supplement).

eTable 1. Subgroup analyses of objective response per blinded independent central review per RECIST version 1.1 in all patients as-treated.

	Cohort A (n=112)	Cohort B (n=102)
Overall ORR	79 (70.5)	72 (70.6)
Age, years		
<65	37 (75.5)	37 (68.5)
≥65	42 (66.7)	35 (72.9)
Gender		
Male	52 (68.4)	45 (72.6)
Female	27 (75.0)	27 (67.5)
Tumor histology		
Squamous	52 (71.2)	0 (NA)
Nonsquamous	27 (69.2)	72 (70.6)
ECOG performance status		
0	37 (72.5)	40 (70.2)
1	42 (68.9)	32 (71.1)
Disease stage		
IIIA	29 (70.7)	28 (71.8)
IIIB	46 (73.0)	29 (69.0)
Smoking status[a]		
Former/current smoker	75 (70.8)	70 (72.2)
PD-L1 status[b]		
TPS <1%	14 (66.7)	20 (71.4)

TPS ≥1%	50 (75.8)	29 (72.5)

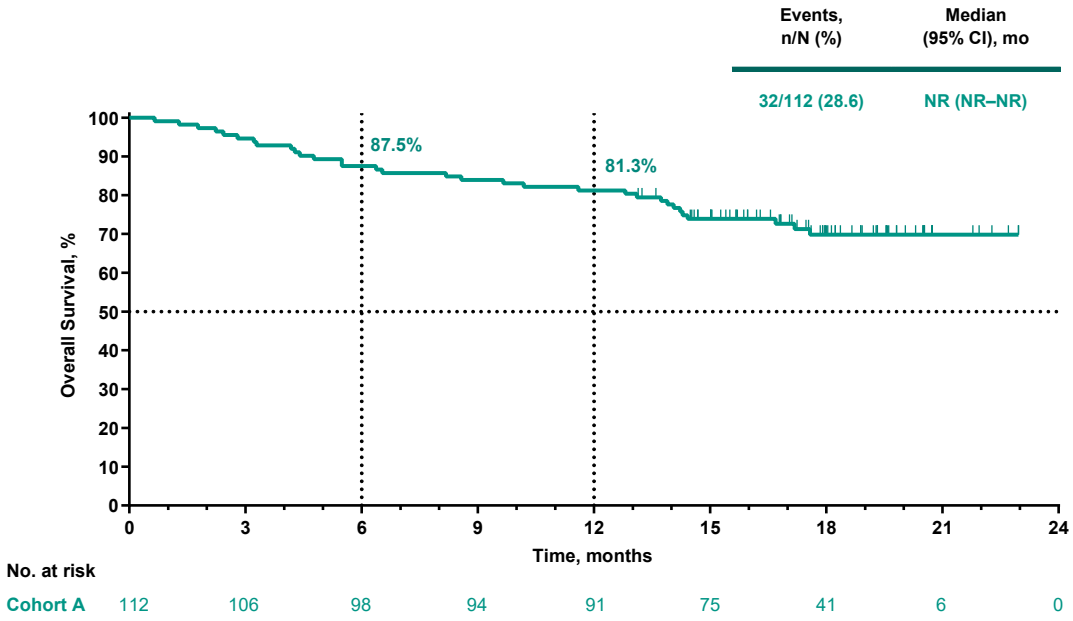
NA, Not applicable; ORR, objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1.
Values are presented as n (%) unless stated otherwise.
[a]There were only 11 patients in the 'never smoker' subgroup (6 in cohort A, 5 in cohort B) which precluded further analysis.
[b]Patients with PD-L1 not evaluable or unknown are not included in the subgroup analysis.

eTable 2. Summary of radiotherapy dose specification in patients who experienced grade 3–5 pneumonitis (all of whom received radiotherapy).

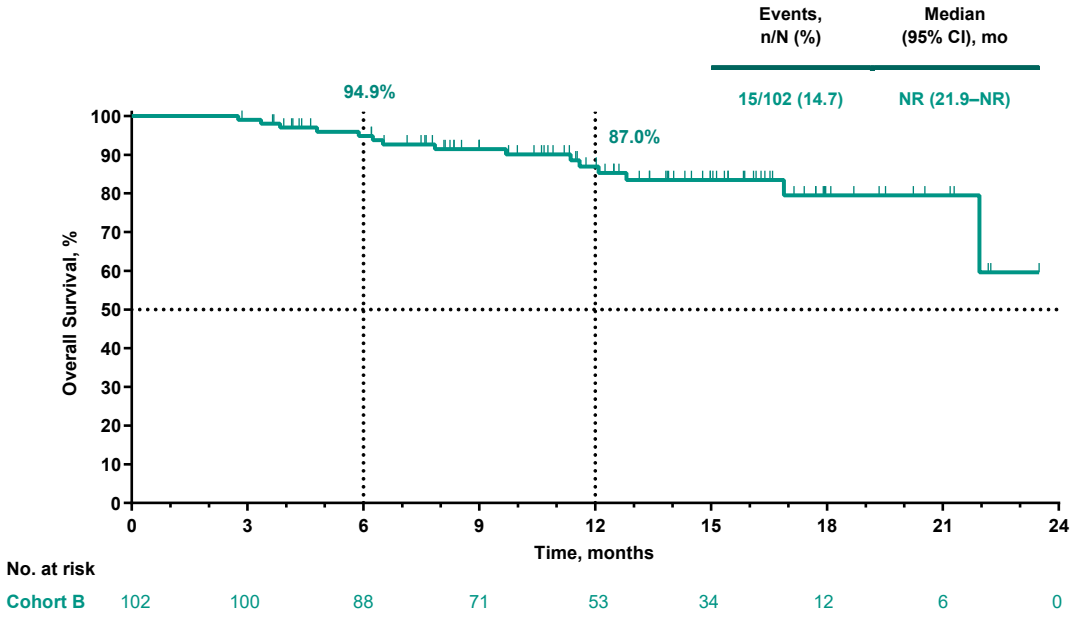
	Cohort A (n=9)	**Cohort B (n=7)**
Actual total lung V20 (%)	n=8	n=6
Mean (SD)	27.3 (4.13)	24.8 (5.74)
Median (range)	27.0 (22.0–34.0)	25.0 (17.0–32.0)
≤31%, n (%)	6 (75.0)	5 (83.3)
>31%, n (%)	2 (25.0)	1 (16.7)
Actual Total Lung V5 (%)	n=8	n=6
Mean (SD)	57.8 (4.40)	55.0 (9.76)
Median (range)	59.0 (51.0–63.0)	58.5 (36.0–62.0)
≤60%, n (%)	6 (75.0)	4 (66.7)
>60%, n (%)	2 (25.0)	2 (33.3)
Mean Lung Dose (cGy)	n=8	n=6
Mean (SD)	1525.0 (190.89)	1455.0 (276.21)
Median (range)	1573.0 (1288.0–1849.0)	1466.5 (1076.0–1814.0)
Mean Heart Dose (cGy)	n=8	n=6
Mean (SD)	1178.1 (477.81)	769.2 (337.56)
Median	1037.0 (644.0–1825.0)	838.0 (250.0–1178.0)
Tumor Volume (CC)	n=8	n=6
Mean (SD)	133.9 (73.50)	86.7 (133.61)
Median (range)	116.5 (39.0–244.0)	31.0 (7.0–353.0)

eFigure. Kaplan-Meier estimates of overall survival in (A) cohort A and (B) cohort B and progression-free survival in (C) cohort A and (D) cohort B. NR, not reached.

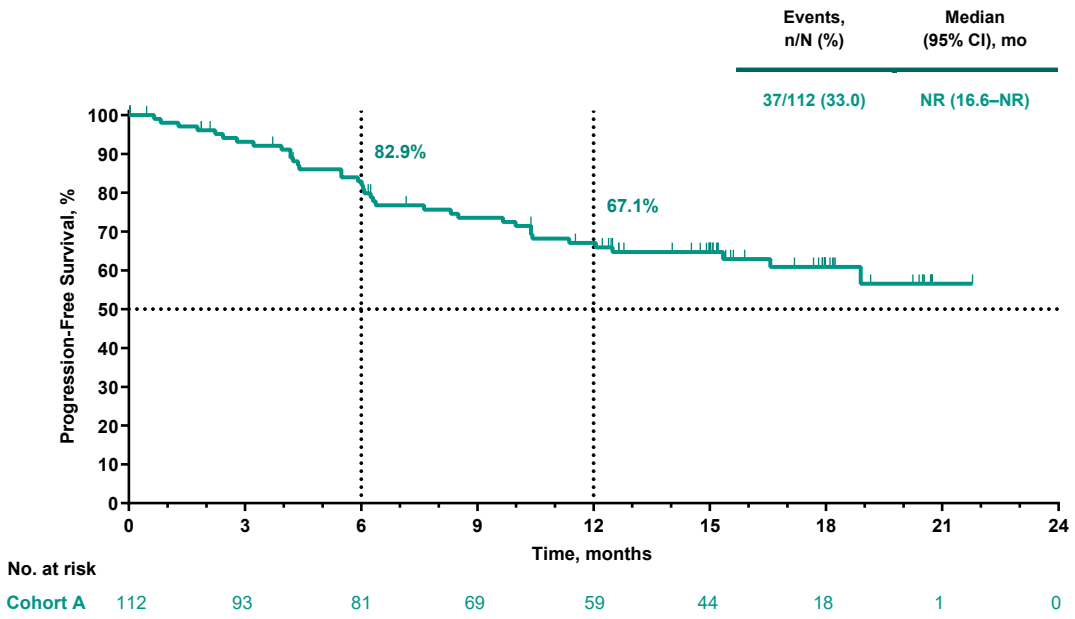
(A)



(B)



(C)



(D)