Official Title: A Phase II, Open-Label, Multicenter, Single-Arm Study to Investigate the Efficacy and Safety of Atezolizumab as Neoadjuvant and Adjuvant Therapy in Patients With Stage IB, II, IIIA or Selected IIIB Resectable and Untreated Non-Small Cell Lung Cancer

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STATISTICAL ANALYSIS PLAN

Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080

A PHASE II, OPEN-LABEL, MULTICENTER, SINGLE-ARM STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF ATEZOLIZUMAB AS NEOADJUVANT AND ADJUVANT THERAPY IN PATIENTS WITH STAGE IB, II, IIIA OR SELECTED IIIB RESECTABLE AND UNTREATED NON-SMALL CELL LUNG CANCER

Protocol No: ML39236 Version 5

Prepared by:
[redacted]
Syneos Health

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SIGNATURE PAGE

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[redacted] **Ph.D.,** [redacted]
Genentech, Inc.
• [redacted]
Approval Date
• 22-MAY-2020

[redacted] **Ph.D.,** [redacted]
Genentech, Inc.
Approval Date

• [redacted]
• 16-JUN-2020

Syneos Health
• [redacted]
Approval Date
• 22-MAY-2020

[redacted]
Syneos Health
• [redacted]
Approval Date
• 22-MAY-2020

TABLE OF CONTENTS

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
CNB	core needle biopsy
CR	complete response
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
DFS	disease-free survival
ECOG	Eastern Cooperative Oncology Group
EFS	event-free survival
eCRF	electronic Case Report Form
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
IF	immunofluorescence
IHC	immunohistochemistry
INR	International normalized ratio
IRB	Institutional Review Board
MRI	magnetic resonance imaging
NCI	National Cancer Institute
NSCLC	non–small cell lung cancer
ORR	objective response rate
OS	overall survival
PCR	polymerase chain reaction
PD-1	programmed death-1
PD-L1	programmed death-ligand 1
PET	positron emission tomography
PFT	pulmonary function test
q21d	every 21 days
q3w	every 3 weeks
RECIST	Response Evaluation Criteria in Solid Tumors
SOC	standard of care
UC	urothelial cancer
WES	whole-exome sequencing

1. INTRODUCTION

1.1 Background on Non-small Cell Lung Cancer

Lung cancer is the leading cause of cancer death worldwide. In the United States about 200,000 cases are diagnosed each year with approximately 150,000 deaths occurring and a progressive increase in mortality with age (Siegel et al. 2015). Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancers and is divided into squamous cell carcinoma, large cell carcinoma, and adenocarcinoma subtypes. The majority of patients present with advanced metastatic disease that cannot be cured with current therapies. A minority of patients (about 25%) present with localized disease that is sometimes (about 50%) cured by surgical resection. Of those not cured by surgical resection, the majority recur in distant sites that could not be detected prior to surgical resection. For these Stage IB-IIIA patients, the addition of systemic chemotherapy before or after surgery improved 5-year survival rates by about 5% (Pignon et al. 2008). Chemotherapy before surgery (neoadjuvant) results in slightly higher response rates compared to chemotherapy for advanced stages but there are essentially no complete responses (CRs). Recently, immunotherapy with antibodies that bind to checkpoint inhibitors such as programmed death 1 (PD-1) and programmed death ligand (PD-L1) have been shown to produce long lasting responses in some patients with advanced NSCLC who were refractory to standard chemotherapy (Rizvi et al. 2015).

Subsequent randomized clinical trials showed that these antibodies produce superior survival compared to docetaxel chemotherapy in patients who progressed after systemic platinum doublet chemotherapy (Borghaei et al. 2015; Brahmer et al. 2015; Fehrenbacher et al. 2016). The clinical benefits were greater in patients with high PD-L1 expression although survival was similar to docetaxel even in patients lacking PD-L1 expression. Early studies with these antibodies in the first line therapy setting showed even better results especially in patients with high PD-L1 expression (Gettinger 2015; Garon et al. 2015). Because PD-L1 expression is a continuous variable and not a perfect predictive biomarker, many investigators are exploring other potential biomarkers of predictive therapeutic benefit. The number of mutations determined by whole-exome sequencing (WES) has been shown to perform as another potential predictive biomarker (Rizvi et al. 2015). The expression of many other genes and proteins is being explored, but this is complicated by the lack of tissue and a limited understanding of its association with objective response rates (ORR) and survival.

1.2 Background on Atezolizumab

PD-L1 is an extracellular protein that down regulates immune responses primarily in peripheral tissues through binding to its two receptors PD-1 and B7.1. PD-1 is an inhibitory receptor expressed on T cells following T-cell activation, which is sustained in states of chronic stimulation such as in chronic infection or cancer (Blank et al. 2005; Keir et al. 2008). Binding of PD-L1 with PD-1 inhibits T-cell proliferation, cytokine production, and cytolytic activity, leading to the functional inactivation or exhaustion of T cells. B7.1 is a molecule expressed on antigen-presenting cells and activated T cells. PD-L1 binding to B7.1 on T cells and antigen-presenting cells can mediate down regulation of immune responses, including inhibition of T-cell activation and cytokine production (Butte et al. 2007; Yang et al. 2011).

Overexpression of PD-L1 on tumor cells (TCs) and the tumor microenvironment has been reported to impede anti-tumor immunity, resulting in immune evasion (Blank and Mackensen 2007). Therefore, interruption of the PD-L1/PD-1 pathway represents an attractive strategy to reinvigorate tumor-specific T-cell immunity.

Atezolizumab (Tecentriq™ , formerly MPDL3280A) is a humanized IgG1 monoclonal antibody consisting of two heavy chains (448 amino acids) and two light chains (214 amino acids), and is produced in Chinese hamster ovary cells. Atezolizumab was engineered to eliminate Fc-effector function via a single amino acid substitution at position 298 on the heavy chain, which results in a non-glycosylated antibody that has minimal binding to Fc receptors and prevents Fc-effector function at expected concentrations in humans. Atezolizumab targets human PD-L1 and inhibits its interaction with its receptors, PD-1 and B7.1 (CD80, B7-1). Both of these interactions are reported to provide inhibitory signals to T cells. Direct targeting of PD-L1 leaves the PD-L2-PD-1 interaction intact, potentially avoiding effects on immune homoeostasis.

Atezolizumab is approved in the United States for the treatment of locally advanced or metastatic urothelial cancer (UC), and metastatic NSCLC that has progressed during or following treatment with a platinum-containing regimen. Atezolizumab is also being investigated as a potential therapy against solid tumors and hematologic malignancies in humans.

1.3 Study Rationale and Benefit-Risk Assessment

It is hypothesized that administration of atezolizumab, an engineered IgG1 monoclonal antibody targeting PD-L1, will demonstrate a good safety profile and produce objective responses in clinical Stage IB-IIIA NSCLC, especially in tumors which express PD-L1 prior to resection. PD-L1 expression by tumor and immune cells results in impaired anti-tumor immune responses by inhibiting T-cell proliferation, cytokine production, and cytotoxic activity. As a result there is significant interest in developing therapeutics to block the immunosuppressive effects of PD-L1 and to identify patients who will benefit from this treatment strategy.

While the addition of adjuvant cisplatin based chemotherapy following surgical resection of early stage NSCLC has produced significant survival benefits (Pignon et al. 2008), rates of local and distant disease relapse leading to death remain unacceptably high. Studies show that neoadjuvant chemotherapy has approximately the same benefit as adjuvant (Felip et al. 2010). Thus, it is critical to investigate the use of atezolizumab and similar agents in treating early stage resectable disease where one can assess the immune environment before and after treatment. It is also critical to develop highly predictive biomarkers of benefit and to study the evolution of immune-related markers with treatment with atezolizumab.

There will be two parts to this study: the first part (Neoadjuvant Atezolizumab Therapy Phase) will evaluate the ability of atezolizumab, an engineered IgG1 monoclonal antibody targeting PD-L1, to produce pathologic responses in the neoadjuvant setting in patients with early stage NSCLC who have a pretreatment biopsy.

The subsequent resection of tumors from these patients will allow determination of pathologic response rates and potential predictive biomarkers from the pretreatment biopsy and evolution of cancer-/immune- related markers associated with response in the tumor biopsy specimen after treatment.

The primary endpoint of the study will be major pathologic response rate (defined as ≤ 10% of viable tumor cells) determined from the surgical resection (Hellmann et al. 2014). In addition, response rates according to RECIST v1.1 will be determined from chest CT scans obtained before and after the atezolizumab therapy and before surgical resection.

The Neoadjuvant Atezolizumab Therapy Phase will only include patients with Stage IB, II, IIIA, or selected IIIB disease and who are deemed suitable for surgical resection without metastatic disease but with sufficient material for initial biopsy to analyze biomarkers. Clinical staging of NSCLC is based on computed tomography (CT) of the chest and upper abdomen, positron emission tomography (PET) and brain CT or magnetic resonance imaging (MRI) to rule out metastatic disease and assess the potential for curative-intent resection. Resection represents the best chance for prolonged survival for patients with non-advanced NSCLC.

After surgical resection, routine clinical surveillance will involve repeated radiographic imaging and monitoring of clinical symptoms for disease recurrence. All patients that complete surgical resection, will be monitored for disease recurrence using extended CT scans with IV contrast every 6 weeks to 3 months. Blood samples will be obtained along with chest CT scans to explore the association of blood-based biomarkers, such as ctDNA positivity with clinical outcome, for up to 2 years. Early detection of biomarkers that predict relapse of disease may help identify personalized treatment options to limit disease recurrence for patients in the future. Blood-based assay approaches, such as detection of circulating tumor DNA (ctDNA), may represent an innovative tool to complement disease surveillance in NSCLC.

Following resection, the risk for relapse correlates with clinical and pathological stage, but the addition of cisplatin based adjuvant chemotherapy improves survival for patients with Stage II and IIIA disease (Pignon et al. 2008), and potentially for some Stage IB patients with lesions greater than 4 cm (Butts et al. 2010).

Therefore, this study will also include a second (exploratory) part, the Adjuvant Atezolizumab Therapy Phase, which will enroll patients who demonstrated clinical benefit (defined as evidence of pathologic response or absence of radiographic progression) with neoadjuvant atezolizumab, to receive up to 12 additional months of adjuvant atezolizumab. Patients can choose to receive standard-of-care (SOC) adjuvant chemotherapy (with or without radiation) before receiving atezolizumab post-surgical resection.

There is little data to guide the duration of adjuvant immunotherapy in lung cancer. An ongoing Phase III study is evaluating 12 months of atezolizumab treatment after cisplatin-based chemotherapy in patients with completely resected Stage IB.IIIA NSCLC with high PD-L1 expression. Another Phase III study is currently recruiting patients with unresectable stage III NSCLC to receive 1 year of consolidation anti-PD-1 therapy after definitive chemo-radiation. Adjuvant immunotherapy has also been explored in other solid tumors. Adjuvant immunotherapy treatment for 1 year with interferon alfa-2b prolongs the relapse-free interval and OS of high-risk resected melanoma patients (Kirkwood et al. 1996). One year of adjuvant anti-PD-1 therapy is considered standard of care for resected melanoma based on the data from the CHECKMATE-238 study (Weber at el. 2017).

Follow-up of all patients will allow for exploration of atezolizumab treatment, as well as non-protocol specified, post-study cancer treatment, on long term survival outcomes, disease-free survival [DFS], event-free survival [EFS], overall survival [OS]) and further improve our understanding of predictive biomarkers.

Blood samples, tumor biopsies, normal lung parenchyma, lymph node samples and bronchial brushings will also be obtained for secondary and exploratory laboratory studies to evaluate potential predictive and prognostic biomarkers and to assess the immune response to atezolizumab.

2. STUDY OBJECTIVES

This study will evaluate the efficacy and safety of atezolizumab in patients with NSCLC. Specific objectives and corresponding endpoints for the study are outlined in Table 1.

Table 1 Objectives and Corresponding Endpoints

Objectives	Corresponding Endpoints
Primary Efficacy Objective:	
• To evaluate the efficacy of atezolizumab as neoadjuvant treatment for Stage IB, II, IIIA, and selected IIIB NSCLC	• Major pathologic response (defined as ≤ 10% of viable tumor cells), scored by a pathologist, based on surgical resection as defined by prior studies (Hellmann et al. 2014)
Secondary Efficacy Objectives:	
• To evaluate the efficacy of atezolizumab as neoadjuvant treatment for Stage IB, II, IIIA, and selected IIIB NSCLC	• Pathological response in PD-L1-positive and PD-L1 negative groups
• To evaluate response to atezolizumab in patients with PD-L1-positive vs. PD-L1-negative tumors	• Investigator-assessed response rate per RECIST v1.1
• To evaluate the association of mutational load, neoantigen score, gene expression signatures, and response to atezolizumab	• Response by: mutation load, neoantigen score, gene expression signatures
Exploratory Efficacy Objectives:	
• To evaluate the efficacy of atezolizumab as neoadjuvant or adjuvant treatment	• OS, DFS and EFS

Safety Objectives:	
• To evaluate the safety and tolerability of atezolizumab as neoadjuvant or adjuvant treatment	• Incidence of adverse events, with severity per NCI CTCAE v4.0
Exploratory Biomarker Objectives:	
• To evaluate the immune response to atezolizumab and assess mechanisms of immune escape	• Assessment of immune response by flow cytometry, IHC, IF, and/or NGS, including but not limited to the characterization of T-cell subsets, NK cells, MDSC, and B cells in whole blood and tissue samples and to correlate with clinical outcome
• To investigate changes in tumor cell infiltrate in tissue samples • To study the association of gene expression or mutation profiles in tumor tissue and/or blood with clinical outcome • Assessment of ctDNA in blood samples obtained pre-, post-neoadjuvant therapy and throughout surveillance after surgical resection and correlation with clinical outcome measures	• Pathological analyses of tissue samples pre- and post- neoadjuvant therapy, at disease progression or recurrence (if available)

CNB = core needle biopsy; ctDNA = circulating tumor DNA; DFS = disease-free survival; EFS = event-free survival; IF = immunofluorescence; IHC = immunohistochemistry; NCI CTCAE v4.0 = National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0; NGS = next-generation sequencing; NK = natural killer (cells); NSCLC= non–small cell lung cancer; MDSC = myeloid-derived suppressor cell; ORR= objective response rate; OS = overall survival; PD-L1= programmed death ligand 1; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors, version 1.1; WES = whole exome sequencing.

3. STUDY DESIGN

3.1 Overview of Study Design

This is a Phase II, open-label, single-arm study, designed to evaluate the efficacy of atezolizumab as a neoadjuvant therapy in patients with Stage IB, II, IIIA, or selected IIIB NSCLC scheduled for curative-intent resection by evaluating response to treatment. In addition, the safety of atezolizumab will be evaluated in this treatment setting. The study is also designed to investigate a number of laboratory correlative studies to further define the mechanism of anti-tumor activity of atezolizumab and several potential predictive biomarkers, which will help identify patients who are more likely to respond to treatment, and to aid in the design of future clinical trials. A

strong correlation between PD-L1 expression and response to the anti -PD-1/PD-L1 antibodies has been demonstrated (Brahmer et al. 2010; Garon et al. 2015; Vansteenkiste et al. 2015), indicating that PD-L1 is potentially useful as a predictive biomarker. Finally, the study will also include DFS, EFS and OS as exploratory endpoints.

Approximately 180 patients with NSCLC will be enrolled in this study at approximately 15 study centers in the United States. The study will be conducted in two parts, a Neoadjuvant Atezolizumab Therapy Phase and an Adjuvant Atezolizumab Therapy Phase. During the Neoadjuvant Atezolizumab Therapy Phase, approximately 180 patients with pathologically documented Stage IB, II, IIIA, and selected IIIB NSCLC and who are eligible for surgical resection with curative intent will be enrolled to receive two doses of atezolizumab as neoadjuvant therapy. Primary and secondary efficacy analyses, safety analyses, and exploratory biomarker analyses will be conducted on this cohort.

All patients who undergo surgery will enter a Surveillance period and will be monitored for disease recurrence using extended chest CT and serial blood samples for biomarker assessments for up to 2 years after surgery. Patients who do not undergo surgery will move directly to Survival Follow-up.

Patients who undergo surgery and receive adjuvant atezolizumab therapy will enter the Adjuvant Atezolizumab Therapy Phase. The Adjuvant Atezolizumab Therapy Phase is exploratory and will evaluate atezolizumab adjuvant therapy for up to a maximum of 12 months (up to 18 cycles) in patients who demonstrate clinical benefit (evidence of pathologic response or absence of radiographic progression) from the Neoadjuvant Atezolizumab Therapy Phase. After surgical resection, patients may receive SOC adjuvant chemotherapy (with or without radiation) before starting atezolizumab adjuvant therapy Any adjuvant treatment (optional SOC chemotherapy ± radiotherapy and/or adjuvant atezolizumab) will be done concomitantly with Surveillance.

For clarity of assessments during the Surveillance period, patients will be grouped by adjuvant treatment and overall:

- Subgroup A: No Adjuvant Treatment
- Subgroup B: Adjuvant Atezolizumab Treatment
- Subgroup C: SOC Chemotherapy (± Radiotherapy) Only
- Subgroup D: SOC Chemotherapy (± Radiotherapy) + Adjuvant Atezolizumab Treatment

Neoadjuvant treatment (Neoadjuvant Atezolizumab Therapy Phase) with atezolizumab 1200 mg every 21 days (one cycle = 21 days) will be given for a maximum of 2 cycles, and adjuvant treatment (Surveillance/Survival Follow-up Phase) with atezolizumab 1200 mg every 21 days will be given for a maximum of 12 months.

Patients could be asked to consent to an optional prescreening tumor biopsy, which will then be used for tissue analysis if the patient is eligible to participate in the study based on pathologically documented NSCLC and other eligibility criteria. This prescreening consent form also includes optional collection of bronchial brushing samples and lymph node samples.

Additionally, patients whose disease progresses or recurs anytime between the neoadjuvant phase and end of surveillance period will be asked to consent to an optional tissue biopsy (tumor and

lymph node, if available) at the time of progression/recurrence. Images will be collected at the time of progression and reviewed.

Patients will be closely monitored for safety and tolerability throughout the study. Safety assessments will include collection and monitoring of adverse events and laboratory abnormalities graded per the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0 (NCI CTCAE v4.0). Laboratory safety assessments will include the regular monitoring of hematology and blood chemistry. Tumor tissue samples, normal lung parenchyma, whole blood samples, and optional lymph node samples will be collected for biomarker assessments.

After Surveillance completion, patients will enter the Survival Follow-up period and will be followed per SOC, but information on off-protocol cancer-treatment, recurrence and survival will be collected every 6 months for up to 3 years after the patient receives the last dose of atezolizumab on study. Patients who discontinue the study due to adverse events will be followed until resolution or stabilization of the adverse event.

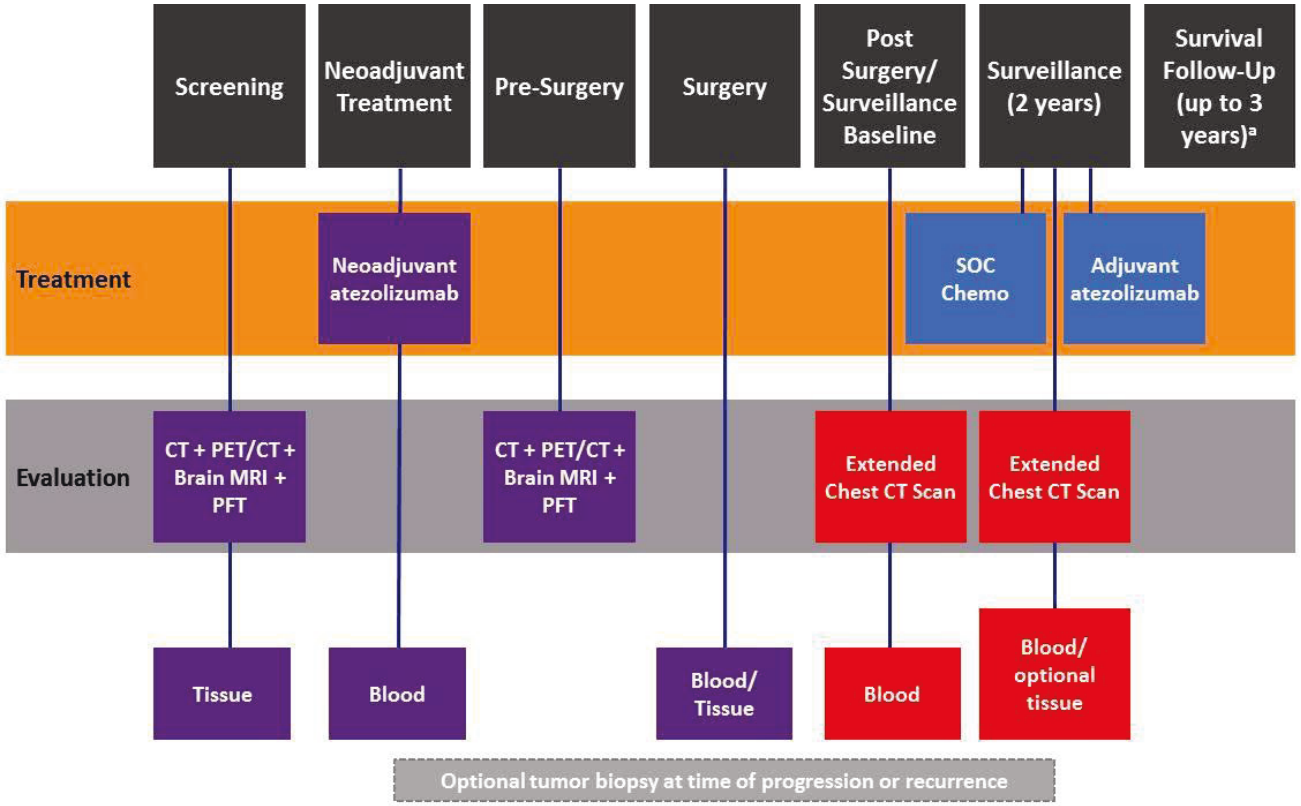
The Neoadjuvant Atezolizumab Therapy Phase will end when the last data point required for primary efficacy analysis (i.e., pathology evaluation at time of surgery) is obtained. This is expected to occur approximately 30 days after the last patient's surgery.

The Surveillance period will end 2 years after the post-surgery visit. After completing neoadjuvant or adjuvant treatment with atezolizumab, patients will be followed for survival for up to 3 years. For patients that undergo surgery and enter Surveillance, time in Surveillance will overlap with time in Survival Follow-up.

The total length of the study, from screening of the first patient to the end of the study, is expected to be approximately 6 years.

The study schema is illustrated in Figure 1, and a schedule of assessments is presented in Section 4 of this statistical analysis plan.

Figure 1 **Study Schema**



CT=computed tomography; MRI=magnetic resonance imaging; PET= positron emission tomography; PFT = pulmonary function test; SOC = standard of care.

a Refer to Appendix 2 in the protocol , Timing of Surveillance Assessments.

4. SCHEDULE OF ASSESSMENTS

Assessment	Screening [a]		Part 1 – Atezolizumab Neoadjuvant Treatment		Surgery			Neo-adjuvant Atezo Treatment Completion/ D/C [d]	Surveillance				Disease Progression or Recurrence [g]	Survival Follow-up [h]
									All Subgroups	For Subgroups B and D only				
					Pre-surgery [b]	Surgery	Post-Surgery/ Surveillance Baseline [c]		Surveillance for All Treatment Subgroups See Appendix 2	Adjuvant Atezo Treatment [e, f]	Adjuvant Atezo Treatment [c, f]	Adjuvant Atezo Treatment Completion / D/C [d]		
(Window [Days])	Day −42 to −1	Day −14 to −1	C1D1 (Day 1 ±3)	C2D1 (Day 22 ±3) [i]	Day 36 (±3)	Day 40 (±10) [j]	4–6 weeks after surgery	30 (± 5) days after last dose	Every 6 weeks to 3 months for up to 2 years [k]	Adjuvant Cycle 1, Day 1, (±5) days	Adjuvant Cycle 2–17, Day 1 (±5) days [i]	30 (± 5) days after last dose	30 days after progression/ recurrence (± 5) days [l]	Up to 3 years
Informed consent (prescreening ICF and main ICF) [m]	x													
Prescreening biopsy	See footnote [n]													
Medical history and demographic data [o]	x													
Weight	x									x	x			
Height	x													
Complete physical examination [p]	x				x [q]									

Assessment	Screening [a]		Part 1 – Atezolizumab Neoadjuvant Treatment		Surgery			Neo-adjuvant Atezo Treatment Completion/ D/C [d]	Surveillance				Disease Progression or Recurrence [g]	Survival Follow-up [h]
									All Subgroups	For Subgroups B and D only				
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(Window [Days])	Day −42 to −1	Day −14 to −1	C1D1 (Day 1 ±3)	C2D1 (Day 22 ±3) [i]	Day 36 (±3)	Day 40 (±10) [j]	4–6 weeks after surgery	30 (± 5) days after last dose	Every 6 weeks to 3 months for up to 2 years [k]	Adjuvant Cycle 1, Day 1, (±5) days	Adjuvant Cycle 2–17, Day 1 (±5) days [l]	30 (± 5) days after last dose	30 days after progression/ recurrence (± 5) days [l]	Up to 3 years
Limited physical examination [r]						X		X		X	X[s]	X		
ECOG Performance Status [t]	X							X		X [t]	X [t]	X		
Vital signs [u]	X		X [u]	X		X		X		X [u]	X [u]	X		
Tumor and response evaluations [v]	X				X		X[w, x]		X [w]	X [y, x]	X [z]			
Pathologic response assessment [z]							X							
Pulmonary function tests	X[aa]				X									
Hematology [bb]		X		X	X					X				
Chemistry [cc]		X		X	X					X				

Assessment	Screening [a]		Part 1 – Atezolizumab Neoadjuvant Treatment		Surgery			Neo-adjuvant Atezo Treatment Completion/ D/C [d]	Surveillance				Disease Progression or Recurrence [g]	Survival Follow-up [h]
									All Subgroups	For Subgroups B and D only				
					Pre-surgery [b]	Surgery	Post-Surgery/ Surveillance Baseline [c]		Surveillance for All Treatment Subgroups See Appendix 2	Adjuvant Atezo Treatment [e, f]	Adjuvant Atezo Treatment [c, f]	Adjuvant Atezo Treatment Completion / D/C [d]		
(Window [Days])	Day −42 to −1	Day −14 to −1	C1D1 (Day 1 ±3)	C2D1 (Day 22 ±3) [i]	Day 36 (±3)	Day 40 (±10) [j]	4–6 weeks after surgery	30 (± 5) days after last dose	Every 6 weeks to 3 months for up to 2 years [k]	Adjuvant Cycle 1, Day 1, (±5) days	Adjuvant Cycle 2–17, Day 1 (±5) days [l]	30 (± 5) days after last dose	30 days after progression/ recurrence (± 5) days [l]	Up to 3 years
Coagulation (aPTT and INR)		x												
Pregnancy test [dd]		x												
Urinalysis [ee]		x												
Thyroid function test (TSH, free T3, and free T4) [ff]		x			x		x			x	x (q3 cycles)			
C-reactive protein		x												
Viral serology [gg]		x												
Biomarker samples (tissue) [hh]	x[ll]					x							x [jj]	
Biomarker samples (blood-based) [hh, kk]			x			x	x [x]	x	x[ll]	x	x [mm]	x	x	

Assessment	Screening [a]		Part 1 – Atezolizumab Neoadjuvant Treatment		Surgery			Neo-adjuvant Atezo Treatment Completion/ D/C [d]	Surveillance				Disease Progression or Recurrence [g]	Survival Follow-up [h]
									All Subgroups	For Subgroups B and D only				
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Optional bronchial brushing [nn]	x										x[oo]			
Atezolizumab administration [pp]			x	x						x	x			
Concomitant medications [qq]	x	x	x	x	x	x	x			x	x			
Adverse events [rr]	x	x	x	x	x	x	x			x	x			
Survival and recurrence follow-up [h]														x

atezo = atezolizumab; C1D1 = Cycle 1, Day 1; C2D1 = Cycle 2, Day 1; D/C = discontinuation; ECG = electrocardiogram; ECOG = Eastern Cooperative Oncology Group; eCRF = electronic Case Report Form; q = every; SOC = standard of care.

Notes: All assessments should be performed within the time windows specified for the scheduled visit. All designated procedures are required

at each visit, even if visit is outside the recommended time window. On treatment days, all assessments should be performed prior to dosing, unless otherwise specified.

[a] Results of SOC tests or examinations performed prior to obtaining informed consent and within 42 days prior to Day 1 (or within 14 days prior to Day 1 for laboratory tests) may be used; such tests do not need to be repeated for screening.

[b] Preferably, assessments at this visit should be performed by the surgeon, if feasible. If not feasible, the assessments may be performed by the Medical Oncologist.

[c] It is acceptable for visit to occur outside the recommended window; all indicated procedures should be still be performed.

[d] For the Adjuvant Atezolizumab Therapy Phase, all vital sign measurements and routine laboratory tests and tumor assessments, will be performed per SOC except biomarkers assessments and Extended Chest CT scan, which will occur per Surveillance schedule of activities (Appendix 2).

[e] Patients who prematurely discontinue neoadjuvant atezolizumab will return to the clinic 30 (+ 5) days after the last dose of atezolizumab treatment. If patients undergo surgery after neoadjuvant atezolizumab discontinuation/completion and will not receive adjuvant atezolizumab, the Treatment Discontinuation Visit assessments can be performed at the Post-Surgery Visit (even if it is more than 30 days after the last dose). If the patient will receive adjuvant atezolizumab, the Treatment Discontinuation Visit will occur when the patient completes/discontinues adjuvant atezolizumab treatment. Patients who do not complete surgery will then be followed for survival. Patients who complete surgery will enter the Surveillance period. The visit at which progressive disease or recurrence occurs may be used as the Treatment Discontinuation Visit.

[f] Any assessments not marked with an "x" should be performed as per SOC.

[g] Disease progression/recurrence must be confirmed by tumor imaging.

[h] Patients who prematurely discontinue neoadjuvant atezolizumab and do not undergo surgery will enter Survival Follow-Up for up to 3 years after the last dose of neoadjuvant atezolizumab. Patients who undergo surgery will enter the Surveillance period (See Appendix 2) and then will enter Survival Follow-Up. During Survival Follow-Up, information on recurrence, off-protocol cancer-related treatment and survival will be collected every 6 months for up to 3 years Surveillance. This information may be obtained at clinic visits or by telephone, mail, or email. The last Survival Follow-up Visit will serve as the Study Completion Visit .

[i] If C2D1 visit is delayed, all subsequent visits will be delayed accordingly.

[j] Delay in surgery due to an adverse event is permitted.

[k] Window for assessments may be altered to align with adjuvant therapy. Allowed timeframe for Surveillance assessments is outlined in Appendix 2. Blood sample and extended chest CT from Post-surgeryVisit will be a part of Surveillance assessments.

[l] Exceptions may be made with Medical Monitor approval.

[m] Informed consent must be documented before any prescreening or screening procedure is performed.

[n] A prescreening biopsy can be conducted for patients who do not have an adequate archival tumor specimen. This biopsy will not need to be repeated at study screening. If a patient has an adequate archival tumor specimen, no additional biopsy will be needed.

[o] Includes clinically significant diseases, surgeries, cancer history (including histology, stage, prior cancer therapies and procedures), smoking

history, asbestos, pleural or pericardial effusion, ascites requiring intervention, exposure, HPV infection and HPV subtypes, associated syndromes, *Helicobacter pylori* infection, relevant mutations, and reproductive status (women).

[p] Includes evaluation of the head, eyes, ears, nose, and throat, and the cardiovascular, dermatological, musculoskeletal, respiratory, gastrointestinal, and neurological systems. Record abnormalities observed at baseline on the General Medical History and Baseline Conditions eCRF. At subsequent visits, record new or worsened clinically significant abnormalities on the Adverse Event eCRF.

[q] Complete physical examination only has to be conducted at either the C2D1 visit or the pre-surgery visit, but not at both.

[r] Perform a limited, symptom-directed examination at specified timepoints or as clinically indicated. Record new or worsened clinically significant abnormalities on the Adverse Event eCRF.

[s] Limited examination should be performed per SOC during adjuvant atezolizumab treatment.

[t] ECOG Performance Status must be of 0 or 1 at screening and before patients can start adjuvant treatment (see Appendix 7).

[u] In the Neoadjuvant Atezolizumab Therapy Phase, measure respiratory rate, pulse rate, systolic and diastolic blood pressure while the patient is in a seated position, temperature, and oxygen saturation by pulse oximetry. For both infusions of atezolizumab, measure the patient's vital signs within 60 minutes before the infusion; and during and after the infusion, if clinically indicated. For the Neoadjuvant Atezolizumab Therapy Phase, measure vital signs per SOC. Record abnormalities observed at screening on the General Medical History and Baseline Conditions eCRF. At subsequent visits, record new or worsened clinically significant abnormalities on the Adverse Event eCRF.

[v] For the Neoadjuvant Atezolizumab Therapy Phase, the patient's tumor will be staged at screening by contrast-enhanced helical CT scan of the chest, PET/CT, and brain MRI, preferably with gadolinium (for Stage II or III disease). If brain MRI is not feasible for technical or patient-related reasons (e.g., pacemaker, severe claustrophobia), brain CT scan with IV contrast should be obtained. All scans will be repeated prior to surgery to confirm surgical eligibility. Radiographic responses will be assessed by the investigator per RECIST v1.1 after the two cycles of atezolizumab. Scans *will* be repeated *and collected* at any time if progressive disease is suspected. For the Adjuvant Atezolizumab Therapy Phase, all tumor assessments will be per Surveillance schedule of activities (see Appendix 2). *All imaging will be collected for further analyses. See imaging manual for specific instructions.*

[w] Extended chest CT scan (including liver and adrenals). All other CT Scans will be performed as per SOC. For additional details on the timing of assessments, see Appendix 2.

[x] Blood sample and extended chest CT scan from Post-surgery Visit will be a part of Baseline Surveillance assessments.

[y] For Group D only: Extended CT chest (including liver and adrenals) needs to be done after completion of SOC adjuvant Chemotherapy/Radiotherapy and before initiation of adjuvant atezolizumab to rule out disease progression/recurrence. If done as part of a surveillance visit, it does not need to be repeated. The other tumor assessments will sync with the surveillance visits (see Appendix 2).

[z] For the Neoadjuvant Atezolizumab Therapy Phase, pathologic responses will be scored by a pathologist based on the surgical resection as defined by (Hellmann et al. 2014).

[aa] Can be performed within 6 months of planned resection and repeated at screening.

[bb] Hematology includes CBC (WBC count, RBC count, hemoglobin, hematocrit, platelet count, differential count [neutrophils, eosinophils,

basophils, monocytes, lymphocytes, other cells]).

[cc] Chemistry panel (serum) includes sodium, potassium, chloride, bicarbonate, glucose, BUN or urea, creatinine, total protein, albumin, phosphorus, calcium, total and direct bilirubin, alkaline phosphatase, ALT, AST, uric acid, LDH.

[dd] All women of childbearing potential, including those who have had a tubal ligation, will have a serum pregnancy test at screening.

[ee] Includes specific gravity, pH, glucose, protein, ketones, and blood.

[ff] Perform thyroid function tests at baseline, the pre-surgery visit, at post-surgery visit and then approximately every 9 weeks (3 cycles) during adjuvant atezolizumab treatment in the Adjuvant Atezolizumab Therapy Phase.

[gg] Viral serology includes HIV, Hepatitis B (HBsAg, antibodies against HBsAg, hepatitis B core antigen; HBV DNA is required positive anti-HBc antibody test), and HCV antibody (anti-HCV).

[hh] See Appendix 3 for detailed schedule.

[ii] Tumor tissue may be archival; it does not need to be collected within 42 days of enrollment.

[jj] Tissue biopsy (tumor and lymph node, if available); at disease progression/recurrence is optional and requires a separate ICF signature. Tissue collection by CNB is preferred, however collection by EBUS, or bronchoscopy are acceptable alternatives.

[kk] The biomarker blood sample may be collected up to 7 days prior to the visit. *Whole blood sample for biomarker assessments should preferably be collected on the day of surgery (prior to surgery and prior to antibiotic administration). It is acceptable to collect the sample up to 7 days prior to surgery (including the day of surgery, and prior to antibiotic administration). If sample needs to be collected outside of the recommended window, please contact the Medical Monitor for guidance and approval.*

[ll] Plasma, serum and, at selected timepoints, also PBMCs will be collected (see Appendix 2).

[mm] Biomarker blood samples will be collected approximately at every 6 weeks to 3 months but can be adjusted to synchronize with Surveillance visits (See Appendix 2).

[nn] Encouraged for patients undergoing EBUS and/or bronchoscopy. See lab manual for exact nomenclature and specific areas to be sampled during procedure.

[oo] Should be performed after approximately 3-4 months of first adjuvant atezolizumab treatment.

[pp] In the Neoadjuvant Atezolizumab Therapy Phase, neoadjuvant treatment with atezolizumab 1200 mg will be given q21d for a maximum of 2 cycles. In Adjuvant Atezolizumab Therapy Phase, adjuvant treatment with atezolizumab 1200 mg will be given q21d for maximum of 12 months (maximum 17 cycles). Patients may need to remain in the clinic post-infusion for monitoring if needed. See Section 4.3.2 for administration instructions.

[qq] Includes any medication (e.g., prescription drugs, over-the-counter drugs, vaccines, herbal or homeopathic remedies, nutritional supplements) used by a patient from 7 days prior to initiation of atezolizumab treatment until the until the following visit: 1) For patients who will receive adjuvant atezolizumab treatment – until the Adjuvant Atezolizumab Completion/ Discontinuation Visit (whichever visit will occur last), or 2) For patients who will not receive adjuvant atezolizumab treatment – until the Post-surgery Visit.

[rr] After informed consent has been obtained but prior to initiation of atezolizumab treatment, only serious adverse events caused by a protocol-mandated intervention should be reported. After initiation of atezolizumab treatment, adverse events will be reported until 30 days after the last

dose of atezolizumab (neoadjuvant or adjuvant, whichever occurs last). Serious adverse events and adverse events of special interest will be reported until 90 days after the last dose of atezolizumab (neoadjuvant or adjuvant, whichever occurs last; see Section 5.3.1). All adverse events associated with CT scans, blood sample collection, and the optional biopsy (collected at the time of disease progression/recurrence) that occur after the 90 day reporting window, but during the Surveillance period, will also be collected and reported. After the designated reporting period, the Sponsor should be notified if the investigator becomes aware of any serious adverse event that is believed to be related to prior atezolizumab treatment. The investigator should follow each adverse event until the event has resolved to baseline grade or better, the event is assessed as stable by the investigator, the patient is lost to follow-up, or the patient withdraws consent. Every effort should be made to follow all serious adverse events and adverse events of special interest considered to be related to atezolizumab treatment or trial-related procedures until a final outcome can be reported.

5. ANALYSIS POPULATIONS

Data will be summarized using the following analysis populations.

- All Enrolled Subjects: This analysis population will include all enrolled subjects, regardless of whether they received any amount of study drug. The all enrolled subjects population will be used for the summarization of subject disposition.
- Safety Population: This analysis population will include all enrolled subjects who have received any dose of study drug. The safety population will be used for the analysis of safety measures.
- Efficacy Population: This analysis population will include all enrolled patients who have received at least one dose of the study drug and who do not have EGFR or ALK mutant tumors.
- Primary Efficacy Population: This analysis population will include all efficacy population subjects, excluding patients who have not received surgery after neoadjuvant treatment with Atezolizumab, and excluding subjects who have not had a complete resection. This population will be used for primary efficacy analysis. For the primary efficacy population, if major pathological response is unable to be assessed, then it will remain undetermined and the subject will be removed from this population.

6. STATISTICAL METHODOLOGY

Data related to exploratory biomarker objectives will not be analyzed by Syneos Health and will not be mentioned further in this SAP.

6.1 Statistical and Analytical Issues

6.1.1 Statistical Methods

Continuous data will be summarized by descriptive statistics, including mean, standard deviation, median, minimum, and maximum. Categorical data will be summarized by the number and percentage of subjects. Percentages will be based on non-missing data unless specified otherwise. Specific details regarding statistical testing will be found in Section 6.3 of this SAP.

Baseline values will be the latest assessment prior to the start of the first cycle of study drug. The same baseline will be used for each study phase.

Statistical analyses will be carried out using SAS® software version 9.3 or higher (Copyright, SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute, Inc., Cary, North Carolina, USA).

6.1.2 Handling of Dropouts and Missing Data

Adverse Events

- Adverse events for which the relation to study drug is not reported will be assumed related to study drug.

- Adverse events for which the NCI CTCAE grade is not reported will not have a grade imputed and will be summarized as "No Grade".
- Missing AE onset and end date components will be conservatively imputed for the purpose of determining treatment emergent status of any events with incomplete dates. Originally reported (and possibly missing or partial) onset and end date information will be presented listings. Imputation for missing AE date components will be handled as follows.
    - If only month and year are present for AE onset, the 1st day of the month and year will be imputed. If the available month and year of AE onset equal the month and year of date of first dose of study drug, and the resulting imputed date will not exceed an available complete end date of the event, then the date of the first dose of study drug will instead be imputed.
    - If only year is present for AE onset, the 1st day of January of the year will be imputed. If the available year of AE onset equals the year of date of first dose of study drug, and the resulting imputed date will not exceed an available complete end date of the event, then the date of the first dose of study drug will instead be imputed.
    - If only month and year are present for AE end, the last day of the month and year will be imputed (taking into account February in leap years). If the available month and year of AE end equal the month and year of study completion/discontinuation date, then the date of study completion/discontinuation will instead be imputed.
    - If only year is present for AE end, the 31st of December of the year will be imputed. If the available year of AE end equals the year of study completion/discontinuation date, then the date of study completion/discontinuation will instead be imputed.
    - AE onset and end dates which are entirely missing will not be imputed.
    - The chronological order of AE onset and end dates will be maintained.

Efficacy Analysis

Handling of missing data for efficacy analysis will be discussed in the respective sections below in this SAP.

6.1.3 Pooling of Investigative Sites

Data from all sites will be pooled for summarization and analyses.

6.1.4 Determination of Sample Size

The primary objective of this study is to determine the major pathological response rate. If there is evidence that the major pathologic response rate is at least 15% then there will be further consideration for the testing of atezolizumab in neoadjuvant lung cancer. This is a single-arm study, and all patients will be treated with atezolizumab. The primary endpoint is assessed by a statistical test of a single proportion of responders against the simple alternative of 5% response.

This design provides 95% statistical power to detect a difference of 10% (15% vs. 5%) at a significance level of 0.05 (1-sided test, variance of the test statistic calculated under the alternative hypothesis). To achieve this, approximately 180 patients will be enrolled in this study. At the final analysis (after 180 patients are enrolled), if there are at least 17 patients who respond then the statistical test rejects the null hypothesis of a 5% response rate in favor of a higher response rate.

This study includes one interim analysis to assess futility after 90 patients are assessed. The non-binding futility interim boundary satisfies conditional power of 0.30. Thus, the probability that the statistical test at the final analysis will be significant at the specified power and test level is at least 0.30, conditional on the data available at the time of the interim analysis. At the interim analysis, if there are seven or fewer responders out of 90 patients then the conditional power of the study drops below 0.30, and enrollment into the study may be terminated.

Differential response by PD-L1 status (positive versus negative) will be assessed. While the composition of PD-L1 status in this patient population is not known, the study will aim to include at least 60 PD-L1 positive patients. With 60 PD-L1 positive patients, the one-sided 95% CI excludes 20% if the major pathologic response rate is 30% (18 responders out of 60 patients). Final enrollment numbers may be expanded accordingly.

6.2 Subject Characteristics

6.2.1 Subject Disposition

Neoadjuvant Atezolizumab Therapy Phase

Calculating the percentages based on the number of subjects who received neoadjuvant atezolizumab treatment, summarize the following:

- The number of subjects who receive neoadjuvant atezolizumab (treated)
- The number and percentage of subjects who had surgery
- The number and percentage of treated subjects who completed Neoadjuvant Atezolizumab treatment
- The number and percentage of subjects who do not complete Neoadjuvant Atezolizumab treatment
- The number and percentage of subjects who do not complete Neoadjuvant Atezolizumab treatment by reason

Adjuvant Atezolizumab Therapy Phase

Calculating the percentages based on the number of subjects treated with adjuvant atezolizumab, summarize the following:

- The number of subjects who receive adjuvant atezolizumab (treated)
- The number and percentage of treated subjects who completed adjuvant atezolizumab treatment
- The number and percentage of subjects who do not complete adjuvant Atezolizumab treatment
- The number and percentage of subjects who do not complete adjuvant Atezolizumab treatment by reason

Surveillance/Survival Follow-up Phase

Calculating the percentages based on the number of subjects entering the surveillance period, summarize the following by subgroup and overall:

- The number of subjects who enter the Surveillance/Survival Follow-up Phase
- The number and percentage of subjects who completed surveillance,
- The number and percentage of subjects who do not complete surveillance
- The number and percentage of subjects who do not complete surveillance by reason

Using subgroups:

- Subgroup A: No Adjuvant Treatment
- Subgroup B: Adjuvant Atezolizumab Treatment
- Subgroup C: SOC Chemotherapy (± Radiotherapy) Only
- Subgroup D: SOC Chemotherapy (± Radiotherapy) + Adjuvant Atezolizumab Treatment

Study Discontinuation

Calculating the percentages based on the number of subjects enrolled, summarize the following:

- The number and percentage of subjects who completed the study,
- The number and percentage of subjects who discontinued the study
- The number and percentage of subjects who discontinued the study by reason

6.2.2 Protocol Deviations

Protocol deviations will be documented and explained by the investigator and classified as major or minor by the clinical monitor.

The number and percentage of subjects with at least one major protocol deviation will be summarized for each protocol deviation category based on the safety population.

All protocol deviations will be listed.

6.2.3 Background and Demographic Characteristics

Demographic information including age at first dose in years, sex, ethnicity, race, height in meters, weight in kilograms, body mass index in kg/m^2, and ECOG performance status will be tabulated for the safety population. Descriptive statistics, including number of patients, mean, standard deviation, median, minimum, and maximum for continuous parameters, as well as percentages for categorical parameters, will be presented.

Age in years at the date of first dose will be computed as an integer using the date of birth and the date of first dose.

Body mass index will be computed as (weight in kilograms / (height in meters)^2).

Tobacco use history (never, current, previous) and for those with current or previous tobacco use the number of years a subjects is/was a smoker and the average number of cigarettes, cigars, pipes, and pack of chewing tobacco per week, will be summarized descriptively for the safety population.

Non-metastatic lung cancer history will be summarized for the safety population by presenting summary statistics for histology (squamous, non-squamous, and type of non-squamous), initial diagnosis staging (Stages IB, II, IIIA, and selected IIIB), and time from initial diagnosis to first dose. Time from initial diagnosis to first dose is computed as the date of first dose in Cycle 1 minus the date of initial diagnosis, plus one day.

Lung cancer molecular profile will be summarized for the safety population by presenting descriptive statistics for derived Epidermal Growth Factor Receptor (EGFR) mutation (positive, negative/unknown), derived anaplastic lymphoma kinase (ALK) rearrangement detection status (yes, no/ unknown), and number and percentage for each binary group category and combined mutually exclusive group category of PD-L1 IHC status by SP142 method. This lung cancer molecular profile will be used in efficacy analyses.

PD-L1 status of patients using SP142 method can be derived as such: group the Tumor Cell (TC) score and Immune Cell (IC) score (both range from 0 – 100) into the following groups:

- Total Perc Cells Membrane Stain: TC0 [0,1), TC1 [1,5), TC2 [5,50), TC3 [50-100]
- Perc Positive Infiltrate In Tumor Mass: IC0 [0,1), IC1 [1,5), IC2 [5,10), IC3 [10,100]

Derive the binary grouping scores: TC3/IC3 (categorized as TC3IC3, TC012IC012, unknown), TC2/IC2 (categorized as TC23IC23, TC01IC01, unknown) and TC1/IC1 (categorized as TC123IC123, TC0IC0, unknown) and the combined mutually exclusive grouping score: TCIC4GRP (categorized as TC3 or IC3, TC0 or IC0, TC2/3 or IC2/3, TC1/2/3 or IC1/2/3, unknown).

For derived EGFR status and derived ALK status, local lab (CRF) value will be used first; if there is missing data in local lab value, central lab value at screening will be used second, and finally if there is missing data in central lab value at screening, central lab value at surgery will be used.

Local lung cancer molecular profile per CRF will be summarized for the safety population by presenting descriptive statistics for Epidermal Growth Factor Receptor (EGFR) mutation (positive, negative, and unknown), anaplastic lymphoma kinase (ALK) rearrangement detection status (yes, no, unknown), and PD-L1 IHC status (negative, positive, unknown).

Results of the ventilation/perfusion scan performed at screening will be summarized for the safety population by presenting summary statistics for scan performed (yes, no) and specific results (no perfusion deficit, perfusion deficit with matched ventilation deficit, ventilation perfusion mismatch, perfusion deficit that corresponds to parenchymal abnormality on chest x-ray, multiple segmental perfusion deficits with normal ventilation).

6.2.4 Treatment Exposure and Compliance

Neoadjuvant Atezolizumab Therapy Phase

Treatment exposure and compliance will be examined in the Neoadjuvant Atezolizumab Therapy Phase of the study by summarizing overall the number of cycles initiated, infusion cycle intervention status (yes, no), and reason for infusion intervention (infusion related reaction [IRR], adverse event not considered IRR, other) for the safety population.

Surveillance/Survival Follow-up Phase

The same treatment exposure and compliance will also be summarized for the Surveillance/Survival Follow-up Phase.

6.2.5 Prior and Concomitant Medications and Therapies

All reported medications and therapies, whether determined to be prior or concomitant uses, will be coded using the Genentech, Inc. Drug Thesaurus. Levels of summarization will include drug class and standardized term.

Concomitant medications are defined as non-study medications with a stop date on or after the first dose of study drug, and a start date on or before the date of the subject's last visit in the study. Medications that started prior to the first dose of study drug and are ongoing will be classified as concomitant. Medications that have a stop date prior to the first dose of study drug will be flagged as 'prior'.

At each level of summarization (drug class and standardized term), a subject will be counted only once for each medication he/she has within that level. Prior and concomitant medications will be summarized in separate tables for each study phase separately. The percentage of safety population subjects having had at least one prior or concomitant medication at each level will be calculated.

Data listings will be provided for all prior and concomitant medications.

6.2.6 Medical Histories

Medical conditions will be coded to system organ classes and preferred terms using Medical Dictionary for Regulatory Activities version 19.1 or higher if available.

The number and percentage of safety population subjects who have any medical history and any medical history within the system organ class and preferred term levels will be summarized.

6.2.7 Surgeries and Procedures

Surgeries and procedures will be coded to standardized terminology.

The number and percentage of safety population subjects with any surgery or procedure, any surgery, and any procedure will be summarized.

6.3 Efficacy Analysis

6.3.1 Primary Efficacy Analysis

The number of subjects with major pathologic response (n) and the major pathologic response rate (n/N x 100) will be summarized for the primary efficacy population (N). A one sample exact binomial test will be performed to test the null hypothesis that the major pathologic response rate is 5%, versus the alternative hypothesis is the major pathologic response rate is > 5%. If the null hypothesis is rejected then this is evidence that the response rate exceeds 5% when atezolizumab is given before resection. The one-sided 95% confidence interval (CI) for major pathologic response rate will be reported.

6.3.2 Secondary Efficacy Analysis

The proportion of subjects who experienced a major pathologic response in the PD-L1 positive group (TC123IC123) and PD-L1 (TC0IC0) negative group will be compared using the Pearson's chi-square test in the primary efficacy population. If the number of subjects in one of the table cells is less than 5, then Fisher's exact test will be used instead. The lower bound of the 80% Wald CI for the difference in proportions between the two groups will be obtained. The number and the proportion of subjects with major pathologic response will be summarized by PD-L1 positive group (TC123IC123) vs. PD-L1 negative group (TC0IC0).

A similar analysis will also be performed for objective response rate: the proportion of subjects who are objective responders (Complete Response and Partial Response are considered as responders, Stable Disease, Progressive Disease and Not Evaluable are considered as non-responders) in the PD-L1 positive (TC123IC123) and negative (TC0IC0) groups will be compared using Pearson's chi-square test in the efficacy population. If the number of subjects in one of the table cells is less than 5, then Fisher's exact test will be used instead. The lower bound of the 80% Wald CI for the difference in proportions between the two groups (PD-L1 positive (TC123IC123) and negative (TC0IC0)) will be obtained. The number and proportion of subjects who are objective responders will be summarized by PD-L1 positive (TC123IC123) and negative (TC0IC0) groups.

A forest plot of major pathological responders will be produced, including the following categories:

- Sex
- Race
- Ethnicity
- ECOG performance status
- Non-metastatic lung cancer histology
- Initial diagnosis staging
- PD-L1 positive (TC123IC123) and PD-L1 negative (TC0IC0)

6.3.3 Exploratory Analysis

Overall survival (OS) will be analyzed in efficacy population. OS is defined as the time from the date of first dose until the date of death from any cause. This is the length of time from the start of treatment that patients are still alive. Subjects alive at the end of the study or lost to follow-up will be censored on the date of last follow-up disease assessment.

Disease-free survival (DFS) will be analyzed in primary efficacy population. DFS is defined as the time from the first date of no disease (i.e., date of surgery with complete resection) to local or distant recurrence or death due to any cause, whichever occurs first. DFS will be analyzed only for patients who underwent surgery with complete resection. After surgery with complete resection, data for patients who withdraw from the study without disease recurrence or death will be censored at the date of last disease follow-up assessment. Patients without post-surgery disease follow-up assessments but known to be alive will be censored at the date of surgery with complete resection plus one day.

Event-free survival (EFS) will be analyzed in efficacy population. EFS is defined as the time from the date of first dose to any of the following events, whichever occurs first:

- Progression of disease per RECIST v1.1 that precludes surgery with complete resection
- Local or distant disease recurrence
- Death due to any cause

Patients who have not experienced disease progression that precludes surgery with complete resection, local or distant disease recurrence, or death at the time of analysis will be censored at the time of last tumor or disease follow-up assessment. Patients with no post-baseline tumor or disease follow-up assessment but known to be alive will be censored at the date of first dose plus one day.

The durations of overall survival, disease-free survival and event-free survival will be computed in months as:

$$\frac{(End\ Date - Start\ Date + 1)}{\left({}^{365.25}/_{12}\right)}$$

The overall survival, disease-free survival and event-free survival will be analyzed using the Kaplan-Meier method for the efficacy population. To describe overall survival, the survival rate, death rate, and overall median, 95% CI, 25th and 75th percentiles, and range will be reported. Furthermore, the patients remaining alive, survival rate, and 95% CI will be reported every 6 months (at 6, 12, 18, 24, 30, and 36 months). To describe disease-free survival and event-free survival, the disease-free rate, not disease-free rate, counts of patients by contributing events, and overall median, 95% CI, 25th and 75th percentiles, and range will be reported. Furthermore, the patients remaining disease-free, disease-free rate, and 95% CI will be reported every 6 months (at 6, 12, 18, 24, 30, and 36 months).

These analyses will also be repeated for each subgroup of major pathologic responder and non-responder, and by subgroups of PD-L1 negative (TC0IC0) and positive (TC123IC123). Subgroups will be compared using a log-rank test.

6.4 Safety Analysis

6.4.1 Adverse Events (AE)

All reported adverse events terms will be coded to a system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities version 19.1 or higher if available.

Treatment related adverse events are those adverse events flagged as suspected to be caused by Atezolizumab.

Neoadjuvant Atezolizumab Therapy Phase

For the Neoadjuvant Atezolizumab Therapy Phase of the study, an adverse event will be any event that starts following the start of the first dose of study drug for those subjects not continuing in the Surveillance/Survival Follow-up Phase of the study, and through the day immediately preceding the start date of the first adjuvant cycle for subjects continuing in the Surveillance/Survival Follow-up Phase of the study.

If the onset date and/or resolution date of an adverse event is incomplete (for example, only the month and year are available), the event will be assumed to start after the first dose of study drug, as long as the available information does not conclusively indicate that the event emerged prior to the start date of the first cycle of study drug administration.

An overview of adverse events will present the number and percentage of safety population subjects who have at least one AE, at least one Grade 3 or higher AE, at least one treatment related AE, at least one serious AE, at least one AE of special interest, at least one AE leading to study drug withdrawal, at least one AE leading to death, and at least one treatment related AE leading to death, overall (subjects counted only once if any AE is experienced) and by highest NCI CTCAE grade (subjects counted only once at the highest grade level experienced).

The number and percentage of safety population subjects with AEs will be summarized by SOC and PT in total, and by highest NCI CTCAE grade. At each summary level, a subject will be counted only once if he/she experiences at least one AE, and when summarizing by highest NCI CTCAE grade, a subject will be counted only once at the highest grade level experienced. AE summary tables will be sorted by descending occurrence rate according to the SOC, and then by descending occurrence rate within PT. The following types of AE summaries will be prepared:

- All AE
- Grade >=3 AE
- Onset date prior to date of surgery (Neoadjuvant Atezolizumab Therapy Phase only)
- Onset date on or after date of surgery, for safety population with surgery date (Neoadjuvant Atezolizumab Therapy Phase only)
- Treatment related AE
- Serious AE
- AE of special interest
- AE leading to death
- Treatment related AE leading to death
- AEs leading to study drug withdrawal

All adverse events will be listed including the AEs which start before the first dose of study drug, and additional separate listings will be created for AEs leading to death, serious AEs, and AEs leading to study drug withdrawal.

Surveillance/Survival Follow-up Phase

For the Surveillance/Survival Follow-up Phase of the study, an adverse event will be any event that starts following the start of the first dose of study drug for those subjects continued in the Surveillance/Survival Follow-up Phase of the study.

If the onset date and/or resolution date of an adverse event is incomplete (for example, only the month and year are available), the event will be assumed to start after the first dose of study drug,

as long as the available information does not conclusively indicate that the event emerged prior to the start date of the first cycle of study drug administration.

AEs in the Surveillance/Survival Follow-up Phase will be summarized and listed in the same form as aforementioned in the Neoadjuvant Atezolizumab Therapy Phase.

AE by highest NCI CTCAE grade will also be summarized for both study phases combined.

6.4.2 Laboratory Parameters

Serum chemistry and hematology parameters will be converted to a standard set of units to be agreed upon with the sponsor.

Neoadjuvant Atezolizumab Therapy Phase

Converted laboratory parameter values will be summarized descriptively (n, mean, standard deviation, median, minimum, and maximum) for safety population subjects at each scheduled data collection time point. Change from baseline (the latest value collected prior to first dose) to each scheduled data collection time point will also be summarized descriptively for safety population subjects.

Shift tables will present a cross tabulation of baseline results categories (values falling in low, normal, high categories relative to normal ranges, or values being associated with grades) versus result categories at each follow up visit. The number and percentage of safety population subjects falling within each cross tabulation cell will be presented; the denominator for each percentage will be the number of safety population subjects with a baseline result and a follow-up result at the given visit for the given parameter.

Surveillance/Survival Follow-up Phase

Same analysis will be done for the Surveillance/Survival Follow-up Phase using the same baseline as the Neoadjuvant Atezolizumab Therapy Phase.

6.4.3 Vital Signs

Vital signs will be summarized descriptively (n, mean, standard deviation, median, minimum, and maximum) for safety population subjects at each scheduled data collection time point. Raw and change from baseline vital sign values, including systolic and diastolic blood pressure, heart rate, height, weight, body temperature for both oral and auricular, and respiratory rate, will be summarized using descriptive statistics at baseline and each assessment time point at post-dose visits for each of the two study phases.

6.4.4 Physical Examination

Complete physical examination at screening and limited physical examination at each scheduled data collection time point will be listed for both phases of the study.

6.4.5 Pulmonary Function Test

Raw and change from baseline for pulmonary function test will be summarized descriptively (n, mean, standard deviation, median, minimum, and maximum) and listed at each scheduled data collection time point for the Neoadjuvant Atezolizumab Therapy Phase.

6.4.6 ECOG Performance Status

Number and percentage for each ECOG performance status will be summarized and listed at each scheduled data collection time point for both phases of the study.

6.4.7 Analyses of Other Safety Assessments

The data for coagulation (aPTT and INR) tests, Pregnancy test, urinalysis, thyroid function test (TSH, Free T3 and Free T4), C-reactive protein, viral serology will be listed.

6.5 Interim Analysis

The study will continue during the planned interim analyses.

6.5.1 Planned Interim Analysis

6.5.1.1 Planned Interim Safety Analysis

After the first 30 patients complete protocol-specified atezolizumab treatment and undergo the planned surgical resection of their tumor, all safety population subjects at that time will be evaluated for tolerability and safety of the neoadjuvant regimen. If, at the time of the safety interim analysis, three or more patients have experienced Grade 5 adverse events related to protocol treatment, then the study may be discontinued.

Outputs from this SAP which will facilitate the planned interim safety analysis are flagged in Section 9 of this SAP.

6.5.1.2 Planned Interim Efficacy Analysis

The study includes one interim analysis to assess futility after 90 patients are assessed for MPR. The non-binding futility interim boundary satisfies conditional power at a cut-off of 0.30.

The analysis for the primary endpoint will be conducted and assessed against the futility boundary. If there are 7 or fewer responders out of 90 patients, then the conditional power of the study drops below 0.30, and enrollment may be terminated.

Outputs from this SAP which will facilitate the planned interim efficacy analysis are flagged in Section 9 of this SAP.

6.5.2 Optional Interim Analysis

Given the hypothesis-generating nature of this study, the sponsor may choose to conduct additional interim efficacy analyses. The decision to conduct an optional interim analysis, and the timing of the analysis, will be documented in the sponsor's trial master file prior to the conduct of the interim analysis. The interim analysis will be performed and interpreted by sponsor study team personnel.

6.6 Changes to Methods Planned in the Protocol

There is no change in the SAP which is deviate from protocol.

7. TABLES, LISTINGS, AND FIGURES

Programmed output will have the following features.

- Courier New Font, 9 point.
- All outputs will be landscape orientation with 1.00 inch left, right, and bottom margins, and a 1.25-inch top margin.
- General header format – analysis population will not appear on listings:

```
Genentech, Inc.                                          Page X of Y
ML39236
                [output type name] [output number]
                          [output title]
                   ([analysis population name])
```

- Source program name and program run date will appear in output footer.
- Unless specified otherwise, minimum and maximum will be displayed with the same precision as recorded data, mean and median will be displayed with one decimal place more than the recorded data, and standard deviation will be displayed with two decimal places more than the recorded data.

Table, listing, and figure shells can be found in the attached document, Genentech_ML39236_SAP_shells_client_v_2_0.docx. A table of contents for outputs to be provided is in Table 3.

Table 3 Tables, Listings, and Figures to Be Produced

Interim Analysis Flag	Output Type and Number	Output Title	Output Population
S, E, P	Table 14.1.1.1	Subject Disposition, Neoadjuvant Atezolizumab Therapy Phase	All Enrolled Subjects
S, E, P	Table 14.1.1.2	Subject Disposition, Adjuvant Atezolizumab Therapy Phase	All Enrolled Subjects
S, E, P	Table 14.1.1.3	Subject Disposition, Surveillance/Survival Follow-up Phase	All Enrolled Subjects
P	Table 14.1.1.4	Subject Discontinuation	All Enrolled Subjects
S, E, P	Table 14.1.2	Demographics and Baseline Characteristics, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Table 14.1.3	General Medical History and Baseline Conditions	Safety Population
	Table 14.1.4	Surgeries and Procedures	Safety Population
S, E, P	Table 14.1.5	Tobacco Use History, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Table 14.1.6	Non-metastatic Lung Cancer History, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Table 14.1.7.1	Lung Cancer Molecular Profile, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Table 14.1.7.2	Derived Lung Cancer Molecular Profile, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S	Table 14.1.8	Screening Ventilation / Perfusion Scan Results	Safety Population
P	Table 14.1.9	Major Protocol Deviations	Safety Population
S, E, P	Table 14.1.10.1	Study Drug Exposure, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.1.10.2	Study Drug Exposure, Surveillance/Survival Follow-up Phase	Safety Population
S, P	Table 14.1.11.1	Prior Medications	Safety Population
S, P	Table 14.1.11.2	Concomitant Medications, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.1.11.3	Concomitant Medications, Surveillance/Survival Follow-up Phase	Safety Population
E, P	Table 14.2.1	Primary Efficacy Analysis for Major Pathologic Response Rate	Primary Efficacy Population
E, P	Table 14.2.2.1	Major Pathologic Response Rate within PD-L1 Group	Efficacy Population
E, P	Table 14.2.2.2	Investigator-assessed Response Rate within PD-L1 Group	Efficacy Population
E, P	Table 14.2.3.1	Survival Analysis for Overall Survival (OS)	Efficacy Population

Interim Analysis Flag	Output Type and Number	Output Title	Output Population
E, P	Table 14.2.3.2	Survival Analysis for Disease-Free Survival (DFS)	Primary Efficacy Population
E, P	Table 14.2.3.3	Survival Analysis for Event-Free Survival (EFS)	Efficacy Population
E, P	Table 14.2.3.4	Survival Analysis for Overall Survival (OS)	Efficacy Population
E, P	Table 14.2.3.5	Survival Analysis for Disease-Free Survival (DFS) by Major Pathologic Responder (MPR)	Primary Efficacy Population
E, P	Table 14.2.3.6	Survival Analysis for Event-Free Survival (EFS) by Major Pathologic Responder (MPR)	Efficacy Population
E, P	Table 14.2.3.7	Survival Analysis for Overall Survival (OS) by PD-L1 Group	Efficacy Population
E, P	Table 14.2.3.8	Survival Analysis for Disease-Free Survival (DFS) by PD-L1 Group	Primary Efficacy Population
E, P	Table 14.2.3.9	Survival Analysis for Event-Free Survival (EFS) by PD-L1 Group	Efficacy Population
S, E, P	Table 14.3.1.1.1	Overview of Adverse Events by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.1.1.2	Overview of Adverse Events by Highest NCI CTCAE Grade, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Table 14.3.1.2.1	Adverse Events by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.1.2.2	Adverse Events by Highest NCI CTCAE Grade, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Table 14.3.1.2a	Adverse Events by Highest NCI CTCAE Grade, Both Study Phases	Safety Population
S, E, P	Table 14.3.1.2b	Adverse Events With Onset Prior to Date of Surgery by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Table 14.3.1.2c	Adverse Events With Onset On or After Date of Surgery by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population With Surgery
S, E, P	Table 14.3.1.3.1	Grade >=3 Adverse Events by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population

Interim Analysis Flag	Output Type and Number	Output Title	Output Population
	Table 14.3.1.3.2	Grade >=3 Adverse Events by Highest NCI CTCAE Grade, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Table 14.3.1.4.1	Treatment Related Adverse Events by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.1.4.2	Treatment Related Adverse Events by Highest NCI CTCAE Grade, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Table 14.3.1.4a	Treatment Related Adverse Events With Onset Prior to Date of Surgery by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Table 14.3.1.4b	Treatment Related Adverse Events With Onset On or After Date of Surgery by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population With Surgery
S, E, P	Table 14.3.1.5.1	Serious Adverse Events by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.1.5.2	Serious Adverse Events by Highest NCI CTCAE Grade, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Table 14.3.1.5a	Treatment Related Serious Adverse Events by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Table 14.3.1.5b	Serious Adverse Events With Onset Prior to Date of Surgery by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Table 14.3.1.5c	Serious Adverse Events With Onset On or After Date of Surgery by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population With Surgery
S, E, P	Table 14.3.1.6.1	Adverse Events of Special Interest by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.1.6.2	Adverse Events of Special Interest by Highest NCI CTCAE Grade, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Table 14.3.1.7.1	Adverse Events Leading to Study Drug Withdrawal by Highest NCI CTCAE Grade, Neoadjuvant Atezolizumab Therapy Phase	Safety Population

Interim Analysis Flag	Output Type and Number	Output Title	Output Population
	Table 14.3.1.7.2	Adverse Events Leading to Study Drug Withdrawal by Highest NCI CTCAE Grade, Surveillance/Survival Follow-up Phase	Safety Population
P	Table 14.3.1.8.1	Adverse Events Leading to Death, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
P	Table 14.3.1.8.2	Adverse Events Leading to Death, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Table 14.3.1.9.1	Treatment Related Adverse Events Leading to Death, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.1.9.2	Treatment Related Adverse Events Leading to Death, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Listing 14.3.2.1.1	Listing of Adverse Events Leading to Death, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
P	Listing 14.3.2.1.2	Listing of Adverse Events Leading to Death, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Listing 14.3.2.2.1	Listing of Serious Adverse Events, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Listing 14.3.2.2.2	Listing of Serious Adverse Events, Surveillance/Survival Follow-up Phase	Safety Population
S, E, P	Listing 14.3.2.3.1	Listing of Adverse Events Leading to Study Drug Withdrawal, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Listing 14.3.2.3.2	Listing of Adverse Events Leading to Study Drug Withdrawal, Surveillance/Survival Follow-up Phase	Safety Population
S, P	Table 14.3.3.1.1	Serum Chemistry Values Over Time, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.3.1.2	Serum Chemistry Values Over Time, Surveillance/Survival Follow-up Phase	Safety Population
S, P	Table 14.3.3.2.1	Hematology Values Over Time, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.3.2.2	Hematology Values Over Time, Surveillance/Survival Follow-up Phase	Safety Population
	Table 14.3.3.3.1	Shift Table of Serum Chemistry Values, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.3.3.2	Shift Table of Serum Chemistry Values, Surveillance/Survival Follow-up Phase	Safety Population
	Table 14.3.3.4.1	Shift Table of Hematology Values, Neoadjuvant Atezolizumab Therapy Phase	Safety Population

Interim Analysis Flag	Output Type and Number	Output Title	Output Population
	Table 14.3.3.4.2	Shift Table of Hematology Values, Surveillance/Survival Follow-up Phase	Safety Population
P	Table 14.3.4.1	Vital Sign Values Over Time, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.4.2	Vital Sign Values Over Time, Surveillance/Survival Follow-up Phase	Safety Population
	Table 14.3.5.1	Pulmonary Function Test Over Time, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
P	Table 14.3.6.1	Number and Percentage for ECOG, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Table 14.3.6.2	Number and Percentage for ECOG, Surveillance/Survival Follow-up Phase	Safety Population
P	Listing 16.2.1.1	Listing of Subject Disposition, Neoadjuvant Atezolizumab Therapy Phase	All Enrolled Subjects
	Listing 16.2.1.2	Listing of Subject Disposition, Surveillance/Survival Follow-up Phase	All Enrolled Subjects
P	Listing 16.2.2.1	Listing of Baseline Demographics	All Enrolled Subjects
P	Listing 16.2.2.2	Listing of Baseline Characteristics	Safety Population
	Listing 16.2.3.1	Listing of Tobacco Use History, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Listing 16.2.3.2	Listing of Non-metastatic Lung Cancer History, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
S, E, P	Listing 16.2.3.3	Listing of Lung Cancer Molecular Profile, Neoadjuvant Atezolizumab Therapy Phase	Safety Population
	Listing 16.2.3.4	Listing of Screening Ventilation / Perfusion Scan	Safety Population
	Listing 16.2.4.1	Listing of General Medical History and Baseline Conditions	Safety Population
	Listing 16.2.4.2	Listing of Surgeries and Procedures	Safety Population
	Listing 16.2.4.3	Listing of Prior and Concomitant Medications	Safety Population
P	Listing 16.2.4.4	Protocol Deviation	Safety Population
S, E, P	Listing 16.2.5	Listing of Study Drug Administration	Safety Population
E, P	Listing 16.2.6.1	Pathological Response	Efficacy Population
P	Listing 16.2.6.2	RECIST 1.1 – Tumor Assessment (Target Lesions)	Efficacy Population
P	Listing 16.2.6.3	RECIST 1.1 – Tumor Assessment (Non - Target Lesions)	Efficacy Population
P	Listing 16.2.6.4	RECIST 1.1 – Tumor Assessment New Lesion	Efficacy Population
E, P	Listing 16.2.6.5	RECIST 1.1 – Radiographic Response Assessment	Efficacy Population

Interim Analysis Flag	Output Type and Number	Output Title	Output Population
	Listing 16.2.6.6	FFPE and Fresh Frozen Tumor Tissue (Archival)	Efficacy Population
	Listing 16.2.6.7	FFPE and Fresh Frozen Tumor Tissue (Screening)	Efficacy Population
	Listing 16.2.6.8	FFPE Tumor Tissue Surgical Resection	Efficacy Population
	Listing 16.2.6.9	Fresh Frozen Tumor Tissue Surgical Resection	Efficacy Population
	Listing 16.2.6.10	Fresh Lymph Node	Efficacy Population
P	Listing 16.2.6.11	Post Neoadjuvant Treatment Surgery	Efficacy Population
	Listing 16.2.6.12	Adjuvant Chemotherapy	Efficacy Population
	Listing 16.2.6.13	Cancer Radiotherapy	Efficacy Population
	Listing 16.2.6.14	Survival and Recurrence Follow-up	Efficacy Population
	Listing 16.2.6.15	Listing of Individual Efficacy Data	Efficacy Population
S, E, P	Listing 16.2.7.1	Listing of Adverse Events	Safety Population
S, E, P	Listing 16.2.7.2	Listing of Serious Adverse Event Details	Safety Population
	Listing 16.2.8.1	Listing of Serum Chemistry	Safety Population
	Listing 16.2.8.2	Listing of Hematology	Safety Population
	Listing 16.2.8.3	Listing of Vital Signs	Safety Population
	Listing 16.2.8.4	Complete Physical Examination	Safety Population
	Listing 16.2.8.5	Pulmonary Function Tests	Safety Population
	Listing 16.2.8.6	ECOG Performance Status	Safety Population
	Listing 16.2.8.7	Other Safety Assessments	Safety Population
P	Figure 1.1	Forest Plot of Major Pathological Responders	Efficacy Population
P	Figure 1.2.1	Kaplan – Meier Plot for Overall Survival	Efficacy Population
P	Figure 1.2.2	Kaplan – Meier Plot for Disease-Free Survival	Primary Efficacy Population
P	Figure 1.2.3	Kaplan – Meier Plot for Event-Free Survival	Efficacy Population
P	Figure 1.2.4	Kaplan – Meier Plot for Overall Survival by Major Pathologic Responder	Efficacy Population
P	Figure 1.2.5	Kaplan – Meier Plot for Disease-Free Survival by Major Pathologic Responder	Primary Efficacy Population
P	Figure 1.2.6	Kaplan – Meier Plot for Event -Free Survival by Major Pathologic Responder	Efficacy Population

Interim Analysis Flag	Output Type and Number	Output Title	Output Population
P	Figure 1.2.7	Kaplan – Meier Plot for Overall Survival by PD-L1 Subgroup	Efficacy Population
P	Figure 1.2.8	Kaplan – Meier Plot for Disease-Free Survival by PD-L1 Subgroup	Primary Efficacy Population
P	Figure 1.2.9	Kaplan – Meier Plot for Event -Free Survival by PD-L1 Subgroup	Efficacy Population

Note: Interim analysis flags are S = Safety Interim Analysis and E = Efficacy Interim Analysis. P = Primary Analysis.

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