BR31 Final Statistical Analysis Plan

A PHASE III PROSPECTIVE DOUBLE-BLIND PLACEBO CONTROLLED RANDOMIZED STUDY OF ADJUVANT MEDI4736 IN COMPLETELY RESECTED NON-SMALL CELL LUNG CANCER

A Lung Immunotherapy NSCLC Consortium (LINC) Trial of the CCTG, IFCT, CEEOG, NCI-Naples, NVALT, KCSG, ALTG and NHMRC CTC, SLCG, WJOG

CCTG Protocol Number: **BR.31**
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1. INTRODUCTION

1.1. Study description

BR31 is an international multicenter, double blinded, placebo controlled, prospective, adjuvant phase III randomized trial. The primary objective is to assess the efficacy of adjuvant therapy with MEDI4736 given by intravenous infusion for one year on the disease free survival in patients with completely resected (stage IB $\geq$ 4cm, stage II or IIIA), non-small cell lung cancer with PD-L1 $\geq$ 25%, PD-L1 $\geq$ 1% as well as all patients regardless of PD-L1 status. Patients were randomized to receive either MEDI4736 or placebo in a 2:1 ratio using the dynamic minimization method stratified by:

- Disease stage (IB ($\geq$ 4cm) vs II vs IIIA)
- Pre-treatment PD-L1 expression level (A [$\geq$ 50%] vs. B [25-49%] vs. C[1-24%] vs. D [< 1%])
- Adjuvant platinum based chemotherapy ($\geq$ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy)
- Accruing centre
- Nodal sampling/dissection conducted in accordance with the European Society of Thoracic Surgeon (ESTS) guidelines (yes vs. no).

Rationale

In advanced NSCLC, inhibition of PD-1 immune checkpoint pathway has been shown to induce durable clinical responses across all histologies and is therefore of broad clinical relevance, particularly among patients with squamous histology who have not benefited from other recent therapeutic interventions. MEDI4736 has a favorable safety profile and limited off-target T cell effects and has good pharmacokinetic and pharmacodynamics properties. Results of early trials with MEDI4736 in advanced cancers are consistent with a class effect of early and sustained tumor control that has been observed previously with other inhibitors of the PD-1 immune checkpoint pathway. Presuming the maturing safety and efficacy data confirm these initial observations, MEDI4736 is particularly attractive as a therapeutic strategy in the adjuvant setting as it may generate immunologic memory and persistent activity in memory B cells, allowing for active and sustained surveillance and killing of tumor cells and possibly long term cure. NSCLC patients with PD-L1 expression positive resected tumors may be particularly sensitive to immunotherapy with MEDI4736 given accumulating evidence in patients with advanced disease. The study design and primary endpoint of this trial have been chosen to allow for the concurrent assessment of MEDI4736 efficacy in delaying disease relapse in all patients and in those with different levels of PD-L1 expression.

Hypothesis

Inhibition of the PD-L1 by MEDI4736 in patients with completely resected Stage IB-IIIA NSCLC will result in improved disease-free and overall survival.

Based on last study protocol amendment, for all patients randomized to the trial, six patient sub-populations are defined according to the PD-L1 expression stratum as determined at

randomization, and the epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) mutation status determined retrospectively. The "EGFR-/ALK-" sub-population excludes only those with common activating EGFR mutations (defined as exon 21 L858R mutation or exon 19 deletions) or with ALK gene rearrangements (ALK+). For patients whose EGR/ALK mutation status can not be determined, they will be included as EGFR-/ALK-. The six study populations are as follows:

- PD-L1 TC ≥ 25% and EGFR-/ALK-
- PD-L1 TC ≥ 1% and EGFR-/ALK-
- All EGFR-/ALK-
- All PD-L1 TC ≥ 25%
- All PD-L1 TC ≥ 1%
- All randomized patients

1.2. Study objectives

The primary objective is to assess in comparison to placebo, the impact of adjuvant therapy with MEDI4736 given by intravenous infusion for one year on the overall survival in patients with completely resected (stage IB > 4cm, stage II or IIIA) NSCLC and with PD-L1 expression TC ≥ 25%, EGFR-/ALK-.

Secondary objectives will evaluate study treatment effect:

- To compare the DFS in the MEDI4736 arm to the placebo arm in the remaining 5 patient sub-populations defined by PD-L1 expression levels and EGFR/ALK status.
- To compare the overall survival (OS) in the MEDI4736 arm to the placebo arm in the six patient sub-populations defined by PD-L1 expression levels and EGFR/ALK status.
- To compare lung cancer specific survival in the MEDI4736 arm to the placebo arm in the six patient sub-populations defined by PD-L1 expression levels and EGFR/ALK status.
- To evaluate the nature, severity, and frequency of toxicities, between the two treatment arms.
- To evaluate the quality of life between the two treatment arms in the six patient sub-populations defined by PD-L1 expression levels and EGFR-/ALK-.
- To determine the survival benefits participants judge necessary to make adjuvant immunotherapy worthwhile, and the factors influencing their preferences.
- To determine the incremental cost effectiveness and cost utility ratios for MEDI4736.
- To evaluate the prognostic and predictive significance of PD-L1 expression.
- To evaluate changes in plasma/serum cytokines and other blood and tissue based biomarkers after treatment with MEDI4736 or placebo and at time of disease relapse/new invasive primary malignancy.
- To explore polymorphisms that may be associated with outcomes

1.3. Study design and modifications

BR31 is an international multicenter, double blinded, placebo controlled, prospective, adjuvant phase III randomized trial. The trial was initially designed to test the DFS between 2 treatment arms among patients with PD-L1 expression TC ≥ 25%, and subsequently test the DFS in all randomized patients. To detect a HR of 0.645 with 90% power for patients with TC ≥ 25%, and a HR of 0.73 in all randomized patients, a sample size of around 680 is required for patients PD-L1 ≥ 25% and approximately 1100 patients irrespective of PD-L1 expression levels. The trial will accrue first 600 patients irrespectively of the PD-L1 expression level, then only accrue next 500 patients with PD-L1≥ 25%. Hierarchal test procedure will be used to maintain the overall type I error.

In 2015, the trial's design was modified with primary objectives to test the DFS between 2 treatment arms in dual primary populations of patients with PD-L1 expression TC ≥ 25% and those of all randomized patients. To detect a HR of 0.645 in patients with PD-L1 ≥ 25%, and a HR of 0.725 in all randomized patients with 80% power using a 5% 2-sided test, a sample size of 1360 is required with approximately 530 patients with PD-L1 ≥ 25%. All eligible patients will be accrued irrespective of their PD-L1's expression levels. The type I error was allocated to the dual populations using the weighted Bonferroni method, with type I error of 4% allocated to the PD-L1≥ 25% subgroup, and 1% allocated to the all randomized patients test in primary analyses of DFS.

In 2020, the trial's design was modified again with primary objectives to assess the effect of MEDI4736 by comparing disease-free survival (DFS) between the two treatment arms in patients with NSCLC that is PD-L1 expression TC ≥25%, in patients with PD-L1 expression TC ≥1% and in all randomized patients. A trial wise one-sided type I error of 2.5% will be used in comparisons between 2 treatment arms across the three primary populations for primary endpoint of DFS and key secondary endpoint of OS.

Late in 2020, in response to the emergence of treatment with Osimertinib for patients with Epidermal Growth Factor Receptor mutated (EGFRm) NSCLC and a corresponding meta-analyses that shows limited effect of study treatment in EGFRm or Anaplastic Lymphoma Kinase gene mutation (ALK+) NSCLC, the primary study patient population is modified to NSCLC patients with PD-L1 ≥ 25% and EGFR-/ALK- sub-population in the Amendment #7 of the study protocol, i.e. exclusion of patients with EGFR exon 21 L858R mutation or exon 19 deletions, or ALK gene rearrangements, from the primary analysis population.

This file is prepared based on the Amendment #7.

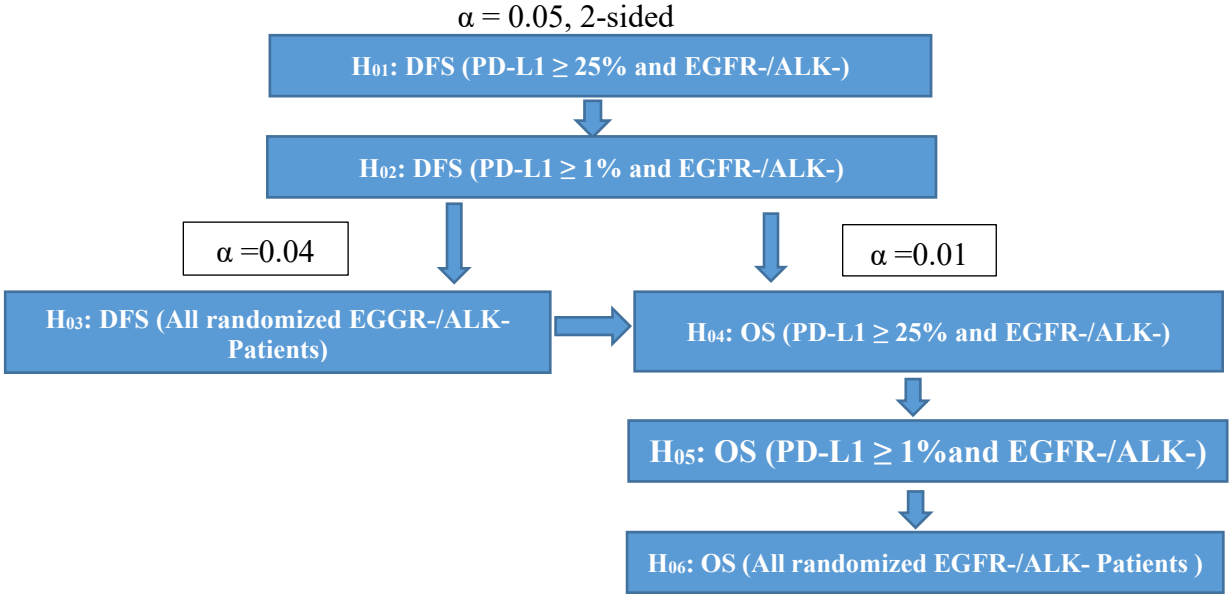
1.4. Sample size

The sample size for this study was determined to compare DFS in patients with NSCLC that is PD L1 ≥ 25% and EGFR-/ALK- sub-population. The expected 5-year DFS rate of patients on the placebo arm was estimated to be 51%, and 5-year expected OS rate of placebo patients was estimated as 58%.

In order to have 85% power to detect a 35.5% reduction in the risk of disease relapse/new primary malignancy with MEDI4376 (i.e. a hazard ratio (HR) for DFS of 0.645) in the PD-L1 ≥ 25% and EGFR-/ALK- patients using a 2-sided 5% significance level test, the required sample size for this study is estimated as 1360 patients (to include approximately 450 PD-L1 ≥ 25% and EGFR-/ALK- patients). Assuming a 5-year patients accrual period, the required number of DFS events for the primary DFS analysis (212 relapses/new primary malignancies or deaths in PD-L1 ≥ 25% and EGFR-/ALK- patients) is estimated to be observed with another 4 years of follow up. The sample size was calculated with a planned interim analysis testing for superiority of the study treatment.

Testing treatment effect on DFS in EGFR-/ALK- patients with PD-L1 ≥ 1%, in all randomized EGFR-/ALK- patients; and on OS in EGFR-/ALK- patients with PD-L1 ≥ 25%, in EGFR-/ALK- patients with PD-L1 ≥ 1%, and in all randomized EGFR-/ALK- patients are key secondary objectives. To control the trial-wise type I error at 5%, the hierarchical testing strategy will be used. The tests will be performed using the Lan-DeMets error spending function with O'Brien-Fleming type boundaries with 2 analyses planned at information fractions of around 0.75 and 1 for DFS. The Type I error will be recycled according to the method of "Multiple testing in group sequential trials using graphical approaches" as proposed by Willi Maurer and Frank Bretz [Maurer 2013]. For the hierarchical test of the PD-L1 ≥ 25% EGFR-/ALK- and PD-L1 ≥ 1% EGFR-/ALK- sub-populations, the tests will be performed at the same significance level for each test at the time in the pre-specified order and further formal testing is stopped at the time of the first non-significant result. The formal test of DFS in all randomized EGFR-/ALK- and of OS of the PD-L1 ≥ 25% EGFR-/ALK- will only be performed when the tests on DFS are positive in both PD-L1 ≥ 25% and EGFR-/ALK-, and PD-L1 ≥ 1% and EGFR-/ALK- sub-populations, the overall hierarchical test strategy for group sequential tests will be conducted according to the method of "Hierarchical testing of multiple endpoints in group-sequential trials" as proposed by Glimm, Maurer and Bretz [Glimm, Maurer and Bretz, 2010] with Haybittle-Peto type of boundaries. The alpha splitting and recycling strategy are given in the figure below.

Figure 1: Over test flow chart



1.5. Treatment Group Assignment

Treatment assignment is performed centrally using Mango, an Interactive Web Response System (IWRS) software located in central office of CCTG. The randomization algorithm minimizes the chance of an imbalance between the two treatment arms within study center with respect to the following stratification factors: 1) disease stage (IB ($\geq$ 4cm) vs II vs IIIA); 2) pre-treatment PD-L1 expression (A [$\geq$ 50%] vs. B [25-49%] vs. C[1-24%] vs. D [< 1%]); 3) adjuvant platinum based chemotherapy ($\geq$ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy), and 4) nodal sampling/dissection conducted in accordance with the European Society of Thoracic Surgeon (ESTS) guidelines (yes vs. no).

1.6. Time of the analysis

There is a planned interim analysis (IA) in addition to the final analysis in the design of this study. The IA was performed on DFS in February 2022 with 169 DFS events in the primary population (PD-L1 $\geq$ 25%, EGFR-/ALK-). The test in difference in DFS between two study treatment arms did not reach to the statistical significance level to claim efficacy of the study treatment, and DSMC recommend continuing as designed for final analysis. Based on O'Brien-Fleming type boundaries with the performed interim analyses using the Lan-DeMets error spending function, the significance level for claiming efficacy of study treatment is 0.043 in favor of treatment arm.

With the hierarchical test strategy, the test for PD-L1$\geq$ 1% and EGFR-/ALK- patient and other populations will be performed with the significant level determined for the PD-L1$\geq$ 25% and EGFR-/ALK- population. The details of the test strategy are as given in figure 1.

This document is to describe the statistical analysis plan for the final analysis according to the study protocol. The statistical report will be sent out to the study chair for preparation of scientific publication. And the drug company will prepare the statistical analysis submitted to regularity authority for drug approval if applicable.

1.7. Data Collection and the trial's database

Data are collected, entered, and managed by CCTG, Kingston, Ontario, according to the group standard data management procedures. A data cutoff point based on the required number of events for the primary endpoint in the predefined populations will be determined for data included in the analysis. A snapshot of the trial's database will be frozen for this analysis.

1.8. China Extension

As a definitive, international phase III trial with potential registrational intent, the BR.31 trial seeks to enrol a globally representative population of participants. In keeping with this goal, the study originally intended to recruit 170 of its target of 1360 patients from China.

However, patients accrual started late in China, when the study closed to further global recruitment of registered patients on October 18, 2019, only 45 patients have been enrolled from China, which would be the total number of patients from China included in the global cohort of the main study of BR31.

In order to ensure that an adequate number of patients from China are enrolled to permit an assessment/confirmation of the potential efficacy and safety of the study therapy in this sub-group by the National Medicinal Products Administration (NMPA), continued enrolment of patients from China will be permitted beyond closure to accrual of the study in the Rest of World, i.e. a "China Extension". The "China Extension" will continue to accrue patients in China. Any statistical analysis to be conducted based solely on patients accrued from China will be described in a separate SAP.

2. Methods and Analyses

2.1 Analyses Populations

Analysis populations for this analysis include the intention to treat (ITT) in all pre-specified 6 populations (i.e. all as randomized patients to the treatment arm in each specified population) and the as-treated population (i.e. all patients who received at least one dose of MEDI4736 or placebo in each specified population).

Analysis of pretreatment characteristics and all efficacy endpoints, such as DFS, will be based on the ITT population for each specified group. Safety and drug exposure analyses will be performed on the as-treated population for each specified group.

2.2 Conventions for Key Data

Baseline evaluations are those collected closest, but prior to or on the first day of study medication for treated subjects or on the day of randomization.

When either day or month of a date is missing, the missing day and/or month will be inputted by the midpoints within the smallest known interval. However, logic checks will be performed to ensure that no imputed data date is after the patient's death or after the data cutoff date.

The stratification factor of "nodal sampling/dissection conducted in accordance with the European Society of Thoracic Surgeon (ESTS) guidelines (yes vs. no)", which was introduced after the trial had accrued some patients, however, it is available in baseline data collection, and we will use those values as stratification values for the variable.

2.3 Analysis Conventions

All comparisons are by treatment arm unless otherwise specified. Discrete variables are generally summarized with the frequency and proportion of subjects falling into each category and compared using Chi-square or Fisher exact test where appropriate. Continuous and ordinal categorical variables are summarized using the mean, median, standard error, minimum and maximum and inter-quartiles values and when appropriate, compared using the Wilcoxon test or t-test. For the time to event outcomes, the

distributions by treatment arm will be estimated with Kaplan-Meier product-limit method, and compared using stratified log-rank test, summarized with median survival, and estimated of HR and its confidence intervals using stratified Cox regression model. In the stratified analysis, if some stratum size is too small (Say, with less than 5 events), it will be merged into the other stratum that is closest to it.

The following baseline factors that will be used in the adjusted analyses where appropriate:

- Disease stage (IB/II vs IIIA)
- Pre-treatment PD-L1 expression (PD-L1 $\geq$ 25% vs. PD-L1 1-24% vs PD-L1 < 1%
- Adjuvant platinum based chemotherapy ($\geq$ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy)

2.4. Randomization and Pre-treatment Characteristics

2.4.1 Definitions and Variables

2.4.1.1 Accrual

X Number (%) of randomized patients per study center (Table 1).

2.4.1.2 Randomization/Stratification

X disease stage (IB ($\geq$ 4cm) vs II vs IIIA)

X pre-treatment PD-L1 expression ($\geq$50% vs. $\geq$25-49% vs. 1-24% vs. < 1%)

X adjuvant platinum based chemotherapy ($\geq$ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy)

X nodal sampling/dissection conducted in accordance with the European Society of Thoracic Surgeon (ESTS) guidelines (yes vs. no) (table 2)

(Note: An unknown/missing category will be added to each factor whenever appropriate.)

- Treatment randomized to receive will be compared with the first dose of actual treatment received during the treatment period to identify any discrepancies (Table 3)
- Baseline patient characteristics will be compared with the patient's corresponding stratification assignment to identify any discrepancies (Table 4)

2.4.1.3 Ineligibility and major protocol violation/deviations (Table 5)

Eligibility and violations of inclusion or exclusion criteria are detailed in study protocol, and all randomized patients' eligibility status are centrally reviewed by CCTG; a field (y/n) for eligibility status and reason for ineligibility is entered in the database. A protocol deviation is defined as accidental or unintentional changes to, or non-compliance with the research protocol that does not increase risk; does not have a significant effect on the subject's rights, safety or welfare; but could affect the efficacy and/or on the integrity of

the data. Deviations may result from the action of the subject, researcher, or research staff. Protocol Violations (PVs) are defined as accidental or unintentional change to, or non-compliance with the IRB approved protocol without prior sponsor and IRB approval. Violations generally increase risk or decrease benefit, affect the subject's rights, safety, or welfare, or the integrity of the data. Protocol deviation and PVs are standardized coded by CCTG.

- Eligible patients: % yes, no
- Reasons for ineligibility: % for each reason and combination of reasons of ineligibility.
- Major protocol violations/deviations: number and % for each deviation.

2.4.1.4 Summary of Follow-up

The follow up time for DFS is defined as the time from the date of randomization to the date of last disease assessment or censored at the date of disease relapse or the occurrence of a new invasive primary malignancy or date of death without disease relapse.
The median (estimated by the Kaplan-Meier method with reverse DFS status), min, max and inter-quartiles of the follow-up time (among disease free patients) will be presented by treatment group and for all patients included in the analysis for the 6 populations i.e., PD-L1 TC $\geq$ 25% and EGFR-/ALK-, PD-L1 TC $\geq$ 1% and EGFR-/ALK- and all EGFR-/ALK- populations (Table 6).

The follow up time for OS is defined as the time from the date of randomization to the date of last known alive or censored at the date of death.
The median (estimated by the Kaplan-Meier method with reverse OS status), min, max and inter-quartiles of the follow-up time (among alive patients) will be presented by treatment group and for all patients included in the analysis for the 6 populations (Table 6b, in the same format as of table 6).

2.4.1.5 Patient Characteristics (Table 7)

- Sex: % male, female
- Race: % Caucasian, Black or African American, Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, Not reported (or refused), Other.
- Ethnicity (Hispanic or Latino vs. Not Hispanic nor Latino).
- Age: < 65 vs. $\geq$ 65, median, min and max;
- Height: Mean (std), median, min and max;
- Weight: Mean (std), median, min and max;
- ECOG Performance status: % 0, 1;
- Smoking history (Ever smoked vs. Never);
- Current smoking status (Yes vs. No);
- Histology type (Adenocarcinoma vs. squamous vs. Adenosquamous vs. others);
- Method of disease diagnoses (Histologically vs. cytologically vs. both);
- Tumor grade (Well differentiated vs. intermediate VS. poor VS. undifferentiated);
- EGFR Mutation status (exon 21 L858R mutation or exon 19 deletions vs, other mutations vs. wild type vs. unknown);

- KRAS status (mutation vs. no mutation vs. unknown);
- BRAF mutation (Mutation vs. wild type VS. unknown);
- ALK (positive vs. negative vs. unknown)
- Received prior systemic therapy (Yes vs. No vs. unknown);
- Prior systemic therapy (Bevacizumab, Carboplatin, Cetuximab, Cisplatin, Docetaxel …);
- Prior radiation therapy (Yes, vs No)
- Disease stage (IB (≥ 4cm) vs II vs IIIA)
- Pre-treatment PD-L1 expression ((≥50% vs. ≥25-49% vs. 1-24% vs. < 1%)
- Prior surgery (Pneumonectomy, Bilobectomy, Sleeve resection, Lobectomy, wedge resections, segmentectomies)

Tables will be generated for all 6 populations.

2.4.1.6 Baseline symptoms (Table 8)

The NCI CTCAE V4.0 will be used for the categorization of all baseline symptoms.

- Any event per patient: % yes, no
- Event by body system
- Grade of type of event (1, 2, 3, 4)

Tables will be generated for all 6 populations.

2.4.1.7 Baseline Hematology/Biochemistry (Table 9)

CTC grades according to CTCAE v4.0 will be used to summarize the baseline hematology/biochemistry data.

	% by CTC grades
X	WBC
X	Hemoglobin
X	Platelets
X	Differential (neutrophils and lymphocytes)
X	Creatinine clearance .
X	Total bilirubin
X	Alkaline phosphatase
X	ALT (SGPT)
X	AST (SGOT)
X	Hypoalbuminemia
X	INR
X	PTT
X	Amylase
X	Lipase

Tables will be generated for all 6 populations.

2.4. 1.8 Concomitant Medications on study entry (Table 10)

A concomitant medication is defined as a medication, which was taken within 2 weeks prior to date of randomization.

X Any concomitant medication: % yes, no
X Number of patients for each type of medication.

Tables will be generated for all 6 populations.

2.4. 1.9 Major Medical Problems (Table 11)

A major medical problem (MMP) is defined as a history of a significant condition or a medical problem ongoing at baseline.

X Any major problem: % yes, no
X Number of patients from each type of the major problem: % diabetes, cardiac, etc.

Tables will be generated for all 6 populations.

2.4.2 Analysis of pre-treatment characteristics

No formal statistical tests will be performed to assess the balance of baseline characteristics between the arms. Categorical variables will be tabulated by treatment arm and for all patients in each test populations. Continuous variables (e.g., age) will be presented using summary statistics (n, median, min and max) by treatment arm based on all randomized patients by arm according to the ITT population in each test populations.

2.5 Efficacy

For the efficacy analysis, formal test on primary endpoint of DFS and key secondary endpoints OS will be performed as given in Over test flow chart (Figure 1). If any of the subpopulations does not reach the threshold for statistical significance, then, the late analysis will be exploratory supportive analysis.

2.5.1 Definitions and Variables

2.5.1.1 Disease free survival

For all randomized patients, DFS is defined as the time from the date of randomization to the date of first documented disease relapse or the occurrence of a new invasive primary malignancy or death from any cause. For patients who had residual disease at study entry after consensus review, the DFS will be censored at the date of randomization. Patients who are alive and disease/new invasive primary malignancy-free at the time of each analysis will be censored at their last disease assessment date.

For a special case, the patient was found that the original NSCLC diagnosis was erroneous, and the patient had metastatic testicular cancer prior to randomization, confirmed retrospectively by immunophenotyping. Since the patient did not have completely resected NSCLC, instead having metastatic testicular cancer at the time of the enrollment such that was never “disease-free”, the database will reflect a “new primary malignancy” disease event occurring before the date of randomization. **Thus, the patient will be censored at randomization date for DFS.**

DFS Time (months) = [(date of disease relapse or the occurrence of a new invasive primary malignancy or death from any cause - date of randomization) + 1] / 30.4375.

2.5.1.2 Overall survival

Overall survival (OS) is defined as the time from the date of randomization to the date of death of any cause, or censored at their last known alive date before or on data cutoff date.

Overall Survival Time (months) = ((date of death or Last known alive date - date of randomization) + 1) / 30.4375.

2.5.2 Analysis of Key Parameters

All analyses will be presented by treatment arm with 2-sided p-value for test of significance.

2.5.2.1 Comparison of Disease-Free Survival between treatment arms

2.5.2.1.1 Disease Free Survival for PD-L1 ≥25% and EGFR-/ALK- Patients

Kaplan-Meier curves for the distribution of DFS in each treatment arm will be displayed. The primary test of the difference between the two treatment arms will be the log-rank test stratified by stratification factors used at randomization* (values collected at randomization)

- Disease stage (IB / II vs IIIA),
- Adjuvant platinum based chemotherapy ($\geq$ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy).

*If any stratum that is too small in size, i.e., with less than 10 events, we will merge it with its closest stratum in analysis. The same will be applied to all other comparison between treatment groups.

Sensitive analysis 1: Ventana Medical Systems Inc reported that there are 6.7% (95/1415) of the randomized patients in BR.31 had PD-L1 data generated using affected dispensers, and PD-L1 data for those patients were re-tested with new samples. To check the potential effect on analysis, a sensitive analysis, log-rank test stratified above listed stratification at randomization will be performed with PD-L1 data from the retested value if available, or values at randomization in determining the patients in PD-L1≥25% group.

Sensitive analysis 2: Samples re-scored for PD-L1 using validated 1% cutoff: For the PD-L1 data used at randomization, the values of 1-24% were in fact values of 5-24%, i.e., those with PD-L1 1-4% were include in the <1% subgroup. PD-L1 data were rescored, mainly affected the 1-24% subgroup, but affected all subgroups. A sensitive analysis will be performed using the rescored PD-L1 data to determine the patients in each PD-L1 subgroups (Use rescored data if available and use data at randomization if no rescored data). A log-rank test stratified by the stratification at randomization for disease stage and adjuvant platinum-based chemotherapy will be performed.

Sensitive analysis 3: As a sensitivity analysis, log rank test stratified by stratification factors with data collected/corrected at baseline (For PD-L1data: Use the re-tested/rescored PD-L1 data if available as baseline data, or the stratification data if there is no re-tested/rescored PD-L1data in the primary population. For disease stage and adjuvant

platinum-based chemotherapy, use baseline data if available, otherwise, use data at randomization.) to test the difference between treatment arms.

The estimated hazard ratio (HR) and its confidence intervals at the significance level of test (MEDI4736 vs. placebo (Referent group)) from the Cox regression model (Efron's approximation will be used for tied events, based on the profile likelihood method) stratified by stratification factors listed above will be reported (table 12). The 3-year DFS rate will estimated.

An unstratified analysis will also be performed.

For patients who developed DFS events, the number of patients for each type of the event will be summarized by treatment arm (Table 13).

For patients who had disease relapse, the treatment received after disease relapse will be summarized in table 14.

Subgroup Analysis: The analysis of DFS will be presented for each level of stratification factors (Values collected at baseline evaluation, if missing at baseline, use values from randomization), PD-L1 expression levels (≥50% vs. ≥25-49%), disease stage (IB (≥ 4cm) vs II vs IIIA), adjuvant platinum based chemotherapy (≥ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy), and nodal sampling/dissection conducted in accordance with the European Society of Thoracic Surgeon (ESTS) guidelines (yes vs. no) to check the homogeneity of treatment effect across the levels of those factors.
Median survivals for each level of stratification factors, HR and its 95% C.I. in comparison between treatment arms will be presented. To test the homogeneity of treatment effect across the level of stratification factors, Cox regression model will be used with interaction terms included (Exclude those with missing for test the interaction) (Table 15).

The same analysis will be performed for all randomized patients with PD-L1 ≥25% population.

A specific analysis will be performed for patients with PD-L1 ≥25% and EFFR+/ALK+ (K-M curves by treatment arm with output of median DFS, and 95% C.I. by treatment arm and estimated HR and its 95% C.I.)

2.5.2.1.2 Disease Free Survival for PD-L1 ≥1% and EGFR-/ALK- Patients

If tests of DFS are positive for the PD-L1 ≥ 25% and EGFR-/ALK- cohort, the formal test of DFS in the PD-L1 ≥1% and EGFR-/ALK- population will be performed. Otherwise, the same analysis will be performed as exploratory analysis. Kaplan-Meier curves for the distribution of DFS in each treatment arm will be displayed. The primary test of the difference between the two treatment arms will be the log-rank test stratified by stratification factors used at randomization* (values collected at randomization)

- Disease stage (IB /II vs IIIA),

- Pre-treatment PD-L1 expression (PD-L1≥ 25% vs. PD-L1 1-24%),
- Adjuvant platinum-based chemotherapy (≥ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy),

Sensitive analysis 1: As a sensitive analysis, log-rank test stratified above listed stratification at randomization will be performed with PD-L1 data from the retested value if available, or values at randomization in determining the patients in PD-L1≥ 25% and PD-L1 1-24% group.

Sensitive analysis 2: Samples re-scored for PD-L1 using validated 1% cutoff: For the PD-L1 data used at randomization, the values of 1-24% are in fact values 5-24%, i.e., those wit PD-L1 1-4% were include in the <1% subgroup. PD-L1 data were rescored, mainly affected the 1-24% subgroup. A sensitive analysis will be performed using the rescored PD-L1 data to determine the patients in PD-L1 ≥ 25% and PD-L1 1-24% groups. A log-rank test stratified by the stratification at randomization for disease stage and adjuvant platinum-based chemotherapy will be performed. The significant results for the PD-L1 ≥1% and EGFR-/ALK- will be claimed only when both the primary analysis and this sensitive analysis are both significant at the pre-specified significance level.

Sensitive analysis 3: Log-rank test stratified use stratification values collected at baseline evaluation. For PD-L1 data, use the re-tested and rescored data if available, otherwise use data at randomization, while for disease stage and adjuvant platinum-based chemotherapy, use data reported at baseline if different from those at randomization, otherwise, use data at randomization.

The estimated hazard ratio (HR) and its confidence intervals at the significance level of test (MEDI4736 vs. placebo (Referent group)) from the Cox regression model (Efron's approximation will be used for tied events) stratified by stratification factors listed above will be reported (table 12b). The 3-year DFS rate will estimated.

An unstratified analysis will also be performed.

For patients who developed DFS events, the number of patients for each type of the event will be summarized by treatment arm (Table 13b).

For patients who had disease relapse, the treatment received after disease relapse will be summarized in table 14b.

Subgroup Analysis: The analysis of DFS will be presented for each level of stratification factors (Values collected at baseline evaluation, if missing at baseline, use values from randomization), PD-L1 expression levels (≥50% vs. ≥25-49% vs. 1-24%), disease stage (IB (≥ 4cm) vs II vs IIIA), adjuvant platinum based chemotherapy (≥ 300 mg/m2 cisplatin/equivalent vs. < 300 mg/m2 vs. no chemotherapy), and nodal sampling/dissection conducted in accordance with the European Society of Thoracic Surgeon (ESTS) guidelines (yes vs. no) to check the homogeneity of treatment effect across the levels of those factors.

Median survivals for each level of stratification factors, HR and its 95% C.I. in comparison between treatment arms will be presented. To test the homogeneity of treatment effect across the level of stratification factors, Cox regression model will be used with interaction terms included (Exclude those with missing for test the interaction) (Table 15b).

The same analysis will be performed for all randomized patients with PD-L1 ≥1% population.
A specific analysis will be performed for patients with PD-L1 ≥1% and EFFR+/ALK+ (K-M curves by treatment arm with output of median DFS, and 95% C.I. by treatment arm and estimated HR and its 95% C.I.

2.5.2.1.3 Disease Free Survival for All Randomized EGFR-/ALK- Patients

If tests of DFS are positive for both PD-L1 ≥ 25% EGFR-/ALK- and PD-L1 ≥ 1% EGFR-/ALK- cohorts, the formal test of DFS in all randomized EGFR-/ALK- population will be performed. Otherwise, the same analysis will be performed as exploratory analysis. Kaplan-Meier curves for the distribution of DFS in each treatment arm will be displayed. The primary test of the difference between the two treatment arms will be the log-rank test stratified by stratification factors used at randomization (values collected at randomization)

- Disease stage (IB (≥ 4cm)/II vs IIIA),
- Pre-treatment PD-L1 expression (PD-L1≥ 25% vs. PD-L1 1-24% vs. PD-L1 < 1%),
- Adjuvant platinum based chemotherapy (≥ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy),

Sensitive analysis 1: As a sensitive analysis, log-rank test stratified above listed stratification at randomization will be performed with PD-L1 data from the retested value if available, or values at randomization in determining the patients in PD-L1≥ 25%, PD-L1 1-24% and <1% groups.

Sensitive analysis 2: A sensitive analysis will be performed using the rescored PD-L1 data to determine the patients in PD-L1 ≥ 25%, PD-L1 1-24% and <1% groups. A log-rank test stratified by the stratification at randomization for disease stage and adjuvant platinum-based chemotherapy will be performed.

Sensitive analysis 3: Log-rank test stratified use stratification values collected at baseline evaluation. For PD-L1 data, use the re-tested and rescored data if available, otherwise use data at randomization, while for disease stage and adjuvant platinum-based chemotherapy, use data reported at baseline if different from those at randomization, otherwise, use data at randomization.

The 2–sided p-value for the above tests will be presented.

The estimated hazard ratio (HR) and its confidence intervals at the significance level of test (MEDI4736 vs. placebo (Referent group)) from the Cox regression model (Efron's approximation will be used for tied events) stratified by stratification factors listed above will be reported (table 12c). The 3-year of DFS rate will be estimated.

An unstratified analysis will also be performed.

For patients who developed DFS events, the number of patients for each type of the event will be summarized (Table 13c).

Table 12b, c and Table 13b, c are the same as table 12 and 13, but for different analysis populations.

For patients who had disease relapse, the treatment received after disease relapse will be summarized in table 14c.

Subgroup Analysis: The analysis of DFS will be presented for each level of stratification factors (Values collected at baseline evaluation, if missing at baseline, use values from randomization), PD-L1 expression levels (≥50% vs. ≥25-49% vs. 1-24% vs. < 1%), disease stage (IB (≥ 4cm) vs II vs IIIA), adjuvant platinum based chemotherapy (≥ 300 mg/m2 cisplatin/equivalent vs. < 300 mg/m2 vs. no chemotherapy), and nodal sampling/dissection conducted in accordance with the European Society of Thoracic Surgeon (ESTS) guidelines (yes vs. no) to check the homogeneity of treatment effect across the levels of those factors.
Median survivals for each level of stratification factors, HR and its 95% C.I. in comparison between treatment arms will be presented. To test the homogeneity of treatment effect across the level of stratification factors, Cox regression model will be used with interaction terms included (Exclude those with missing for test the interaction) (Table 15c).

Prognostic significance of PD-L1 expression levels

For patients on Placebo arm, Kaplan-Meier curves for the distribution of DFS in each PD-L1 expression level (< 1% vs. 1-24% vs. 25-49% vs. ≥50%, use the re-tested and rescored values) will be presented with output of median DFS, and 95% C.I. by levels of PD-L1 expression and estimated HR and its 95% C.I. (<1% as reference group), p-value from log-rank test.

Predictive significance of PD-L1 expression levels

For all randomized EGFR-/ALK- patients, Cox regression model with PD-L1 expression levels (< 1% vs. 1-24% vs. 25-49% vs. ≥50%, use the re-tested and rescored values), treatment arm indicator of MEDI4736 and their interaction terms to fit the DFS data with output of estimated HRs and their 95% C.I.s and p-values from Wald's test.

The same analysis will be performed for all randomized patient's population.

A specific analysis will be performed for patients with EFFR+/ALK+ (K-M curves by treatment arm with output of median DFS, and 95% C.I. by treatment arm and estimated HR and its 95% C.I., p-value from log rank test.)

Prognostic significance of EGFR/ALK mutations

For patients on Placebo arm, Kaplan-Meier curves for the distribution of DFS by EGFR/ALK mutation status (EGFR+/ALK+ vs. EGFR-/ALK-) will be presented with output of median DFS, and 95% C.I. by levels of PD-L1 expression and estimated HR and its 95% C.I. EGFR-/ALK- as reference group), p-value from log-rank test.

Predictive significance of EGFR/ALK mutations

For all randomized patients, Cox regression model with EGFR/ALK mutation status, treatment arm indicator of MEDI4736 and their interaction terms to fit the DFS data with output of estimated HRs and their 95% C.I.s and p-values from Wald's test.

2.5.2.2 Comparison of Overall Survival between treatment arms

2.5.2.2.1 Overall Survival for PD-L1 ≥25% and EGFR-/ALK- Patients

The formal tests on OS will be performed only if the tests of DFS are positive for PD-L1 $\geq$ 25% and EGFR-/ALK-, PD-L1 $\geq$ 1% populations. Otherwise, descriptive analysis on OS will be performed in the same way.

Kaplan-Meier curves for the distribution of OS in each treatment arm will be displayed. The primary test of the difference between the two treatment arms will be the log-rank test stratified by stratification factors used at randomization (values collected at randomization)

- Disease stage (IB/II vs IIIA),
- Adjuvant platinum based chemotherapy ($\geq$ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy),

*If any stratum that is too small in size, i.e., with less than 5 events, we will merge it with its closest stratum in analysis. The same will be applied to all other comparisons between treatment groups.

As a sensitivity analysis, log rank test stratified by stratification factors with data collected/corrected at baseline (For PD-L1data: Use the re-tested PD-L1data if available as baseline data, or the stratification data if there is no re-tested PD-L1data in the primary population. For disease stage and adjuvant platinum-based chemotherapy, use baseline data if available, otherwise, use data at randomization.) to test the difference between treatment arms.

Sensitive analysis 2: Samples re-scored for PD-L1 using validated 1% cutoff: For the PD-L1 data used at randomization, the values of 1-24% were in fact values of 5-24%, i.e., those with PD-L1 1-4% were include in the <1% subgroup. PD-L1 data were rescored, mainly affected the 1-24% subgroup, but affected all subgroups. A sensitive analysis will be performed using the rescored PD-L1 data to determine the patients in each PD-L1 subgroups (Use rescored data if available and use data at randomization if no rescored data). A log-rank test stratified by the stratification at randomization for disease stage and adjuvant platinum-based chemotherapy will be performed.

A sensitivity analysis 3, log rank test stratified by stratification factors with data collected/corrected at baseline (For PD-L1data: Use the re-tested PD-L1data if available

as baseline data, or the stratification data if there is no re-tested PD-L1data in the primary population. For disease stage and adjuvant platinum-based chemotherapy, use baseline data if available, otherwise, use data at randomization.) to test the difference between treatment arms.

The 2–sided p-value for the above tests will be presented.

The estimated hazard ratio (HR) and its confidence intervals at the significance level of test (MEDI4736 vs. placebo (Referent group)) from the Cox regression model (Efron's approximation will be used for tied events) stratified by stratification factors listed above will be reported (table 16).

An unstratified analysis will also be performed.

For patients who died, the number of patients for each cause of death will be summarized by treatment arm (Table 17).

2.5.2.2.2 Overall Survival for PD-L1 ≥1% and EGFR-/ALK- Patients

The formal test will only be performed when test of OS is positive for PD-L1 ≥25% and EGFR-/ALK- cohort. Kaplan-Meier curves for the distribution of OS in each treatment arm will be displayed. The primary test of the difference between the two treatment arms will be the log-rank test stratified by stratification factors used at randomization (values collected at randomization)

- Disease stage (IB/II vs IIIA),
- Pre-treatment PD-L1 expression (PD-L1≥ 25% vs. PD-L1-1-24%),
- Adjuvant platinum based chemotherapy (≥ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy),

Sensitive analysis 1: As a sensitive analysis, log-rank test stratified above listed stratification at randomization will be performed with PD-L1 data from the retested value if available, or values at randomization in determining the patients in PD-L1≥ 25% and PD-L1 1-24% group.

Sensitive analysis 2: Samples re-scored for PD-L1 using validated 1% cutoff: For the PD-L1 data used at randomization, the values of 1-24% are in fact values 5-24%, i.e., those wit PD-L1 1-4% were include in the <1% subgroup. PD-L1 data were rescored, mainly affected the 1-24% subgroup. A sensitive analysis will be performed using the rescored PD-L1 data to determine the patients in PD-L1 ≥ 25% and PD-L1 1-24% groups. A log-rank test stratified by the stratification at randomization for disease stage and adjuvant platinum-based chemotherapy will be performed. The significant results for the subgroup will be claimed only when both the primary analysis and this sensitive analysis are both significant at the pre-specified significance level.

Sensitive analysis 3: Log-rank test stratified use stratification values collected at baseline evaluation. For PD-L1 data, use the re-tested and rescored data if available, otherwise use

data at randomization, while for disease stage and adjuvant platinum-based chemotherapy, use data reported at baseline if different from those at randomization, otherwise, use data at randomization. The 2–sided p-value for above tests will be presented.

The estimated hazard ratio (HR) and its confidence intervals at the significance level of test (MEDI4736 vs. placebo (Referent group)) from the Cox regression model (Efron's approximation will be used for tied events) stratified by stratification factors listed above will be reported (table 16b).

An unstratified analysis will also be performed.

For patients who died, the number of patients for each cause of death will be summarized by treatment arm (Table 17b).

2.5.2.2.3 Overall Survival for All Randomized and EGFR-/ALK- Patients

The formal test will only be performed when tests of OS are positive for both PD-L1 $\geq$ 25% and EGFR-/ALK-, PD-L1 $\geq$ 1% and EGFR-/ALK- sub-populations. Kaplan-Meier curves for the distribution of OS in each treatment arm will be displayed. The primary test of the difference between the two treatment arms will be the log-rank test stratified by stratification factors used at randomization (values collected at randomization)

- Disease stage (IB/II vs IIIA),
- Pre-treatment PD-L1 expression (PD-L1 $\geq$ 25% vs. PD-L1 1-24% VS. PD-L1 < 1%),
- Adjuvant platinum based chemotherapy ($\geq$ 300 mg/m^2 cisplatin/equivalent vs. < 300 mg/m^2 vs. no chemotherapy),

Sensitive analysis 1: As a sensitive analysis, log-rank test stratified above listed stratification at randomization will be performed with PD-L1 data from the retested value if available, or values at randomization in determining the patients in PD-L1$\geq$ 25%, PD-L1 1-24% and <1% groups.

Sensitive analysis 2: A sensitive analysis will be performed using the rescored PD-L1 data to determine the patients in PD-L1 $\geq$ 25%, PD-L1 1-24% and <1% groups. A log-rank test stratified by the stratification at randomization for disease stage and adjuvant platinum-based chemotherapy will be performed.

Sensitive analysis 3: Log-rank test stratified use stratification values collected at baseline evaluation. For PD-L1 data, use the re-tested and rescored data if available, otherwise use data at randomization, while for disease stage and adjuvant platinum-based chemotherapy, use data reported at baseline if different from those at randomization, otherwise, use data at randomization.

The 2–sided p-value for the above tests will be presented.

The estimated hazard ratio (HR) and its confidence intervals at the significance level of test (MEDI4736 vs. placebo (Referent group)) from the Cox regression model (Efron's

approximation will be used for tied events) stratified by stratification factors listed above will be reported (table 16c) .

An unstratified analysis will also be performed.

For patients who died, the number of patients for each cause of death will be summarized by treatment arm (Table 17c).

Table 16b, c and Table 17b, 17c are the same as table 16 and 17, but for different analysis populations.

Lung cancer specific survival and the PD-L1's Prognostic/predictive significance on OS will be explored at final analysis of OS.

2.6 Drug Exposure

2.6.1 Definitions and Variables

2.6.1.1 Duration of Study Therapies in Weeks

Duration of study therapy (in weeks) is defined as the time from the first date the patients took MEDI4736 /placebo to the date of final dose given plus 4 weeks.

- Duration of study therapy (weeks) for all patients by treatment arms (Table 18): median, min and max

2.6.1.2 Cumulative dose of MEDI4736 /placebo

The total of MEDI4736 /placebo doses taken by the patients is defined as the sum of MEDI4736 /placebo received by patients during the duration of the study.

- Total of MEDI4736 /placebo doses (mg) (Table 18): median, min and max.

2.6.1.3 Dose adjustment, interruption or discontinuation (Table 19)

MEDI4736/placebo dose may be adjusted (slowing/interruption of infusion rate, omission of a dose, or permanent discontinuation) because of toxicities or other reasons.

- The number of patients with at least one dose adjustment/interruption or discontinuation during the study
- Specify the primary reason for the dose omission/interruption: % of patients with each reason (e.g., hematologic toxicity, other AEs, etc.)
- Number of patients discontinued protocol treatment
- Specify reasons for protocol treatment discontinuation: % of patients with each reason (e.g., Aes, progressive disease, intercurrent illness, etc.)

2.6.2 Analysis

All variables will be summarized for all treated patients by study treatment.

2.7 Concomitant medications, transfusion, and hospitalization

2.7.1 Definition and Variables

Concomitant medications are all other medications (other than study drugs) taken at any time till the 12 weeks after the date of the last treatment/placebo. Hospitalizations are those which occur at any time on-study.

- **X** Any concomitant medications or treatments per patient (Table 20): % yes, no**.**
- X Any prophylactic RT (Table 20): % yes, no
- X Any blood transfusion (Table 20): % yes, no
- X Any hospitalization per patient (Table 20): % yes, no.

2.7.2 Analysis

Supportive and concomitant medications and therapies will be displayed for all treated patients. The data will be presented as shown in the table samples in Table 20.

2.8 Safety

The safety analyses will be based on the all treated population. Adverse events and laboratories are graded and categorized using the CTCAE v4.0 criteria.

2.8.1 Definitions and variables

2.8.1.1 Laboratory tests

Analyses of laboratory data will include analyses of hematology and biochemistry tests. The hematology data include WBC, platelets, neutrophils, hemoglobin and the biochemistry data include AST (SGOT) and ALT (SGPT), total bilirubin, serum creatinine, albumin, (Tables 21-22). Laboratory results will be graded according to the CTC criteria version 4.0.

All laboratory data collected at any time during the study for these tests will be included in the analyses of worst value on study.

All tests specified above:

- CTC grade for worst value on-study (for hematology and biochemistry tests): %0, 1, 2, 3, 4
- Thyroid Function Tests: Overall TSH, T3 free, T3 total, T4 free, T4 total (Table 23).

2.8.1.2 Toxicity/adverse event/intercurrent illness

The CTC version 4.0 will be used to summarize toxicities/adverse events/intercurrent illnesses. Events will be displayed by primary term. All toxicities/adverse events/intercurrent illnesses data collected at any time will be included in the analyses of worst value on study will be included in the analyses of worst value during that cycle. All the analyses will be repeated to include only the toxicities/adverse events/intercurrent illnesses which are drug related (The relation to protocol therapy higher than or equal to 3).

- Any event during the study (Table 24): % yes
- Worst severity per patient per primary term on study (Table 25): % CTC grade 1, 2, 3, 4, unknown
- Toxicity/adverse event/intercurrent illness which are serious (reasons for seriousness in the toxicity table higher than or equal to 1), fatal only (reason for seriousness in the toxicity table equal to 1), leading to hospitalization (reason for seriousness in the toxicity table equal to 3) (Table 26)
- Drug related adverse events are those events with a relation to protocol therapy of 3=possible, 4=probable or 5=definite. (Same as table 23, 26.)
- SAEs that led to drug interruptions (Table 27)
- SAEs that led to drug discontinued (Table 27)
- Deaths within 30 days from last treatment administration (Table 28)
- Cause of death within 30 days from last treatment administration (Table 28).

2.8.2 Analysis

All patients who received at least one dose of study medication will be included in the safety analyses. Top 5 toxicities**,** and drug related grade 3 or higher will be compared using the Fisher's exact test for comparison of the toxicity rates between 2 treatment arms.

2.9 Off-study

2.9.1 Definitions and Variables

X Patients off-MEDI4736/Placebo only (Table 29): Number and % of all treated patients

X Reason for going off- MEDI4736 /Placebo only (Table 29): Number and % of all treated patients for each reason

2.9.2 Analysis

Tables will be presented by treatment arm and for all patients.
For Patients who were off treatment due to toxicities from protocol treatment, a table will be prepared to tabulate the number of patients for each toxicity.

2.10. Quality of life

The quality of life (QoL) of patients are assessed using EORTC QLQ-C30 and the lung cancer module (QLQ-LC13) questionnaires. The EORTC QLQ-C30 is a self-administered

cancer specific questionnaire with multi-dimensional scales. The QLQ-LC13 lung cancer module includes questions assessing lung cancer-associated symptoms (cough, hemoptysis, dyspnea, and site-specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication. The validity and reliability have been studied by the EORTC Study Group on Quality of Life.

j2.10.1 Definitions and Variables

2.10.1.1 EORTC QLQ-C30

There are five functional domains and three symptom domains that can be derived from EORTC QLQ-C30 (see below for definitions). If the number of unanswered questions in each domain is within a limit specified with the definition for each domain, the score is calculated as for function domains:
Score=100-(((Total score for the answered questions/(no. of questions answered))-1)*100/3)
In addition, for symptom domains:
Score = (((Total score for the answered questions/(no. of questions answered))-1)*100/3)
Otherwise, the score will be recorded as "missing". For each single item, the score will be recorded as "missing" if the answer to this item is missing.

Functional Domains:

- Physical: Questions: 1, 2, 3, 4, 5
  Score=missing if number of above questions not answered is greater than 2;
- Role: Questions: 6, 7
  Score=missing if number of above questions not answered is greater than 1.
- Emotional: Questions: 21, 22, 23, 24
  Score=missing if number of above questions not answered is greater than 2;
- Cognitive: Questions: 20, 25
  Score=missing if number of above questions not answered is greater than 1;
- Social: Questions: 26, 27
  Score=missing if number of above questions not answered is greater than 1;

Symptom Domains:

- Fatigue: Questions: 10, 12, 18
  Score=missing if number of above questions not answered is greater than 1;
- Nausea and vomiting: Questions: 14, 15
  Score=missing if number of above questions not answered is greater than 1;
- Pain: Questions: 9, 19
  Score=missing if number of above questions not answered is greater than 1.

There are also six single items in EORTC QLC-C30 pertaining to common symptoms and one global assessment that can be derived from EORTC QLQ-C30. The single items are:
Single Items:

- Dyspnea: Question 8;
- Sleep: Question 11;
- Appetite: Question 13;
- Constipation: Question 16;
- Diarrhea: Question 17;

- Financial: Question 28.

They are all scored using the following formula:
Score = (Answered score to the question-1)*100/3.

The **Global Assessment** includes Questions 29 and 30. If number of these two questions not answered is greater than 1, its score will be "missing"; Otherwise,

Score = ((Total scores for the answered questions/(no. of questions answered))-1)*100/6.

2.10.1.2 EORTC QLQ-LC13

There are one symptom domain and 10 single items that can be derived from EORTC QLQ-LC13 (see below for definitions). The following are the scoring algorithms for these domains/items.

Symptom Domains/Items:

- Cough: Question: 31
  Score=missing if the answer to this item is missing;
  Otherwise, Score = (Answered score to the question-1)*100/3;
- Hemoptysis: Question: 32
  Score=missing if the answer to this item is missing;
  Otherwise, Score = (Answered score to the question-1)*100/3;
- Dyspnea domain: Questions: 33, 34, 35
  Score=missing if number of above questions not answered is greater than 1;
  Otherwise,
  Score = ((Total scores for the answered questions/(no. of questions answered))-1)*100/3.
- Sore mouth: Questions: 36
  Score=missing if the answer to this item is missing;
  Otherwise, Score= (Answer to the question-1)*100/3;
- Trouble swallowing: Questions: 37
  Score=missing if the answer to this item is missing;
  Otherwise, Score= (Answer to the question-1)*100/3;
- Peripheral neuropathy: Questions: 38
  Score=missing if the answer to this item is missing;
  Otherwise, Score= (Answer to the question-1)*100/3;
- Hair loss: Questions: 39
  Score=missing if the answer to this item is missing;
  Otherwise, Score= (Answer to the question-1)*100/3;
- Pain in chest: Questions: 40
  Score=missing if the answer to this item is missing;
  Otherwise, Score= (Answer to the question-1)*100/3;
- Pain in shoulder: Questions: 41
  Score=missing if the answer to this item is missing;
  Otherwise, Score=(Answer to the question-1)*100/3;
- Pain elsewhere: Questions: 42
  Score=missing if the answer to this item is missing;

Otherwise, Score=(Answer to the question-1)*100/3;

- Pain medication: Questions: 43
  For those whose answer is "Yes" for taking pain medication,
  Score=missing if the answer to this item is missing;
  Otherwise, Score=(Answer to the question-1)*100/3;

2.10.2 Analysis

All analyses on quality-of-life scores will be exploratory and will include all randomized patients with baseline and at least I evaluation after randomization in each corresponding prespecified study population. i.e., PD-L1 TC ≥ 25% and EGFR-/ALK-; PD-L1 TC ≥ 1% and EGFR-/ALK and All EGFR-/ALK- patients.

2.10.2.1 Determination of Assessment Times

The following will be the scheme to determining the time frame of a QoL assessment:

1) Baseline: Baseline evaluation is the QoL questionnaire collected within 14 days, but prior to, or on the date of randomization or first date of treatment.
2) At Week 4, 12, 24, 36, 48 evaluations: If the QoL is assessed within 2 weeks before or after the specific time point.
3) At 12 weeks following the completion of the last cycle: if the QoL is assessed within 4 weeks before or after the date when patients are seen in the clinic for their week 12 visit following the last cycle, this assessment is considered as week 12 follow up assessment;
4) Other off treatment periods: patients are supposed to be seen in clinic and complete QOL questionnaire every 12 weeks up to 108 weeks after randomization. If the QoL is assessed within 4 weeks before or after the expected date for a given follow-up period, this assessment is considered as an assessment for that period.

2.10.2.2 Calculation of Compliance Rates

The method used to calculate the compliance rates of QoL assessment (See Tables 30) is calculated as the number of forms received out of the number of forms expected at each assessment point defined based on the following principles:

1) At baseline: the number of forms expected is the total number of patients who are required to fill out QoL questionnaires.
2) During the treatment period: the number expected at each assessment time is the total number of patients who were alive and disease relapse free at the time point, and have baseline QoL data.
3) Twelve weeks following the completion of last cycle: patients are required to fill out one follow-up form at this time point, the number of forms expected is determined by the total number of patients who were alive and disease relapse free at the time point and have baseline QoL data.
4) Other off treatment period: patients are supposed to complete QoL questionnaire every 12 weeks. The expected number of forms is determined by the total number

of patients who were alive and disease relapse free at the time point and have baseline QoL data.

2.10.2.3 Cross-sectional analysis

The mean and standard deviation of QL scores at baseline and mean and standard deviation of QoL change scores from baseline at each assessment time will be calculated (see Table 31). Then Wilcoxon Rank-Sum test is used to compare two treatment arms in terms of change in QOL score at each assessment time from baseline (see Table 32).

2.10.2.4 QoL response analysis

QOL response analysis is the NCIC QoL committee recommended analysis, and is calculated as follows: for a functional domain, a change score of 10 points from baseline was defined as clinically relevant. Patients were considered improved if reported a score 10-points or better than baseline at any time of QOL assessment. Conversely, patients were considered worsened if reported a score minus 10-points or worse than baseline at any time of QOL assessment without above defined 10-point improvement. Patients whose scores were between 10-point changes from baseline at every QOL assessment were considered as stable. In contrast to functional domains, for the determination of patient's QOL response, classification of patients into improved and worsened categories is revered for symptom domains and single items. Chi-square test is then performed to compare the distributions of these three categories between two arms, and Mantel-Haenszel chi-square test for trend is used to test if there is a trend that patients in one treatment arm have higher proportions in the better QoL categories than those on the other arm. (Table 33).

2.10.2.5 QoL Primary Analysis

For the 5 functional domains and global quality of life assessments, a repeated measures analysis will be performed to explore the difference between the two arms on each of QoL item score changed from baseline. The mixed linear models with treatment, time of visit (Months from randomization) and treatment-by-visit time interaction as fixed effects will fit the longitudinal data of each domain score, the covariance structure for the sequence of measurements on each visit will be modeled by the general unstructured form or empirical form. In assessing the treatment effect, standard error based on robust estimate will be used, and the treatment effect is characterized by the initial treatment effect and the interaction of treatment by time.

Model goodness of fit will be checked by Schwartz's Bayesian criteria and Akaike's information criterion.

Maximum likelihood estimates of fitted model parameters and p-value for testing initial treatment effect and treatment effect over time will be presented. (table 34).

2.10.3 EQ-5D-3L

The EQ-5D is a standardized measure of health status developed by the EuroQol Group in order to provide a simple, generic measure of health for clinical and economic appraisal. Applicable to a wide range of health conditions and treatments, it provides a simple

descriptive profile and a single index value for health status that can be used in the clinical and economic evaluation of health care.

The EQ-5D-3L index comprises 5 dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). For each dimension, respondents select which statement best describes their health on that day from a possible 3 options of increasing levels of severity (no problems, some problems, and unable to/extreme problems). A unique EQ-5D health state is referred to by a 5-digit code allowing for a total of 243 health states. For example, state 11111 indicates no problems on any of the 5 dimensions. These data will be converted into a weighted health state index by applying scores from EQ-5D value sets elicited from general population samples (the base case will be the United Kingdom valuation set, with other country value sets applied in scenario analyses). In addition to the descriptive system, respondents also assess their health on the day of assessment on a visual analogue scale, ranging from 0 (worst imaginable health) to 100 (best imaginable health). This score will be reported separately.

3. Tables

Table 1: Accrual by Center

Data set: All Randomized Patients			
	Number of patients (%)		
	MEDI4736 N = ***	Placebo N = ***	Total N = ***
Center #1	*** (**)	*** (**)	*** (**)
Center #2	*** (**)	*** (**)	*** (**)
Center #3	*** (**)	*** (**)	*** (**)
...	*** (**)	*** (**)	*** (**)

Table 2: Accrual by Stratification Factor at Randomization

Data set: All Randomized Patients

	Number of patients (%)		
	MEDI4736 N = ***	Placebo N=***	Total N = ***
Stage			
IB	** (**)	** (**)	** (**)
II	** (**)	** (**)	** (**)
IIA	** (**)	** (**)	** (**)
Nodalsampling/dissection according to ESTS			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Adjuvant platinum based chemotherapy			
≥ 300mg/m^2	** (**)	** (**)	** (**)
< 300mg/m^2	** (**)	** (**)	** (**)
No chemo	** (**)	** (**)	** (**)
Pre-treatment PD-L1 level			
≥50%	** (**)	** (**)	** (**)
25% to 49%	** (**)	** (**)	** (**)
1 to 24%	** (**)	** (**)	** (**)
< 1%	** (**)	** (**)	** (**)

Source: Centralized Randomization File

Table 3: Treatment as Randomized Versus as Treated at Cycle 1

Data set: All Randomized Patients			
	Number of Patients (%) Randomized Arm		
	MEDI4736 N=***	Placebo N=***	Total N=***
Treatment Received			
MEDI4736	*** (**)	*** (**)	*** (**)
Placebo	*** (**)	*** (**)	*** (**)
Not treated	*** (**)	*** (**)	*** (**)

Table 4: Discrepancies between Stratification Level as Randomized and at Baseline

Data set: All Randomized Patients						
	Number of patients (%)					
	MEDI4736 N=***		Placebo N=***		Total N=***	
Any difference	*** (**)		*** (**)		*** (**)	
At baseline	As Randomized		As Randomized		As Randomized	
Stage	IB	II | IIIA	IB	II | IIIA	IB	II | IIIA
IB II	**	** | **	**	** | **	**	** | **
IIIA	**	** | **	**	** | **	**	** | **
Adjuvant platinum based chemotherapy	< 300	≥ 300| No chemo	< 300	≥ 300| No chemo	< 300	≥ 300| No chemo
< 300 mg/m^2	**	** | **	**	** | **	**	** | **
≥ 300 mg/m^2 No Chemo	** **	** | ** ** | **	** **	** | ** ** | **	** **	** | ** ** | **
nodalsampling/dissection According ESTS	Yes	No	Yes	No	Yes	N0
Yes	**	**	**	**	**	**
No	**	**	**	**	**	**

Pre-treatment PD-L1 expression	≥50%	25 – 49% | 1-24%	< 1%
≥50%	***	*** | ***	***
≥25%	***	*** | ***	***
1-24%	***	*** | ***	***
< 1%	***	*** | ***	***

Table 5: Eligibility, Reasons for Ineligibility and Major Protocol Violations

Data set: All Randomized Patients			
	Number of Patients (%)		
	MEDI4736 N=***	Placebo N=***	Total N=***
Eligible	*** (**)	*** (**)	*** (**)
Not Eligible	*** (**)	*** (**)	*** (**)
Reason for ineligibility			
<Reason 1>	**	**	**
<Reason 2>	**	**	**
...	**	**	**
Major protocol violation	**(**)	**(**)	**(**)
<violation 1>	**	**	**
<violation 2>	**	**	**
...	**	**	**

Table 6: DFS Follow-up for Patients included in analysis

Data set: All Randomized Patients			
	MEDI4736 arm	Placebo arm	All patients
Median (95% C,I.)	*** (**, **)	*** (**, **)	*** (**, **)
Min, Max	** -- **	** -- **	** -- **
Inter-quartiles	**, **	**, **	**, **

Table 7: OS Follow-up for Patients included in analysis

Data set: All Randomized Patients			
	MEDI4736 arm	Placebo arm	All patients
Median (95% C,I.)	*** (**, **)	*** (**, **)	*** (**, **)
Min, Max	** -- **	** -- **	** -- **
Inter-quartiles	**, **	**, **	**, **

Table* 8*: Patients Characteristics at Baseline

Data set: All Randomized Patients			
	Number of patients (%)		
	MEDI4736 N=***	Placebo N=***	Total N=***
Sex			
Female	** (**)	** (**)	** (**)
Male	** (**)	** (**)	** (**)
Race			
White	** (**)	** (**)	** (**)
Black	** (**)	** (**)	** (**)
....	** (**)	** (**)	** (**)
Age (years)			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **
≥ 65	** (**)	** (**)	** (**)
< 65	** (**)	** (**)	** (**)
Histology type			
Adeno	** (**)	** (**)	** (**)
squamous	** (**)	** (**)	** (**)
Adenosquamous	** (**)	** (**)	** (**)
others	** (**)	** (**)	** (**)
Disease Stage			
IB	** (**)	** (**)	** (**)
II	** (**)	** (**)	** (**)
IIIA	** (**)	** (**)	** (**)
Smoking history			
Ever Smoked	** (**)	** (**)	**(**)
Never	** (**)	** (**)	** (**)
Prior Systematic Therapy			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Prior Systematic Therapy			
Bevacizumab	** (**)	** (**)	** (**)
Carboplatin	** (**)	** (**)	** (**)
Cisplatin	** (**)	** (**)	** (**)
….	....	…	…
EGFR mutation status			
Common mutation	** (**)	** (**)	** (**)
Exon21 L858R	** (**)	** (**)	** (**)
Exon19 deletion	** (**)	** (**)	** (**)
Other mutation	** (**)	** (**)	** (**)
Wild type	** (**)	** (**)	** (**)
ALK mutation			
Positive	** (**)	** (**)	** (**)

Negative	** (**)	** (**)	** (**)
Pre-treatment PD-L1			
≥50%	** (**)	** (**)	** (**)
25-49%	** (**)	** (**)	** (**)
1-24%	** (**)	** (**)	** (**)
< 1%	** (**)	** (**)	** (**)
Prior surgery	** (**)	** (**)	** (**)
Pneumonectomy	** (**)	** (**)	** (**)
Bilobectomy	** (**)	** (**)	** (**)
Sleeve resection	** (**)	** (**)	** (**)
Lobectomy	…..	……	……
wedge resections			
segmentectomies			
……			

Table 8: Baseline Signs and Symptoms

Data set: All Randomized Patients (MEDI4736 Arm)

	Number of patients (%) N=***					
	Worst grade					Any grade
	NR	1	2	3	4	
Patients with any sign/symptom at baseline	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with particular sign or symptom, within body system:						
Body System 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Body System 2[(1)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)

(1) Patients may have more than one event within a body system

NOTE: Same table to be made for Placebo Arm

Table 9: Baseline Hematology/Biochemistry

Data set: All Randomized Patients			
	Number of Patients (%)		
	MEDI4736 N = ***	Placebo N = ***	Total N=***
Hematology:			
WBC			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Differential			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Platelet			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
neutrophils			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Lymphocytes			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Hemoglobin			
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)

Not reported [1]	** (**)	** (**)	** (**)
Biochemistry:			
serum creatinine			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Alkaline Phosphatase			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
SGOT (AST)			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
SGPT (ALT)			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
…….			

[1] Not done or outside the 14-day window prior to start of therapy

Table 10: Concomitant Medications on Study entry

Data set: All Randomized Patients			
	Number of patients (%)		
	MEDI4736 N=***	Placebo N=***	Total N=***
Any concomitant medication at baseline (1)			
No	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)

(1)Any medication taken within one week prior to start of therapy treatment

Table 11: Major Medical Problems at Baseline

Data set: All Randomized Patients			
	Number of patients (%)		
	MEDI4736 N = ***	Placebo N = ***	Total N=***
Patients Reporting at least one medical problem	** (**)	** (**)	** (**)
Type Medical Problem(1) (from highest to lowest in frequency)			
Diabetes	** (**)	** (**)	** (**)
Bronchopulmonary	** (**)	** (**)	** (**)
Gastrointestinal	** (**)	** (**)	** (**)
Cardiovascular	** (**)	** (**)	** (**)
Hypertension	** (**)	** (**)	** (**)
Endocrine/metabolic	** (**)	** (**)	** (**)
Genitourinary	** (**)	** (**)	** (**)
Musculoskeletal	** (**)	** (**)	** (**)
HENT	** (**)	** (**)	** (**)
...			

(1) patients may report more than one medical problem

Table 12: Log Rank and Cox Regression Model for Disease Free Survival

Univariate Analysis[1]

Treatment Arm	Median DFS (Months)	Hazard Ratio[2] (C.I.)*	Log-rank p-value
Treatment arm			0.***
MEDI4736	**.**	**.**	
Placebo	**.**	(**.**,**.**)	

(1) Stratified (value at randomization)
(2) Estimated from stratified Cox model

* C.I. at significance level of test, which depends on number of events included in the analysis.

Log Rank and Cox Regression Model for Disease Free Survival: PD-L1 ≥25% (Values at retested or randomization)

Univariate Analysis[1]

Treatment Arm	Median DFS (Months)	Hazard Ratio[2] (C.I.)*	Log-rank p-value
Treatment arm			0.***
MEDI4736	**.**	**.**	
Placebo	**.**	(**.**,**.**)	

(1) Stratified (value at randomization)
(2) Estimated from stratified Cox model

* C.I. at significance level of test, which depends on number of events included in the analysis.

Log Rank and Cox Regression Model for Disease Free Survival: PD-L1 ≥25% (Values at rescored or randomization)

Univariate Analysis[1]

Treatment Arm	Median DFS (Months)	Hazard Ratio[2] (C.I.)*	Log-rank p-value
Treatment arm			0.***
MEDI4736	**.**	**.**	
Placebo	**.**	(**.**,**.**)	

(1) Stratified (value at randomization)
(2) Estimated from stratified Cox model
* C.I. at significance level of test, which depends on number of events included in the analysis.

Log Rank and Cox Regression Model for Disease Free Survival: PD-L1 ≥25% (Values at rescored, re-tested or at randomization)

Univariate Analysis(1)

Treatment Arm	Median DFS (Months)	Hazard Ratio(2) (C.I.)*	Log-rank p-value
Treatment arm			0.***
MEDI4736	**.**	**.**	
Placebo	**.**	(**.**,**.**)	

(1) Stratified (value at baseline)
(2) Estimated from stratified Cox model
* C.I. at significance level of test, which depends on number of events included in the analysis.

Table 13: Disease free survival events Summary

Data set: All Randomized Patients with PD-L1≥25% (Values of re-tested or at randomization) and EGFR-/ALK-

	Number of Patients (%)	
	MEDI4736 N=***	Placebo N=***
Number of patients who had disease relapse	*** (**)	*** (**)
Disease relapse on study treatment	**	**
Disease relapse during follow-up	**	**
New primary malignancy	**	**
Death without disease relapse	**	**
Patients who were censored (Alive without disease relapse)	*** (**)	*** (**)

Table 12b, c and Table 13b, c are the same as table 12 and 13, but with PD-L1 ≥1% and EGFR-/ALK- or all EGFR-/ALK- population

jjjjjTable 14: Anti-Cancer Therapy Received After Disease relapse

Data set: All patients with disease relapse during the trial

	Number of patients (%)	
	MEDI4736 N=***	Placebo N =***
Number of patients with any subsequent anticancer therapy after disease relapse	*** (**)	*** (**)
Chemotherapy (1)	*** (**)	*** (**)
Agent (Pemetrexed; taxotere; etc….	*** (**)	*** (**)
Tyrosine Kinase inhibitor (1)	*** (**)	*** (**)
Agent (erlotinib, gefitinib; etc)	*** (**)	*** (**)
Radiotherapy (1)	*** (**)	*** (**)
Immunotherapy (1)	*** (**)	*** (**)
Other (1)	*** (**)	*** (**)

(1) Patients could have more than one type of therapy.

Table 14b: Anti-Cancer Therapy Received for Patients who experienced a second, independent primary tumour as DFS event

Data set: All patients with disease relapse during the trial

	Number of patients (%)	
	MEDI4736 N=***	Placebo N =***
Number of patients with any subsequent anticancer therapy after second, independent primary tumour	*** (**)	*** (**)
Chemotherapy (1)	*** (**)	*** (**)
Agent (Pemetrexed; taxotere; etc….	*** (**)	*** (**)
Tyrosine Kinase inhibitor (1)	*** (**)	*** (**)
Agent (erlotinib, gefitinib; etc)	*** (**)	*** (**)
Radiotherapy (1)	*** (**)	*** (**)
Immunotherapy (1)	*** (**)	*** (**)
Other (1)	*** (**)	*** (**)

(1) Patients could have more than one type of therapy.

Table 15: DFS Subgroup Analysis (PD-L1≥25% and EGFR-/ALK- patients)

	Durva. Arm		Placebo arm			
Factors	N	Median Survival (95% C.I.)	N	Median Survival (95% C.I.)	HR (95% C.I.)	P-value-test interaction
PD-L1						0.***
≥ 50%	**	** (**, **)	**	** (**, **)	** (**, **)	
≥25-49%	**	** (**, **)	**	** (**, **)	** (**, **)	
Disease stage						0.***
IB (≥4cm)	**	** (**, **)	**	** (**, **)	** (**, **)	
II	**	** (**, **)	**	** (**, **)	** (**, **)	
IIIA	**	** (**, **)	**	** (**, **)	** (**, **)	
Adjuvant chemo						0.***
≥ 300 mg/m^2	**	** (**, **)	**	** (**, **)	** (**, **)	
< 300 mg/m^2	**	** (**, **)	**	** (**, **)	** (**, **)	
no chemotherapy	**	** (**, **)	**	** (**, **)	** (**, **)	
Nodal sampling according to ESTS						0.***
Yes	**	** (**, **)	**	** (**, **)	** (**, **)	
No	**	** (**, **)	**	** (**, **)	** (**, **)	

Table 15b: DFS Subgroup Analysis (PD-L1≥1% and EGFR-/ALK- patients)

	Durva. Arm		Placebo arm			
Factors	N	Median Survival (95% C.I.)	N	Median Survival (95% C.I.)	HR (95% C.I.)	P-value-test interaction
PD-L1						0.***
≥ 50%	**	** (**, **)	**	** (**, **)	** (**, **)	
≥25-49%	**	** (**, **)	**	** (**, **)	** (**, **)	
1-24%	**	** (**, **)	**	** (**, **)	** (**, **)	
Disease stage						0.***
IB (≥4cm)	**	** (**, **)	**	** (**, **)	** (**, **)	
II	**	** (**, **)	**	** (**, **)	** (**, **)	
IIIA	**	** (**, **)	**	** (**, **)	** (**, **)	
Adjuvant chemo						0.***
≥ 300 mg/m^2	**	** (**, **)	**	** (**, **)	** (**, **)	
< 300 mg/m^2	**	** (**, **)	**	** (**, **)	** (**, **)	
no chemotherapy	**	** (**, **)	**	** (**, **)	** (**, **)	
Nodal sampling according to ESTS						0.***
Yes	**	** (**, **)	**	** (**, **)	** (**, **)	
No	**	** (**, **)	**	** (**, **)	** (**, **)	

Table 15c: DFS Subgroup Analysis (All randomized EGFR-/ALK- patients)

	Durva. Arm		Placebo arm			
Factors	N	Median Survival (95% C.I.)	N	Median Survival (95% C.I.)	HR (95% C.I.)	P-value-test interaction
PD-L1						0.***
≥ 50%	**	** (**, **)	**	** (**, **)	** (**, **)	
≥25-49%	**	** (**, **)	**	** (**, **)	** (**, **)	
1-24%	**	** (**, **)	**	** (**, **)	** (**, **)	
< 1%	**	** (**, **)	**	** (**, **)	** (**, **)	
Disease stage						0.***
IB (≥4cm)	**	** (**, **)	**	** (**, **)	** (**, **)	
II	**	** (**, **)	**	** (**, **)	** (**, **)	
IIIA	**	** (**, **)	**	** (**, **)	** (**, **)	
Adjuvant chemo						0.***
≥ 300 mg/m^2	**	** (**, **)	**	** (**, **)	** (**, **)	
< 300 mg/m^2	**	** (**, **)	**	** (**, **)	** (**, **)	
no chemotherapy	**	** (**, **)	**	** (**, **)	** (**, **)	
Nodal sampling according to ESTS						0.***
Yes	**	** (**, **)	**	** (**, **)	** (**, **)	
No	**	** (**, **)	**	** (**, **)	** (**, **)	

Table 16: Log Rank and Cox Regression Model for Overall Survival: PD-L1 ≥25% (Values at randomization) and EGFR-/ALK-

Univariate Analysis[1]

Treatment Arm	Median DFS (Months)	Hazard Ratio[2] (C.I.)*	Log-rank p-value
Treatment arm			0.***
MEDI4736	**.**	**.**	
Placebo	**.**	(**.**,**.**)	

(1) Stratified (value at randomization)
(2) Estimated from stratified Cox model
* C.I. at significance level of test, which depends on number of events included in the analysis.

Log Rank and Cox Regression Model for Disease Free Survival: PD-L1 ≥25% (Values at retested or randomization) and EGFR-/ALK-

Univariate Analysis[1]

Treatment Arm	Median DFS (Months)	Hazard Ratio[2] (C.I.)*	Log-rank p-value
Treatment arm			0.***
MEDI4736	**.**	**.**	
Placebo	**.**	(**.**,**.**)	

(1) Stratified (value at randomization)
(2) Estimated from stratified Cox model
* C.I. at significance level of test, which depends on number of events included in the analysis.

Log Rank and Cox Regression Model for Disease Free Survival: PD-L1 ≥25% (Values at rescored or randomization) and EGFR-/ALK-

Univariate Analysis[1]

Treatment Arm	Median DFS (Months)	Hazard Ratio[2] (C.I.)*	Log-rank p-value
Treatment arm			0.***

MEDI4736	**.**	**.**
Placebo	**.**	(**.**,**.**)

(1) Stratified (value at randomization)
(2) Estimated from stratified Cox model
* C.I. at significance level of test, which depends on number of events included in the analysis.

Log Rank and Cox Regression Model for Disease Free Survival: PD-L1 ≥25% (Values at rescored, re-tested or at randomization) and EGFR-/ALK-

Univariate Analysis(1)

Treatment Arm	Median DFS (Months)	Hazard Ratio(2) (C.I.)*	Log-rank p-value
Treatment arm			0.***
MEDI4736	**.**	**.**	
Placebo	**.**	(**.**,**.**)	

(1) Stratified (value at baseline)
(2) Estimated from stratified Cox model
* C.I. at significance level of test, which depends on number of events included in the analysis.

Table 17: Death causes

Data set: All Randomized Patients with PD-L1≥25% (Value at randomization) and EGFR-/ALK-

	Number of Patients (%)	
	MEDI4736 N=***	Placebo N=***
Number of patients who died	*** (**)	*** (**)
Causes of death		
NSCL cancer only	**	**
AE related to other treatment	**	**
Other primary malignancy	**	**
AE related to protocol treatment	**	**
Others	**	**
Patients who were censored (Alive or lost to follow up)	*** (**)	*** (**)

Table 16b, c and Table 17b, c are the same as table 15 and 16, but with** PD-L1 ≥1% **and EGFR-/ALK- or all EGFR-/ALK- populations.

Table 18: Total Treatment Duration and Dose of MEDI4736 /placebo

Data Set: All Treated Patients		
	MEDI4736	Placebo
Duration in weeks:		
N	***	***
Median	*	*
Min – Max	* - *	* - *
Total dose in mg:		
N	***	***
Median	*	*
Min – Max	* - *	* - *

Table 19: Dose Interruption or Discontinuation

Data Set: All Treated Patients

	Number of patients (%)	
	MEDI4736 (N=***)	Placebo (N=***)
Any drug interruption or discontinuation	** (**)	** (**)
Reasons for drug interruption or discontinuation		
<*reason 1*>	** (**)	** (**)
<*reason 2*>	** (**)	** (**)
...	** (**)	** (**)
At least one drug interruption	** (**)	** (**)
Reason for drug interruption		
<*reason 1*>	** (**)	** (**)
<*reason 2*>	** (**)	** (**)
...	** (**)	** (**)
...	** (**)	** (**)
Protocol treatment discontinuation	** (**)	** (**)
Reasons for discontinuation		
<*reason 1*>	** (**)	** (**)
<*reason 2*>	** (**)	** (**)
……	** (**)	** (**)

Table 20: Summary of Supportive and Concomitant Medications and Therapy, Transfusion and hospitalization

Data Set: All Treated Patients						
	Number of patients (%)					
	MEDI4736 (n = ***)		Placebo (n = ***)		TOTAL (n = ***)	
Any concomitant medication	***	(**)	***	(**)	***	(**)
Any blood transfusion	***	(**)	***	(**)	***	(**)
Any hospitalization	***	(**)	***	(**)	***	(**)

* Patients may have received more than one type of concomitant medication

Table 21: Hematology: Worst Ever Grade per Patient on Study

Data set: All Treated Patients		
	Number of patients (%)	
	MEDI4736	Placebo
WBC		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Platelets		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Neutrophils		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hemoglobin		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)

Table 22: Biochemistry: Worst Ever Grade per Patient on Study

Data set: All Treated Patients		
	Number of patients (%)	
	MEDI4736	Placebo
ALT (SGPT)		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
AST (SGOT)		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Total bilirubin		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Creatinine		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Albumin		
Number of patients	**	**
Normal	** (**)	** (**)
Low[(1)]	** (**)	** (**)
High[(2)]	** (**)	** (**)
Amylase		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)

Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Lipase		
Number of patients	**	**
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)

(1) Less than lower normal limit
(2) Greater than upper normal limit
NOTE: Patients can have more than one category (low and/or high)

Table 23: Thyroid Function Tests: Worst during Study

TFTs	MEDI4736 (No. of patient)	Placebo (No. of patients)	Total
T3 free			
Normal	** (**)	** (**)	** (**)
< 0.5 *LLN	** (**)	** (**)	** (**)
1-- 0.5* LLN	** (**)	** (**)	** (**)
Not reported	** (**)	** (**)	** (**)
T3 Total			
Normal	** (**)	** (**)	** (**)
< 0.5 *LLN	** (**)	** (**)	** (**)
1-- 0.5* LLN	** (**)	** (**)	** (**)
Not reported	** (**)	** (**)	** (**)
T4 free			
Normal	** (**)	** (**)	** (**)
< 0.5 *LLN	** (**)	** (**)	** (**)
1-- 0.5* LLN	** (**)	** (**)	** (**)
Not reported	** (**)	** (**)	** (**)
T4 Total			
Normal	** (**)	** (**)	** (**)
< 0.5 *LLN	** (**)	** (**)	** (**)
1-- 0.5* LLN	** (**)	** (**)	** (**)
Not reported	** (**)	** (**)	** (**)
TSH			
Normal	** (**)	** (**)	** (**)
>1- 1.5 *ULN	** (**)	** (**)	** (**)
>1.5-- 2* ULN	** (**)	** (**)	** (**)
>2-- 5* ULN	** (**)	** (**)	** (**)
> 5* ULN	** (**)	** (**)	** (**)
Not reported	** (**)	** (**)	** (**)

Table 24: Toxicity/Adverse Events/Intercurrent Illness (Worst Ever Grade on Study)

Data set: All Treated Patients (MEDI4736 Arm)

	Number of patients (%) N=***					
	Worst grade					Any grade
	NR	1	2	3	4	
Patients with any AE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE within category						
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...						
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...						

(1) Patients may have more than one event within a category.

NOTE: In Placebo Arm, the same type of table will be made. Same type of tables which include only the toxicities/adverse events/intercurrent illnesses which are drug related will be made for both MEDI4736 and placebo arms.

Table 25: Worst Ever Grade Toxicities/Adverse Event/Intercurrent Illness which are Serious, Fatal Only, Leading to Hospitalization, Results in significant disability / incapacity, Congenital anomaly, Required intervention / important medical event

Data set: All Treated Patients (MEDI4736 Arm)

	Number of patients (%) N=***					
	Worst grade					Any grade
	NR	1	2	3	4	
Patients with serious AE within category						
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Patients with fatal AE within category						
Category 1[(1)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Patients with AE leading to hospitalization within category						
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...						
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...						

(1) Patients may have more than one event within a category.

NOTE: In Placebo Arm, the same type of table will be made.
Same type of tables which include only the toxicities/adverse events/intercurrent illnesses which are drug related will be made for both MEDI4736 and placebo arms.

Table 26: SAEs that Led to Dose Discontinuation

Data set: All Treated Patients (MEDI4736 Arm)

	Number of patients (%) N=***					
	grade					Total
	NR	1	2	3	4	
Patients with any SAE led to study drug discontinuation	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with SAE led to study drug discontinuation within category	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3						
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1						
...						

(1) Patients may have more than one event within a category.

NOTE: In Placebo Arm, the same type of table will be made. Same type of tables which include only the toxicities/adverse events/intercurrent illnesses which are drug related will be made for both MEDI4736 and placebo arms.

Table 27: SAEs that Led to Dose Interruption

Data set: All Treated Patients (**MEDI4736** Arm)

	Number of patients (%) N=***					
	Worst grade					Total
	NR	1	2	3	4	
Patients with any AE led to dose interruption	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE led to dose interruption within category	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3						
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1						
...						

(1) Patients may have more than one event within a category.

NOTE: In Placebo Arm, the same type of table will be made. Same type of tables which include only the toxicities/adverse events/intercurrent illnesses which are drug related will be made for both MEDI4736 and placebo arms.

Table 28: Deaths on Study within 30 Days of the Last Treatment

Data set: All Treated Patients		
	Number of Patients (%)	
	MEDI4736 N=***	Placebo N=***
Number of Patients who died within 30 days of last treatment	** (**)	** (**)
Cause of Death		
NSCLC	**	**
Toxicity from protocol treatment	**	**
NSCLC + Toxicity from Protocol Treatment complication	**	**
Non-protocol Treatment Complication	**	**
NSCLC + Non-protocol Treatment Complication	**	**
Other Primary Malignancy	**	**
Other Condition or Circumstance	**	**

Table 29: Reason Off-Protocol Therapy

Data set: All Treated Patients						
	Number of patients (%)					
	MEDI4736 (n = ***)		Placebo (n = ***)		TOTAL (n = ***)	
Number (%) patients off **MEDI4736** / Placebo	**	(**)	**	(**)	**	(**)
Reasons off study						
Treatment complete	**	(**)	**	(**)	**	(**)
Disease relapse	**	(**)	**	(**)	**	(**)
Intercurrent disease	**	(**)	**	(**)	**	(**)
New primary malignancy	**	(**)	**	(**)	**	(**)
Patient refusal (related to AE)	**	(**)	**	(**)	**	(**)
Patient refusal (Not related to AE)	**	(**)	**	(**)	**	(**)
Toxicity to protocol treatment	**	(**)	**	(**)	**	(**)
Death	**	(**)	**	(**)	**	(**)

Other	**	(**)	**	(**)	**	(**)
Unknown	**	(**)	**	(**)	**	(**)
Never treated	**	(**)	**	(**)	**	(**)

Table 30: Compliance (Received/Expected) with QoL Assessment by Treatment Arm

	IO+ Chemotherapy		IO alone	
Period	Expected	Received (%)	Expected	Received (%)
Baseline	***	*** (**.*)	***	*** (**.*)
Week 4	***	*** (**.*)	***	*** (**.*)
Week 12	***	*** (**.*)	***	*** (**.*)
Week 24	***	*** (**.*)	***	*** (**.*)
……	***	*** (**.*)	***	*** (**.*)
12 weeks After Complete Trt	***	*** (**.*)	***	*** (**.*)
Every 12 Wks	***	*** (**.*)	***	*** (**.*)
…	***	*** (**.*)	***	*** (**.*)

Table 31: Baseline Score for Each Domain/item

Domain/item		IO + Chemotherapy	IO alone	P-value
Physical	N	***	***	0.**
	MEAN	**.**	**.**	
	STD DEV	**.**	**.**	
Emotional	N	***	***	0.**
	MEAN	**.**	**.**	
	STD DEV	**.**	**.**	
…	N	***	***	0.**
	MEAN	**.**	**.**	
	STD DEV	**.**	*.**	
……..				

Table 32: Mean QOL Change Scores from Baseline for Global Domain at Each Assessment Time

	IO+ Chemotherapy		IO alone		
Assessment	N	Mean (SD)	N	Mean (SD)	P value*
Week 4	***	**.** (**.**)	***	**.** (**.**)	0.**
Week 12	***	**.** (**.**)	***	**.** (**.**)	0.**
…	***	**.** (**.**)	***	**.** (**.**)	0.**

12 Weeks after Last cycle	***	**.** (**.**)	***	**.** (**.**)	0.**
Every 12 weeks, …	……	**.** (**.**) ……..	***	**.** (**.**)	0.**

*Wilcoxon test.

(There will be one table for each domain/item).

Table 33: Results for QOL Response Analyses

Domain	IO+Chemotherapy Improved N (%)	Stable N (%)	Worsen N (%)	IO alone Improved N (%)	Stable N (%)	Worsen N (%)	P-value
EORTC QLQ-C30							
Physical	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Role	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Emotional	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Cognitive	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Social	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Global	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Pain	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Fatigue	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Nausea	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Dyspnea	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Sleep	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Appetite	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Constipation	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Diarrhea	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Financial	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
EORTC QOL-LC13							
Cough	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Hemoptysis	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Dyspnea	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Sore Month	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Trouble Swallowing	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Peripheral neuropathy	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Hair loss	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Pain in chest	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Pain in shoulder	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Pain elsewhere	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Pain medication	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**

Table 34: QoL Repeated Measure Analysis-- Physical

Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	**.**	**.**	****	**.**	0.****
Arm					
MEDI4736	**.**	**.**	****	**.**	0.****
Placebo					
time	**.**	**.**	****	**.**	0.****
time* MEDI4736	**.**	**.**	****	**.**	0.****

Tables for each of other 4 functional domains and global QoL assessments.