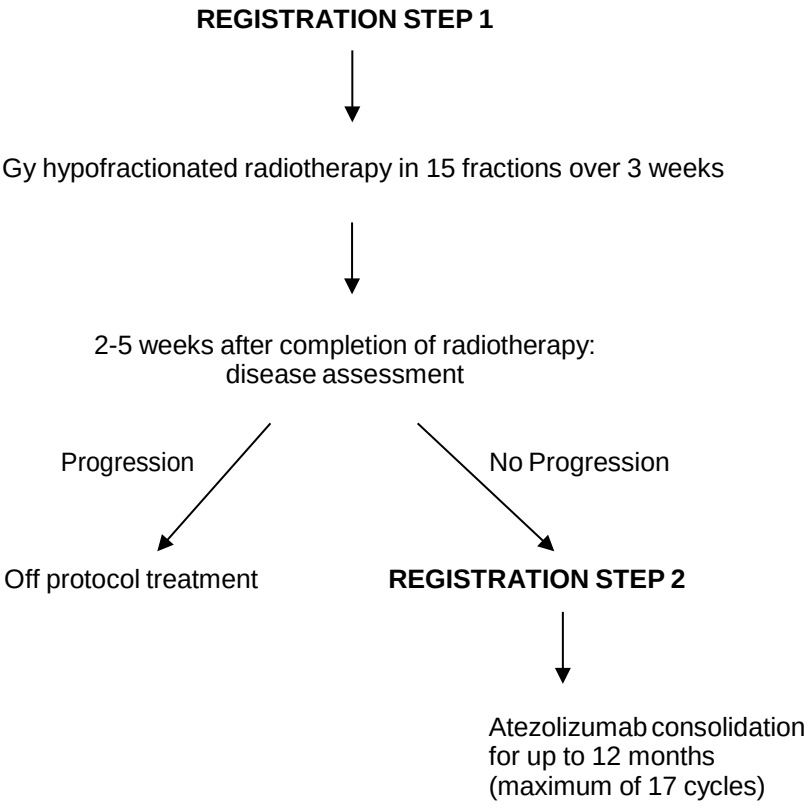
SCHEMA


REGISTRATION STEP 1
60 Gy hypofractionated radiotherapy in 15 fractions over 3 weeks
2-5 weeks after completion of radiotherapy:
disease assessment
Progression
No Progression
Off protocol treatment
REGISTRATION STEP 2
Atezolizumab consolidation
for up to 12 months
(maximum of 17 cycles)

5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a patient to be considered eligible for registration in OPEN. Section 5 may be printed and used by the site, but is not to be uploaded in RAVE (unless specially stated). For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the SWOG SDMC in Seattle at 206/652-2267 or lungquestion@crab.org prior to registration. NCI policy does not allow for waiver of any eligibility criterion (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm).

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 4 weeks later would be considered Day 28. This allows for efficient patient scheduling without exceeding the guidelines. If Day 14, 28, 42, or 90 falls on a weekend or holiday, the limit may be extended to the next working day.

5.1 Registration Step 1

Disease Related Criteria

a. Participants must have pathologic (cytological or histological) proof of non-small cell lung cancer (NSCLC).

b. Participants must have Stage III NSCLC with Zubrod Performance Status of 2 or Stage II NSCLC with Zubrod Performance Status of 0-2 (see Sections 4.0 and 10.4).

c. Participants must not be candidates for surgical resection in the opinion of the treating investigator. Participants whose disease was previously resected must have experienced local or regional recurrence at least 12 months after resection.

d. Participants must not be candidates for concurrent chemoradiation in the opinion of the treating investigator.

e. Participants must have measurable or non-measurable disease (see Section 10.1) documented by CT or MRI. Measurable disease must be assessed within 28 days prior to Registration Step 1. Non-measurable disease must be assessed within 42 days prior to Step 1 registration. The CT from a combined PET/CT may be used only if it is of diagnostic quality as defined in Section 10.1a. All known sites of disease must be assessed and documented on the Baseline Tumor Assessment Form (RECIST 1.1).

f. Participants must have an MRI or CT scan of the brain with contrast within 28 days prior to Registration Step 1.

g. Participants' disease must fit within the radiation constraints detailed in Section 7.2 in the opinion of a local radiation oncologist.

Prior/Concurrent Therapy Criteria

h. Participants may have received prior treatment for their lung cancer, including surgery, chemotherapy, targeted agents, and/or radiation treatment. At least 12 months must have elapsed since last treatment.

i. Participants may have had prior radiation therapy as long as the irradiated area does not overlap with the radiation field targeted for this study.

Clinical/Laboratory Criteria

j. Participants must have recovered from any adverse effects of prior major surgery to the satisfaction of the treating physician. Biopsies and central IV access placement are not considered major surgery.

k. Participants must have adequate bone marrow function as evidenced by all of the following: ANC ≥ 1500/mcl; platelet count ≥ 100,000/mcl; and hemoglobin ≥ 9 grams/dL. These results must be obtained within 28 days prior to Registration Step 1.

l. Participants must have adequate liver function as evidenced by the following: total bilirubin ≤ 1.5 x institutional upper limit of normal (IULN), and aspartate transaminase (AST) and alanine transaminase (ALT) ≤ 2.5 x IULN. These results must be obtained within 28 days prior to Registration Step 1.

m. Participants must have adequate renal function as evidenced by ONE of the following: serum creatinine ≤ 1.5 x IULN OR measured or calculated creatinine clearance ≥ 40 mL/min. This result must have been obtained within 28 days prior to Registration Step 1.

$$\text{Calculated Creatinine Clearance} = \frac{(140 - \text{age}) \times (\text{weight in kg})\ \dagger}{72 \times \text{serum creatinine}\ *}$$

Multiply this number by 0.85 if the patient is a female.

† The kilogram weight is the patient weight with an upper limit of 140% of the IBW.
* Actual lab serum creatinine value with a minimum of 0.8 mg/dL.

n. Participants must have percent predicted diffusing capacity of the lungs for carbon monoxide (DLCO) of at least 50% documented within 90 days prior to Registration Step 1.

o. Patient must not have had a prior history of interstitial lung disease or > Grade 2 (CTCAE Version 5) pneumonitis.

p. Participants must not have active autoimmune disease requiring therapy within the past 6 months.

q. Participants must not have an active infection requiring therapy.

r. Participants must be ≥ 18 years old.

s. Participants must not be pregnant or nursing because atezolizumab has not been studied in pregnant or nursing women and the mechanism of action is expected to cause fetal harm. Women/men of reproductive potential must have agreed to use an effective contraceptive method while on protocol treatment and for five months after last dose of atezolizumab. A woman is considered to be of "reproductive

potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.

t. Participants with known human immunodeficiency virus (HIV) infection must be on effective anti-retroviral therapy and must have undetectable viral load at their most recent viral load test and within 6 months prior to Registration Step 1.

u. Patient must be tested for hepatitis B within 28 days prior to randomization. Patient must not have active (chronic or acute) hepatitis B virus (HBV) infection. Patients may have past or resolved HBV infection.

Active HBV is defined as having a positive hepatitis B surface antigen (HBsAg) test.

Past or resolved HBV is defined as having a negative HBsAG test and a positive total hepatitis B core antibody (HBcAb) test.

v. Patient must be tested for hepatitis C within 28 days prior to randomization. Patient must not have active hepatitis C virus (HCV) infection.

Active HCV is defined as having a positive HCV antibody test followed by a positive HCV RNA test.

w. No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease free for three years. Participants with localized prostate cancer who are being followed by an active surveillance program are also eligible.

Specimen Submission Criteria

x. Participants must be offered optional participation in banking of specimens for future research as described in Section 15.1.

Regulatory Criteria

y. Participants must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.

z. As a part of the OPEN registration process (see Section 13.3 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

5.2 Registration Step 2

a. Participants must be registered to Step 2 within 42 days after completion of radiation treatment. Participants must have received at least 44 Gy of radiation treatment.

b. Participants must have no evidence of progression per RECIST 1.1 on CT scan of the chest, abdomen, and pelvis performed between 2 and 5 weeks after completion of radiation therapy.

c. Any toxicities from radiation therapy must have resolved to < Grade 2.

d. Participants must have adequate bone marrow function as evidenced by all of the following: ANC ≥ 1500/mcl; platelet count ≥ 100,000/mcl; and hemoglobin ≥ 9 grams/dL. These results must be obtained within 28 days prior to Registration Step 2.

e. Participants must have adequate liver function as evidenced by the following: total bilirubin ≤ 1.5 x institutional upper limit of normal (IULN), and AST and ALT ≤ 2.5 x IULN. These results must be obtained within 28 days prior to Registration Step 2.

f. Participants must have adequate renal function as evidenced by ONE of the following: serum creatinine ≤ 1.5 x IULN OR measured or calculated creatinine clearance ≥ 40 mL/min. This result must have been obtained within 28 days prior to Registration Step 2.

$$\text{Calculated Creatinine Clearance} = \frac{(140 - \text{age}) \times (\text{weight in kg})\ \dagger}{72 \times \text{serum creatinine}\ *}$$

Multiply this number by 0.85 if the patient is a female.

† The kilogram weight is the patient weight with an upper limit of 140% of the IBW.
* Actual lab serum creatinine value with a minimum of 0.8 mg/dL.

g. Participants must not have received steroids in doses of more than prednisone 10 mg daily or equivalent within 14 days prior to Registration Step 2.

h. Participants must not have received a live vaccine within 28 days prior to Registration Step 2.