PATIENT POPULATION:
Locally advanced inoperable node-positive non-small cell lung cancer , stage II or III

STRATIFICATION:
- PD-L1 expression (<1%, 1%-49%, 50-100%)
- T-stage (T1-2a vs T2b or higher)

RANDOMIZE*

Arm 1	Arm 2
RT to all sites of known thoracic disease (2 Gy fx/day to a total dose of 60 Gy) with concurrent chemotherapy**	SBRT†† to primary tumor followed by RT to nodal metastases (2 Gy fx/day to a total dose of 60 Gy) with concurrent chemotherapy**
followed by	followed by
Consolidation immunotherapy† x 12 months	Consolidation immunotherapy† x 12 months

*Randomization is 1:1.

**Chemotherapy is given concurrently with radiotherapy (RT). See Section 5.1.1 for details.

††See Section 5.1 for allowable stereotactic body radiation therapy (SBRT) fractionation.

†Consolidation immunotherapy for up to 12 months or alternative consolidation regimens may be given per the treating physician. See Section 5.1.2 for details.

3. ELIGIBILITY AND INELIGIBILITY CRITERIA

Notes: Per NCI guidelines, exceptions to inclusion and exclusion criteria are not permitted. For questions concerning eligibility see protocol cover page. For radiation therapy-related eligibility questions, please contact RTQA (see protocol cover page).

3.1 Eligibility Criteria

A patient cannot be considered eligible for this study unless ALL of the following conditions are met.

3.1.1 Pathologically (histologically or cytologically) proven diagnosis of Stage II or III (AJCC Eighth Edition) non-small cell lung cancer (NSCLC) with known PD-L1 status prior to registration.

- Patients must have an identified primary tumor and at least one nodal metastasis (peribronchial/hilar/intrapulmonary, mediastinal/subcarinal, supraclavicular/scalene)
- Up to 4 cycles of systemic therapy received prior to registration for the current study cancer is allowable; any prior chemotherapy for a different cancer is also permissible.

3.1.2 The patient must be deemed clinically appropriate for curative intent definitive combined modality therapy, based on the following staging assessments:

- History/physical examination prior to registration;
- MRI scan of the brain (preferred) or CT scan of the brain (if available, contrast is preferred for all neuroimaging) prior to registration;
- CT chest with IV contrast (if contrast is available and unless contraindicated, such as for abnormal kidney function) prior to registration. PET/CT may be used if the CT portion is of identical diagnostic quality as achieved in a stand-alone CT.

3.1.3 No evidence of distant metastases based on FDG PET/CT scan obtainedwithin 60 days of registration.

3.1.4 Primary tumor ≤ 7 cm;

3.1.5 Age ≥ 18;

3.1.6 ECOG performance status 0-2;

3.1.7 Hematologic function (e.g. platelets, leukocytes, hemoglobin) amenable, at the discretion of the treating physician, to allow for treatment with chemotherapy and concurrent radiation therapy;

3.1.8 Adequate renal function: Creatinine clearance ≥ 25 mL/min by the Cockcroft-Gault (C-G) equation:

CrCl (mL/min) =	[140 – age (years)] x weight (kg) / 72 x serum creatinine (mg / dL)	{x 0.85 for female patients}

3.1.9 Subjects with non-malignant pleural effusion are eligible provided the effusion is not known or demonstrated to be an exudative effusion.

- If a pleural effusion is present, the following criteria must be met to exclude malignant involvement:
  - When pleural fluid is visible on both the CT scan and on a chest x-ray, a pleuracentesis is required to confirm that the pleural fluid is cytologically negative;
  - Effusions that are minimal (i.e., not visible on chest x-ray) that are too small to safely tap are eligible.

3.1.10 Medical history consistent with the patient being amenable, at the discretion of the treating physician, to allow for treating with consolidation immunotherapy. Patients with known EGFR/ALK mutation at the time of registration are eligible, and these patients can be treated with consolidation durvalumab or chemotherapy at the discretion of the treating physician.

3.1.11 Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen.

3.1.12 Negative pregnancy test ≤ 14 days prior to registration for participants of childbearing potential;

3.1.13 The patient or a legally authorized representative must provide study-specific informed consent prior to study entry and, for patients treated in the U.S., authorization permitting release of personal health information.

3.2 Ineligibility Criteria

Patients with any of the following conditions are NOT eligible for this study.

3.2.1 Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields that is determined by the treating physician to impede the treatment of the study malignancy.

3.2.2 Patients without identifiable primary tumor and at least 1 pathologically enlarged lymph node are not eligible (T3-4N0 or T0N1-3 patients are not eligible). At least 1 radiographically-involved lymph node is required, but pathologic confirmation of involvement is not mandated.

3.2.3 Centrally located primary tumor < 2 cm from involved nodal disease which would result in significant overlap of the primary SBRT and nodal radiation fields. Centrally located is defined as within or touching the zone of the proximal bronchial tree, which is a volume 2 cm in all directions around the proximal bronchial tree (carina, right and left main bronchi, right and left upper lobe bronchi, intermedius bronchus, right middle lobe bronchus, lingular bronchus right and left lower lobe bronchi).

3.2.4 Participants who are pregnant or unwilling to discontinue nursing.

3.2.5 Participants of childbearing potential (participants who may become pregnant or who may impregnate a partner) unwilling to use highly effective contraceptives during therapy and for the FDA-labeled contraception timeframe required after the final dose of the selected chemotherapy regimen, because the treatment in this study may be significantly teratogenic. (See protocol section 9 for definition of highly effective contraception.)