STATISTICAL ANALYSIS PLAN

A RANDOMIZED PHASE II TRIAL OF GEMCITABINE AND NAB-PACLITAXEL VS. GEMCITABINE, NAB-PACLITAXEL, DURVALUMAB AND TREMELIMUMAB AS 1ST LINE THERAPY IN METASTATIC PANCREATIC ADENOCARCINOMA

Protocol CCTG PA.7

Prepared by:	Signature	Date
CCTG/Queen's Statistician	_____ Dongsheng Tu	_____

Reviewed by:	Signature	Date
CCTG/Queen's Senior Investigator	_____ Chris O'Callaghan	_____

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ABBREVIATIONS

AE	Adverse Event
ALP	Alkaline phosphatase
ALT	Alanine Aminotransferase
AST	Serum Glutamic Oxaloacetic Transaminase
BSA	Body Surface Area
BUN	Blood urea nitrogen
CCTG	Canadian Cancer Trials Group
C. I.	Confidence Interval
CMH	Cochran-Mantel-Haenszel
CR	Complete Response
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
CTLA-4	Cytotoxic T-lymphocyte-associated protein 4
DSMC	Data and Safety Monitoring Committee
ECOG	Eastern Cooperative Cancer Group
ECG	Electrocardiography
EORTC	European Organization for Research and Treatment of Cancer
G+N	Gemcitabine and nab-paclitaxel
G+N+D+T	Gemcitabine and nab-paclitaxel with durvalumab and tremelimumab
iCPD	Immune confirmed progression disease
iCR	Immune complete response
IN	Inevaluable
INR	International Normalized Ratio (for Prothrombin Time)
iPR	Immune partial response
irAE	Immune Related Adverse Event
iRECIST	Immune Response Evaluation Criteria in Solid Tumors
iSD	Immune stable disease
iUPD	Immune unconfirmed progression disease
LDH	Serum Lactate Dehydrogenase
LKA	Last day the patient is Known Alive
LLN	Lower Limit of Normal
MPV	Major Protocol Violation
NA	Not Assessed
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
WBC	White Blood Cell Count

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1. Background and Rationale

The purpose of this document is to describe the analysis of PA.7 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. In a number of cancers including pancreatic cancer, overexpression of PD-L1 is associated with reduced survival and unfavourable 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 additional benefits to standard 1st line chemotherapy with gemcitabine/nab-paclitaxel in metastatic pancreatic cancer.

Research Hypothesis:

The primary hypothesis in this study is that durvalumab and tremelimumab combined with standard 1st line chemotherapy with gemcitabine/nab-paclitaxel (Arm G+N+D+T) will have a greater clinical efficacy compared to standard 1st line chemotherapy with gemcitabine/nab-paclitaxel (Arm G+N) in patients with metastatic pancreatic 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

PA.7 is an open-label, randomized, non-blinded, phase II clinical study of durvalumab+tremelimumab in combination with gemcitabine and nab-paclitaxel (Arm G+N+D+T) versus gemcitabine and nab-paclitaxel (Arm G+N) in patients with newly diagnosed, untreated, metastatic pancreatic adenocarcinoma. Prior to the randomized component, 10 patients would first be accrued to ensure safety and tolerability of the combination. After the safety profile of these patients was assessed, 180 patients would be randomized in a 2:1 ratio to Arm G+N+D+T or G+N after stratification by ECOG

performance status (0 vs. 1) and receipt of prior adjuvant therapy (yes versus no). Overall survival (OS) was the primary endpoint of this study. The study was conducted by the Canadian Cancer Trials Group (CCTG), with the support of AstraZeneca. CCTG Case Report Forms (CRFs) are used and the database are maintained by CCTG.

This study opened to accrue patients on August 22, 2016. Accrual to safety run-in component of the study was completed on January 23, 2017 with a total of 11 patients enrolled. The first analysis of the run-in patients was performed in March 2017 when all of the patients completed at least one cycle of treatment and, after the review of the results, accrual to randomized Phase II component was opened on April 10, 2017. With permission from the DSMC, an analysis was performed in the middle of January 2018 on a database locked on January 12, 2018 to generate tables and figures for the internal planning of AstraZeneca. The results of this analysis were also presented to DSMC at beginning of February 2018 with a proposal to transition the trial to phase III by CCTG. After reviewing the results, DSMC Chair recommended to continue the phase II trial as currently designed and place the transition "on hold". This recommendation was affirmed by DSMC after reviewing an updated analysis at their 2018 Annual Spring Meeting in April 2018. The accrual of the trial was closed on July 28, 2018 after its accrual goal of 180 patients has been achieved. At its Fall Teleconference in November 2018, the DSMC reviewed a request by the trial team to support an unplanned interim analysis based on the endpoint of overall survival when 100 deaths had occurred for the purpose of informing a potential phase III study design. After reviewing the response to questions raised during the review, this request was approved by the DSMC on March 18, 2019. The analysis was performed at end of April 2019 on a database locked on April 12, 2019 after all deaths observed before April 8, 2019 were reviewed. DSMC recommended the trial continue on to its final analysis as planned after reviewing the results of this analysis at its meeting on May 3, 2019. This analysis plan describes the analyses performed for the final analysis planned when 180 events are observed.

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 in combination with gemcitabine and nab-paclitaxel (G+N+D+T Arm) and gemcitabine and nab-paclitaxel alone (G+N Arm). The randomization was dynamically balanced by ECOG performance status (0 vs. 1) and receipt of prior adjuvant therapy (yes versus no) 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 metastatic pancreatic cancer treated with durvalumab and tremelimumab combined with gemcitabine and nab-paclitaxel to the overall survival of patients treated with gemcitabine and nab-paclitaxel 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 with gemcitabine and nab-paclitaxel .

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 gemcitabine and nab-paclitaxel by comparing overall survival (OS) between G+N+D+T and G+N 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 4.6 month difference in median survival (a hazard ratio of 0.65) between the two treatment arms assuming a median survival of 8.5 months for the gemcitabine and nab-paclitaxel 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 17 months will be required to reach the necessary number of events.

6. Data Set Descriptions

Three types of analysis samples will be used:

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

Response-Evaluable Patients:
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).

All Treated Patients:
All patients who received at least one dose of protocol treatment. Patients randomized to G+N Arm who have received at least one dose of durvalumab and tremelimumab on study (from Cancer Treatment Section of Treatment Report) will be grouped with patients randomized to G+N+D+T in the 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 (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 initial diagnosis of pancreatic cancer to randomization: median, minimum, maximum values **(Table 7)**
- Metastatic disease at initial diagnosis: Yes, No **(Table 7)**
- Months from diagnosis of metastatic disease following completion of prior surgical/adjuvant therapy: median, minimum, maximum values **(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 radiotherapy for pancreatic cancer **(Table 9)**
- Prior radiotherapy by site **(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 specific drug/agent (**Table 10**)

7.4.5 Extent of Disease

- Number of patients with target lesions**,** number of target lesions, largest measure, site of target lesions **(Table 11)**
- Number of patients with non-target lesions, number of non-target lesions, site of non-target lesions **(Table 12)**

7.4.6 Baseline Exams

- Baseline signs and symptoms **(Table 13)**
- Baseline hematology: WBC, neutrophils, platelets, hemoglobin, RBC, lymphocytes, monocytes, eosinophils, basophils **(Table 14)**
- Baseline serum chemistry: Total bilirubin, AST, ALT, LDH, creatinine clearance, serum creatinine, chloride, sodium, albumin, potassium, calcium, magnesium, ALP, glucose, amylase, lipase, Urea, BUN **(Table 15)**
- Baseline Thyroid Function Tests **(Table 16)**
- Baseline Coagulation Tests (**Table 17**)
- Baseline ECG **(Table 18)**
- Baseline urinalysis **(Table 19)**

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 20)**
- Number of patients with past or current major medical problems ongoing at baseline **(Table 21)**

7.5 Extent of Exposure

Patients included are those who received at least one dose of protocol treatment as defined in Section 6.

7.5.1 Study Therapy

During a 4 week cycle of protocol treatment, the patients on both arms would receive infusion of gemcitabine (1000 mg/m^2) and nab-paclitaxel (125 mg/m^2) on days 1, 8 and 15. Patients on G+N+D+T arm would receive in addition 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 gemcitabine or nab-paclitaxel (in weeks) during the study is defined as follows:

[last date of infusion of gemcitabine or nab-paclitaxel – first date of infusion of gemcitabine or nab-paclitaxel + 14]/7,

where the first and last date of infusion is taken from Gemcitabine Administration or Nab-paclitaxel Administration Section of Treatment Report.

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 treated patients:

- Number of patients by cycle of therapy **(Table 22)**
- Total number of cycles of treatment per patient **(Table 23)**
- Total treatment duration per patient for each drug (**Table 24**)

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

The administration of protocol treatment in a cycle may be modified (delayed, omitted, reduced, 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 with at least one cycle reduced, omitted, delayed, or infusion interrupted **(Table 25)**
- Reason for these dose modifications **(Table 25)**

7.5.3 Cumulative Dose, Dose Intensity and Relative Dose Intensity

The cumulative dose (mg) per patient for durvalumab and tremelimumab is the total dose (mg) that the patient received. The cumulative dose (mg/m^2) per patient for gemcitabine and nab-paclitaxel is defined as the sum over all cycles of the total actual dose received divided by the BSA in a given cycle **(Table 26).**

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

$$\text{Actual Dose Intensity} = \frac{\text{Cumulative dose } (\frac{\text{mg}}{m^2} \text{ or mg})}{\text{Duration of treatment}}.$$

where duration of treatment is defined in 7.5.1 **(Table 27).**

The relative dose intensity per patient for each drug is defined as the dose intensity (mg/m^2/week or mg/week) divided by the planned weekly dose as assigned in the protocol, which is 375 mg/week for durvalumab, 18.75 mg/week for tremelimumab, 750 mg/m^2/week for gemcitabine, and 93.75 mg/m^2/week for nab-paclitaxel.

The patient relative dose intensities will be grouped according to the following categories: < 60%,≥ 60% - < 80%, ≥ 80% - < 90%, ≥ 90% (**Table 28**).

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 29):**

- 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 (last date of infusion of gemcitabine, nab-paclitaxel, durvalumab or tremelimumab in Treatment Report, Date of Attendance/Last Contact on 4-Week Post Treatment Report, Follow-up Report, Short Follow Up Report, and Minimal Follow-up 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 30**). 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 31)** stratified by the factors coded as:

Stratification Factors (at randomization)		
Performance status	1 = ECOG 0	0 = ECOG 1
Prior adjuvant chemotherapy	1=Yes	0=No

The hazard ratio of durvalumab and tremelimumab combined with gemcitabine and nab-paclitaxel (G+N+D+T Arm) over gemcitabine and nab-paclitaxel alone (G+N Arm) and two-sided 90% CI will be calculated **(Table 31)** based on the Cox regression model stratified by above stratification factors, and with treatment arm coded as G+N+D+T Arm=1 and G+N Arm=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 31).**

Prognostic factors (at baseline)		
Gender	0 = Female	1 = Male
Age	0 = ≥65	1 = < 65
Number of organ sites	0 = >2	1= ≤ 2

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 gemcitabine and nab-paclitaxel (G+N+D+T Arm) over gemcitabine and nab-paclitaxel alone (G+N Arm) **(Table 32):**

- Gender: male, female
- Age: <65, ≥65
- Race: white, black, other
- Performance status at baseline: ECOG 0, 1
- Number of organ sites involved at baseline: ≤ 2 versus > 2

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 33):**

- 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 34).** A stratified Cox regression model will estimate the durvalumab and tremelimumab combined with gemcitabine and nab-paclitaxel (G+N+D+T Arm) over gemcitabine and nab-paclitaxel alone (G+N Arm) PFS hazard ratio and 90% C. I. **(Table 34).** 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 34).**

Coding for treatment arm, stratification variables and prognostic factors is identical to that presented in **Section 7.6.1**.

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 35).**

7.6.5 Treatment Objective Response

All patients will have their best objective 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 collected in "Best Overall Response" 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 objective response is defined as the "best verified" objective 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.

Best objective response to protocol treatment will be summarized for all randomized patients **(Table 36).**

The primary analysis of objective 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 37)** 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 37**). 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 Objective 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 38)**. 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)
- Number of organ sites involved at baseline (≤ 2 versus > 2).

7.6.7 Duration of Objective Response

For patients whose best objective responses are classified as CR or PR at any reporting period during the study, the duration of objective 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 objective response and associated 95% confidence intervals will be computed and compared by the stratified log-rank test adjusting for stratification factors at randomization **(Table 39).**

7.6.8 Treatment Immune Response (iRECIST)

All patients will also have their response classified every 8 weeks using the modified iRECIST guidelines. The best immune response (iRECIST) to protocol treatment is collected in "Best Objective Response i-RECIST" 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 immune 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 "Investigator Assessment-i-RECIST" section of TREATMENT REPORT.

All analyses performed for objective response as listed above will be performed similarly for immune response (**Table 40** to **Table 43**Error! Reference source not found.).

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 will be defined as acute (on treatment) adverse events; Events reported on Follow-up Report or Short Follow-up Report will be defined as delayed adverse events.

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 acute 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.

- Acute Adverse events: worst CTCAE grade per patient **(Table 44)**
- Severe acute adverse events: worst CTCAE grade per patient **(Table 45)**
- Drug related acute adverse events: worst CTCAE grade per patient **(Table 46)**
- Immune-related acute adverse event: worst CTCAE grade per patient (**Table 47**)
- Severe immune-related acute adverse event: worst CTCAE grade per patient (**Table 48**)
- Delayed adverse events: worst CTCAE grade per patient (**Table 49**)

7.7.2 Laboratory Evaluations

Laboratory evaluations reported on Treatment Report or 4-Week Post-Treatment Follow-Up Report will be included in the calculation for acute (on treatment) laboratory adverse events. All laboratory evaluations reported on Follow-up Report or Short Follow-up Reports will be included in the calculation for delayed (during follow-up) 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.

7.7.2.1 Hematology

- Hemoglobin, platelets, WBC, neutrophils, RBC, lymphocytes, monocytes, eosinophils, basophils on treatment: worst CTC grade per patient **(Table 50)**
- Hemoglobin, platelets, WBC, neutrophils, RBC, lymphocytes, monocytes, eosinophils, basophils during follow-up: worst CTC grade per patient **(Table 51)**

7.7.2.2 Serum Chemistry

- Total bilirubin, AST, ALT, LDH, creatinine clearance, serum creatinine, chloride, sodium, albumin, potassium, calcium, magnesium, ALP, glucose, amylase, lipase, Urea/BUN, CA 19-9 on treatment: worst CTC grade per patient **(Table 52)**
- Total bilirubin, AST, ALT, LDH, serum creatinine, chloride, sodium, albumin, potassium, calcium, magnesium, ALP, amylase, lipase during follow-up: worst CTC grade per patient **(Table 53)**

7.7.2.3 Thyroid Function Tests

- TSH, T3 free, T3 total, T4 free, T4 total on treatment **(Table 54)**
- TSH, T3 free, T3 total, T4 free, T4 total during follow-up **(Table 55)**

7.7.2.3 Coagulation

- PT, INR, PTT on treatment **(Table 56)**
- PT, INR, PTT during follow-up **(Table 57)**

7.7.3 Other Safety

7.7.3.1 ECG

Cardiac function of patients is evaluated as clinically indicated by ECG during protocol treatment with results reported on Treatment Report.

- Number of patients by normal or abnormal ECG, by treatment group **(Table 58)**

7.7.3.2 Urinalysis

Dipstick urinalysis is performed as clinically indicated during protocol treatment . with results reported on Treatment Report.

- Results of urinalysis, by treatment group **(Table 59)**

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

- Deaths during treatment or within 4 weeks of last protocol treatment: number of patients who died and cause of death from Date/Cause of Death Section of Death Report **(Table 60)**
- Number of patients with adverse events leading to discontinuations of protocol treatment as identified from Off Protocol Treatment - Adverse Events of End of Treatment Report **(Table 61)**

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 for pancreatic cancer 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 during or 4 weeks after protocol treatment (reported on Treatment Report and 4-Week Post-Treatment Follow-Up Report) **(Table 62)**
- Other anti-cancer treatments for pancreatic cancer during or 4 weeks after protocol treatment (reported on Treatment Report and 4 Weeks 4-Week Post-Treatment Follow-Up Report) (**Table 63**)
- Other anti-cancer treatments for pancreatic cancer during follow-up (reported on Follow-up Report or Short Follow-up Reports) **(Table 63)**

- Major medical problem during or 4 weeks after protocol treatment (reported on Treatment Report and 4-Week Post-Treatment Follow-Up Report) **(Table 64)**

7.9 Quality of Life

The quality of life of patients in this study is assessed at 4, 8, 12, 16 and 24 weeks from randomization during protocol treatment and then every 3 months until PD or the initiation of another chemotherapy treatment 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.

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 65).**

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 66)**. 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 66)**.

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 67)**.

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 68** and **Table 69**).

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 70**).

8. Appendices

Appendix 1: Tables and Figure

Table 1: Patient Disposition

Data set: All Randomized Patients			
	Number of patients (%)		
	G+N+D+T	G+N	Total
Randomized	N=***	N=***	N=***
Treated	*** (**)	*** (**)	*** (**)
On study	*** (**)	*** (**)	*** (**)
Off study(1)	*** (**)	*** (**)	*** (**)
Never Treated	*** (**)	*** (**)	*** (**)

(1) Off all study therapies.

Table 2: Follow-up of Patients

Data set: All Randomized Patients			
	Number of patients (%)		
	G+N+D+T	G+N	Total
Number of patients alive	*** (%)	*** (%)	*** (%)
Follow-up (months)			
median	**	**	**
Minimum-maximum	**-**	**-**	**-**

Table 3: Accrual by Center

Data set: All Randomized Patients			
	Number of patients (%)		
	G+N+D+T N = ***	G+N 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 (%)		
	G+N+D+T N = ***	G+N N=***	Total N = ***
Performance Status			
ECOG 0	** (**)	** (**)	** (**)
ECOG 1	** (**)	** (**)	** (**)
Prior adjuvant therapy			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)

Source: Centralized Randomization File

Figure 1: Accrual by Calendar Time

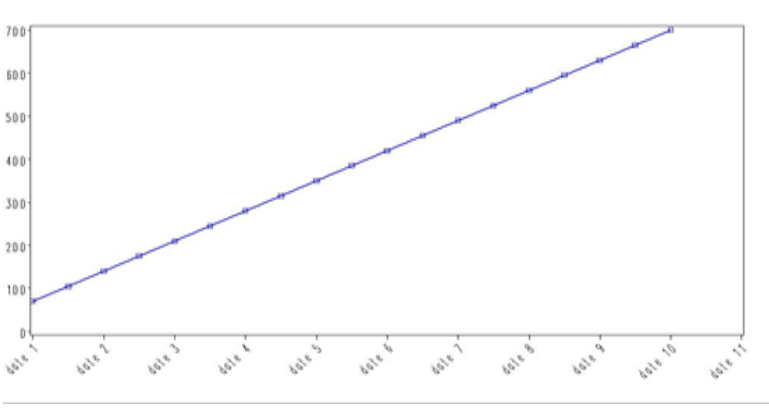

Table 5: Eligibility and Reasons for Ineligibility and Major Protocol Violations

Data set: All Randomized Patients			
	Number of Patients (%)		
	G+N+D+T N=***	G+N 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		
	G+N+D+T N=***	G+N N=***	Total N=***
Treatment received			
All G+N+D+T	*** (**)	*** (**)	*** (**)
Durvalumab only	*** (**)	*** (**)	*** (**)
Tremelimumab only	*** (**)	*** (**)	*** (**)
G+N Only	*** (**)	*** (**)	*** (**)
Not treated	*** (**)	*** (**)	*** (**)

Table 7: Pretreatment Characteristics at Baseline

Data set: All Randomized Patients			
	Number of patients (%)		
	G+N+D+T N=***	G+N 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 initial diagnosis to randomization			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **
Metastatic disease at initial diagnosis			
Yes	**(**)	**(**)	** (**)
No	**(**)	**(**)	**(**)
Months from diagnosis of metastatic disease following completion of prior surgical/adjuvant therapy			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **

Table 8: Prior Surgery

Data set: All Randomized Patients			
	Number of Patients (%)		
	G+N+D+T N=***	G+N 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 (%)		
	G+N+D+T N=***	G+N N=***	Total N=***
Any Prior Radiotherapy			
No	*** (**)	*** (**)	*** (**)
Yes	*** (**)	*** (**)	*** (**)
Site of any prior radiotherapy[(1)]			
Site #1	*** (**)	*** (**)	*** (**)
Site #2	*** (**)	*** (**)	*** (**)
...	*** (**)	***(**)	***(**)

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

Table 10: Prior Systemic Therapy

Data set: All Randomized Patients			
	Number of patients (%)		
	G+N+D+T N=***	G+N 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	*** (**)	*** (**)	*** (**)
Specific drug/agent[(1)]			
Drug/agent #1	*** (**)	*** (**)	*** (**)
Drug/agent #2	*** (**)	*** (**)	*** (**)
…	*** (**)	*** (**)	*** (**)

[(1)] Patient may have more than one drug/agent.

Table 11: Extent of Disease (Target Lesions)

Data set: All Randomized Patients			
	Number of Patients with Target Lesions (%)		
	G+N+D+T N=***	G+N 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 12: Extent of Disease (Non-Target Lesions)

Data set: All Randomized Patients			
	Number of Patients (%)		
	G+N+D+T N=***	G+N 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 13: Baseline Signs and Symptoms

Data set: All Randomized Patients (G+N+D+T 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 G+N Arm

Table 14: Baseline Hematology

Data set: All Randomized Patients			
	Number of Patients (%)		
	G+N+D+T N = ***	G+N 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 15: Baseline Chemistry

Data set: All Randomized Patients			
	Number of Patients (%)		
	G+N+D+T N = ***	G+N N = ***	Total N=***
Total bilirubin			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Creatinine clearance			
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]	** (**)	** (**)	** (**)
ALP			
Normal	** (**)	** (**)	** (**)
High [2]	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Lipase			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [1]	** (**)	** (**)	** (**)
Urea/BUN			
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 16: Baseline Thyroid Function Tests

Data set: All Randomized Patients			
	Number of Patients (%)		
	G+N+D+T N = ***	G+N 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 17: Baseline Coagulation Tests

Data set: All Randomized Patients			
	Number of Patients (%)		
	G+N+D+T N = ***	G+N 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 18: Baseline ECG

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

Table 19 : Baseline Urinalysis

Data set: All Randomized Patients			
	Number of patients (%)		
	G+N+D+T N=***	G+N 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 20: Concomitant Medications at Baseline

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

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

Table 21: Major Medical Problems at Baseline

Data set: All Randomized Patients			
	Number of patients (%)		
	G+N+D+T N = ***	G+N 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 22: Number of Patients by Cycle

Data Set: All Treated Patients			
		Number of Patients (%)	
		G+N+D+T Arm	G+N Arm
Cycle	1	** (**)	** (**)
	2	** (**)	** (**)
	3	** (**)	** (**)
	...		

Table 23: Number of Cycles of Protocol Therapy per Patient

Data Set: All Treated Patients		
	G+N+D+T Arm	G+N Arm
Number of Cycles:		
N	***	***
Median	*	*
Min – Max	* - *	* - *

Table 24: Total Treatment Duration

Data Set: All Treated Patients						
	G+N+D+T Arm				G+N Arm	
	Durva-lumab	Tremeli-mumab	Gemcita-bine	Nab-paclitaxel	Gemcita-bine	Nab-paclitaxel
Duration in weeks						
N	***	***	***	***	***	***
Median	*	*	*	*	*	*
Min – Max	* - *	* - *	* - *	* - *	* - *	* - *

Table 25: Dose Reduction, Omission or Delay and Infusion Interruption

Data Set: All Treated Patients						
	Number of patients (%)					
	G+N+D+T Arm				G+N Arm	
	Durvalu-mab (N=***)	Tremeli-mumab (N=***)	Gemcita-bine (N=***)	Nab-paclitaxel (N=***)	Gemcita-bine (N=***)	Nab-paclitaxel (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>	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
...	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
At least one infusion interruption	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Reason for interruption:						
<reason 1>	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
<reason 2>	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
...	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)

Table 26: Cumulative Dose

Data Set: All Treated Patients						
	G+N+D+T Arm				G+N Arm	
	Durva-lumab	Tremeli-mumab	Gemcita-bine	Nab-paclitaxel	Gemcita-bine	Nab-paclitaxel
Cumulative dose						
N	***	***	***	***	***	***
Mean (STD)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Median	*	*	*	*	*	*
Min – Max	* - *	* - *	* - *	* - *	* - *	* - *

Table 27: Dose Intensity

Data Set: All Treated Patients						
	G+N+D+T Arm				G+N Arm	
	Durva-lumab	Tremeli-mumab	Gemcita-bine	Nab-paclitaxel	Gemcita-bine	Nab-paclitaxel
Dose Intensity						
N	***	***	***	***	***	***
Mean (STD)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Median	*	*	*	*	*	*
Min – Max	* - *	* - *	* - *	* - *	* - *	* - *

Table 28: Relative Dose Intensity

Data Set: All Treated Patients						
	G+N+D+T Arm				G+N Arm	
	Durvalumab (N=***)	Tremelimumab (N=***)	Gemcitabine (N=***)	Nab-paclitaxel (N=***)	Gemcitabine (N=***)	Nab-paclitaxel (N=***)
Relative Dose intensity						
≥ 90% planned intensity	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
≥ 80% - < 90% planned intensity	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
≥ 60% - < 80% planned intensity	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
< 60% planned intensity	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)

Table 29: Off Treatment Summary

Data Set: All Treated Patients						
	G+N+D+T Arm				G+N Arm	
	Durvalumab (N=***)	Tremelimumab (N=***)	Gemcitabine (N=***)	Nab-paclitaxel (N=***)	Gemcitabine (N=***)	Nab-paclitaxel (N=***)
Off treatment	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Reason off treatment						
Treatment Completed	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Progressive disease (objective)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Symptomatic progression	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Intercurrent Illness – adverse events unrelated to protocol treatment	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Adverse events related to protocol therapy	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patient Refusal (not related to adverse event)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Death	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Other reason	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)

Table 30: All Deaths

Data set: All Randomized Patients		
	Number of Patients (%)	
	G+N+D+T N=***	G+N N=***
Number of Patients who died	** (**)	** (**)
Cause of Death		
Pancreatic cancer only	**	**
Toxicity from protocol treatment	**	**
Pancreatic 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

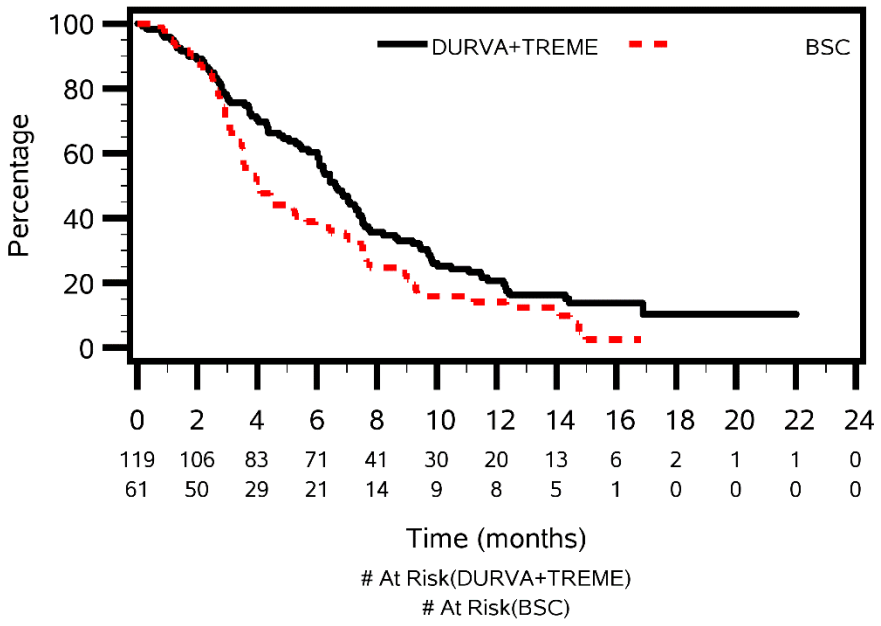

Table 31: Log Rank and Cox Regression Model for Overall Survival

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 model
Treatment arm				0.***		0.***
G+N+D+T	***	**.**	**.**		**.**	
G+N	***	**.**	(**.**,**.**)		(**.**,**.**)	
Gender				0.***		0.***
Male	***	**.**	NC [3]		**.**	
Female	***	**.**			(**.**,**.**)	
Age				0.***		0.***
<65	***	**.**	NC		**.**	
≥65	***	**.**			(**.**,**.**)	
Number of organ sites				0.***		0.***
≤ 2	***	**.**	NC		**.**	
>2	***	**.**			(**.**,**.**)	

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

Table 32: Survival by Subsets

Data set: All Randomized Patients						
		G+N+D+T		G+N		
Factors	Value	N	Median Survival (90% C.I.)	N	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	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Number of organ sites	≤2	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	>2	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)

(1) G+N+D+T over G+N hazard ratio (Unstratified)

Table 33: Progression Summary

Data set: All Randomized Patients

	Number of Patients (%)	
	G+N+D+T N=***	G+N N=***
Patients who progressed	*** (**)	*** (**)
Progression on protocol treatment	**	**
Progression off protocol treatment	**	**
Death (without documented progression)	**	**
Patients who were censored	*** (**)	*** (**)
Reason Censored		
Lost to follow-up	**	**
Not progressed	**	**

Figure 3: Kaplan-Meier Curves for Progression Free Survival

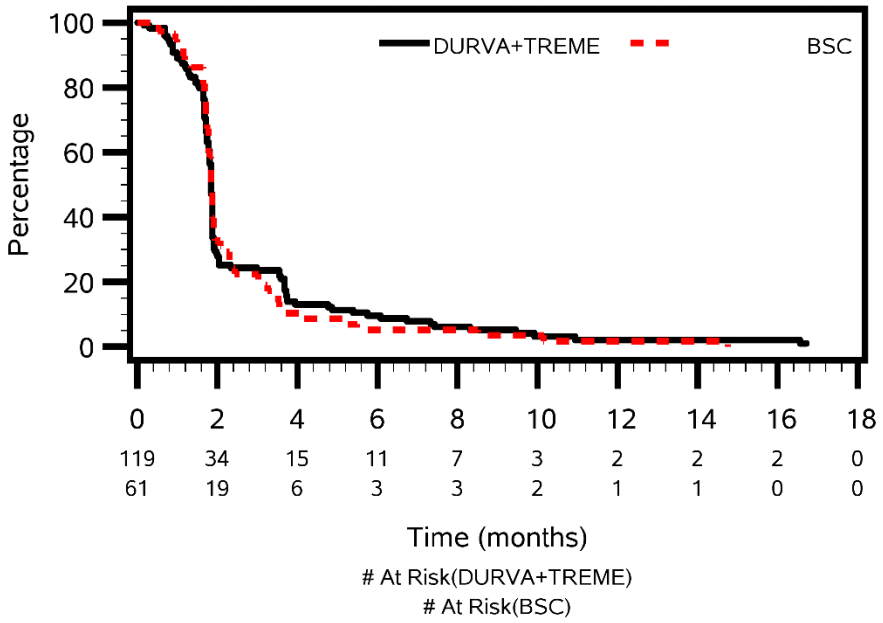

Table 34: Log Rank and Cox Regression Model for Progression Free Survival (PFS)

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 model
Treatment arm				0.***		0.***
G+N+D+T	***	**.**	**.**		**.**	
G+N	***	**.**	(**.**,**.**)		(**.**,**.**)	
Gender				0.***		0.***
Male	***	**.**	NC [3]		**.**	
Female	***	**.**			(**.**,**.**)	
Age				0.***		0.***
<65	***	**.**	NC		**.**	
≥65	***	**.**			(**.**,**.**)	
Number of organ sites				0.***		0.***
≤ 2	***	**.**	NC		**.**	
>2	***	**.**			(**.**,**.**)	

(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 35: Progression Free Survival (PFS) by Subsets

Data set: All Randomized Patients						
Factors	Value	N	G+N+D+T Median Survival (90% C.I.)	N	G+N 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	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
Number of organ sites	≤2	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)
	>2	**	**.** (**.**,**.**)	**	**.** (**.**,**.**)	**.** (**.**,**.**)

(1) G+N+D+T over G+N hazard ratio (Unstratified)

Table 36: Treatment Objective Response

Data set: All Randomized Patients

	Number of Patients (%)[a] N=***	
	G+N+D+T N=***	G+N 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 37: Cochran Mantel Haenszel and Logistic Regression Model for Objective 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.***
G+N+D+T: G+N	**.** (**.**,**.**)		**.** (**.**,**.**)	
Gender		0.***		0.***
Male: Female	NC [3]		**.** (**.**,**.**)	
Age		0.***		0.***
<65: ≥65	NC		**.** (**.**,**.**)	
Number of organ sites		0.***		0.***
≤2: >2	NC		**.** (**.**,**.**)	

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

Table 38: Objective Response According to Pretreatment Characteristics

Data set: All Randomized Patients		
	Number of Objective Responses/Number of Patients (%)	
	G+N+D+T N=***	G+N N=***
Gender		
Male	**/** (**)	**/** (**)
Female	**/** (**)	**/** (**)
Age		
< 65 years	**/** (**)	**/** (**)
≥ 65 years	**/** (**)	**/** (**)
Race		
White	**/** (**)	**/** (**)
Black	**/** (**)	**/** (**)
Other	**/** (**)	**/** (**)
Baseline performance status		
ECOG 0-1	**/** (**)	**/** (**)
ECOG 2	**/** (**)	**/** (**)
Number of organ sites		
≤ 2	**/** (**)	**/** (**)
>2	**/** (**)	**/** (**)

Table 39: Duration of Objective Response

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

(1) Stratified

Table 40: Immune Response (iRECIST)

Data set: All Randomized Patients		
	Number of Patients (%)[a] N=***	
	G+N+D+T N=***	G+N N=***
Patients with at least one target lesion	N=***	N=***
Response-evaluable	N=***	N=***
Immune Complete response (iCR)	** (**)	** (**)
Immune Partial response (iPR)	** (**)	** (**)
Immune Stable disease (iSD)	** (**)	** (**)
Immune confirmed progression (iCPD)	** (**)	** (**)
Immune unconfirmed progression (iUPD)	** (**)	** (**)
Inevaluable for response (IN)	** (**)	** (**)
<Reason 1>	**	**
<Reason 2>	**	**
....	...	....
Not response evaluable	N=***	N=***
Never treated	**	**
Not assessed (NA)	**	**
Patients without any target lesion	N=***	N=***
Immune confirmed progression (iCPD)	**	**
Immune unconfirmed progression (iUPD)	** (**)	** (**)
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 41: Cochran Mantel Haenszel and Logistic Regression Model for Immune 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.***
G+N+D+T: G+N	**.** (**.**,**.**)		**.** (**.**,**.**)	
Gender		0.***		0.***
Male: Female	NC [3]		**.** (**.**,**.**)	
Age		0.***		0.***
<65: ≥65	NC		**.** (**.**,**.**)	
Number of organ sites		0.***		0.***
≤2: >2	NC		**.** (**.**,**.**)	

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

Table 42: Immune Response According to Pretreatment Characteristics

Data set: All Randomized Patients		
	Number of Immune Responses/Number of Patients (%)	
	G+N+D+T N=***	G+N N=***
Gender		
Male	**/** (**)	**/** (**)
Female	**/** (**)	**/** (**)
Age		
< 65 years	**/** (**)	**/** (**)
≥ 65 years	**/** (**)	**/** (**)
Race		
White	**/** (**)	**/** (**)
Black	**/** (**)	**/** (**)
Other	**/** (**)	**/** (**)
Baseline performance status		
ECOG 0-1	**/** (**)	**/** (**)
ECOG 2	**/** (**)	**/** (**)
Number of organ sites		
≤ 2	**/** (**)	**/** (**)
>2	**/** (**)	**/** (**)

Table 43: Duration of Immune Response

Data set: All Randomized Patients with iCR or iPR			
	G+N+D+T N=***	G+N N=***	P-value(1)
Median Duration of Immune Response (months) (90% CI)	*** (**-**)	*** (**-**)	.**

(1) Stratified

Table 44: Acute (On Treatment) Adverse Events

Data set: All Treated Patients on G+N+D+T 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.

Note: Same table will be made for patients on G+N Arm.

Table 45: Severe Acute (On Treatment) Adverse Events

Data set: All Treated Patients on G+N+D+T 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.

Note: Same table will be made for patients on G+N Arm.

Table 46: Drug Related Acute (on Treatment) Adverse Events

(1) Related to Durvalumab

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

(5) Related to Gemcitabine

Data set: All Treated Patients on G+N+D+T Arm						
	Number of patients (%) N=***					
	Worst grade					Any grade
	1	2	3	4	5	
	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE related to Gemecitabine 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.

Note: Same table will be made for patients on G+N Arm.

(6) Related to Nab-paclitaxel

Data set: All Treated Patients on G+N+D+T Arm						
	Number of patients (%) N=***					
	Worst grade					Any grade
	1	2	3	4	5	
	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE related to Nab-paclitaxel 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.

Note: Same table will be made for patients on G+N Arm.

Table 47: Immune-related Acute (On Treatment) Adverse Events

Data set: All Treated Patients on G+N+D+T Arm						
	Number of patients (%) N=***					
	Worst grade					Any grade
	1	2	3	4	5	
Patients with any irAE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with irAE 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: Same table will be made for patients on G+N Arm.

Table 48: Severe Acute (On Treatment) Immune-related Adverse Events

Data set: All Treated Patients on G+N+D+T Arm				
	Number of patients (%) N=***			
	Worst grade			Any grade 3 or higher irrAE
	3	4	5	
Patients with any irAE	** (**)	** (**)	** (**)	** (**)
Patients with irAE 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: Same table will be made for patients on G+N Arm.

Table 49: Delayed (During Follow-up) Adverse Events

Data set: All Treated Patients on G+N+D+T Arm						
	Number of patients (%) N=***					
	Worst grade					Any grade
	1	2	3	4	5	
Patients with any delayed AE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with delayed 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 G+N Arm.

Table 50: Hematology During Protocol Treatment: Worst Grade per Patient

Data set: All Treated Patients		
	Number of Patients (%)	
	G+N+D+T N = ***	G+N 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 51: Hematology During Follow-up: Worst Grade per Patient

Data set: All Treated Patients		
	Number of Patients (%)	
	G+N+D+T N = ***	G+N 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 52: Serum Chemistry during Protocol Treatment: Worst Grade per Patient

Data set: All Treated Patients		
	Number of Patients (%)	
	G+N+D+T N = ***	G+N N = ***
Total bilirubin		
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Not reported [(1)]	** (**)	** (**)
Creatinine clearance		
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]	** (**)	** (**)
ALP		
Normal	** (**)	** (**)
High [2]	** (**)	** (**)
Not reported [1]	** (**)	** (**)
Lipase		
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Not reported [1]	** (**)	** (**)
Urea/BUN		
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Not reported [1]	** (**)	** (**)

[1] Greater than upper normal limit

Table 53: Serum Chemistry During Follow-up: Worst Grade per Patient

Data set: All Treated Patients		
	Number of Patients (%)	
	G+N+D+T N = ***	G+N N = ***
Total bilirubin		
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Not reported (1)	** (**)	** (**)
Creatinine clearance		
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)]	** (**)	** (**)
ALP		
Normal	** (**)	** (**)
High [(2)]	** (**)	** (**)
Not reported [(1)]	** (**)	** (**)
Lipase		
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Not reported [(1)]	** (**)	** (**)
Urea/BUN		
Grade 0	** (**)	** (**)
Grade 1	** (**)	** (**)
Grade 2	** (**)	** (**)
Grade 3	** (**)	** (**)
Grade 4	** (**)	** (**)
Not reported [(1)]	** (**)	** (**)

[(1)] Greater than upper normal limit

Table 54: Thyroid Function Tests: Worst During Protocol Treatment

Data set: All Treated Patients		
	Number of Patients (%)	
	G+N+D+T N = ***	G+N 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 55: Thyroid Function Tests: Worst during Follow-up

Data set: All Treated Patients		
	Number of Patients (%)	
	G+N+D+T N = ***	G+N 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 56: Coagulation Tests: Worst During Protocol Treatment

Data set: All Treated Patients		
	Number of Patients (%)	
	G+N+D+T N = ***	G+N 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 57: Coagulation Tests: Worst During Follow-up

Data set: All Treated Patients		
	Number of Patients (%)	
	G+N+D+T N = ***	G+N 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 58: ECG Results During Protocol Treatment

Data set: All Treated Patients		
	Number of patients (%)	
	G+N+D+T N=***	G+N 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 59 : Urinalysis During Protocol Treatment

Data set: All Treated Patients		
	Number of patients (%)	
	G+N+D+T N=***	G+N 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 60: Deaths During or within 4 weeks of Last Protocol Treatment

Data set: All Treated Patients		
	Number of Patients (%)	
	G+N+D+T N=***	G+N N=***
Number of Patients who died during or within 4 weeks of last protocol 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 61: Adverse Event leading to Discontinuation of protocol Treatment[(a)]

Data set: All Treated Patients		
	Number of patients (%)	
	G+N+D+T N=***	G+N 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>	**	**
....	**	**
Number discontinued Gemcitabine from adverse events	***(***)	***(***)
<Adverse event 1>		
<Adverse event 2>	***	***
....	***	***
Number discontinued Nan-paclitaxel 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 62: Concomitant Medications

Data set: All Treated Patients		
	Number of patients (%)	
	G+N+D+T N = ***	G+N N=***
Any concomitant medication during or 4 weeks after protocol treatment		
No	** (**)	** (**)
Yes	** (**)	** (**)
Type of concomitant medications[(1)]		
Medication A	** (**)	** (**)
…		

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

Table 63: Anti-Cancer Treatment

	Number of patients (%)	
	G+N+D+T N=***	G+N N =***
Number of patients with any anti-cancer treatment during or 4 weeks after protocol 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 during follow-up	*** (**)	*** (**)
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 64: Major Medical Problems

Data set: All Treated Patients		
	Number of patients (%)	
	G+N+D+T N = ***	G+N N=***
Any major medical problem during or 4 weeks after protocol treatment		
No	** (**)	** (**)
Yes	** (**)	** (**)
Type of major medical problems[(1)]		
Medication A	** (**)	** (**)
…		

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

Table 65: Compliance Rate with QoL Assessment by Treatment Arm

	G+N+D+T		G+N	
	Expected	Received (%)	Expected	Received (%)
Baseline	***	** (**)	***	** (**)
During protocol treatment				
4 weeks	***	** (**)	***	** (**)
8 weeks	***	** (**)	***	** (**)
12 weeks	***	** (**)	***	** (**)
16 weeks	***	** (**)	***	** (**)
24 weeks	***	** (**)	***	** (**)
After protocol treatment				
3 months	***	** (**)	***	** (**)
6 months	***	** (**)	***	** (**)
12 months	***	** (**)	***	** (**)
15 months	***	** (**)	***	** (**)
18 months	***	** (**)	***	** (**)
21 months	***	** (**)	***	** (**)
24 months	***	** (**)	***	** (**)

Table 66: Proportion of Patients with Deterioration, Improvement or Stable QoL

	N	G+N+D+T N (%)	G+N 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 67: Time to Deterioration in QoL Primary Endpoints

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

Table 68: QoL: Summary Baseline Scores

	G+N+D+T	G+N	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 69: Summary QOL Change Scores from Baseline for Scale/Domain/Item at Each Time Period*

	G+N+D+T	G+N	P Value**
Scale/Domain/Item			
During protocol treatment 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)	 ** (**)	 ** (**)	.**
After protocol treatment 3 months N Mean (STD)	 *** ** (**)	 *** ** (**)	.**
6 months N Mean (STD)	 ** (**)	 ** (**)	.**
9 months N Mean (STD)	 ** (**)	 ** (**)	.**
12 months N Mean (STD)	 ** (**)	 ** (**)	.**
15 months N Mean (STD)	 ** (**)	 ** (**)	.**
18 months N Mean (STD)	 ** (**)	 ** (**)	.**
21 months N Mean (STD)	 ** (**)	 ** (**)	.**
24 months N Mean (STD)	 ** (**)	 ** (**)	.**

* Table will be provided for each scale/domain/item.
** Wilcoxon rank sum test

Table 70: Results for QOL Response Analyses

Domain	G+N+D+T			G+N			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