Supplementary

Table S1 Baseline Evaluation assessments during standard care of definitive chemoradiation therapy (dCRT) (only for patients consented prior to dCRT)

Procedure/scale	Definitive chemoradiation (dCRT) phase							
	Week 1 and 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9
	Screening (-28 days to 0 day)	Visit No. 3	Visit No. 4	Visit No. 5	Visit No. 6	Visit No. 7	Visit No. 8	Visit No. 9
Informed consent for preliminary enrollment	X							
Eligibility criteria	X							
Demographics	X							
Medical history	X							
Physical exam (full)	X							
ECOG performance status	X							
Targeted physical exam based on symptoms		X	X	X	X	X	X	X
Vital Signs & weight & height	X	X	X	X	X	X	X	X
ECG	X							
Pulmonary function test	X							
Laboratory assessments								
Clinical chemistry	X	X	X	X	X	X	X	
Creatinine clearance	X							
Hematology	X	X	X	X	X	X	X	
Coagulation (PT/INR/PTT)	X	---------- As clinically indicated ----------						
TSH, T4 (reflex free T3)	X	---------- As clinically indicated ----------						
Pregnancy test	X							
Urinalysis	X							
Monitoring								
Adverse event monitoring		X	X	X	X	X	X	X
Review of prior/concomitant medications	X							
Other assessments and assays								
PD-L1 (optional) testing from tissue	X							
Imaging by PET/CT/MRI	X							
Tumor pathology review	X							
CT simulation (for planning definitive CRT)	X							
Definitive CRT (30-33 fractions RT, with two or more cycles of chemotherapy)					X			
Immunohistochemistry staining for immune cell markers including confocal microscopy (archival biopsy tissue)	X							
Blood draw for tumor marker research (exploratory endpoint)	X		X		X			X

Table S2 Meeting the following dose constraints with conventional fractionated RT as part of the definitive chemoradiation is mandatory for eligibility of the current trial

Critical organ	Max dose limit	Volume/dose constraint
Total lung-CTV	<110% of PD	V20 Gy <30%[a] (accept <35%); mean dose <15 Gy (accept <20 Gy)
Esophagus	<105% of PD	mean dose <34 Gy
Cord	45 Gy	
Heart		V50 Gy <25%; V45 Gy <67%; V40 Gy <100%; mean <35 Gy
Brachial plexus	60 Gy preferred, accept 66 Gy	

[a], V20 Gy <30%: no more than 30% of the volume of total lung minus the CTV should receive 20 Gy or more dose; CTV clinical tumor volume; PD prescribed dose; Normal tissue constraints shall be prioritized in the following order for treatment planning: 1=spinal cord, 2=lungs, 3=esophagus, 4=brachial plexus, and 5=heart.

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Table S3 Schedule of study procedures

Study procedure	Screening	C1	CT sim	C2	RT (1st boost)	RT (2nd boost)	C3 to C26 or PD
	Day -28 to 0	Day 1[a]	Day 8-14	Day 15-21	Day 22-35	Day 22-35	Q14 ± 3 days unless dosing needs to be held for toxicity reasons
Informed consent/registration							
Review of eligibility criteria	X						
Demographics	X						
Physical exam (full)	X						
Targeted physical exam (based on symptoms)/ Routine follow-ups	X		X		X		X
Medical history	X						
ECOG performance status	X	X		X	X		X
Vital signs (including weight and height)	X	X		X	X		X
ECG	X				As clinically indicated		
Laboratory assessments							
Clinical chemistry	X	X		X			X
Creatinine clearance	X	X					
Hematology	X	X		X			X
Coagulation labs (PT/INR/PTT)	X				---------- As clinically indicated ----------		
TSH, T4, (reflex free T3)	X	X			---------- As clinically indicated ----------		
Pregnancy test (if applicable)	X	X		X			X
Urinalysis	X						
Monitoring							
Concomitant medications	<----------						---------->
AE/SAE assessment	<----------						---------->
IP administration/therapy							
Durvalumab		X		X			X
hfRT (QOD)					X	X	
CT simulation (for planning hfRT)			X				
Other assessments and assays							
EORTC QLQ-C30 v.3 and LC13 module	X	X		X			X
Tumor biopsy (archival or newly acquired)	X						
Tumor biopsy (archival, if available, for patients who submit a newly acquired biopsy at screening for PD-L1 status)	X						
Tumor biopsy (after hfRT) (optional)							X
Blood draws for exploratory research endpoint	X		X		X	X	X
Pulmonary function test	X						X
Efficacy evaluations							
Tumor assessment (PET/CT/MRI) (RECIST 1.1)	X	Q12w ± 1w for the first 48 weeks [relative to the date of registration (day 0)], and thereafter until confirmed objective disease progression/death (whichever comes first). The schedule of q12w ± 1 week for first 48 weeks and thereafter MUST be followed regardless of any delays in dosing					

[a], every effort should be made to minimize the time between screening and starting durvalumab treatment [i.e., within 1 day of completion of screening, but allow the first infusion to start up to 28 days after initial phase of radiation therapy (with concurrent chemotherapy)]. AE, Adverse event; C, Cycle; ECG, Electrocardiogram; IM, Intramuscular; LFT, Liver function test; q12w, Every 12 weeks; QOD, Every other day; SAE, Serious adverse event; T3, Triiodothyronine; T4, Thyroxine; TSH, Thyroid-stimulating hormone.

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Table S4 Normal tissue constraints for consolidative RT (serial tissues)

Serial Tissue	Volume	Volume Max (Gy)	Dmax (Gy)	Complications
Spinal Cord	<0.03 cc	5.5 Gy (2.75 Gy/fx)		Myelitis
Ipsilateral brachial plexus	<0.03 cc	6 Gy (3 G/fx)		neuropathy
Rib*	<1 cc	16 Gy (8 Gy/fx)	17.6 Gy (8.6 Gy/fx)	Pain or fracture
Skin*	<10 cc	14 Gy (7 Gy/fx)	12.8 Gy (6.4 Gy/fx)	ulceration
Stomach	<10 cc	7.2 Gy (3.6 Gy/fx)	12.8 Gy (6.4 Gy/fx)	Ulceration/fistula

*, exceeded any of these limits by 5% is a protocol violation except for skin and rib with dose constraints provided for suggested planning.

Table S5 Normal tissue constraints for consolidative RT (parallel tissues)

Parallel tissue	Volume	Volume Max (Gy)	Dmax (Gy)	Complications
Lung, Total	1500 cc	5 Gy (2.5 Gy/fx)		Basic Lung Function
Lung, Total	<25%	2.5 Gy (1.25 Gy/fx)		Pneumonitis
	<15%	5 Gy (2.5 Gy/fx)		
	<5%	10Gy (5 Gy/fx)		
	<1.5%	20Gy (10 Gy/fx)		
	1000 cc	5.4 Gy(2.7Gy/fx)		
Esophagus, non-adjacent wall	<5 cc	11 Gy (5.5 Gy/fx)	16Gy (8 Gy/fx)	Stenosis/fistula
Heart/pericardium	<15 cc	12.8 Gy (6.4 Gy/fx)	16Gy (8 Gy/fx)	Pericarditis
Trachea and ipsilateral bronchus**	<4 cc	6.6 Gy (3.3 Gy/fx)	14 Gy (7 Gy/fx)	Stenosis/fistula
Trachea and ipsilateral bronchus, non-adjacent wall	<4 cc	7.2 Gy (3.6 Gy/fx)	12 Gy (6 Gy/fx)	Stenosis/fistula
Great vessels, non-adjacent wall			12 Gy (6 Gy/fx)	Aneurysm

**, circumferential volume of trachea and ipsilateral bronchus dose constraints are only required for proximally located tumor.

Table S6 Conformality of prescribed dose for calculations based on deposition of photon beam energy in heterogeneous tissue

PTV Volume (cc)	Ratio of Prescription Isodose Volume to the PTV Volume		Ratio of 50% Prescription Isodose Volume to the PTV Volume, $R_{50\%}$		Maximum Dose (in % of dose prescribed) @ 2 cm from PTV in Any Direction, D_{2cm} (%)		Percent of Lung Receiving 20 Gy Total or More, V_{20} (%)	
	Deviation		Deviation		Deviation		Deviation	
	None	Minor	None	Minor	None	Minor	None	Minor
1.8	<1.2	<1.5	<5.9	<7.5	<50	<57	<10	<15
3.8	<1.2	<1.5	<5.9	<6.5	<50	<57	<10	<15
7.4	<1.2	<1.5	<5.1	<6.0	<50	<58	<10	<15
13.2	<1.2	<1.5	<4.7	<5.8	<50	<58	<10	<15
22.0	<1.2	<1.5	<4.5	<5.5	<54	<63	<10	<15
34.0	<1.2	<1.5	<4.3	<5.3	<58	<68	<10	<15
50.0	<1.2	<1.5	<4.0	<5.0	<62	<77	<10	<15
70.0	<1.2	<1.5	<3.5	<4.8	<66	<86	<10	<15
95.0	<1.2	<1.5	<3.3	<4.4	<70	<89	<10	<15
126.0	<1.2	<1.5	<3.1	<4.0	<73	<91	<10	<15
163.0	<1.2	<1.5	<2.9	<3.7	<77	<94	<10	<15

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