STATISTICAL ANALYSIS PLAN

A PHASE II RANDOMIZED STUDY OF DURVALUMAB AND TREMELIMUMAB AND BEST SUPPORTIVE CARE VS BEST SUPPORTIVE CARE ALONE IN PATIENTS WITH ADVANCED COLORECTAL ADENOCARCINOMA REFRACTORY TO STANDARD THERAPIES

Protocol CCTG CO.26

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May 9, 2018

Revised: September 6, 2018

ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Serum Glutamic Oxaloacetic Transaminase
BSA	Body Surface Area
BSC	Best Supportive Care
CCTG	Canadian Cancer Trials Group
CEA	Carcinoembryonic antigen
C. I.	Confidence Interval
CMH	Cochran-Mantel-Haenszel
CR	Complete Response
CRC	Colorectal Cancer
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
ECOG	Eastern Cooperative Cancer Group
ECG	Electrocardiography
EORTC	European Organization for Research and Treatment of Cancer
IN	Inevaluable
IV	Intravenous
INR	International Normalized Ratio (for Prothrombin Time)
LDH	Serum Lactate Dehydrogenase
LKA	Last day the patient is Known Alive
LLN	Lower Limit of Normal
MPV	Major Protocol Violation
MSI	Microsatellite Instability
MSI-H	Microsatellite Instability-High
MSI-L	Microsatellite Instability-Low
MSS	Microsatellite Stable
NA	Not Assessed
NAP	Not Applicable
NC	Not Computed
ORR	Objective Response Rate
OS	Overall Survival
PD	Progression Disease
PD1	Programmed cell death protein 1
PD-L1	Programmed cell death ligand 1
PFS	Progression-free survival
PR	Partial Response
PT	Prothrombin Time
PTT	Partial Thromboplastin Time
QLQ	Quality of Life Questionnaire
QOL	Quality of Life
RBC	Red Blood Cell Count
RECIST	Response Evaluation Criteria in Solid Tumors

SAS	Statistical Analysis System
SD	Stable Disease
STD	Standard Deviation
TSH	Thyroid-stimulating hormone
VEGF	Vascular Endothelial Growth Factor
WBC	White Blood Cell Count

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1. Background and Rationale

The purpose of this document is to describe the analysis of CO.26 for the writing of a Canadian Cancer Trials Group (CCTG) study report on this study. The data are collected and cleaned by CCTG. All analyses will be performed by a senior biostatistician in CCTG and a final statistical analysis report will be prepared. A copy of this report will be sent to the study chair for the writing of the manuscript and to AstraZeneca.

Rationale of the Study:

Programmed cell death ligand 1 (PD-L1), the ligand for programmed cell death protein 1 (PD1), is part of a complex system of receptors and ligands that are involved in controlling T-cell activation, which acts at multiple sites in the body to help regulate normal immune responses and is utilized by tumours to help evade detection and elimination by the host immune system. Overexpression of PD-L1 in colorectal cancer (CRC) is associated with poor prognosis. Clinically, blockade of the PD-1 inhibitory checkpoint pathway by inhibiting PD-L1/ PD-1 engagement has been shown to induce tumour regression across many cancer types, including melanoma and renal cell, colon and lung cancers. CTLA-4 is another co-inhibitory receptor expressed on activated T cells and regulates early stage T cell activation, reducing the amplitude of T-cell activation. Targeting both PD-1 and CTLA-4 pathways may have additive or synergistic activity because the mechanisms of action of CTLA-4 and PD-1 are non-redundant. This study was designed to evaluate whether combining PD-1/PD-L1 and CTLA-4 inhibition with durvalumab and tremelimumab will lead to improved patient survivals compared to best supportive care in advanced colorectal cancer.

Research Hypothesis:

The primary hypothesis in this study is that durvalumab and tremelimumab combined with best supportive care (Durva+Treme) will have a greater clinical efficacy compared to best supportive care alone (BSC) in patients with refractory, advanced colorectal cancer as measured by overall survival.

Schedule of Analyses:

Only one analysis will be performed, when 150 events (deaths) have been observed.

2. Study Description

2.1 Study Design

Study CCTG CO.26 is a multi-centre, open-label, randomized phase II trial of durvalumab and tremelimumab combined with best supportive care *versus* best supportive care alone (where best supportive care is defined as those measures

designed to provide palliation of symptoms and improve quality of life as much as possible) in patients with refractory, advanced colorectal carcinoma. Patients are stratified by ECOG performance status (0 vs. 1) and site of tumour (right colon vs. transverse colon vs. left colon vs. rectum vs. unknown) prior to randomization. This study is conducted by CCTG with support from AstraZeneca. CCTG Case Report Forms (CRFs) are used and the database are maintained by CCTG.

A total of 180 patients would be enrolled (120 on Durva+Treme and 60 on BSC). The final analyses will be performed by CCTG when the required number of deaths (150) is recorded. This analysis plan describes the analyses performed at the completion of the study.

This study was activated on August 10, 2016 and closed to randomization of patients on June 29, 2017 after 180 patients were randomized. The CCTG Data Safety Monitoring Committee has been reviewing safety data every six months (usually at the time of the bi-annual CCTG Spring and Fall meetings) and as otherwise required. These analyses have been prepared by a CCTG/Queen's Senior Biostatistician.

2.2 Treatment Allocation

The study is planned to randomize 180 subjects using a 2:1 allocation to durvalumab and tremelimumab combined with best supportive care (Durva+Treme Arm or ARM 2) and best supportive care alone (BSC Arm or ARM 1). The randomization was dynamically balanced by ECOG performance status (0 vs. 1) and site of tumour (right colon vs. transverse colon vs. left colon vs. rectum vs. unknown) using the method of minimization. A centralized system was used to randomize all patients in this study.

3. Objectives

3.1 Primary

The primary objective of this study is to compare overall survival of patients with advanced colorectal cancer who are refractory to all available therapy treated with durvalumab and tremelimumab combined with best supportive care to the overall survival of patients treated with best supportive care alone.

3.2 Secondary

Secondary objectives are to:

- Compare progression-free survival (PFS) between the two treatment arms.
- Compare objective response rates (ORR) between the two treatment arms.
- Assess the toxicity and safety profile of the combination of durvalumab and tremelimumab and best supportive care.

4. Endpoints

4.1 Primary Efficacy

The primary efficacy endpoint is overall survival.

4.2 Secondary Efficacy

The secondary efficacy endpoints are progression-free survival and objective response rate.

4.3 Safety

The safety endpoints are serious and non-serious adverse events (clinical and laboratory), laboratory parameters, dosing data (including dose interruptions, total delivered dose and dose modifications) and reasons off treatment.

5. Sample Size and Power

The primary objective of this study is to assess the additional effect of durvalumab and tremelimumab to best supportive care by comparing overall survival (OS) between Durva+Treme and BSC arms among all randomized patients. It was calculated that with a 2-sided alpha of 10%, a total of 180 patients with 150 events (deaths) would be required to provide 80% power to detect a 2.4 month difference in median survival (a hazard ratio of 0.65) between the two treatment arms assuming a median survival of 4.5 months for the BSC alone arm. The final analysis will be conducted after at least 150 events have been recorded. It is estimated that 180 patients accrued over 18 months and followed for 6 months will be required to reach the necessary number of events.

6. Data Set Descriptions

Three types of analysis samples will be used:

<u>All Randomized Patients</u>:
All patients who have been randomized in the study with the treatment arm being as randomized.

<u>Response-Evaluable Patients</u>:
All patients who have received at least one cycle of therapy and have their disease re-evaluated will be considered evaluable for response (exceptions will be those who exhibit objective disease progression prior to the end of cycle 1 who will also be considered evaluable).

<u>All Treated Patients</u>:
All patients on Durva+Treme who received at least one dose of durvalumab and tremelimumab and on BSC who had at least one Best Supportive Care Report.

Patients randomized to BSC who have received at least one dose of durvalumab and tremelimumab on study (from Cancer Treatment Section of Best Supportive Care Report) will be grouped with patients randomized to Durva+Treme in analyses of safety.

7. Statistical Analysis

7.1 General Methods

All comparisons between treatment arms will be carried out using a two-sided test at an alpha level of 10% unless otherwise specified.

When appropriate, discrete variables are summarized with the number and proportion of subjects falling into each category, and compared using Fisher's exact test. Continuous and ordinal categorical variables are summarized using the mean, median, standard error, minimum and maximum values and when appropriate, compared using the Wilcoxon test. All confidence intervals are computed based on normal approximations except those for rates, which will be computed based on the exact method.

Time to event variables are summarized using Kaplan-Meier plots. Primary comparisons of the treatment groups are made using the stratified log-rank test. Primary estimates of the treatment differences are obtained with the hazard ratios and 90% confidence intervals from stratified Cox regression models using treatment arm as the single factor.

Percentages given in the summary tables will be rounded and may therefore not always add up to exactly 100%. Listings, tabulations, and statistical analyses will be carried out using the SAS (Statistical Analysis System, SAS Institute, North Carolina, USA) software.

Unless otherwise specified, date of randomization and stratification factors will be taken from the Centralized Randomization File.

Baseline evaluations will be those collected on Eligibility Checklist and Baseline Report and closest to, but no later than, the first day of study medication for treated subjects and closest to, but no later than, the date of randomization, for subjects who were randomized but who never received treatment.

Laboratory results, adverse events, and other symptoms are coded and graded using the Common Terminology Criteria for Adverse Events (CTCAE v4.0).

7.2 Data Conventions

When converting a number of days to other units, the following conversion factors will be used:
1 year = 365.25 days

1 month = 30.4375 days

When either day or month of a date is missing, the missing day and/or month will be imputed by the midpoint within the smallest known interval. For example, if the day of the month is missing for any date used in a calculation, the 15th of the month will be used to replace the missing day. If the month and day of the year are missing for any date used in a calculation, the first of July of the year will be used to replace the missing date.

7.3 Study Conduct

All randomized patients are included in the analyses of study conduct. Information will be tabulated by randomized treatment (unless otherwise indicated) and pooled treatments.

7.3.1 Patient Disposition

- Number of patients randomized, treated (for patients on Durva+Treme arm only: on study, off study), never treated **(Table 1)**
- Number of alive patients **(Table 2)**
- Median (estimated by Kaplan-Meier method) and range (minimum and maximum) **(Table 2)** of the follow-up time (months) defined as time from the day of randomization (as recorded in centralized randomization file) to the last day the patient is known alive (LKA) as the last recorded date known alive or censored at the time of death and calculated as

$$[(\text{date of death or LKA} - \text{date of randomization}) + 1)]/30.4375.$$

7.3.2 Accrual Patterns

- Number of patients randomized by center **(Table 3)**
- Number of patients by stratification factors at randomization **(Table 4)**
- Accrual of patients by calendar time pooled across two treatment arms **(Figure 1)**

7.3.3 Eligibility Violations/Protocol Deviations

Eligibility violations of inclusion or exclusion criteria are centrally reviewed by CCTG; a field (y/n) for eligibility status and reason for ineligibility is entered in the database. A major protocol violation (MPV) is defined as a deviation from the protocol, initiated by the centre or the investigator, serious enough to mean that the patient's data contributes little, if any, information on the efficacy or toxicity of the regimen under study. MPVs are coded by CCTG based on its standard codes.

- Number of patients eligible, not eligible **(Table 5)**
- Reasons for ineligibility **(Table 5)**
- Major protocol violations: % for each type of violations **(Table 5)**.

Deviations from randomization will be summarized as follows:

- Treatment as randomized versus as treated **(Table 6)**

7.4 Study Population

All randomized patients are included in the study population analyses. Information will be tabulated by randomized treatment (unless otherwise indicated) and pooled treatments.

7.4.1 Patient Pretreatment Characteristics

- Gender **(Table 7)**
- Race **(Table 7)**
- Age: median, minimum, maximum values**;** number <65, ≥65 **(Table 7)**
- ECOG Performance Status: 0, 1 **(Table 7)**
- BSA: median, minimum, maximum values **(Table 7)**
- Months from first histological diagnosis of colorectal cancer to randomization: median, minimum, maximum values **(Table 7)**
- Histology: adeno-carcinoma, etc. **(Table 7)**
- Site of tumour: right colon, transverse colon, left colon, rectum, unkown **(Table 7)**
- KRAS mutation status: wild-type, mutated, unknown **(Table 7)**
- NRAS mutation status: wild-type, mutated, unknown **(Table 7)**
- BRAF mutation status: wild-type, mutated, unknown **(Table 7)**
- MSI status: MSI-H, MSI-L, MSS, Unknown **(Table 7)**

7.4.2 Prior Surgery

- Number of patients with prior surgery for colorectal cancer **(Table 8)**
- Procedure/site of prior surgery **(Table 8)**

7.4.3 Prior radiotherapy

- Number of patients with prior adjuvant or palliative radiotherapy. **(Table 9)**
- Prior radiotherapy by site and type (adjuvant or palliative) **(Table 9)**

7.4.4 Prior Systemic Therapy

- Number of subjects with prior systemic therapy and type of prior systemic therapy (adjuvant, metastatic, neo-adjuvant) **(Table 10)**
- Number of patients with prior thymidylate synthase inhibitor (**Table 11**)
- Number of patients with prior irinotecan containing regimen **(Table 11)**
- Number of patients with prior oxaliplatin containing regimen **(Table 11)**
- Number of patients with prior cetuximab or panitumumab containing regimen (**Table 11**)
- Number of patients with prior VEGF targeting therapy **(Table 11)**
- Number of patients with prior TAS-102 therapy **(Table 11)**

7.4.5 Extent of Disease

- Number of patients with target lesions**,** number of target lesions, largest measure, site of target lesions **(Table 12)**

- Number of patients with non-target lesions, number of non-target lesions, site of non-target lesions **(Table 13)**

7.4.6 Baseline Exams

- Baseline signs and symptoms **(Table 14)**
- Baseline hematology: WBC, neutrophils, platelets, hemoglobin, RBC, lymphocytes, monocytes, eosinophils, basophils **(Table 15)**
- Baseline serum chemistry: Total bilirubin, AST, ALT, alkaline phosphatase, LDH, serum creatinine, chloride, sodium, albumin, potassium, calcium, magnesium, ALP, glucose, amylase, lipase, CEA **(Table 16)**
- Baseline Thyroid Function Tests **(Table 17)**
- Baseline Coagulation Tests (**Table 18**)
- Baseline ECG **(Table 19)**
- Baseline urinalysis **(Table 20)**

7.4.7 Concomitant Medications and Major Medical Problems at Baseline

- Number of patients with concomitant medication within 14 days prior to the date of randomization **(Table 21)**
- Number of patients with past or current major medical problems ongoing at baseline **(Table 22)**

7.5 Extent of Exposure to Durvalumab and Tremelimumab

Patients included are those who received at least one dose of durvalumab or tremelimumab as defined in Section 6.

7.5.1 Study Therapy

During a 4 week cycle of protocol treatment, the patients received infusion of durvalumab (1500 mg) on day 1 and tremelimumab (75 mg) on day 1 of cycles 1, 2, 3 and 4 only.

Duration of durvalumab or tremelimumab (in weeks) during the study is defined as follows:

> [last date of infusion of durvalumab or tremelimumab – first date of infusion of durvalumab or tremelimumab + 28]/7,

where the first and last date of infusion is taken from Durvalumab Administration or Tremelimumab Administration Section of Treatment Report).

The following variable will be summarized using the data set of all patients treated by durvalumab or tremelimumab:

- Number of patients by cycle of therapy **(Table 23)**
- Total number of cycles of treatment per patient **(Table 24)**
- Total treatment duration of durvalumab or tremelimumab per patient (**Table 25**)

7.5.2 Dose Reduction, Omission, Discontinuation, or IV Rate Decrease or Infusion Interruption to Durvalumab or Tremelimumab

The administration of durvalumab or tremelimumab in a cycle may be modified (reduced, omitted, delayed, and IV rate decreased and infusion interrupted) because of toxicity or other reasons. For each drug, the following variables will be summarized using the data set of all treated patients:

- Number of patients who had all of their drug administrations according to protocol (**Table 26**)
- Number of patients with at least one cycle reduced, omitted, delayed, or IV rate decreased and infusion interrupted **(Table 27)**
- Reason for these dose modifications **(Table 27)**

7.5.3 Cumulative Dose, Dose Intensity and Relative Dose Intensity of Durvalumab or Tremelimumab

The cumulative dose (mg) per patient for each drug is the total dose (mg) the patient received, which is defined as the sum of the actual dose level (mg) over the study **(Table 28).**

The actual dose intensity of a drug (mg/week) per patient is defined as:

$$\text{Actual Dose Intensity} = \frac{\text{Cumulative dose (mg)}}{[\text{last dosing date} - \text{first dosing date} + 28]/7}.$$

where first and last dosing date is taken from Durvalumab Administration or Tremelimumab Administration Section of Treatment Report **(Table 29).**

The relative dose intensity of durvalumab or tremelimumab per patient is defined as the dose intensity (mg/week) divided by the planned weekly dose as assigned in the protocol, which is 375 mg/week for durvalumab and 18.75 mg/week for tremelimumab.

The patient relative dose intensities will be grouped according to the following categories: < 60%,≥ 60% - < 80%, ≥ 80% - < 90%, ≥ 90% (**Table 30**).

7.5.4 Off Study Therapy

The reason for off of each study therapy will be taken from End of Treatment Section of End Of Treatment Report.

The following information will be summarized for each of protocol treatment **(Table 31):**

- Number of patients off study treatment
- Reason off protocol therapy

7.6 Efficacy

7.6.1 Overall survival

For all randomized patients, survival is calculated from the day of randomization (as recorded in Centralized Randomization File) to death (Date/Cause of Death Section of Death Report). For alive patients, survival is censored at the last day the patient is known alive (LKA) as the last recorded date known alive (Date of Attendance/Last Contact on Best Support Care Report, 4-Week Post Treatment Report, Follow-up Report, Short Follow Up Report, and Minimal Follow-up Report; or last date of infusion of durvalumab or tremelimumab in Treatment Report). Survival time (in months) is defined as

[(date of death or LKA – date of randomization) + 1)]/30.4375.

A frequency table for the number of patients who died and cause of death in each treatment arm will be provided (**Table 32**). Kaplan-Meier curve for proportions of survival in each treatment arm will be displayed (**Figure 2**).

The comparison of overall survival between the two treatment arms is the primary objective of this study. The primary analysis will be the log-rank test **(Table 33)** stratified by the factors coded as:

<u>Stratification Factors (at randomization)</u>

Performance status	1 = ECOG 0 0 = ECOG 1
Site of tumour	1=right colon; 2=transverse colon; 3=left colon; 4=rectum; 5=unknown

The hazard ratio of durvalumab and tremelimumab combined with best supportive care (ARM 2) over best supportive care alone (ARM 1) and two-sided 90% CI will be calculated **(Table 33)** based on the Cox regression model stratified by above stratification factors, and with treatment arm coded as ARM 2=1 and ARM 1=0. The 90% confidence intervals for the median survival will be computed using the method of Brookmeyer and Crowley [2].

In order to assess the influence of the potential prognostic factors shown and coded below on the comparison of survival between treatment arms, a stratified Cox regression model will be used with all variables (treatment arm and prognostic factors) included to estimate hazard ratios and 90% confidence intervals **(Table 33).**

<u>Prognostic factors (at baseline)</u>

Gender	0 = Female	1 = Male
Age	0 = ≥65	1 = < 65
Number of organ sites	0 = >2	1= ≤ 2
Presence of liver metastases	0= Yes	1= No

No interactions will be considered in the model**.**

7.6.2 Overall Survival by Subsets

For each level of the following baseline variables, a Kaplan-Meier plot of survival by treatment arm will be produced as well as medians with 90% C.I. and the hazard ratio (unstratified) with 90% CI of durvalumab or tremelimumab combined with best supportive care (ARM 2) over best supportive care alone (ARM 1) **(Table 34):**

- Gender: male, female
- Age: <65, ≥65
- Race: white, black, other
- Performance status at baseline: ECOG 0, 1
- Site of tumour: right colon, transverse colon, left colon, rectum, unknown
- KRAS status: wildtype, mutated
- NRAS status: wildtype, mutated
- BRAF status: wildtype, mutated
- MSI status: MSI-H, MSI-L, MSS

7.6.3 Progression-free Survival

Progression-free survival (PFS) will be calculated for all patients from the day of randomization until the first observation of disease progression (date of objective relapse or progression of Relapse/Progression Report) or death due to any cause (recorded in Date/Cause of Death Section of Death Report) as the (difference+1).

If a patient has not progressed or died, PFS will be censored on the date of last disease assessment defined as the earliest test date of target lesion or non-target lesions (if patient has no target lesions), whichever is latest.

A frequency table will be provided describing progression and censoring as follows **(Table 35):**

- Number of patients who progress (documented progression, death without documented progression)
- Number of patients censored (alive and not progressed)

Analyses for PFS will be similar to that for overall survival as previously described. A Kaplan-Meier curve for PFS in each treatment arm will be displayed (**Figure 3**). In the primary analysis, median PFS for the two treatments will be compared using the stratified log-rank test **(Table 36).** A stratified Cox regression model will estimate the durvalumab and tremelimumab combined with best supportive care (ARM 2) over best supportive care alone (ARM 1) PFS hazard ratio and 90% C. I. **(Table 36).** In addition, a stratified Cox regression model adjusted for covariates will be applied to verify the impact of the prognostic factors on the treatment effect **(Table 36).**

Coding for treatment arm, stratification variables and prognostic factors is identical to that presented in **Section 7.5.1**.

Some patients received other anti-cancer therapy before progression or death. Sensitivity analyses will be performed by censoring those who have received anti-cancer therapy prior to documentation of disease relapse/progression or death on the earliest date cancer treatment began or treating them as having PFS events at the earliest date when the treatment began.

7.6.4 Progression-free survival by Subsets

Subset analyses performed for overall survival will also be performed for PFS (**Table 37).**

7.6.5 Treatment Response

All patients will have their best response on study classified every 8 weeks until disease progression, using the RECIST (Response Evaluation Criteria in Solid Tumors) criteria 1.1. The best response to protocol treatment is determined by investigators for patients who permanently discontinued protocol treatment and collected in "Best Objective Response RECIST 1.1" section of END OF TREATMENT REPPORT. For patients who are still on protocol treatment and followed for response at final clinical cut-off, their best response is defined as the "best verified" response they have achieved up to the time of clinical cut-off determined by CCTG Senior Investigator based on data on "Response Assessment" section of TREATMENT REPORT or BEST SUPPORTIVE CARE REPORT.

Best response to protocol treatment will be summarized for all randomized patients **(Table 38).**

The primary analysis of response will be the comparison of the objective response rate (CR+PR) between treatment arms among all the randomized patients using the Cochran-Mantel-Haenszel (CMH) statistic adjusted for stratification factor for all randomized patients **(Table 39)** as defined in Section 6.

In addition, a stratified logistic regression model adjusted for covariates will be applied to verify the impact of the prognostic factors on the treatment effect **(Table 39**). For all stratified logistic regression models, estimates of the odds ratio(s) and 90% confidence interval(s) will be given.

Stratified logistic regression odds ratios will be estimated using PROC PHREG in SAS [5]. A dummy time variable will be created, where all responders will be classified as events with an arbitrary time = t_0, and non-responders as censored with time t_1, where $t_1 > t_0$. The DISCRETE option will be used for tied observations.

Coding for treatment, stratification variable and prognostic factors is identical to that presented in Section 7.4.1.

7.6.6 Treatment Response by Subsets

For all randomized patients, the objective response rate will be presented for each treatment arm in the subgroups defined by the categorical variables listed below **(Table 40)**. No formal comparisons are planned:

- gender (male, female)
- age (<65 years, ≥65 years)
- race (white, black, other)
- performance status at baseline (ECOG 0, ECOG 1)
- Site of tumour (right colon, transverse colon, left colon, rectum)
- KRAS status (wildtype, mutated)
- NRAS status (wildtype, mutated)
- BRAF status (wildtype, mutated)
- MSI status (MSI-H, MSI-L, MSS)

7.6.7 Duration of Response

For patients whose best responses are classified as CR or PR at any reporting period during the study, the duration of response is calculated as the time from CR or PR is documented (whichever is the first) until first observation of objective disease relapse or progression or death due to any cause. If a patient has not relapsed/progressed or died, duration of response will be censored on the date of last disease assessment defined as the earliest test date of target lesion or non-target lesions (if patient has no target lesions), whichever is latest.

All randomized patients with CR or PR are included in this analysis. The median duration of response and associated 95% confidence intervals will be computed and compared by the stratified log-rank test adjusting for stratification factors at randomization **(Table 41).**

7.7 Safety

The safety analyses will based on the All Treated population defined in Section 6. Adverse events and laboratories are graded and categorized using the CTCAE v4.0 criteria except where CTCAE grades are not available.

7.7.1 Adverse Events

Adverse events will be recorded on the CCTG toxicity/adverse event-intercurrent illness case report form. Events reported on Treatment Report or 4-Week Post-Treatment Follow-Up Report for patients on the Durva+Treme arm will be defined as adverse events on Durva+Treme; Events reported on any case report forms except Form 1 will be summarized separately for patients on both arms as overall adverse events during the (whole) study.

Drug related adverse events are those events with a relation to protocol therapy of 3=possible, 4=probable or 5=definite.

Severe adverse events are those events reported with a CTCAE Grade of 3 or higher.

Comparisons between treatment arms on overall adverse events (any vs. other, severe vs. other) will be carried out using a two sided Fisher's exact test at an alpha level of two-sided 10%.

The following variables are summarized. Tabulations of overall adverse events will be presented by treatment group.

- Adverse events on Durva+Treme: worst CTCAE grade per patient **(Table 42)**
- Severe adverse events on Durva+Treme: worst CTCAE grade per patient **(Table 43)**
- Drug related adverse events on Durva+Treme: worst CTCAE grade per patient **(Table 44)**
- Overall adverse events: worst CTCAE grade per patient **(Table 45)**
- Severe overall adverse events: worst CTCAE grade per patient **(Table 46)**

7.7.2 Laboratory Evaluations

For patients on Durva+Treme, laboratory evaluations reported on Treatment Report or 4-Week Post-Treatment Follow-Up Report for patients on the Durva+Treme arm will be included in the calculation for laboratory adverse events on Durva+Treme. All laboratory evaluations reported after baseline assessment will be included in the calculation for overall laboratory adverse events. Laboratory results will be classified according to CTCAE version 4.0. Laboratory tests that are not covered by the CTCAE grading system will be summarized according to the following categories: normal and above the upper normal limits.

7.6.2.1 Hematology

- Hemoglobin, platelets, WBC, neutrophils, RBC, lymphocytes, monocytes, eosinophils, basophils on Durva+Treme: worst CTC grade per patient **(Table 47)**
- Overall hemoglobin, platelets, WBC, neutrophils, RBC, lymphocytes, monocytes, eosinophils, basophils: worst CTC grade per patient **(Table 48)**

7.6.2.2 Serum Chemistry

- Total bilirubin, AST, ALT, alkaline phosphatase, LDH, serum creatinine, chloride, sodium, albumin, potassium, calcium, magnesium, ALP, amylase, lipase, CEA on Durva+Treme: worst CTC grade per patient **(Table 49)**
- Overall total bilirubin, AST, ALT, alkaline phosphatase, LDH, serum creatinine, chloride, sodium, albumin, potassium, calcium, magnesium, ALP, amylase, lipase, CEA: worst CTC grade per patient **(Table 50)**

7.6.2.3 Thyroid Function Tests

- TSH, T3 free, T3 total, T4 free, T4 total on Durva+Treme **(Table 51)**
- Overall TSH, T3 free, T3 total, T4 free, T4 total **(Table 52)**

7.6.2.3 Coagulation

- PT, INR, PTT on Durva+Treme **(Table 53)**
- Overall PT, INR, PTT **(Table 54)**

7.7.3 Other Safety

7.6.3.1 ECG

Cardiac function of patients is evaluated as clinically indicated by ECG during protocol treatment for patients on Durva+Treme with results reported on Treatment Report and before progression for patients on BSC with results reported on Best Supportive Care Report.

- Overall number of patients by normal or abnormal ECG, by treatment group **(Table 55)**

7.6.3.2 Urinalysis

Dipstick urinalysis is performed as clinically indicated during protocol treatment for patients on Durva+Treme with results reported on Treatment Report and before progression for patients on BSC with results reported on Best Supportive Care Report.

- Results of urinalysis, by treatment group **(Table 56)**

7.7.4 Deaths on Study/Adverse Events Leading to Discontinuations of Protocol Treatment

- Deaths during durvalumab and tremelimumab treatment or within 4 weeks of last durvalumab and tremelimumab treatment (DURVA+TREME Arm only): number of patients who died and cause of death from Date/Cause of Death Section of Death Report **(Table 57)**
- Number of patients with adverse events leading to discontinuations of durvalumab as identified from Off Protocol Treatment - Adverse Events of End of Treatment Report (DURVA+TREME Arm only) **(Table 58)**
- Number of patients with adverse events leading to discontinuations of tremelimumab as identified from Off Protocol Treatment - Adverse Events of End of Treatment Report (**Table 58**)

7.8 Concomitant Medications, Other Anti-Cancer Treatments, and Major Medical Problems

Investigators may prescribe concomitant medications or treatments deemed necessary to provide adequate prophylactic or supportive care. Administration of any other anti-cancer therapy is not permitted while the patient is receiving protocol therapy.

Thereafter, patients may be treated at the investigator's discretion. Major medical problems are those thought unrelated to protocol treatment.

- Concomitant medications for patients on DURVA+TREME Arm during or 4 weeks after Durvalumab and Tremelimumab Treatment (reported on Treatment Report and 4-Week Post-Treatment Follow-Up Report) and on BSC Arm prior to objective disease progression (reported on Best Supportive Care Report) **(Table 59)**
- Anti-cancer treatments during or 4 weeks after Durvalumab and Tremelimumab Treatment (reported on Treatment Report and 4 Weeks 4-Week Post-Treatment Follow-Up Report) (DURVA+TREME Arm only) (**Table 60**)
- Anti-cancer treatments before progression (reported on Treatment Report 4-Week Post-Treatment Follow-Up Report, and Fellow-up Report for patients on DURVA+TREME Arm and Best Supportive Care Report on BSC), by treatment group **(Table 60)**
- Anti-cancer treatments for all patients after progression (reported on Short Follow-up Report), by treatment group **(Table 60)**
- Major medical problem before progression (reported on Treatment Report 4-Week Post-Treatment Follow-Up Report, and Fellow-up Report for patients on DURVA+TREME Arm and Best Supportive Care Report on BSC), by treatment group **(Table 61)**

7.9 Quality of Life

The quality of life of patients in this study is assessed at 4, 8, 12, 16 and 24 months from randomization by using EORTC QLQ-C30 (version 3.0). The following are the scoring algorithms for this instrument.

7.9.1 EORTC QLQ-C30

The EORTC core questionnaire, QLQ-C30 (version 3.0), consists of five Functional Scales, Global Health Status, and nine Symptoms Scales. Each scale in the questionnaire will be scored (0 to 100) according to the EORTC recommendations in the EORTC QLQ-C30 Scoring Manual. The scoring method is summarized below. In this summary Qi refers to the ith question on the QLQ-C30.

Functional scale's scores:

- Physical functioning: (1 - ((Q1+Q2+Q3+Q4+Q5)/5 -1)/3) * 100
- Role functioning: (1 - ((Q6+Q7)/2-1)/3) * 100
- Emotional functioning: (1 - ((Q21+Q22+Q23+Q24)/4-1)/3) * 100
- Cognitive functioning: (1 - ((Q20+Q25)/2-1)/3) * 100
- Social functioning: (1 - ((Q26+Q27)/2-1)/3) * 100

Global health status score:

- Global health status/QOL: ((Q29+Q30)/2-1)/6 * 100

Symptom scale's scores:

- Fatigue: ((Q10+Q12+Q18)/3-1)/3 * 100
- Nausea and vomiting: ((Q14+Q15)/2-1)/3 * 100
- Pain: ((Q9+Q19)/2-1)/3 * 100
- Dyspnea: ((Q8-1)/3 * 100
- Insomnia: (Q11-1)/3 * 100
- Appetite loss: (Q13-1)/3 * 100
- Constipation: (Q16-1)/3 * 100
- Diarrhea: (Q17-1)/3 * 100
- Financial difficulties: (Q28-1)/3 * 100

Missing items in a scale will be handled by the methods outlined in the scoring manual. In particular, values will be imputed for missing items by "assuming that the missing items have values equal to the average of those items which are present" for any scale in which at least half the items are completed. A scale in which less than half of the items are completed will be treated as missing.

7.9.2 Data Sets

The analyses of quality of life data will be restricted to randomized patients who have a measurement at baseline and at least one measurement after baseline.

The QOL assessment is performed prior to randomization and during chemotherapy/BSC at 4, 8, 16, and 24 weeks from randomization. Since exact time of assessment may vary from subject to subject, it is necessary to provide a window for each QOL time point. What follows is a description of how to assign a questionnaire to a discrete time point:

Time Point	Windows (i.e., time periods)
Baseline	14 days prior to up to the day of randomization
Week 4	2 weeks - < 6 weeks
Week 8	6 weeks - < 10 weeks
Week 12	10 weeks - < 14 weeks
Week 16	14 weeks - < 20 weeks
Week 24	20 weeks -< 28 weeks

If more than one questionnaire is available for the baseline window, then the latest non-missing measurement, per question, will be considered. If more than one questionnaire is available at a time point other than baseline, then the average (per question) of the non-missing measurements will be used.

Summary statistics, plots and longitudinal comparisons will be based on changes of the quality of life scores from baseline.

7.9.3 Compliance

Compliance will be described, by time of evaluation, by the number and percentage of subjects who filled out a questionnaire (per subject, at least one question answered) in that period of evaluation. The denominator used in calculating the percentage for baseline will be all randomized subjects. The denominator used for all other time points will be the number of subjects known to be alive at the start of the time period **(Table 62).**

7.9.4 Primary Analyses of QOL

The primary endpoints for the comparison of QOL between treatment arms will be proportions of patients who had deterioration in physical function and Global Health Status at 8 weeks and 16 weeks after the randomization. The deterioration is defined as a change score from baseline which is –10 points or lower [6]. Fisher's exact test will be used to compare the proportions of patients with deterioration between two treatment arms at these two time points **(Table 63)**. No multiple adjustment for these comparisons will be made.

The proportions of patients who had improving (defined as change score from baseline of 10 points or higher) or stable (defined as change score from baseline of between –10 and 10 points) physical function and Global Health Status at 8 weeks and 16 weeks after the randomization will also be compared between two treatment arms using Fisher's exact test **(Table 63)**.

The time to definitive deterioration in physical function and Global Health Status is defined as the time from randomization until the change score from baseline is –10 points or lower. For patients whose change scores are always higher than –10 points, the time to definitive deterioration will be censored at their last QoL assessment times. The log-rank test will be used to compare the time to definitive deterioration between two treatment arms **(Table 64)**.

7.9.5 Baseline and Change Score Analysis

Descriptive statistics for EORTC QOL score (mean, standard deviation) will be presented for each scale at baseline. The same statistics will be generated at each time of post-baseline evaluation. The comparability of mean baseline scores and change scores at each time of post-baseline evaluation between treatment groups will be assessed using a Wilcoxon rank sum test (**Table 65** and **Table 66**).

7.9.6 QOL Response Analysis

QOL response for functional scales and global health status is calculated as follows: A change score of 10 points from baseline is defined as clinically relevant. Patients are considered to have clinical improvement if reporting a score 10-points or better than baseline at any time of QOL assessment. Conversely, patients are considered worsened if reporting a score minus 10-points or worse than baseline at any time of QOL assessment without any improvement. Patients whose scores are between 10-point changes from baseline at every QOL assessment will be considered as stable. In

contrast to functional scales, for the determination of patient's QOL response, classification of patients into improved and worsened categories is reversed for symptom scales. A Chi-square test will then be performed to compare the distributions of these three categories between two arms (**Table 67**).

8. Appendices

Appendix 1: Tables and Figure

Table 1: Patient Disposition

Data set: All Randomized Patients			
	Number of patients (%)		
	DURVA+TREME	BSC	Total
Randomized	N=***	N=***	N=***
Treated	*** (**)	*** (**)	*** (**)
On study	*** (**)	NAP(1)	NAP(1)
Off study(2)	*** (**)	NAP(1)	NAP(1)
Never Treated	*** (**)	*** (**)	*** (**)

(1) NAP: Not Applicable; (2) Off all study therapies.

Table 2: Follow-up of Patients

Data set: All Randomized Patients			
	Number of patients (%)		
	Durva+Treme	BSC	Total
Number of patients alive	*** (%)	*** (%)	*** (%)
Follow-up (months)			
median	**	**	**
Minimum-maximum	**-**	**-**	**-**

Table 3: Accrual by Center

Data set: All Randomized Patients			
	Number of patients (%)		
	DURVA+TREME N = ***	BSC N = ***	Total N = ***
Center #1	*** (**)	*** (**)	*** (**)
Center #2	*** (**)	*** (**)	*** (**)
Center #3	*** (**)	*** (**)	*** (**)
...	*** (**)	*** (**)	*** (**)

Table 4: Accrual by Stratification Factor at Randomization

Data set: All Randomized Patients			
	Number of patients (%)		
	DURVA+TREME N = ***	BSC N=***	Total N = ***
Performance Status			
ECOG 0	** (**)	** (**)	** (**)
ECOG 1	** (**)	** (**)	** (**)
Site of Tumour			
Right colon	** (**)	** (**)	** (**)
Transverse colon	** (**)	** (**)	** (**)
Left colon	** (**)	** (**)	** (**)
Rectum	** (**)	** (**)	** (**)
Unknown	** (**)	** (**)	** (**)

Source: Centralized Randomization File

Figure 1: Accrual by Calendar Time

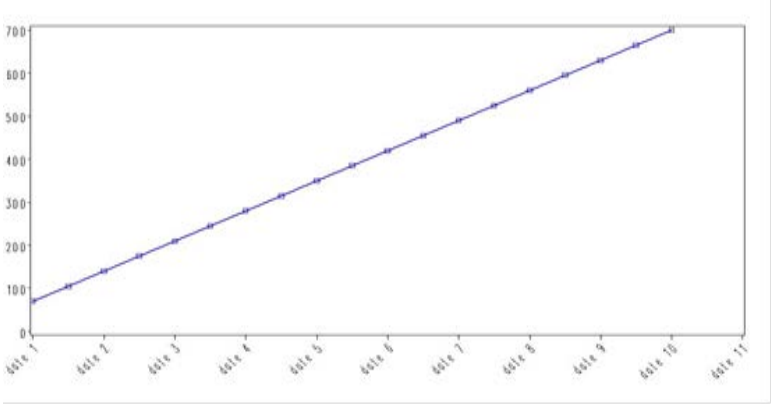

Table 5: Eligibility and Reasons for Ineligibility and Major Protocol Violations

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

Table 6: Treatment as Randomized Versus as Treated

Data set: All Randomized Patients			
	Number of Patients (%) Randomized Arm		
	DURVA+TREME N=***	BSC N=***	Total N=***
Treatment received			
Both durvalumab and tremelimumab	*** (**)	*** (**)	*** (**)
Durvalumab only			
Tremelimumab only			
BSC Only	*** (**)	*** (**)	*** (**)
Not treated	*** (**)	*** (**)	*** (**)

Table 7: Pretreatment Characteristics at Baseline

Data set: All Randomized Patients			
	Number of patients (%)		
	DURVA+TREME N=***	BSC N=***	Total N=***
Gender			
Female	** (**)	** (**)	** (**)
Male	** (**)	** (**)	** (**)
Race			
White	** (**)	** (**)	** (**)
Black or African American	** (**)	** (**)	** (**)
....	** (**)	** (**)	** (**)
Age (years)			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **
< 65	** (**)	** (**)	** (**)
≥ 65	** (**)	** (**)	** (**)
ECOG Performance Status			
0	** (**)	** (**)	** (**)
1	** (**)	** (**)	** (**)
BSA (m^2)			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **
Months from First Histological Diagnosis to Randomization			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **
Histology			
Adeno-carcinoma	**(**)	**(**)	** (**)
Squamous	**(**)	**(**)	**(**)
Other	**(**)	**(**)	**(**)
Site of tumour			
Right colon	** (**)	** (**)	** (**)
Transverse colon	** (**)	** (**)	** (**)
Left colon	** (**)	** (**)	** (**)
Rectum	** (**)	** (**)	** (**)
Unknown	** (**)	** (**)	** (**)
KRAS status			
Wildtype	** (**)	** (**)	** (**)
Mutated	** (**)	** (**)	** (**)
Unknown	** (**)	** (**)	** (**)
NRAS status			
Wildtype	** (**)	** (**)	** (**)
Mutated	** (**)	** (**)	** (**)
Unknown	** (**)	** (**)	** (**)

BRAF status			
Wildtype	** (**)	** (**)	** (**)
Mutated	** (**)	** (**)	** (**)
Unknown	** (**)	** (**)	** (**)
Microsatellite instability (MSI) status			
MSI high (MSI-H)	** (**)	** (**)	** (**)
MSI low (MSI-L)	** (**)	** (**)	** (**)
Microsatellite stable (MSS)	** (**)	** (**)	** (**)
Unknown	** (**)	** (**)	** (**)

Table 8: Prior Surgery

Data set: All Randomized Patients

	Number of Patients (%)		
	DURVA+TREME N=***	BSC N=***	Total N=***
Prior surgery			
No	*** (**)	*** (**)	*** (**)
Yes	*** (**)	*** (**)	*** (**)
Procedure / Site			
Procedure / Site 1	*** (**)	*** (**)	*** (**)
Procedure / Site 2	*** (**)	*** (**)	*** (**)
....	*** (**)	*** (**)	*** (**)

Table 9: Prior Radiotherapy

Data set: All Randomized Patients

	Number of patients (%)		
	DURVA+TREME N=***	BSC N=***	Total N=***
Any Prior Radiotherapy			
No	*** (**)	*** (**)	*** (**)
Yes	*** (**)	*** (**)	*** (**)
Type of Any Prior Radiotherapy			
Adjuvant	*** (**)	*** (**)	*** (**)
Palliative	*** (**)	*** (**)	*** (**)
Adjuvant + Palliative	*** (**)	***(**)	***(**)
Site of any prior radiotherapy[(1)]			
Site #1	*** (**)	*** (**)	*** (**)
Site #2	*** (**)	*** (**)	*** (**)
Site #3	*** (**)	***(**)	***(**)
...			
Total Dose of radiotherapy (cGy)	*** (**)	***(**)	***(**)

[(1)] Patient may have more than one site of radiotherapy

Table 10: Prior Systemic Therapy

Data set: All Randomized Patients			
	Number of patients (%)		
	DURVA+TREME N=***	BSC N=***	Total N=***
With at least one prior systemic therapy	*** (**)	*** (**)	*** (**)
Type of prior systemic therapy			
At least one adjuvant	*** (**)	*** (**)	*** (**)
At least one neo-adjuvant	*** (**)	*** (**)	*** (**)
At least one metastatic	*** (**)	*** (**)	*** (**)

Table 11: Specific Prior Chemotherapy

Data set: All Randomized Patients

	Number of patients (%)		
	Durva+Treme N=***	BSC N=***	Total N=***
Prior thymidylate synthase inhibitor			
Yes	*** (**)	*** (**)	*** (**)
No	*** (**)	*** (**)	*** (**)
Prior irinotecan containing regimen			
Yes and failed	*** (**)	*** (**)	*** (**)
Reason of failure			
Progression	*** (**)	*** (**)	*** (**)
Intolerance	*** (**)	*** (**)	*** (**)
Yes and relapsed within 6 months	*** (**)	*** (**)	*** (**)
No but with documented unsuitability	*** (**)	*** (**)	*** (**)
Reason unsuitable[(1)]			
Hypersensitivity	*** (**)	*** (**)	*** (**)
Abnormal glucuronidation of bilirubin	*** (**)	*** (**)	*** (**)
Gilbert's syndrome	*** (**)	*** (**)	*** (**)
Previous pelvic/abdominal irradiation	*** (**)	*** (**)	*** (**)
Other	*** (**)	*** (**)	*** (**)
No without documented unsuitability	*** (**)	*** (**)	*** (**)
Prior oxaliplatin containing regimen			
Yes and failed	*** (**)	*** (**)	*** (**)
Reason of failure			
Progression	*** (**)	*** (**)	*** (**)
Intolerance	*** (**)	*** (**)	*** (**)
Yes and relapsed within 6 months	*** (**)	*** (**)	*** (**)
No but with documented unsuitability	*** (**)	*** (**)	*** (**)
Reason unsuitable[(1)]			
Hypersensitivity	*** (**)	*** (**)	*** (**)
Pre-existing renal impairement	*** (**)	*** (**)	*** (**)
≥ grade 2 neurosensory neuropathy	*** (**)	*** (**)	*** (**)
Other	*** (**)	*** (**)	*** (**)
No without documented unsuitability	*** (**)	*** (**)	*** (**)
Prior cetuximab or panitumumab containing regimen			
Not applicable (not RAS wildtype)	*** (**)	*** (**)	*** (**)
Yes and failed	*** (**)	*** (**)	*** (**)
Reason of failure			
Progression	*** (**)	*** (**)	*** (**)
Intolerance	*** (**)	*** (**)	*** (**)
No but with documented unsuitability	*** (**)	*** (**)	*** (**)
Reason unsuitable[(1)]			
Hypersensitivity	*** (**)	*** (**)	*** (**)
Other	*** (**)	*** (**)	*** (**)
No for RAS wildtype patients without documented unsuitability	*** (**)	*** (**)	*** (**)

Prior VEGF targeting therapy			
Yes	*** (**)	*** (**)	*** (**)
No	*** (**)	*** (**)	*** (**)
Prior TAS-102 therapy			
Yes	*** (**)	*** (**)	*** (**)
No	*** (**)	*** (**)	*** (**)

(1) Patient may have more than one unsuitable reason

Table 12: Extent of Disease (Target Lesions)

Data set: All Randomized Patients			
	Number of Patients with Target Lesions (%)		
	DURVA+TREME N=***	BSC N=***	Total N=***
Presence of Target Lesions			
Patients with at least one target lesion	*** (**)	*** (**)	*** (**)
Number of Target Lesions			
1	*** (**)	*** (**)	*** (**)
2	*** (**)	*** (**)	*** (**)
3	*** (**)	*** (**)	*** (**)
4	*** (**)	*** (**)	*** (**)
5	*** (**)	*** (**)	*** (**)
Largest Target Lesion in cm			
< 2	*** (**)	*** (**)	*** (**)
2-5	*** (**)	*** (**)	*** (**)
> 5-10	*** (**)	*** (**)	*** (**)
> 10	*** (**)	*** (**)	*** (**)
Site of Target Lesion[(1)]			
Abdomen	*** (**)	*** (**)	*** (**)
Adrenals	*** (**)	*** (**)	*** (**)
Bone	*** (**)	*** (**)	*** (**)
Brain	*** (**)	*** (**)	*** (**)
Liver	*** (**)	*** (**)	*** (**)
Lung	*** (**)	*** (**)	*** (**)
Nodes	*** (**)	*** (**)	*** (**)
Pleura	*** (**)	*** (**)	*** (**)
Skin	*** (**)	*** (**)	*** (**)
Subcutaneous Tissue	*** (**)	*** (**)	*** (**)
....	*** (**)	*** (**)	*** (**)

[(1)] Patients may have target lesions at more than one site

Table 13: Extent of Disease (Non-Target Lesions)

Data set: All Randomized Patients			
	Number of Patients (%)		
	DURVA+TREME N=***	BSC N=***	Total N=***
Patients with no-target lesion	*** (**)	*** (**)	*** (**)
Site of non-target lesion[(1)]			
Abdomen	*** (**)	*** (**)	*** (**)
Adrenals	*** (**)	*** (**)	*** (**)
Bone	*** (**)	*** (**)	*** (**)
Brain	*** (**)	*** (**)	*** (**)
Liver	*** (**)	*** (**)	*** (**)
Lung	*** (**)	*** (**)	*** (**)
Nodes	*** (**)	*** (**)	*** (**)
Pleura	*** (**)	*** (**)	*** (**)
Skin	*** (**)	*** (**)	*** (**)
Subcutaneous Tissue	*** (**)	*** (**)	*** (**)
Other	*** (**)	*** (**)	*** (**)
Number of non-target lesions			
1	*** (**)	*** (**)	*** (**)
2	*** (**)	*** (**)	*** (**)
3	*** (**)	*** (**)	*** (**)
4	*** (**)	*** (**)	*** (**)
≥5	*** (**)	*** (**)	*** (**)

[(1)] Patients may have non-target lesions at more than one site

Table 14: Baseline Signs and Symptoms

Data set: All Randomized Patients (DURVA+TREME 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 BSC Arm

Table 15: Baseline Hematology

Data set: All Randomized Patients			
	Number of Patients (%)		
	DURVA+TREME N = ***	BSC N = ***	Total N=***
Hemoglobin			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Platelets			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
WBC			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Neutrophils			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Lymphocytes			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
RBC			
Normal	** (**)	** (**)	** (**)
High [2]	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Monocytes			
Normal	** (**)	** (**)	** (**)
High [2]	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Eosinophils			
Normal	** (**)	** (**)	** (**)
High [2]	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Basophils			
Normal	** (**)	** (**)	** (**)
High [2]	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)

[1] Not done or outside the 14-day window prior to start of therapy
[2] High than upper lower limit

Table 16: Baseline Chemistry

Data set: All Randomized Patients			
	Number of Patients (%)		
	DURVA+TREME N = ***	BSC N = ***	Total N=***
Total bilirubin			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Alkaline phosphatase			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
ALT			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
AST			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
LDH			
Normal	** (**)	** (**)	** (**)
High(2)	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Serum Creatinine			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Hypernatremia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Hyponatremia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Hyperkalemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)

Not reported [1]	** (**)	** (**)	** (**)
Hypokalemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Hypercalcemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Hypocalcemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Hypermagnesemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Hypomagnesemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Hyperglycemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Hypoglycemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Hyperalbuminemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)

Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Hypoalbuminemia			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Chloride			
Normal	** (**)	** (**)	** (**)
High [2]	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Amylase			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
CEA			
Normal	** (**)	** (**)	** (**)
High [2]	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Lipase			
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
[2] High than upper lower limit

Table 17: Baseline Thyroid Function Tests

Data set: All Randomized Patients			
	Number of Patients (%)		
	DURVA+TREME N = ***	BSC N = ***	Total N = ***
TSH			
Normal	** (**)	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)	** (**)
<0.1xLLN	** (**)	** (**)	** (**)
T3 Free			
Normal	** (**)	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)	** (**)
<0.1xLLN	** (**)	** (**)	** (**)
T3 Total			
Normal	** (**)	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)	** (**)
<0.1xLLN	** (**)	** (**)	** (**)
T4 Free			
Normal	** (**)	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)	** (**)
<0.1xLLN	** (**)	** (**)	** (**)
T4 Total			
Normal	** (**)	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)	** (**)
<0.1xLLN	** (**)	** (**)	** (**)

Table 18: Baseline Coagulation Tests

Data set: All Randomized Patients			
	Number of Patients (%)		
	DURVA+TREME N = ***	BSC N = ***	Total N = ***
PT			
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
INR			
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
PTT			
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)

Table 19: Baseline ECG

Data set: All Randomized Patients			
	Number of patients (%)		
	DURVA+TREME N=***	BSC N=***	Total N=***
Baseline ECG: Results			
Normal	*** (**)	*** (**)	*** (**)
Abnormal	*** (**)	*** (**)	*** (**)
ECG not performed	*** (**)	*** (**)	*** (**)

Table 20 : Baseline Urinalysis

Data set: All Randomized Patients			
	Number of patients (%)		
	DURVA+TREME N=***	BSC N=***	Total N=***
Urinalysis – SPOT Test			
Negative/trace	**(**)	**(**)	**(**)
1+(>20 mg/dL–30 mg/dL)	**(**)	**(**)	**(**)
2+(>30 mg/dL–100 mg/dL)	**(**)	**(**)	**(**)
3+(>100 mg/dL– 300 mg/dL)	**(**)	**(**)	**(**)
4+(>300 mg/dL)	**(**)	**(**)	**(**)
Urinalysis – 24-Hour Test (g/day)			
Grade			
1	**(**)	**(**)	**(**)
2	**(**)	**(**)	**(**)
3	**(**)	**(**)	**(**)

Table 21: Concomitant Medications at Baseline

Data set: All Randomized Patients			
	Number of patients (%)		
	DURVA+TREME N=***	BSC N=***	Total N=***
Any concomitant medication [(1)]			
No	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)

[(1)]Any medication taken within 14 days prior to randomization.

Table 22: Major Medical Problems at Baseline

Data set: All Randomized Patients			
	Number of patients (%)		
	DURVA+TREME N = ***	BSC N = ***	Total N=***
Patients with at least one past or current major medical problem	** (**)	** (**)	** (**)
Medical Problem[(1)]			
(from highest to lowest in frequency)			
Diabetes	** (**)	** (**)	** (**)
...			

(1) patients may report more than one medical problem reported

Table 23: Number of Patients on DURVA+TREME Arm by Cycle

Data Set: All Treated Patients on DURVA+TREME Arm		
		Number of Patients (%)
		DURVA+TREME Arm
Cycle	1	** (**)
	2	** (**)
	3	** (**)
	...	

Table 24: Number of Cycles of Protocol Therapy per Patient on DURVA+TREME Arm

Data Set: All Treated Patients on DURVA+TREME Arm	
	DURVA+TREME Arm
Number of Cycles:	
N	***
Median	*
Min – Max	* - *

Table 25: Total Treatment Duration of Durvalumab and Tremelimumab

Data Set: All Treated Patients on DURVA+TREME Arm		
	Durvalumab	Tremelimumab
Duration in weeks:		
N	***	***
Median	*	*
Min – Max	* - *	* - *

Table 26: Compliance with Durvalumab and Tremelimumab Administration

Data Set: All Treated Patients on DURVA+TREME Arm	
	DURVA+TREME Arm
All Durvalumab Administrations According to Protocol	
Yes	** (**)
No	** (**)
All Tremelimumab Administrations According to Protocol	
Yes	** (**)
No	** (**)

Table 27: Dose Reduction, Omission or Delay and IV Rate Decrease and Infusion Interruption for Durvalumab and Tremelimumab

Data Set: All Treated Patients on DURVA+TREME Arm

	Number of patients (%)	
	Durvalumab (N=***)	Tremelimumab (N=***)
At least one dose reduction	** (**)	** (**)
Reason for dose reduction:		
<*reason 1*>	** (**)	** (**)
<*reason 2*>	** (**)	** (**)
...	** (**)	** (**)
At least one dose omission	** (**)	** (**)
Reason for dose omission:		
<*reason 1*>	** (**)	** (**)
<*reason 2*>	** (**)	** (**)
...	** (**)	** (**)
At least one dose delay	** (**)	** (**)
Reason for delay:		
<*reason 1*>	** (**)	** (**)
<*reason 2*>	** (**)	** (**)
...	** (**)	** (**)
IV rate decrease and infusion interruption	** (**)	** (**)
Reason for decrease and interruption:		
<*reason 1*>	** (**)	** (**)
<*reason 2*>	** (**)	** (**)
...	** (**)	** (**)

Table 28: Cumulative Dose of Durvalumab and Tremelimumab

Data Set: All Treated Patients on DURVA+TREME Arm		
	Durvalumab	Tremelimumab
Cumulative dose per patient		
N	***	***
Mean (STD)	** (**)	** (**)
Median	**	**
Min-Max	** - **	** - **

Table 29: Dose Intensity of Durvalumab and Tremelimumab

Data Set: All Treated Patients on DURVA+TREME Arm		
	Durvalumab	Tremelimumab
Dose intensity per patient		
N	***	***
Mean (STD)	** (**)	** (**)
Median	**	**
Min-Max	** - **	** - **

Table 30: Relative Dose Intensity of Durvalumab and Tremelimumab

Data Set: All Treated Patients on DURVA+TREME Arm		
	Durvalumab	Tremelimumab
Relative Dose intensity		
≥ 90% planned intensity	** (**)	** (**)
≥ 80% - < 90% planned intensity	** (**)	** (**)
≥ 60% - < 80% planned intensity	** (**)	** (**)
< 60% planned intensity	** (**)	** (**)

Table 31: **Off Durvalumab and Tremelimumab Treatment Summary**

Data set: All Treated Patients on DURVA+TREME Arm		
	Number of patients (%)	
	Durvalumab N=***	Tremelimumab N=***
Patients off Treatment	N = ** (**)	N = ** (**)
Reason off protocol therapy		
Treatment Completed	**	**
Progressive Disease (objective)	**	**
Symptomatic Progression	**	**
Intercurrent Illness – adverse events unrelated to treatment	**	**
Adverse events related to protocol therapy	**	**
Patient Refusal (not related to adverse event)	**	**
Death	**	**
Other Reason	**	**

Table 32: All Deaths

Data set: All Randomized Patients		
	Number of Patients (%)	
	DURVA+TREME N=***	BSC N=***
Number of Patients who died	** (**)	** (**)
Cause of Death		
Colorectal cancer only	**	**
Toxicity from protocol treatment	**	**
Colorectal cancer + Toxicity from protocol treatment complication	**	**
Non-protocol Treatment Complication	**	**
Colorectal cancer + Non-protocol Treatment Complication	**	**
Other Primary Malignancy	**	**
Other Condition or Circumstance	**	**

Figure 2: Kaplan-Meier Curves for Overall Survival

Table 33: Log Rank and Cox Regression Model for Overall Survival

Data set: All Randomized Patients						
	N	Univariate Analysis[1]			Multivariate Analysis[2]	
Treatment Arm/ Prognostic Factors at Baseline		Median Survival (Months)	Hazard Ratio[4] (90% CI)	Log-rank p-value	Hazard Ratio[4] (90% C.I.)	P-value from Cox regre-ssion
Treatment arm				0.***		0.***
DURVA+TREME	***	**.**	**.**		**.**	
BSC	***	**.**	(**.**,**.**)		(**.**,**.**)	
Gender				0.***		0.***
Male	***	**.**	NC [3]		**.**	
Female	***	**.**			(**.**,**.**)	
Age				0.***		0.***
<65	***	**.**	NC		**.**	
≥65	***	**.**			(**.**,**.**)	
Number of organ sites				0.***		0.***
≤ 2	***	**.**	NC		**.**	
>2	***	**.**			(**.**,**.**)	
Presence of liver metastases				0.***		0.***
Yes	***	**.**	NC		**.**	
No	***	**.**			(**.**,**.**)	

(1) Stratified; (2) Stratified Cox regression with all factors included; (3) NC = not computed
(4) Hazard ratio of first category over second category

Table 34: Survival by Subsets

Data set: All Randomized Patients

Factors	Value	DURVA+TREME N	DURVA+TREME Median Survival 90% C.I.	BSC N	BSC Median Survival 90% C.I.	Hazard Ratio[(1)] 90% C.I.
Performance Status at baseline	ECOG 0	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	ECOG 1	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Age	<65	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	≥65	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Gender	Female	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Male	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Race	White	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Black	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Other	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Site of tumour	Right colon	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Transverse colon	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Left colon	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Rectum	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
KRAS Status	Wildtype	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Mutated	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
NRAS Status	Wildtype	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Mutated	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
BRAF Status	Wildtype	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Mutated	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
MSI status	MSI-H	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	MSI-L	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	MSS	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)

(1) DURVA+TREME over BSC hazard ratio (Unstratified)

Table 35: Progression Summary

Data set: All Randomized Patients

	Number of Patients (%)	
	DURVA+TREME N=***	BSC N=***
Patients who progressed	*** (**)	*** (**)
Progression on Durva+Treme	**	NAP(1)
Progression off Durva+Treme	**	NAP(1)
Death (without documented progression)	**	**
Patients who were censored	*** (**)	*** (**)
Reason Censored		
Lost to follow-up	**	**
Not progressed	**	**

(1) NAP: not applicable

Figure 3: Kaplan-Meier Curves for Progression Free Survival

Table 36: Log Rank and Cox Regression Model for Progression Free Survival (PFS)

Data set: All Randomized Patients						
	N	Univariate Analysis[1]			Multivariate Analysis[2]	
Treatment Arm/ Prognostic Factors at Baseline		Median PFS (Months)	Hazard Ratio[4] (90% CI)	Log-rank p-value	Hazard Ratio[4] (90% C.I.)	P-value from Cox regre-ssion
Treatment arm				0.***		0.***
DURVA+TREME	***	**.**	**.**		**.**	
BSC	***	**.**	(**.**,**.**)		(**.**,**.**)	
Gender				0.***		0.***
Male	***	**.**	NC [3]		**.**	
Female	***	**.**			(**.**,**.**)	
Age				0.***		0.***
<65	***	**.**	NC		**.**	
≥65	***	**.**			(**.**,**.**)	
Number of organ sites				0.***		0.***
≤ 2	***	**.**	NC		**.**	
>2	***	**.**			(**.**,**.**)	
Presence of liver metastases				0.***		0.***
Yes	***	**.**	NC		**.**	
No	***	**.**			(**.**,**.**)	

(1) Stratified; (2) Stratified Cox regression with all factors included; (3) NC = not computed
(4) Hazard ratio of first category over second category

Note: Same table will be made for sensitivity analyses which (1) censor the patients who have received other anti-cancer treatments prior to documentation of disease relapse/progression or death at the earliest time when these treatments began or (2) treat them as having PFS events at the earliest time when these treatments began.

Table 37: Progression Free Survival (PFS) by Subsets

Data set: All Randomized Patients						
		DURVA+TREME		BSC		
Factors	Value	N	Median PFS 90% C.I.	N	Median PFS 90% C.I.	Hazard Ratio[(1)] 90% C.I.
Performance Status at baseline	ECOG 0	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	ECOG 1	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Age	<65	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	≥65	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Gender	Female	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Male	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Race	White	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Black	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Other	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Site of tumour	Right colon	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Transverse colon	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Left colon	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Rectum	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
KRAS Status	Wildtype	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Mutated	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
NRAS Status	Wildtype	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Mutated	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
BRAF Status	Wildtype	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	Mutated	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
MSI status	MSI-H	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	MSI-L	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	MSS	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)

(1) DURVA+TREME over BSC hazard ratio (Unstratified)

Table 38: Treatment Response

Data set: All Randomized Patients

	Number of Patients (%)[a] N=***	
	DURVA+TREME N=***	BSC N=***
Patients with at least one target lesion	N=***	N=***
Response-evaluable	N=***	N=***
Complete response (CR)	** (**)	** (**)
Partial response (PR)	** (**)	** (**)
Stable disease (SD)	** (**)	** (**)
Progressive disease (PD)	** (**)	** (**)
Inevaluable for response (IN)	** (**)	** (**)
<Reason 1>	**	**
<Reason 2>	**	**
....	...	....
Not response evaluable	N=***	N=***
Never treated	**	**
Not assessed (NA)	**	**
Patients with no target lesions	N=***	N=***
Progressive disease (PD)	**	**
Inevaluable for response (IN)	**	**
<Reason 1>	**	**
<Reason 2>	**	**
....	...	....
Not assessed (NA)	**	**
Never treated	**	**

[a] percentages are calculated out of the number of randomized patients

Table 39: Cochran Mantel Haenszel and Logistic Regression Model for Response

Data set: All Randomized Patients				
	Univariate Analysis [1]		Multivariate Analysis [2]	
Treatment/ Prognostic Factors	Odds Ratio [4] (90%CI)	CMH p-value	Odds Ratio [4] (90% C.I.)	p-value from logistic regression
Treatment arm		0.***		0.***
DURVA+TREME: BSC	**.** (**.**,**.**)		**.** (**.**,**.**)	
Gender		0.***		0.***
Male: Female	NC [3]		**.** (**.**,**.**)	
Age		0.***		0.***
<65: ≥65	NC		**.** (**.**,**.**)	
Number of organ sites		0.***		0.***
≤2: >2	NC		**.** (**.**,**.**)	
Number of previous chemo drug classes		0.***		0.***
≤2: >2	NC		**.** (**.**,**.**)	
Presence of liver metastases		0.***		0.***
No: Yes	NC		**.** (**.**,**.**)	

(1) Stratified
(2) Stratified Logistic regression, all factors included
(3) NC = not computed
(4) Odds ratio of first category over second category

Table 40: Response According to Pretreatment Characteristics

Data set: All Randomized Patients		
	Number of Responses/Number of Patients (%)	
	DURVA+TREME N=***	BSC N=***
Gender		
Male	**/** (**)	**/** (**)
Female	**/** (**)	**/** (**)
Age		
< 65 years	**/** (**)	**/** (**)
≥ 65 years	**/** (**)	**/** (**)
Race		
White	**/** (**)	**/** (**)
Black	**/** (**)	**/** (**)
Other	**/** (**)	**/** (**)
Baseline performance status		
ECOG 0-1	**/** (**)	**/** (**)
ECOG 2	**/** (**)	**/** (**)
Site of Tumour		
Right colon	**/** (**)	**/** (**)
Transverse colon	**/** (**)	**/** (**)
Left colon	**/** (**)	**/** (**)
Rectum	**/** (**)	**/** (**)
KRAS status		
Wildtype	**/** (**)	**/** (**)
Mutated	**/** (**)	**/** (**)
NRAS status		
Wildtype	**/** (**)	**/** (**)
Mutated	**/** (**)	**/** (**)
BRAF status		
Wildtype	**/** (**)	**/** (**)
Mutated	**/** (**)	**/** (**)
MSI status		
MSI-H	**/** (**)	**/** (**)
MSI-L	**/** (**)	**/** (**)
MSS	**/** (**)	**/** (**)

Table 41: Duration of Response

Data set: All Randomized Patients with CR or PR			
	DURVA+TREME N=***	BSC N=***	P-value(1)
Median Duration of Response (months) (90% CI)	*** (**-**)	*** (**-**)	.**

(1) Stratified

Table 42: Adverse Events on Durvalumab and Tremelimumab Treatment

Data set: All Treated Patients on DURVA+TREME Arm

	Number of patients (%) N=***						
	Worst grade						Any grade
	NR	1	2	3	4	5	
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.

Table 43: Severe Adverse Events on Durvalumab and Tremelimumab Treatment

Data set: All Treated Patients on DURVA+TREME Arm

	Number of patients (%) N=***			
	Worst grade			Any grade 3 or higher AE
	3	4	5	
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.

Table 44: Drug Related Adverse Events during Durvalumab and Tremelimumab Treatment

(1) Related to Durvalumab

Data set: All Treated Patients on DURVA+TREME Arm						
	Number of patients (%) N=***					
	Worst grade					Any grade
	1	2	3	4	5	
	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE related to durvalumab within category						
Category 1[(a)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(a)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)

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

(2) Related to Tremelimumab

Data set: All Treated Patients on DURVA+TREME Arm						
	Number of patients (%) N=***					
	Worst grade					Any grade
	1	2	3	4	5	
	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE related to Tremelimumab within category						
Category 1[(a)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(a)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)

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

(3) Related to Durvalumab or Tremelimumab

Data set: All Treated Patients on DURVA+TREME Arm						
	Number of patients (%) N=***					
	Worst grade					Any grade
	1	2	3	4	5	
	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE related to Tremelimumab within category						
Category 1[(a)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(a)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)

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

(4) Related to Both Durvalumab and Tremelimumab

Data set: All Treated Patients on DURVA+TREME Arm						
	Number of patients (%) N=***					
	Worst grade					Any grade
	1	2	3	4	5	
	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE related to Tremelimumab within category						
Category 1[(a)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(a)]						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)

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

Table 45: Overall Adverse Events

Data set: All Treated Patients on DURVA+TREME Arm

	Number of patients (%) N=***					
	Worst grade					Any grade
	1	2	3	4	5	
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: The same type of table will be made for BSC arm.

Table 46: Severe Overall Adverse Events

Data set: All Treated Patients						
	Number of patients (%)					
	DURVA+TREME N=***			BSC N=***		
	Worse Grade					
	Grade 3	Grade 4	Grade 5	Grade 3	Grade 4	Grade 5
Patients with any serve AE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with serve 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.

Table 47: Hematology during Durvalumab and Tremelimumab Treatment

Data set: All Treated Patients on DURVA+TREME Arm	
	Number of Patients (%)
	DURVA+TREME N = ***
Hemoglobin	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Platelet	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
WBC	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Neutrophils	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
RBC	
Normal	** (**)
High [(1)]	** (**)
Lymphocytes	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Monocytes	
Normal	** (**)
High [(1)]	** (**)
Eosinophils	
Normal	** (**)
High [(1)]	** (**)
Basophils	
Normal	** (**)
High [(1)]	** (**)

[(1)] Greater than upper normal limit

Table 48: Overall Hematology: Worst Grade per Patient

Data set: All Treated Patients		
	Number of Patients (%)	
	DURVA+TREME N = ***	BSC N = ***
Hemoglobin		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Platelet		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
WBC		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Neutrophils		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
RBC		
Normal	** (**)	** (**)
High [(1)]	** (**)	** (**)
Lymphocytes		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Monocytes		
Normal	** (**)	** (**)
High [(1)]	** (**)	** (**)
Eosinophils		
Normal	** (**)	** (**)
High [(1)]	** (**)	** (**)
Basophils		
Normal	** (**)	** (**)
High [(1)]	** (**)	** (**)

[(1)] Greater than upper normal limit

Table 49: Serum Chemistry during Durvalumab and Tremelimumab Treatment: Worst Grade per Patient

Data set: All Treated Patients on DURVA+TREME Arm	
	Number of Patients (%)
	DURVA+TREME N = ***
Total bilirubin	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Alkaline phosphatase	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
ALT	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
AST	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
LDH	
Normal	** (**)
High [(1)]	** (**)
Serum Creatinine	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Hypernatremia	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	
Hyponatremia	** (**)
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Hyperkalemia	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Hypokalemia	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)

Grade 4	** (**)
Hypercalcemia	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Hypocalcemia	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Hypermagnesemia	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Hypomagnesemia	** (**)
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	
Hyperalbuminemia	** (**)
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Hypoalbuminemia	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Chloride	
Normal	** (**)
High [(1)]	** (**)
ALP	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Amylase	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
Lipase	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
CEA	
Normal	** (**)
High [(1)]	** (**)

[(1)] Greater than upper normal limit

Table 50: Overall Serum Chemistry: Worst Grade per Patient

Data set: All Treated Patients		
	Number of Patients (%)	
	DURVA+TREME N = ***	BSC N = ***
Total bilirubin		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Alkaline phosphatase		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
ALT		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
AST		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
LDH		
Normal	** (**)	** (**)
High [(1)]	** (**)	** (**)
Serum Creatinine		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hypernatremia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hyponatremia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hyperkalemia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hypokalemia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)

Hypercalcemia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hypocalcemia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hypermagnesemia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hypomagnesemia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hyperalbuminemia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Hypoalbuminemia		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Chloride		
Normal	** (**)	** (**)
High [(1)]	** (**)	** (**)
Amylase		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Lipase		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
CEA		
Normal	** (**)	** (**)
High [(1)]	** (**)	** (**)

[(1)] Greater than upper normal limit

Table 51: Thyroid Function Tests: Worst during Durvalumab and Tremelimumab Treatment

Data set: All Treated Patients on DURVA+TREME Arm	
	Number of Patients (%)
	DURVA+TREME N = ***
TSH	
Normal	** (**)
<1-0.5xLLN	** (**)
<0.5-0.1xLLN	** (**)
<0.1xLLN	
T3 Free	** (**)
Normal	** (**)
<1-0.5xLLN	** (**)
<0.5-0.1xLLN	** (**)
<0.1xLLN	** (**)
T3 Total	
Normal	** (**)
<1-0.5xLLN	** (**)
<0.5-0.1xLLN	** (**)
<0.1xLLN	** (**)
T4 Free	
Normal	** (**)
<1-0.5xLLN	** (**)
<0.5-0.1xLLN	** (**)
<0.1xLLN	** (**)
T4 Total	
Normal	** (**)
<1-0.5xLLN	** (**)
<0.5-0.1xLLN	** (**)
<0.1xLLN	** (**)

Table 52: Thyroid Function Tests: Worst during Study

Data set: All Treated Patients		
	Number of Patients (%)	
	DURVA+TREME N = ***	BSC N = ***
TSH		
Normal	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)
<0.1xLLN	** (**)	** (**)
T3 Free		
Normal	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)
<0.1xLLN	** (**)	** (**)
T3 Total		
Normal	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)

<0.1xLLN	** (**)	** (**)
T4 Free		
Normal	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)
<0.1xLLN	** (**)	** (**)
T4 Total		
Normal	** (**)	** (**)
<1-0.5xLLN	** (**)	** (**)
<0.5-0.1xLLN	** (**)	** (**)
<0.1xLLN	** (**)	** (**)

Table 53: Coagulation Tests: Worst during Durvalumab and Tremelimumab Treatment

Data set: All Treated Patients on DURVA+TREME	
	Number of Patients (%)
	DURVA+TREME N = ***
PT	
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)
INR	** (**)
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	
PTT	** (**)
Grade 1	** (**)
Grade 2	** (**)
Grade 3	** (**)
Grade 4	** (**)

Table 54: Coagulation Tests: Worst during Study

Data set: All Treated Patients		
	Number of Patients (%)	
	DURVA+TREME N = ***	BSC N = ***
PT		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
INR		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
PTT		
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)

Table 55: ECG Results

Data set: All Treated Patients		
	Number of patients (%)	
	DURVA+TREME N=***	BSC N=***
ECG reported	*** (**)	*** (**)
All Normal	**	**
At least one abnormal but none clinically important	**	**
At least one abnormal and clinically important		
ECG not reported/not performed	*** (**)	*** (**)

Table 56 : Urinalysis

Data set: All Treated Patients		
	Number of patients (%)	
	ARM A N = **	ARM B N = **
Urinalysis – SPOT Test		
Negative/trace	**(**)	**(**)
1+(>20 mg/dL–30 mg/dL)	**(**)	**(**)
2+(>30 mg/dL–100 mg/dL)	**(**)	**(**)
3+(>100 mg/dL– 300 mg/dL)	**(**)	**(**)
4+(>300 mg/dL)	**(**)	**(**)
Urinalysis – 24-Hour Test (g/day)		
Grade		
1	**(**)	**(**)
2	**(**)	**(**)
3	**(**)	**(**)

Table 57: Deaths During Durvalumab and Tremelimumab Treatment or within 4 weeks of Last Durvalumab and Tremelimumab Treatment

Data set: All Treated Patients on DURVA+TREME Arm	
	Number of Patients (%)
	DURVA+TREME N=***
Number of Patients who died during or within 4 weeks of last Durvalumab and Tremelimumab treatment	** (**)
Cause of Death	
Colorectal cancer	**
Toxicity from protocol treatment	**
Colorectal cancer + Toxicity from protocol treatment complication	**
Non-protocol Treatment Complication	**
Colorectal cancer + Non-protocol Treatment Complication	**
Other Primary Malignancy	**
Other Condition or Circumstance	**

Table 58: Adverse Event leading to Discontinuation of Durvalumab or Tremelimumab[(a)]

Data set: All Treated Patients on DURVA+TREME Arm	
	Number of patients (%)
	DURVA+TREME N=***
Number discontinued durvalumab from adverse events	** (**)
<Adverse event 1>	
<Adverse event 2>	**
....	**
Number discontinued Tremelimunab from adverse events	** (**)
<Adverse event 1>	
<Adverse event 2>	**
....	**

(a) From End of Treatment Form with off reasons= ="Adverse events related to protocol therapy".

Table 59: Concomitant Medications

Data set: All Treated Patients		
	Number of patients (%)	
	DURVA+TREME N = ***	BSC N=***
Any concomitant medication during or 4 weeks after Durvalumab and Tremelimumab Treatment for patients on DURVA+TREME and before objective progression on BSC		
No	** (**)	** (**)
Yes	** (**)	** (**)
Type of concomitant medications[(1)]		
Medication A	** (**)	** (**)
…		

(1): patients may have received more than one concomitant medication.

Table 60: Anti-Cancer Treatment

	Number of patients (%)	
	DURVA+TREME N=***	BSC N =***
Number of patients with any anti-cancer treatment during or 4 weeks after Durvalumab and Tremelimumab Treatment	*** (**)	NAP (NAP)
Chemotherapy [(1)]	*** (**)	NAP (NAP)
Drug 1 …	*** (**)	NAP (NAP)
Radiotherapy [(1)]	*** (**)	NAP (NAP)
Hormonal therapy [(1)]	*** (**)	NAP (NAP)
Drug 1 …	*** (**)	NAP (NAP)
Immunotherapy [(1)]	*** (**)	NAP (NAP)
Drug 1 …	*** (**)	NAP (NAP)
Other [(1)]	*** (**)	NAP (NAP)
Drug 1 …	*** (**)	NAP (NAP)
Number of patients with any anti-cancer treatment before progression	*** (**)	*** (**)
Chemotherapy [(1)]	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)
Radiotherapy [(1)]	*** (**)	*** (**)
Hormonal therapy [(1)]	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)
Immunotherapy [(1)]	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)
Other [(1)]	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)
Number of patients with any anti-cancer treatment after progression	*** (**)	*** (**)
Chemotherapy [(1)]	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)
Radiotherapy [(1)]	*** (**)	*** (**)
Hormonal therapy [(1)]	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)
Immunotherapy [(1)]	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)
Other [(1)]	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)

(1) Patients could have more than one type of anti-cancer treatment. NA=Not applicable.

Table 61: Major Medical Problems

Data set: All Treated Patients		
	Number of patients (%)	
	DURVA+TREME N = ***	BSC N=***
Any major medical problem during or 4 weeks after Durvalumab and Tremelimumab Treatment for patients on DURVA+TREME and before objective progression on BSC		
No	** (**)	** (**)
Yes	** (**)	** (**)
Type of major medical problems(1)		
Medication A	** (**)	** (**)
…		

(1): patients may have more than one major medical problem.

Table 62: Compliance Rate with QoL Assessment by Treatment Arm

	DURVA+TREME		BSC	
	Expected	Received (%)	Expected	Received (%)
Baseline	***	** (**)	***	** (**)
4 weeks	***	** (**)	***	** (**)
8 weeks	***	** (**)	***	** (**)
12 weeks	***	** (**)	***	** (**)
16 weeks	***	** (**)	***	** (**)
24 weeks	***	** (**)	***	** (**)

Table 63: Proportion of Patients with Deterioration, Improvement or Stable QoL

	N	DURVA+TREME N (%)	BSC N (%)	P value*
Deterioration				
Physical function				0.***
Week 8	***	*** (**.**)	*** (**.**)	
Week 16	***	*** (**.**)	*** (**.**)	
Global health status				0.***
Week 8	***	*** (**.**)	*** (**.**)	
Week 16	***	*** (**.**)	*** (**.**)	
Improvement				
Physical function				0.***
Week 8	***	*** (**.**)	*** (**.**)	
Week 16	***	*** (**.**)	*** (**.**)	
Global health status				0.***
Week 8	***	*** (**.**)	*** (**.**)	
Week 16	***	*** (**.**)	*** (**.**)	
Stable				
Physical function				0.***
Week 8	***	*** (**.**)	*** (**.**)	
Week 16	***	*** (**.**)	*** (**.**)	
Global health status				0.***
Week 8	***	*** (**.**)	*** (**.**)	
Week 16	***	*** (**.**)	*** (**.**)	

* Fisher's exact test

Table 64: Time to Deterioration in QoL Primary Endpoints

Data set: All patients who had baseline and at least one follow-up QoL assessment				
	DURVA+TREME		BSC	
	N	Median (months) (90% CI)	N	Median (months) (90% CI)
Physical function	***	**.** (**.**, **.**)	***	**.** (**.**, **.**)
Global Health Scale	***	**.** (**.**, **.**)	***	**.** (**.**, **.**)

Table 65: QoL: Summary Baseline Scores

	DURVA+TREME	BSC	P value*
Functional scales			
Physical			0.***
N	***	***	
Mean	***	***	
STD	***	***	
...	...	...	
Global health status			0.***
N	***	***	
Mean	***	***	
STD	***	***	
Symptom scales			
Fatigue			0.***
N	***	***	
Mean	***	***	
STD	***	***	
…	…	…	

* Wilcoxon rank sum test

Table 66: Summary QOL Change Scores from Baseline for Scale/Domain/Item at Each Time Period*

	DURVA+TREME	BSC	P Value**
Scale/Domain/Item			
Week 4			.**
N	***	***	
Mean	***	***	
STD	***	***	
Week 8			.**
N			
Mean	***	***	
STD	***	***	
Week 12			.**
N			
Mean	***	***	
STD	***	***	
Week 16			.**
N			
Mean	***	***	
STD	***	***	
Week 24			.**
N			
Mean	***	***	
STD	***	***	

* Table will be provided for each scale/domain/item.

** Wilcoxon rank sum test

Table 67: Results for QOL Response Analyses

Domain	DURVA+TREME			BSC			P-value*
	Improved	Stable	Worsened	Improved	Stable	Worsened	
	N (%)			N (%)			
EORTC QLQ-C30							
Physical	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Role	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Emotional	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Cognitive	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Social	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Global	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Pain	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Fatigue	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Nausea	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Dyspnea	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Sleep	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Appetite	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Constipation	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Diarrhea	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**
Financial	***(**)	***(**)	***(**)	***(**)	***(**)	***(**)	.**

* Chi-square test