Statistical Analysis Plan

OncoMed Pharmaceuticals, Inc.

Study 59R5-003 (Phase 2 Portion)

A Phase-1b/2 Study of Tarextumab (OMP-59R5) in Combination with Etoposide and Platinum Therapy in Subjects with Untreated Extensive Stage Small Cell Lung Cancer

PINNACLE: Phase-1b/2 INvestigation of anti-Notch Antibody Therapy with Etoposide and Platinum Therapy in Small Cell Lung Carcinoma Safety and Efficacy

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Approval

Upon review of this document, including table, listing, and figure shells, the undersigned approves the Statistical Analysis Plan. The analysis methods and data presentation are acceptable.

[redacted]

SynteractHCR

3/23/2017
Date

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OncoMed Pharmaceuticals, Inc.

3/23/2017
Date

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LIST OF ABBREVIATIONS

AE	Adverse event
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
ATC	Anatomical/Therapeutic/Chemical (class)
AUC	Area under curve
BMI	Body mass index
BSA	Body surface area
CRF	Case report form
CNS	Central nervous system
CR	Complete response
CSR	Clinical study report
CTCAE	Common terminology criteria for adverse events
DOR	Duration of response
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EP	Etoposide and platinum (therapy)
ES-SCLC	Extensive stage small cell lung cancer
HR	Hazard ratio
ITT	Intent-to-treat (patient population)
KM	Kaplan-Meier
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum tolerated dose
N3RPI	NOTCH-3-ralated PFS index
NE	Inevaluable (by RECIST criteria)
ORR	Overall response rate
OS	Overall survival
PCI	Prophylactic cranial irradiation
PD	Progressive disease
PFS	Progression free survival
PH	Proportional hazards
PK	Pharmacokinetics
PP	Per-protocol (patient population)
PR	Partial response
RECIST	Response evaluation criteria in solid tumors (version 1.1)
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Stable disease
SLD	Sum of longest diameters
TEAE	Treatment-emergent adverse event
TFLs	Tables, figures and listings
WBR	Whole brain radiation
WHO	World Health Organization

DEFINITIONS

Adverse event	Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research, or any baseline conditions that worsened during the study.
Baseline value	The last non-missing value recorded prior to the first dose of study drug.
Best overall response	Patient's best investigator-assessed RECIST response to treatment category recorded since the start of the treatment.
On study tumor assessments	Tumor assessments that meet the following criteria: 1. No gap of ≥91 days between successive tumor assessments among those on or prior to the on study tumor assessment. (Note: a tumor assessment for which "Not Evaluated" is entered into the database does not qualify as a tumor assessment.) 2. No prior initiation of non-protocol anticancer therapy.
Overall response rate	The proportion of patients achieving a complete response or partial response to treatment.
Dose intensity	The total dose (in mg) a patient actually received divided by the total dose (in mg) the patient should have received had there been no missed doses, dosing delays or dosage reductions.
Intent-to-treat population	All patients randomized to receive study drug regardless of whether they actually received study drug and regardless of whether evidence is found indicating they failed to meet study inclusion/exclusion criteria or had other protocol violations.
Last contact date	The last contact date is the latest assessment/visit date recorded on any of the following case report forms: Discontinuation, Hematology, Chemistry, RECIST Overall Response Tumor Assessments, Survival Follow Up, Study Drug Infusion, Etoposide Infusion or Platinum Therapy Infusion.
Non-Protocol Anti-Cancer Therapy	Non-protocol anti-cancer therapies used by patients during their participation in this study, if any, will be identified by the sponsor after review of relevant data listings.
Per-protocol population	The subset of safety population who either (a) have at least one response evaluation on study, or (b) die prior to their first scheduled response evaluation.
Platinum Therapy / Platinum Choice	The physician's choice of platinum therapy (cisplatin or carboplatin) was used as a stratification variable by the dynamic randomization system. Discrepancies, if any, between the platinum therapy used to stratify a patient's treatment assignment and the platinum therapy actually administered during the study will be dealt with as follows. Platinum choice entered in the dynamic randomization system will be used in all efficacy analyses where platinum choice is included as a model

	effect. However, actual platinum received (as documented on earliest Platinum Therapy Infusion CRF [e.g., Cycle 1, Day 1]) will be used when calculating dosing compliance.
Randomization Date	Although each patient's randomization date was recorded by site personnel on the Informed Consent case report form (CRF), the actual randomization date substantiated by the dynamic randomization system used to make blinded treatment assignments will be used in all analyses including calculations of times to events such as OS and PFS.
Randomized Study Drug	Tarextumab or placebo
Safety population	The subset of the intent-to-treat population who received at least one partial dose of tarextumab or Placebo and who have at least one post-dosing safety evaluation (labs, vital signs or adverse events).
Treatment-emergent adverse event	An adverse event that starts or increases in severity any time after the first administration of any randomized study drug (i.e., tarextumab or placebo) up to 30 days following the last administration of any study drug.

1. INTRODUCTION

This document outlines the statistical methods to be implemented for analyzing data collected within the phase-2 portion of OncoMed Pharmaceuticals, Inc. Protocol 59R5-003 (A Phase-1b/2 Study of Tarextumab [OMP-59R5] in Combination with Etoposide and Platinum Therapy in Subjects with Untreated Extensive Stage Small Cell Lung Cancer), amendment 6 dated 22 April 2016. The purpose of this statistical analysis plan (SAP) is to provide specific guidelines from which the statistical analyses will proceed. Any deviations from this plan will be documented in the clinical study report (CSR). The definitive analyses of efficacy data for making statistical inference with respect to the objectives the Phase-2 portion of the study and the definitive analyses of safety data will be performed using data from a formal data cut taken planned to occur in April 2017. Randomized treatment assignments will be unblinded at that time. Any subsequent data analyses that may be performed to include data accrued into the database following the April-2017 data cut will be considered secondary efficacy and/or safety analyses.

Investigating the pharmacokinetics (PK) of tarextumab in combination with EP is an objective of this study, but a detailed analysis plan is outside the scope of this document.

Throughout this SAP, the terms patient and subject are used synonymously to refer to an individual who was enrolled to participate in the clinical trial.

2. STUDY OBJECTIVES

2.1. Primary Objectives

The primary objectives of this study are:

- Phase-1b portion: To determine the maximum tolerated dose (MTD) of tarextumab when administered on Day 1 of each 21 day cycle along with etoposide 100 mg/m^2 on Days 1, 2 and 3 and cisplatin 80 mg/m^2 or carboplatin to an area under curve (AUC) of 5 mg/mL/min on Day 1 in subjects with untreated extensive stage small cell lung cancer (ES-SCLC).
- Phase-2 portion: To determine the improvement in progression free survival (PFS) resulting from the addition of tarextumab to etoposide and platinum therapy (EP) in subjects receiving first-line therapy for ES- SCLC. (Platinum therapy for the phase-2 portion was similar to phase-1b [i.e., cisplatin or carboplatin], but the cisplatin dose was changed to 75 mg/m^2.)

Statistical analyses concerning the primary objective for the phase-1b portion of this study will not be addressed in this SAP.

2.2. Secondary Objectives

The secondary objectives of this study are:

- Phase-1b and -2 portions: To determine the PK of tarextumab in combination with EP in subjects receiving first-line therapy for ES-SCLC
- Phase-1b and -2 portions: To determine the immunogenicity of tarextumab in combination with EP in subjects receiving first-line therapy for ES-SCLC
- Phase-2 portion: To estimate the improvement in overall survival (OS), 12-month survival and overall response rate (ORR) resulting from the addition of tarextumab to EP in subjects receiving first-line therapy for ES-SCLC

- Phase-2 portion: To correlate the treatment effect in PFS, OS, 12-month survival and ORR resulting from the addition of tarextumab to EP in subjects with Notch3, Hey2, Hes1, Hey1 and Hes6 expression
- Phase-1b portion: To determine the safety and tolerability of tarextumab in combination with EP in subjects who are receiving first-line therapy for ES-SCLC
- Phase-2 portion: To compare the safety and tolerability of tarextumab in combination with EP relative to EP alone in all subjects who are receiving first-line therapy for ES-SCLC

Statistical analyses concerning the secondary objectives for the phase-1b portion of this study will not be addressed in this SAP.

2.3. Exploratory Objective

An exploratory objective of this study is:

- Phase-1b and -2 portions: To describe the changes in exploratory pharmacodynamic biomarkers, including Notch pathway related genes and proteins and circulating tumor cells following tarextumab treatment

3. STUDY DESIGN AND PLAN

The following descriptions of the study design and plan were copied from the study protocol. Since this SAP only covers analyses planned for the phase-2 portion of the study, some portions of the study design and plan related only to the phase-1b portion were omitted intentionally.

The study consists of a phase-1b lead-in portion to determine the MTD of tarextumab in combination with EP for 6 cycles followed by treatment with tarextumab alone until unacceptable toxicity or disease progression. The initial dose escalations of tarextumab will be conducted with etoposide and cisplatin. The dose of tarextumab will not exceed 15 mg/kg. Following the establishment of the highest tolerable dose of tarextumab in combination with etoposide and cisplatin, a cohort of 6 subjects will be treated at this dose in combination with etoposide and carboplatin. Once the safety and tolerability of tarextumab at this dose is also confirmed with etoposide and carboplatin, the protocol will transition to a phase-2, multicenter, randomized, placebo-controlled portion comparing the efficacy and safety of tarextumab at the highest tolerable dose in combination with EP for 6 cycles followed by single agent tarextumab relative to EP alone for 6 cycles in subjects receiving first-line therapy for ES-SCLC. However, if a DLT is observed in 2 or more subjects in the cohort of 6 subjects treated with the highest tolerable dose of tarextumab with etoposide and carboplatin, a new cohort of 3 to 6 subjects will be enrolled at the next lower dose level of tarextumab with etoposide and carboplatin. The highest tarextumab dose that is tolerable with both platinum options will be used in phase-2 portion of the study.

In phase-2 portion of the study, subjects may be treated with cisplatin or carboplatin as determined by the investigator prior to randomization. Alteration to the choice of platinum therapy is not permitted once the subject is randomized.

Etoposide 100 mg/m^2 will be administered on Days 1, 2 and 3 along with cisplatin 80 mg/m^2 for phase-1b and 75 mg/m^2 for the phase-2 portion of the study or carboplatin to an AUC of 5 mg/mL/min on Day 1 of every 21-day cycle for 6 cycles, tarextumab or placebo will be given on Day 1 of every 21-day cycle prior to the administration of EP.

Subjects may continue one of the chemotherapy drugs if the other is held or discontinued prior to completing 6 cycles of EP and prior to disease progression. Subjects should continue EP alone for a total of 6 cycles if tarextumab is held or discontinued prior to the completion of 6 cycles of EP. Subjects may continue study drug if one or both of the chemotherapy drugs is held or discontinued prior to completing 6 cycles of EP and prior to disease progression.

The phase-2 portion of the study may commence after the safety and tolerability of the highest tolerable dose of tarextumab has been confirmed in both cohorts of subjects with etoposide and cisplatin/carboplatin during phase-1b. The highest tarextumab dose that is tolerable with both platinum options will be used in the phase-2 portion of the study. For example: if tarextumab at 15 mg/kg is tolerable with etoposide and cisplatin, but not tolerable with etoposide and carboplatin; and tarextumab at 12.5 mg/kg is tolerable with etoposide and carboplatin, then tarextumab at 12.5 mg/kg will be the dose used in phase-2. The phase-2 portion includes a blinded treatment phase and follow-up phase. It is a multicenter, randomized, placebo-controlled portion evaluating the efficacy and safety of tarextumab in combination with etoposide and platinum therapy in subjects with previously untreated ES-SCLC. Subjects may be treated with cisplatin or carboplatin as determined by the Investigator prior to randomization. Alteration to the choice of platinum therapy is not permitted once the subject is randomized.

Approximately 135 evaluable subjects will be enrolled to the phase-2 portion of the study. Evaluable subjects are those who received at least one dose of study drug (either tarextumab or placebo).

Version 1.1 of standard response evaluation criteria in solid tumors (RECIST) criteria [Ref-1] was used to evaluate patients' responses to treatment. RECIST response categories include complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD). In addition to these four primary ratings, a patient's response to treatment is classified as unevaluable (abbreviated NE) when no imaging/measurement is performed at a particular time point.

3.1. Blinded Treatment Phase

Subjects who qualify for enrollment into the phase-2 portion of the study will be randomized in a 1:1 ratio to receive study treatment of EP with placebo or EP with tarextumab. The randomization will be balanced on the choice of platinum therapy (cisplatin versus carboplatin) and the prior use of whole brain radiation (WBR) or prophylactic cranial irradiation (PCI). Changing the choice of platinum therapy is not permitted once the subject is randomized. Treatment for each subject will begin on Cycle1, Day 1 (the first dosing day). Etoposide 100 mg/m^2 will be given on Days 1, 2 and 3 and cisplatin 75 mg/m^2 or carboplatin to an AUC of 5 mg/mL/min will be given on Day 1 of every 21-day cycle for 6 cycles. Subjects may remain in the blinded treatment phase to continue one of the chemotherapy drugs if the other is held or discontinued prior to completing 6 cycles of EP and prior to disease progression. For subjects who have study drug held or discontinued for tolerability reasons, EP chemotherapy should continue to the completion of 6 cycles. Subjects may continue study drug if one or both of the chemotherapy drugs is held or discontinued prior to completing 6 cycles of EP and prior to disease progression.

After the completion of 6 cycles of EP, subjects who do not have disease progression and have not had WBR or PCI prior to study entry and are good candidates for PCI according to the

investigator should receive PCI within 8 weeks after the last dose of chemotherapy at a total dose of 25 Gy in 10 fractions. If subjects discontinue EP with treatment-related toxicities prior to completing 6 cycles and are good candidates for PCI per the investigator, PCI can be initiated at any time determined appropriate by the investigator. Subjects who do not receive PCI within 8 weeks after the last dose of chemotherapy can have PCI later during the study as determined by the investigator. Study drug (tarextumab or placebo) administration should continue at every 21-day cycle between the completion of chemotherapy and the initiation of PCI. PCI should not be initiated within 2 weeks of study drug administration and study drug will be held during the PCI treatment period. Subjects will resume study drug alone ≥14 days after completion of PCI, until disease progression or unacceptable treatment-related toxicities or withdrawal of consent. Subjects will discontinue study treatment if there is evidence of central nervous system (CNS) metastasis.

3.2. Follow-Up

Subjects who discontinue study treatment for any reason other than disease progression will be followed with tumor assessment every 6 weeks (42 ±5 days) during follow-up until documented disease progression or initiation of new anti-cancer therapy, whichever is sooner. Additionally, subjects who are discontinued from study treatment will be followed for survival and any subsequent anti-cancer therapies. Survival follow-up information and subsequent anti-cancer therapies, including systemic therapies, surgery (resection of metastatic disease), and radiation therapy will be collected during telephone calls, through subjects medical records, and/or clinic visits every 3 months starting from the last study treatment until death, loss to follow-up, or study termination by the sponsor. The study staff may use a public information source (e.g., county records) to obtain information about survival status only.

4. DETERMINATION OF SAMPLE SIZE

The following assumptions and methods for determining the sample size for the study were copied from the study protocol. Since this SAP only covers analyses planned for the phase-2 portion of the study, details on the determination of sample size for the phase-1b portion of the study have been omitted intentionally.

At the final analysis we will evaluate the effect of tarextumab on PFS in subjects in the intention to treat (ITT) population (defined in section 6.1). The final analysis will take place when 91 progression events have been observed or 10 months after the completion of enrollment whichever occurs first.

Denote the treatment effect in terms of the log of the hazard ratio (HR) by θ_1.

The null hypotheses for testing homogeneity of PFS distributions across treatment arms is:

$$H_0: \theta_1 = 0$$

And the alternative hypothesis is:

$$H_A: \theta_1 < 0$$

The power and type-1 error rate for the log rank test of this hypothesis is presented in Table 1.

Table 1. Progression-Free Survival: Power for the Alternative Hypothesis

	Analysis 1	Analysis 2	Final Analysis
Total Number of Events	61	76	91
Z-Statistic (reject the null) [1]	3.168	2.301	1.036
P-value (1 sided)	0.00077	0.011	0.15
Z statistic (reject the Alt) [2]	-1.773	-1.486	-1.079
P-value (1 sided)	0.038	0.0690	0.1400
Cumulative Type 1 Error (1-sided)	8e-04	0.0107	0.1501
Cumulative Power			
HR=0.75	0.0204	0.1479	0.6318
HR=0.67	0.0543	0.2897	0.8090
HR=0.65	0.0687	0.3365	0.8460
HR=0.60	0.1204	0.4709	0.9194
HR=0.50	0.3223	0.7647	0.9884
Cumulative Probability of Stopping for Harm			
Alternative	4e-04	8e-04	0.0018
Null	0.0381	0.0762	0.1501
HR=1.33 (1/0.75)	0.2580	0.4246	0.6275
HR=1.49 (1/0.67)	0.4172	0.6170	0.8052
HR=2.00 (1/0.50)	0.8248	0.9412	0.9877

[1] The boundary for rejecting the null hypothesis for efficacy is obtained from the gamma(-16) alpha spending function.
[2] The boundary for rejecting the null hypothesis for harm is obtained from the gamma(-4) alpha spending function.

With 91 events at the final analysis, there is 80% power with 0.15 type 1 error to detect an HR of 0.67. There is a 7.6% chance of stopping early for harm under the null hypothesis; a 42.5% chance of stopping early for harm if the HR=1.33 (1/0.75); a 61.7% chance of stopping early for harm if the HR=1.49 (1/0.67); and a 94.1% chance of stopping early for harm if the HR=2.00 (1/0.5).

Analyses 1 and 2 will take place at the last two quarterly safety review meeting of the Data Safety Monitoring Board (DSMB). The estimated numbers of events at these times are presented in Table 1. If the number of events differs from what is presented, then the efficacy and safety boundaries will be recalculated using the spending functions which are footnoted in Table 1.

Overall survival is a secondary endpoint in this study. An analysis of OS will take place at the time of each analysis for PFS as well as at the time that the final analysis of PFS takes place. The final analysis of OS will take place when there are 98 events or 6 months after the final analysis for PFS, whichever occurs first. Table 2 and Figure 1 present enrollment, PFS events and Deaths over time assuming a control hazard of progression beyond 9 months of 0.1386.

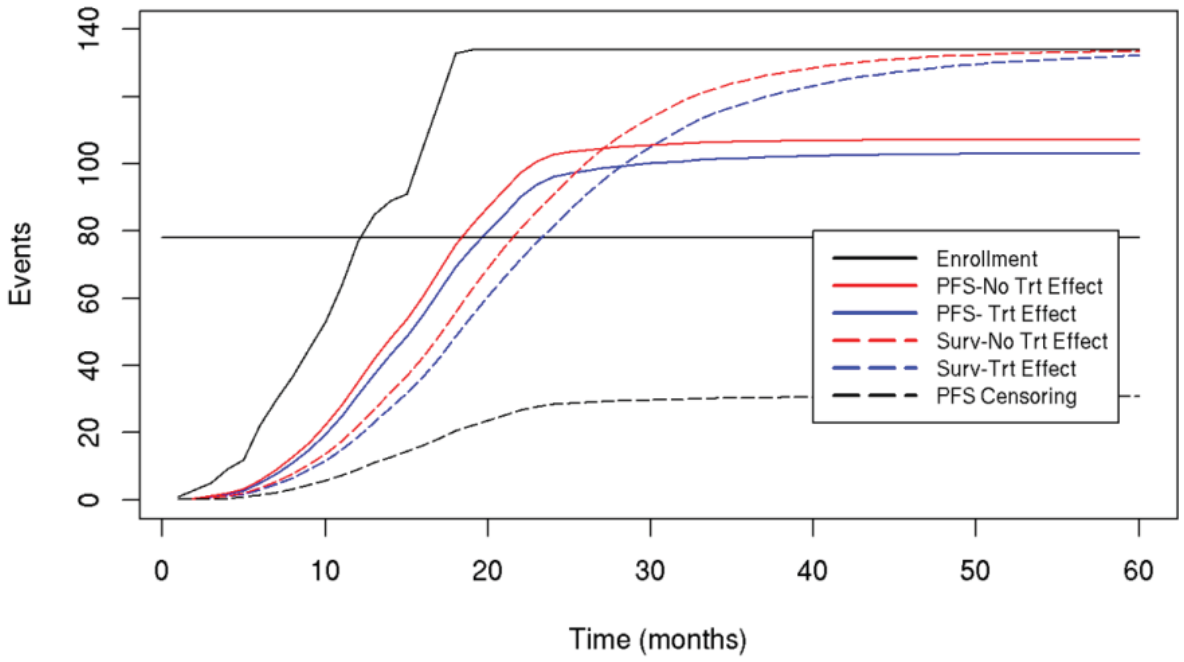
Table 2. Enrollment, Progressions and Deaths over Time – Control Hazard of Progression of 0.1386 Beyond 9 Months

Study Time (months)	6	12	13	14	15	16	17	18	19	20
Cumulative Enrolment	22	77	85	89	91	105	119	133	134	134
Total PFS Events	5	31	38	43	49	55	62	69	75	80
Total PFS Events-2 [1]	6	35	42	48	54	61	68	76	82	87
Total Deaths	3	19	23	27	32	37	42	49	55	61
Total Deaths-2 [1]	4	22	27	32	37	42	49	56	63	69
Censored PFS (tarextumab)	1	5	6	7	8	9	10	11	12	13
Censored PFS (placebo)	1	4	5	6	7	8	9	9	10	11

Study Time (months)	21	22	23	24	25	26	27	28	29	30
Cumulative Enrolment	134	134	134	134	134	134	134	134	134	134
Total PFS Events	85	90	94	96	97	98	99	99	100	100
Total PFS Events-2 [1]	92	98	101	103	104	104	105	105	105	106
Total Deaths	66	72	77	81	86	91	95	99	102	105
Total Deaths-2 [1]	75	81	86	91	96	100	104	108	111	114
Censored PFS (tarextumab)	14	15	15	16	16	16	16	16	16	17
Censored PFS (placebo)	12	12	13	13	13	13	13	13	13	13

[1] Total PFS Events-2 and Total Deaths-2 refer, respectively, to the expected numbers of progressions and deaths when tarextumab does not prolong progression or death.

Figure 1. Enrollment, Progressions and Deaths over Time – Control Hazard of Progression of 0.1386 Beyond 9 months



Calculations in Table 2 and Figure 1 take into account non constant hazards for PFS and OS described in Table 3 and Table 4, respectively. Estimates of non constant hazard are from Kaplan-Meier (KM) curves for PFS and Survival in Noda et al [Ref-2] and Hanna et al [Ref-3]. Regarding enrollment it was initially assumed that there is a ramp up time of 5 months with a starting enrollment of 4 subjects per months and that the maximum enrollment rate is 6 subjects per month. The enrollment in Table 10 and Figure 1 represents the observed enrollment up to January 2016 and the remaining enrollment is assumed to be 15 subjects per month.

The censoring rate was initially assumed to be 40% of the rate at which events occur in the control arm and 60% of the rate at which events occur in the tarextumab arm. When 79 PFS events accrued in the study, there were 39 censored observations for a censoring rate of 39/(39+79)=33%. This information was used to recalibrate the total number of events at the final analysis, the type 1 error rate and power.

Table 3. Hazards for Piece-Wise Exponential Model of Progression Free Survival

Period	0-5 months	5-7 months	7-8 months	>8 months
% Change in Proportion without an event (Change in PFS)	0.50 (1.00 to 0.50)	0.50 (0.50 to 0.25)	0.50 (0.25 to 0.125)	0.50 (0.125 to 0.0625) 8-18 months [1] 8-11 months [2]
Hazard Control	0.1386	0.3466	0.6931	0.0693, 0.2310
Hazard Treatment	0.0901	0.2253	0.4505	0.0451, 0.1502
Hazard Ratio	0.65	0.65	0.65	0.65

[1] Noda et al [Ref-2]
[2] Hanna et al [Ref-3]

Table 4. Hazards for Piece-Wise Exponential Model of Overall Survival

Period	0-5 months	5-7 months	7-8 months	>8 months
% Change in Proportion without an event	0.50 (1.00 to 0.50)	0.50 (0.50 to 0.25)	0.60 (0.25 to 0.10)	0.467 (0.15 to 0.08) 18-24 months [1]
Hazard Control	0.07702	0.1155	0.1703	0.127
Hazard Treatment	0.05006	0.07509	0.1107	0.0825
Hazard Ratio	0.65	0.65	0.65	0.65

[1] Hanna et al [Ref-3]

We see from Table 2 that approximately 70% of the 98 deaths required for the final analysis of survival are expected to be observed at the time of the final analysis for PFS. Table 5 presents the power to detect benefit in OS for several HRs assuming that type 1 error is controlled at the 0.15 level and additional analyses take place at approximately 50%, 67% and 83% of full information. These additional analyses will take place at the quarterly DSMB review meetings. If the actual number of events at the review meetings differs from what is presented in the table, the efficacy and safety boundaries will be recalculated using the spending functions footnoted in Table 5.

Table 5. Overall Survival: Power for the Alternative Hypothesis

	Analysis 1	Analysis 2	Analysis 3	Final Analysis
Total Number of Events	49	66	81	98
Z-Statistic (reject the null) [1]	3.889	3.174	2.333	1.036
P-value (1 sided)	0.000050	0.00075	0.0098	0.15
Z statistic (reject the Alt) [2]	-2.1	-1.848	-1.511	-1.082
P-value (1 sided)	0.018	0.032	0.0658	0.139
Cumulative Type 1 Error (1-sided)	1e-04	8e-04	0.0099	0.1501
Cumulative Power				
HR=0.75	0.0020	0.0226	0.1499	0.6511
HR=0.682	0.0054	0.0530	0.2711	0.8047
HR=0.65	0.0086	0.0777	0.3471	0.8637
HR=0.60	0.0178	0.1365	0. 4869	0.9324
HR=0.50	0.0717	0. 3610	0. 7846	0. 9918
Cumulative Probability of Stopping for Harm				
Alternative	3e-04	5e-04	9e-04	0.0019
Null	0.0179	0.0381	0.0744	0.1501
HR=1.33 (1/0.75)	0.1372	0.2660	0.4332	0.6470

	Analysis 1	Analysis 2	Analysis 3	Final Analysis
HR=1.47 (1/0.682)	0.2235	0.4037	0.6007	0.8000
HR=2.00 (1/0.50)	0.6278	0.8426	0.9496	0.9911

[1] The boundary for rejecting the null hypothesis for efficacy is obtained from the gamma(-16) alpha spending function.
[2] The boundary for rejecting the null hypothesis for harm is obtained from the gamma(-4) alpha spending function.

With 98 deaths at the final analysis, there is 80% power with 0.15 type 1 error to detect a HR of 0.682. There is a 7.4% chance of stopping early for harm under the null hypothesis, a 43.3% chance of stopping early for harm if the HR=1.33 (1/0.75); a 60.1% chance of stopping early for harm if the HR=1.47 (1/0.682); and a 95.0% chance of stopping early for harm if the HR=2.00 (1/0.5).

5. GENERAL ANALYSIS CONSIDERATIONS

The statistical analyses will be reported using summary tables, figures and listings (TFLs). Unless otherwise noted, all statistical testing will be two-sided and will be performed at the 0.05 level of significance.

- Continuous variables will be summarized with the number of non-missing values, estimated means, standard deviations, medians, 25th and 75th percentiles, and observed minimum and maximum values.
- Categorical variables will be summarized by counts and by percentages. The percentage of patients within a category will be displayed in parentheses rounded to the nearest tenth of one percent. However, when the number of patients within a category is 0, then the percentage (i.e., 0.0%) will be omitted.
- Time-to-event variables will be summarized by KM estimates of quartiles, observed minimum and maximum values, and the number of censored observations. The hazard will be estimated by the sum of all individual follow-up times in days divided by 365.25.

Any durations of time expressed in months will be reported in proportional “months” according to the formula

$$\text{months} = \frac{365.25}{12} \text{ days.}$$

Summary tables will be presented by treatment group. Individual subject data will be presented in data listings.

The analyses described in this plan are considered *a priori*, in that they have been defined prior to database lock and prior to breaking the treatment blind. If any *a posteriori* analyses (i.e., analyses not included in this SAP) are performed, they will be identified as such in the CSR where the objective and rationale for executing any *a posteriori* analyses will be documented.

5.1. Analysis Software

In general, data analyses and tabulations will be executed using SAS® version 9.2 or higher. SAS® programing statements will be validated by an independent programmer and SAS® output will undergo a senior-level statistical review to confirm that that all data manipulations and calculations are accurate and statistically valid methods have been implemented. Checks will be made to ensure accuracy and consistency with this plan and within and between TFLs. Upon

completion of validation and quality-review procedures, all documentation will be collected and filed by the project statistician or designee.

5.2. Baseline Values

Unless otherwise noted, baseline is defined as the last non-missing value recorded prior to the first dose of study drug. Therefore, data collected during any unscheduled visits will be used in the determination of baseline values, as applicable.

5.3. Missing Values

No imputations will be made for missing values. Summaries will be based on observed data only.

5.4. Subgroup Analyses

Plans for analyses of subgroups based on the presence or absence of anti-tarextumab antibodies are presented in section 11.7 below.

No analyses by baseline characteristics or study center are planned.

Subgroup analyses by baseline Notch3, Hes1, Hey2, Hey1 and Hes6 expression levels are not planned, but the impact these potentially important covariates have on the efficacy of tarextumab will be assessed through statistical modeling (see sections 8.1, 8.3, 8.6 and 8.7).

5.5. Multiple Comparisons/Multiplicity

A gamma(-12) spending function will be used to control the type-1 error for the assessment of efficacy and a gamma(-4) spending function will be used to control the type-1 error for harm arising from multiple analyses of PFS (see Table 1). The same spending functions will be used to control for multiplicity when testing OS (see Table 5).

6. ANALYSIS DATA SETS

The analysis set for the phase-2 portion of the study will include data from all subjects who were randomized in the phase-2 portion to receive either tarextumab or control. Data from subjects who were enrolled in the phase-1b portion of the study will be excluded from the analysis set.

The planned data cut for the formal final analysis of PFS will take place at the point where 91 PD events have occurred or 10 months after the completion of enrollment, whichever occurs first. However, the actual data cut for the final formal analysis of PFS may be extended beyond 10 months after the completion of enrollment for reasons concerning study conduct (e.g., if patients are randomized but not treated). This will ensure that the study will have 81% power to detect an HR of 0.67 (improvement in median PFS from 4.8 months to 7.2 months) with an associated total one sided type-1 error rate of 0.15 (see section 4).

When the data cut for the formal analysis of PFS is taken, the following rules will be applied to determine which data are included in statistical analyses and data summaries. The goal of these data filtering rules is to ensure that that only certain data records occurring after the cutoff date 01-DEC-2016 are included.

1. No filter will be applied to the Death Report CRF or Follow Up After Discontinuation of Study Treatment CRF.

2. On CRF pages with a start/stop date (such as AE and CM), the data will be kept if either the start or stop date is on or prior to the cut off date. Note: if the start date is on or prior to the cut off, the record will be retained, therefore there may be stop dates that appear in listings that are post the cut off date.
3. If the outcome for an AE is death, the record will be retained even if the death occurred after the cut off date. Note: the record will be kept only for the purpose of preserving the death date (for efficacy analysis). The AE however will not be used in summaries of AEs.
4. In the event a partial date is reported and there is a chance the event/occurrence could be on or prior to the cutoff date, then that record will be kept for analyses and summaries. For instance, a record with a partial date of "2016" would be kept for analysis. Likewise, a record of "DEC-2016" would also be kept since the actual event date could have been 01DEC2016.

An additional data filtering rule specific to analyses of PFS and DOR is that deaths reported on the Death Report CRF and AE CRF where death is reported after the cut off date will not be considered.

Additional data filtering rules specific to analyses of OS are:

1. Death reported on Death Report CRF and AE CRF (end date of AE), regardless of date will be included in OS analyses. That is deaths reported after the cutoff date will not be filtered.
2. If the date of death reported on the Death Report CRF and an AE CRF is not the same, the date of death reported on the Death Report CRF will be used. SynteractHCR will notify the sponsor of the discrepancy.
3. The Follow-Up Discontinuation CRF does not explicitly collect date of death. The form only collects the Date of Survival Assessment and Last Known Survival Date. If a patient's death is reported only on the Follow-Up Discontinuation CRF, then SynteractHCR will notify the sponsor, and the sponsor will advise SynteractHCR how to proceed.

Upon request, a listing of death dates can be generated to show which patients have died and which CRF page was used to acquire the death date.

The planned data cut for the final analysis of OS will be 6 months after the data cut for PFS or when 98 deaths have been observed, whichever occurs first. Once again, the actual data cut for the final formal analysis of OS may be extended beyond 6 months after the PFS data cut for reasons concerning study conduct.

6.1. Analysis Populations

The following five groups of study patients will be used for statistical analyses.

1. The ITT patient population includes all patients randomized to receive study drug regardless of whether they actually received study drug and regardless of whether evidence is found indicating they failed to meet study inclusion/exclusion criteria or had other protocol violations. When the ITT patient population is analyzed, patients are grouped according to

their randomized treatment regardless of actual treatment received. The ITT patient population is the analysis population for demographics and baseline characteristics and for all statistical inference and primary tests of hypotheses related to efficacy endpoints.

2. The safety patient population is the subset of ITT patients who received at least one dose of study drug. When the safety patient population is analyzed, patients are grouped according to actual treatment received. Tarextumab is considered a patient's "treatment received" in the safety patient population if the patient received at least one dose of tarextumab (complete or incomplete dose) any time during the study. The safety patient population is the analysis population for all analyses of safety data.
3. The per-protocol (PP) patient population is the subset of safety patients who either (a) have at least one response evaluation on study, or (b) die prior to their first scheduled response evaluation. When the per-protocol patient population is analyzed, patients are grouped according to actual treatment received. The per-protocol population is used for sensitivity (secondary, supportive) analyses of efficacy endpoints.
4. The pharmacokinetic (PK) patient population is comprised of all subjects who received at least one complete dose of tarextumab and have at least one post-dose PK sample.
5. The immunogenicity patient population is comprised of all subjects who had a baseline and one or more follow-up samples obtained for quantifying anti-tarextumab antibody.

7. SUMMARIES OF PATIENT CHARACTERISTICS

7.1. Subject Disposition

Subject disposition information will be summarized for all subjects by treatment arm. Summaries will include the number of subjects randomized, the number of subjects in each analysis population, the primary reason for stopping each study drug (randomized treatment [tarextumab or placebo], selected platinum therapy [cisplatin or carboplatin] and etoposide), and the primary reason for withdrawing from the study.

The physician's choice of platinum therapy (cisplatin or carboplatin) was used as a stratification variable by the dynamic randomization system. The actual platinum received (as documented on earliest Platinum Therapy Infusion CRF [e.g., Cycle 1, Day 1]) will be summarized in a 2x2 frequency table against the platinum-therapy strata under which a patient was randomized.

7.2. Protocol Deviations

Protocol deviations will be collected and provided by the sponsor. Major protocol deviations that could potentially affect the integrity of efficacy/safety analysis results will be identified prior to database lock and categorized. Major protocol deviations categories may include, but are not limited to enrollment violations, dosing violations, prohibited concomitant therapy violations, and continuation of therapy when treatment should have been discontinued. Major protocol deviations will be summarized by deviation category and treatment group.

7.3. Demographics and Baseline Characteristics

Demographic variables include age, sex, child-bearing potential for females, ethnicity and race. Age will be calculated in years relative to the informed consent date. Baseline characteristics include height, weight, body mass index (BMI), smoking history and Eastern Cooperative

Oncology Group (ECOG) performance status. Descriptive statistics will be presented for age, height and weight; and frequency counts and percentages will be presented for sex, child-bearing potential, ethnicity, race, smoking history (never smoked, ex-smoker, or current smoker) and ECOG performance status. Demographic and baseline characteristics will be summarized for the ITT, safety, PP and immunogenicity populations.

ES-SCLC history, including time since ES-SCLC diagnosis, histological/cytological type (small cell only, mixed type, or other), anatomical location of primary tumor, and number of disease sites (1, 2 or ≥3) at study entry will be summarized by treatment group for the ITT and safety populations. The time from ES-SCLC diagnosis to randomization will be quantified in months according to the formula shown in section 5. Summary statistics for baseline values of total tumor length (abbreviated SLD for sum of longest diameters) will be included in the analyses of efficacy endpoints.

Baseline levels of Notch3, Hes1, Hey2, Hey1 and Hes6 will be summarized as a continuous variable in the ITT, safety and per-protocol populations.

Prior therapies (surgeries and radiotherapies) for ES-SCLC will be summarized for the ITT and safety populations.

Patients' medical and surgical histories will be displayed in a data listing.

8. EFFICACY ENDPOINTS

Primary analyses of efficacy endpoints will use data from the ITT population. Additional efficacy analyses will be performed using data from only the PP population, but these analyses are considered secondary.

Efficacy endpoints include investigator-assessed PFS, assessment of SLD as a continuous variable, ORR defined as the proportion of patients achieving a CR or PR, duration of response (DOR), sites of progression, OS and landmark survival at 180, 360, 540 and 720 days.

As mentioned in section 5 above,

- Continuous variables will be summarized with the number of non-missing values, estimated means, standard deviations, medians, 25th and 75th percentiles, and observed minimum and maximum values.
- Categorical variables will be summarized by counts and by percentages. The percentage of patients within a category will be displayed in parentheses rounded to the nearest tenth of one percent. However, when the number of patients within a category is 0, then the percentage (i.e., 0.0%) will be omitted.
- Time-to-event variables will be summarized by KM estimates of quartiles, observed minimum and maximum values, and the number of censored observations. The hazard will be estimated by the sum of all individual follow-up times in days divided by 365.25.

8.1. Progression-Free Survival

On study tumor assessments are those that meet the following criteria:

1. No gap of >91 days between successive tumor assessments among those on or prior to the on study tumor assessment. (Note: a tumor assessment for which "Not Evaluated" is entered into the database does not qualify as a tumor assessment.)
2. No prior initiation of non-protocol anticancer therapy.

PFS, the primary endpoint of the study, is defined as the time from randomization (Day 1) until the first occurrence of death or disease progression based on investigator assessments of tumor response per the RECIST criteria. Progressions that are not determined from on study tumor assessments as well as deaths occurring more than 49 days from the last on-study tumor assessment are not treated as progression events. Subjects without a progression event will be censored at their last on study tumor assessment.

In addition two special cases will be handled in a manner consistent with the above rules as follows:

1. Patients whose first tumor assessment is >91 days from randomization will be censored on the date of randomization with a PFS of 1 day.
2. Patients who never had an on study tumor assessment and who did not die within 49 days (the scheduled time between tumor assessments plus 7 days) after randomization will be censored on the date of randomization with a PFS of 1 day.

The KM method will be used to estimate the proportions of subjects over time without progression or death and the median progression-free survival time. KM curves will be plotted by treatment group. The 95% confidence intervals for median progression-free survival time will also be calculated for each treatment arm. The p-value for treatment effect will be generated using a stratified log rank test using platinum choice (cisplatin or carboplatin; see page 6) and prior treatment modality (WBRT or PCI) as stratification factors. The HR and its 95% confidence interval will be estimated using a Cox proportional hazards (PH) model with main effects for treatment and the aforementioned stratification factors.

According to the study design, administrations of randomized treatment (tarextumab or placebo only; without EP) may continue in 21-day cycles from the completion of 6 cycles of EP until the initiation of PCI. The following analysis of PFS will be conducted in order to determine if there is a treatment benefit when tarextumab is administered in combination with EP. Subjects who have not progressed will have their PFS censored 35 days (the scheduled time for 1 treatment cycle plus 7 days) following the last dose of Carboplatin/Cisplatin or EP. KM and Cox PH analyses will be the same as those described above.

The impact of the biomarkers Notch3, Hes1, Hey2, Hey1 and Hes6 on PFS will be evaluated with a Cox PH model with treatment, biomarker and treatment-by-biomarker interaction included in the model as independent variables. A separate Cox PH model will be used for each biomarker.

Sensitivity analyses for PFS include replicating the primary log-rank analysis using the PP population and unstratified log-rank tests using the ITT and PP populations.

The planned timing for the primary analysis of PFS is stated in section 5.5 above.

8.2. Total Tumor Length

Total tumor length is the sum of the longest diameters (SLD) for the target lesions as defined by RECIST criteria. Standard summary statistics for a continuous variable (identified in section 5) will be computed for SLD at baseline and the Cycle-3, Day-1 (C3D1) and Cycle-5, Day-1 (C5D1) assessments. Summary statistics will also be presented for changes from baseline at the C3D1 and C5D1 tumor assessments. Ninety-five percent confidence intervals for the mean SLD at each time point will also be computed. Two analysis of covariance (ANCOVA) models for SLD will be used to test the hypothesis that there is no difference between treatment arms with regard to changes in tumor length from baseline at the C3D1 assessment.

- The difference between the follow-up and baseline SLD (e.g., $SLD_{C3D1} - SLD_{baseline}$) will be the dependent variable in the first ANCOVA model. Treatment, platinum choice (cisplatin versus carboplatin) and prior treatment modality (WBRT or PCI) will be categorical factors in the model, and $SLD_{baseline}$ will be included as a continuous covariate.
- The log of the ratio of follow-up to baseline SLD (e.g., log $[SLD_{C3D1}/SLD_{baseline}]$) is the dependent variable in the ANCOVA model. Treatment, platinum choice and prior treatment modality will be categorical factors in the model, and log $SLD_{baseline}$ will be included as a continuous covariate.

Missing values will not be imputed.

Separate but similar analyses will be performed for changes in tumor length from baseline at the C5D1 assessment.

A waterfall plot of best percent change in SLD across all tumor assessments relative to baseline will be presented.

Rates of change in SLD from baseline to C3D1, C5D1 and at progression will be evaluated.

The rate of change in SLD at C*x*D1 is defined as

$$100\left(\frac{SLD_{CxD1} - SLD_{baseline}}{SLD_{baseline}}\right)/d_2$$

where d_2 is the number of days between the baseline assessment (Day 1) and the C*x*D1 assessment.

Rate of change in SLD at C*x*D1 will be missing for subjects who did not have a RECIST assessment corresponding to the C*x*D1 visit.

The rate of change in SLD from its on-study nadir to progression is defined as

$$100\left(\frac{SLD_{progression} - SLD_{nadir}}{SLD_{nadir}}\right)/d_1$$

where d_1 is the number of days between the on-study SLD nadir and progression.

Rate of change in SLD at progression will be missing for subjects who did not have a RECIST assessment of PD on study and for subjects whose on-study $SLD_{nadir} = 0$.

Comparisons of these rates of change between the two treatment arms will be made using an analysis of variance (ANOVA) model with treatment, platinum choice (cisplatin versus carboplatin) and prior treatment modality (WBRT or PCI) as categorical independent variables.

8.3. Overall Response Rate

A patient's best overall response is defined as the best investigator-assessed RECIST response to treatment category recorded since the start of the treatment. The hierarchy of response ratings, best to worst, is CR, PR, SD, PD, followed by NE. The numbers and percentages of subjects achieving each of these response categories will be summarized within treatment group.

The ORR, defined as the proportion of patients achieving a CR or PR, and its 95% confidence interval will be computed within treatment group. The p-value for equality between treatment groups will be calculated for the two groups using a logistic regression model including treatment, platinum choice (cisplatin versus carboplatin) and prior treatment modality (WBRT or PCI) as categorical independent variables. Patients without any post-baseline tumor assessments will be classified among those never achieving a CR or PR.

The impact of the biomarkers Notch3, Hes1, Hey2, Hey1 and Hes6 on ORR will be evaluated with a logistic regression model with treatment, biomarker and treatment-by-biomarker interaction included in the model as independent variables. A separate logistic regression model will be used for each biomarker.

8.4. Duration of Response

Analyses of DOR include only patients who achieved a CR or PR; patients failing to achieve a CR or PR during the study are omitted from analyses of DOR. If the number of patients achieving a CR or PR is not sufficient to produce meaningful KM curves, then the planned analyses for DOR may be abandoned.

DOR is defined as the number of days from the first CR or PR until the first occurrence of death or disease progression based on investigator assessments of tumor response per the RECIST criteria. Progressions that are not determined from on study tumor assessments as well as deaths occurring more than 49 days from the last on-study tumor assessment are not treated as progression events. Subjects achieving a CR/PR but without a subsequent progression event will be censored at their last on study tumor assessment.

In addition two special cases will be handled in a manner consistent with the above rules as follows:

1. Patients whose next tumor assessment (following the first CR/PR) is >91 days after the first CR/PR will be censored on the date of the first CR/PR with a DOR of 1 day.
2. Patients who never had an on study tumor assessment after the first CR/PR and who did not die within 49 days (the scheduled time between tumor assessments plus 7 days) after the first CR/PR will be censored on the date of first CR/PR with a DOR of 1 day.

The KM method will be used to estimate the proportions of CR/PR patients over time who have not experienced RECIST disease progression and the median DOR. KM curves will be plotted and 95% confidence intervals for median DOR will also be calculated for each treatment arm. The HR, its 95% confidence interval and the p-value for testing the statistical significance of the

treatment effect will be generated using a Cox PH model with main effects for treatment, platinum choice (cisplatin versus carboplatin) and prior treatment modality (WBRT or PCI).

8.5. Sites of Progression

Sites of progression will be categorized as stemming from (1) a new lesion or (2) progression of an existing lesion. Treatment-group distributions based on this binomial categorization will be tested using a chi-square test. Then "new lesions" will be further categorized by anatomical site. Patients with new lesions at multiple anatomical locations will be classified as a single category. The resulting multinomial distributions will also be compared across treatment groups using a chi-square test.

8.6. Overall Survival

OS is defined as the number of days from randomization (Day 1) until death. The following rules will be used to define censored observations and censoring times for OS.

1. A patient for whom no death date is reported will have OS censored on the last contact date (defined on page 6). When evaluating the last contact date using the 'Follow-Up After Discontinuation of Study Treatment' CRF, both of the 'date of survival assessment' (if checked 'alive' for 'subject status') and the 'last known survival date' (if checked 'alive or 'lost to follow-up' for 'subject status) will be considered.
2. Patients lacking data after randomization who do not die have their event time censored on the date of randomization with duration of 1 day.
3. All patients alive on the date of the 98th sequential patient death will have their OS censored on the day following the date on which the 98th patient died. All patient deaths will be counted towards the total of 98, independent of which treatment arm the deceased patients were randomized to.

The KM method will be used to estimate survival proportions over time. KM survival curves will be plotted and 95% confidence intervals for median OS will also be calculated for each treatment arm. The HR, its 95% confidence interval and the p-value for testing the statistical significance of the treatment effect will be generated using a Cox PH model with main effects for treatment, platinum choice (cisplatin versus carboplatin) and prior treatment modality (WBRT or PCI).

OS will also be analyzed separately for two subsets of ITT patients defined by platinum choice (cisplatin or carboplatin). In this case, the p-value for testing the statistical significance of the treatment effect will be generated using a Cox PH model with main effects for treatment and prior treatment modality only.

The impact of the biomarkers Notch3, Hes1, Hey2, Hey1 and Hes6 on OS will be evaluated with a Cox PH model with treatment, biomarker and treatment-by-biomarker interaction included in the model as independent variables. A separate Cox PH model will be used for each biomarker.

The planned timing for the primary analysis of OS is stated in section 5.5 above.

8.7. Landmark Survival

KM estimates of OS at 180, 360, 540 and 720 days will be summarized. Comparisons between the two treatment groups will be made using independent Z tests.

9. EXPLORATORY ANALYSES

An exploratory analysis was undertaken by the sponsor using blinded data to examine the relationship between PFS and the Notch pathway markers HES1, HES6 and NOTCH3. The biomarker values were normalized so that the distributions had mean 0 and variance 1, then a Cox PH model was fit using the three main effects, the three two-way interactions, and the three-way interaction as independent variables. Estimated coefficients are show in Table 6.

Table 6. Cox PH Model between Progression-Free Survival and Three Biomarkers

Independent Variable	Estimated Coefficient	Exponentiated Coefficient	Standard Error	Z-Score	P-Value
HES6	0.17396	1.190	0.192	0.9059	0.3700
HES1	0.00154	1.002	0.134	0.0115	0.9900
NOTCH3	0.01248	1.013	0.189	0.0660	0.9500
HES6*HES1	0.68087	1.976	0.241	2.8300	0.0047
HES6*NOTCH3	–0.56935	0.566	0.247	–2.3021	0.0210
HES1*NOTCH3	0.15654	1.169	0.191	0.8215	0.4100
HES6* HES1*NOTCH3	1.07604	2.933	0.357	3.0175	0.0025

Model notes: n=89 (56 observations deleted due to missing values); number of events=58; Likelihood ratio test=16.3 (7 degrees of freedom); p=0.0222

Judging statistical significance at the two-sided 0.05 level, the two statistically significant terms which included NOTCH3 were used to establish a NOTCH-3-ralated PFS index (N3RPI).

$$\text{N3RPI} = -0.569*\text{HES6}*\text{NOTCH3} + 1.076*\text{HES1}*\text{HES6}*\text{NOTCH3}$$

Patients were then split into two groups (High N3RPI or Low N3RPI) based on whether their score was above or below the median N3RPI (0.066), respectively. A patient whose N3RPI was equal to the median was placed into the Low N3RPI group. Patients in each of these two groups were then split into two additional groups (High NOTCH3 or Low NOTCH3) based on whether their score was above or below the overall median NOTCH3 value (–0.046), respectively. A patient whose NOTCH3 was equal to the median was placed into the Low NOTCH3 group.

The KM curves for PFS and for OS in these four subgroups are presented in Figure 2 and Figure 3, respectively. For patients with an N3RPI above the median N3RPI (i.e., High N3RPI), the difference in PFS between the High and Low NOTCH3 groups is associated with a p-value of 0.09.

Figure 2. Progression-Free Survival Kaplan-Meier Curves for Patients with High and Low N3RPI

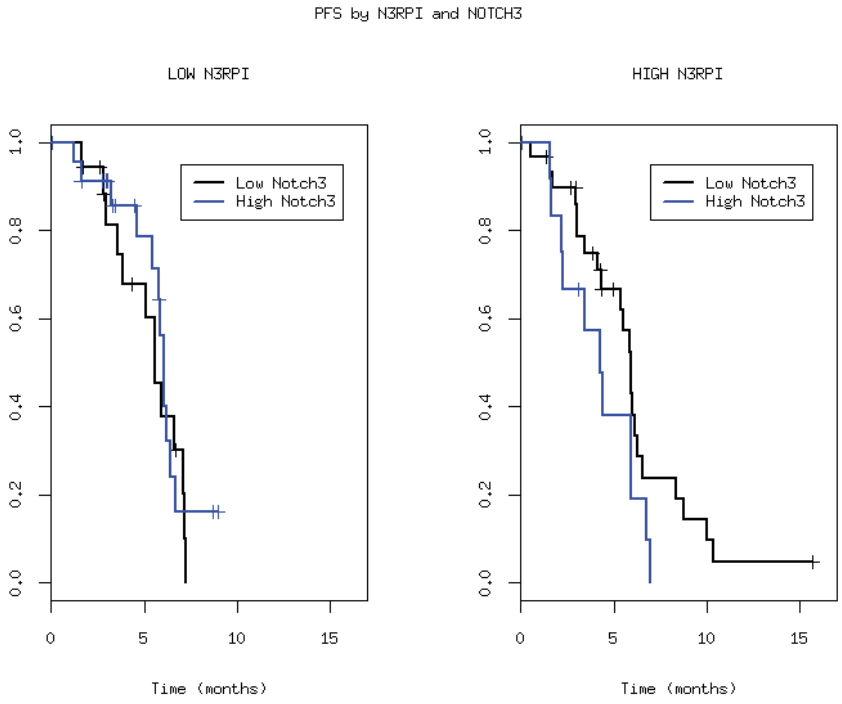
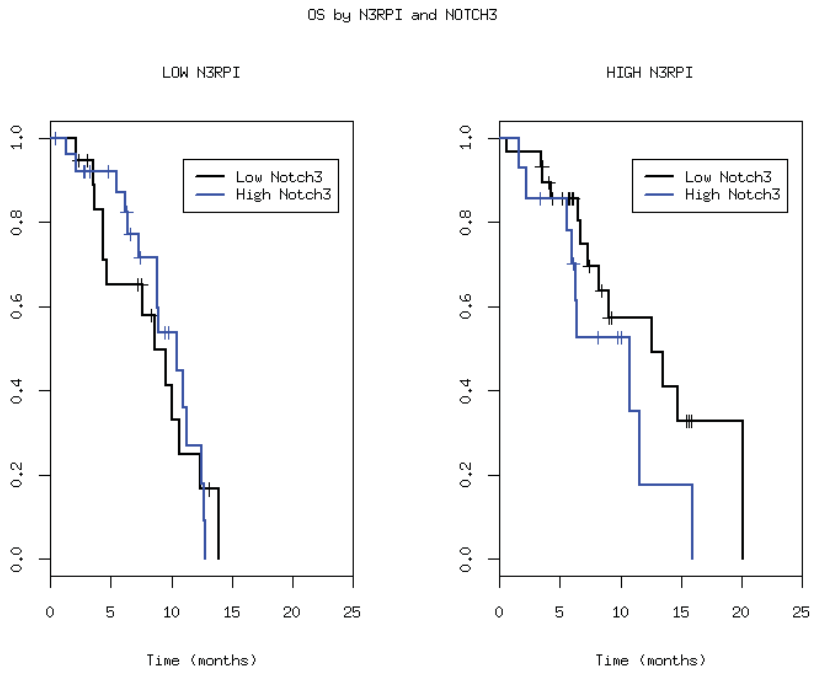


Figure 3. Overall Survival Kaplan-Meier Curves for Patients with High and Low N3RPI



It is noteworthy that high NOTCH3 is trending to be beneficial for patients with low N3RPI, whereas high NOTCH3 appears to be detrimental when N3RPI is high. This prompted the exploratory hypothesis that NOTCH 3 inhibition with tarextumab will improve PFS and OS in patients who have high N3RPI. In the case where N3RPI is high, tarextumab may be able to reduce the detrimental effects associated with high Notch 3 expression.

The following exploratory analyses will be carried out to test this hypothesis. The analysis population (ITT or per-protocol) will be divided into two N3RPI groups: High N3RPI and Low N3RPI (as defined above). Independent Cox PH models will be fit to data from each of the two groups. The models will include effects for treatment (tarextumab or placebo), NOTCH3 value, and the interaction between treatment and NOTCH3. The treatment HR and a 95% CI for the HR will be estimated at the quartiles of the NOTCH3 distribution. The same analysis will be carried out for “high” and “low” patient subgroups based on each of the biomarkers (Hes1, Hes6, Hey1 and Hey2).

10. PHARMACOKINETIC ENDPOINTS

Investigating the PK of tarextumab in combination with EP is an objective of this study, but a detailed analysis plan is outside the scope of this document. Therefore, no PK analyses are discussed here.

11. SAFETY ENDPOINTS

Analyses of safety endpoints will use data from the safety population. Safety endpoints listed in the study protocol include adverse events (AEs), serious adverse events (SAEs), clinical laboratory parameters, and results from testing for anti-tarextumab antibodies. Other safety endpoints include vital signs and electrocardiogram (ECG) results.

11.1. Treatment Cycles and Dosing

Dosing with tarextumab (or placebo), etoposide and EP will be summarized by the number of cycles of treatment administered (duration of treatment), the number of doses of each study medication, and the extent of exposure to each study medication. Placebo exposure will be summarized in tarextumab-equivalent units, that is, by the number of milligrams of tarextumab the placebo "replaced" during treatment-blinded dosing.

Body surface area (BSA) is determined for each visit. The latest assessment of BSA on or before each visit will be used to determine the protocol-specified amount of drug (mg) in a dose.

11.1.1. Dose Intensity

Dose intensity is defined as the total dose a patient actually received divided by the total dose the patient should have received had there been no missed doses, dosing delays or dosage reductions.

$$\text{Dose intensity} = \frac{\text{Total amount of drug received (mg)}}{\text{protocol-specified, planned amount of drug (mg)}}$$

The actual amount of drug received is obtained from the dosing records.

The protocol specified amount of drug to be received for each treatment is provided below.

Etoposide

The number of doses of Etoposide that should be administered per protocol is

$$3 \cdot floor\left(\frac{Stop - Start}{21}\right) + h_{Etop}\left[\frac{Stop - Start}{21} - floor\left(\frac{Stop - Start}{21}\right)\right],$$

where

$$h_{Etop}(x) = \begin{cases} 1 \text{ if } 21 \cdot \mathrm{x} \geq 0 \\ 2 \text{ if } 21 \cdot \mathrm{x} \geq 1 \\ 3 \text{ if } 21 \cdot \mathrm{x} \geq 2 \end{cases}$$

Start is the date of the first dose of treatment. Stop is the last dose of treatment.

The amount of drug contained in a dose of Etoposide is

$$100 mg / m^2 \cdot \mathrm{BSA}$$

Carboplatin/Cisplatin/Study Drug

The number of doses of Carboplatin, Cisplatin or Study Drug that should be administered per protocol is

$$1 \cdot floor\left(\frac{Stop - Start}{21}\right) + h\left[\frac{Stop - Start}{21} - floor\left(\frac{Stop - Start}{21}\right)\right],$$

where

$$h\ (x) = \{1 \text{ if } 21 \cdot \mathrm{x} \geq 0$$

Start is the date of the first dose of treatment and Stop is the last dose of treatment for the respective drugs. Treatment period is (last treatment date – first treatment date + 2), allowing 2 extra days to cover any following early visits.

The mg amount of drug contained in a dose of Carboplatin is

$$(\text{AUC of } 5) \times (GFR + 25)$$

The mg amount of drug contained in a dose of Cisplatin is

$$80mg / m^2 \times BSA$$

The amount of drug contained in a dose of study drug is

$$15mg / kg \cdot \text{weight}$$

Weight, BSA and GFR are to be determined at each visit. Use the latest weight, BSA and/or GFR on or before each dose to determine the amount of drug (mg) in a dose.

11.1.2. Dosing Compliance

Dosing compliance is defined as the ratio of the number of doses administered to the number of doses planned according to the schedule outlined in the study protocol.

$$\text{Dosing compliance} = \frac{N_{administered}}{N_{planned}} \times 100\%$$

where $N_{planned}$ is the number of doses planned according to the schedule outlined in the study protocol and $N_{administered}$ is the number of doses the patient received.

Dosing compliance will be summarized as a continuous variable (see Section 5) and by the numbers of patients with 0% to <20%; 20% to <40%; 40% to <60%; 60% to <80%; 80% to <100%; and 100% compliance. The reasons for delaying and/or withholding doses randomized study drug, selected platinum agent and etoposide will also be summarized.

11.2. Adverse Events

Reported AE terms will be mapped to preferred terminology using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1. All reported events will appear in AE listings, however only treatment-emergent adverse events will be summarized. A treatment-emergent adverse event (TEAE) is an AE that starts or increases in severity any time after the first administration of any randomized study drug (i.e., tarextumab or placebo) up to 30 days following the last administration of any study drug. AE severity was rated by the investigator according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 criteria.

A high-level safety summary will display the numbers of patients within each treatment arm who experience one or more AEs in each of the following categories:

- All TEAEs regardless of severity or presumed relationship to study drug
- TEAEs judged related to tarextumab/placebo
- TEAEs judged related to etoposide
- TEAEs judged related to platinum therapy (cisplatin or carboplatin)
- TEAEs judged related to any study drug
- Treatment-emergent SAEs regardless of severity or presumed relationship to study drug
- Treatment-emergent SAEs judged related to tarextumab
- Treatment-emergent SAEs judged related to EP
- Treatment-emergent SAEs judged related to any study drug
- TEAEs leading to a delay/interruption in the administration of study drug
- TEAEs leading to a reduction in the protocol-specified dose of study drug
- TEAEs leading to discontinuation of study drug
- TEAEs leading to withdrawal from the study
- TEAEs leading to death

The base summary of TEAEs will show treatment-arm incidence rates for each MedDRA primary system organ class (SOC) and/or preferred term (PT) sorted by descending incidence in the tarextumab treatment group. A separate summary will be produced for each of the AE subsets listed above. Additional summaries will be produced by CTCAE severity grade. Patients may have more than one TEAE per MedDRA SOC and/or PT. At each level of summarization, a patient is counted once if he or she reported one or more TEAEs at that level. In AE summaries by CTCAE severity grade, patients will be classified according to the highest reported CTCAE severity for a qualifying event.

11.3. Clinical Laboratory Parameters

Clinical laboratory results (serum chemistry, hematology, coagulation and urinalysis) will be valued using conventional units of measurement and summarized by treatment group using descriptive statistics for baseline, maximum post baseline, minimum post baseline, and last observed values. Changes from baseline will also be summarized. All clinical laboratory results will be listed by patient.

The numbers of patients shifting from a ‘low’ or ‘normal’ test result at baseline to ‘high’ result at any post-baseline assessment will be summarized, as will the numbers of patients shifting from a ‘normal’ or ‘high’ result at baseline to ‘low’ result post baseline. Laboratory parameters with a CTCAE grading scale will be summarized in Range Change Abnormal (RCA) tables which categorize patients according to (1) their most extreme post-baseline severity grade, and (2) the severity grade at their last post-baseline evaluation. Parameters with a CTCAE grading scale for high values and a second scale for low values will be summarized in both directions. Some

urinalysis parameters with categorical outcomes will be summarized with the numbers of patients shifting from normal at baseline (e.g., negative or absent) to an abnormal result post baseline (e.g., positive or present).

11.4. Vital Signs

Vital signs (systolic and diastolic blood pressures, pulse, body temperature and respiration rate) will be summarized by treatment group using descriptive statistics for baseline, maximum post baseline, minimum post baseline, and last observed values. Changes from baseline will also be summarized. All vital signs will be listed by patient.

The numbers of patients with a result above the normal range at any post-baseline assessment will be summarized, as will the numbers of patients with a result below the normal range at any post-baseline visit. Normal ranges are:

- Systolic blood pressure: 90-120 mm Hg
- Diastolic blood pressure: 60-80 mm Hg
- Pulse rate: 60-100 beats/minute
- Body temperature: 97.8-99.1 °F
- Respiratory rate: 12-18 breaths/minute

11.5. Electrocardiogram Results

ECG results (QRS duration, PR interval and QTc Interval) will be summarized by treatment group using descriptive statistics for baseline, maximum post baseline, minimum post baseline, and last observed values. Changes from baseline will also be summarized. All ECG results will be listed by patient.

The numbers of patients with a result above the normal range at any post-baseline assessment will be summarized, as will the numbers of patients with a result below the normal range at any post-baseline visit. Normal ranges are:

- QRS duration: 80-100 msec
- PR interval: 120-200 msec
- QTc interval (Bazett or Fridericia formula): ≤430 msec for males; ≤450 msec for females

The numbers of QTc values in the ranges <480 msec; 480-500 msec; and >500 msec will be presented for the categories baseline, worst (maximum) post-baseline assessment, and last post-baseline assessment.

The overall clinical interpretation of each ECG acquisition will be classified on the ordinal scale normal, abnormal but not clinically significant, and abnormal with clinical significance. Overall clinical interpretation will then be summarized (1) for the categories baseline, worst (maximum) post-baseline assessment, and last post-baseline assessment and (2) in a shift table pairing the baseline and most extreme post-baseline classifications.

11.6. ECOG Performance Status

ECOG performance status will be summarized (1) for the categories baseline, minimum post-baseline value, maximum post-baseline value, and last post-baseline value and (2) in a shift table pairing the baseline assessment and most extreme post-baseline values.

11.7. Immunogenicity

The incidence of anti-tarextumab antibody development in the tarextumab treatment group will be summarized with counts and proportions. In addition, the impact of detectable anti-tarextumab antibodies and neutralizing anti-tarextumab antibodies on the efficacy of tarextumab will be assessed by summarizing PFS and OS in the subgroups of patients with and without these anti-tarextumab antibodies. The impact of detectable anti-tarextumab antibodies and neutralizing anti-tarextumab antibodies on the safety of tarextumab will be assessed by comparing AE incidence rates in the subgroups of patients with and without these anti-tarextumab antibodies. However, these subgroup analyses may not be carried out if the number of subjects with or without anti-tarextumab antibodies does not provide reasonable estimates of PFS and ORR.

11.8. Prior and Concomitant Medications

Medications recorded on case report forms will be mapped to Anatomical/Therapeutic/Chemical (ATC) classes and preferred names in the World Health Organization (WHO) Drug Dictionary Enhanced (version March 1, 2014).

Prior and concomitant medications will be summarized for each treatment group by WHO ATC class and preferred name. Patients may have used more than one prior/concomitant medication per ATC class and preferred name. At each level of summarization, a patient is counted once if he or she reported one or more medications at that level. Summaries will be ordered by descending order of incidence of ATC class and preferred name within each ATC class. All prior and concomitant medications will be listed by patient.

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APPENDIX B. TABLE SHELLS

Table 14.1.1.1
Subject Disposition
All Subjects

	Placebo	Tarextumab	Total
Subjects Randomized	xx	xx	xx
ITT Population[1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Per-Protocol Population[2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Safety Population[3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Immunogenicity Population[4]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pharmacokinetic Population[5]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects Discontinued	xx	xx	xx
Primary Reason for Study Exit			
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-Up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study Terminated by OncoMed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal by Subject	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Primary Reason for Discontinuing Study Drug [6]			
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-Up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Disease Progression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study Terminated by OncoMed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal of Consent / Patient Decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Investigator Decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: Denominators are based on the ITT population.
[1] ITT = Intent-to-Treat. ITT population is comprised of all randomized subjects.
[2] All randomized subjects who received at least one dose of study drug and had at least one post baseline tumor assessment.
[3] All subjects who received at least one partial dose of tarextumab or placebo.
[4] All subjects who had a baseline and at least one follow-up anti-tarextumab antibody sample obtained.
[5] All subjects who received at least one dose of study drug and had at least one post-dose PK sample.
[6] Study drug is Placebo or Tarextumab.
[7] Platinum therapy is cisplatin or carboplatin.

Programmer Notes: (a) add additional set of rows for (i) "Primary Reason for Discontinuing Etoposide" and (ii) "Primary Reason for Discontinuing Platinum Therapy [7]"

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Table 14.1.1.2
Platinum Therapy Randomization Strata Versus Actual Platinum Therapy Received
ITT Population

	Actual Platinum Therapy Received					
	Placebo (N=xx)		Tarextumab (N=xx)		Total (N=xx)	
	Cisplatin	Carboplatin	Cisplatin	Carboplatin	Cisplatin	Carboplatin
Platinum Therapy Randomization Strata						
Cisplatin	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Carboplatin	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 14.1.2.1
Major Protocol Deviations
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)	Total (N=xx)
Any Major Protocol Deviations [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Deviation Category 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Deviation Category 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Deviation Category 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc.	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] Subjects may be included in more than one protocol deviation category.

Programmer note: the actual categories of Major Protocol Deviation will be according to the external protocol deviation file received.

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Table 14.1.3.1
Demographic Characteristics
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)	Total (N=xx)
Age (years) [1]			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
25th, 75th Percentile	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Sex			
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Child Bearing Potential [2]			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity			
Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race			
American Indian or Alaska Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Multiple Races Checked	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] Age on consent date.
[2] For females only.

Programmer notes: (a) percentages under Child Bearing Potential are percentages of female subjects, (b) repeat this table using the safety, per-protocol and immunogenicity populations (c) remove 'Multiple Races Checked' row if all tables have zero count for total.

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59R5-003 (Phase 2)

Table 14.1.3.5
Baseline Characteristics
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)	Total (N=xx)
Height (cm)			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
25th, 75th Percentile	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Weight (kg)			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
25th, 75th Percentile	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Body Mass Index (kg/m^2) [1]			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
25th, 75th Percentile	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
ECOG Performance Status			
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Smoking History			
Never Smoked	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ex Smoker	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Current Smoker	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] BMI (kg/m^2) = weight (kg) / [height (cm)]^2.

Programmer notes: (a) repeat this table using the safety, per-protocol and immunogenicity populations

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Table 14.1.3.9
Small Cell Lung Cancer Disease Characteristics
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)	Total (N=xx)
Months Since Diagnosis [1]			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
25th, 75th Percentile	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Histological/Cytological Type			
Small Cell Only	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mixed Type	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Anatomical Location of Primary Cancer [1]			
Right Upper Lung	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Right Lower Lung	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Middle of Right Lung	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Left Upper Lung	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of Sites of Disease at Study Entry			
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
≥3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sites of Disease at Study Entry [2]			
Bone	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Brain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pleura	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Adrenal Gland	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lymph Nodes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other Nodes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] Months since diagnosis to the date of randomization.
[2] Subjects may be included in more than one category. Therefore percentages may add to more than 100%.

Programmer notes: (a) repeat this table using the safety population

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59R5-003 (Phase 2)

Table 14.1.3.11
Prior Therapies for Small Cell Lung Cancer
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)	Total (N=xx)
Prior Surgery for Lung Cancer			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Prior Radiotherapy for Lung Cancer			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Programmer notes: (a) repeat this table using the safety population

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Table 14.1.3.13
Baseline Gene Expression
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)	Total (N=xx)
Notch3 Expression			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
25th, 75th Percentile	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Hes1 Expression			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
25th, 75th Percentile	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Hey1 Expression			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
25th, 75th Percentile	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx

Programmer notes: (a) add additional rows for Hey2 Expression and Hes6 Expression, (b) repeat this table using the safety and per-protocol populations

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Table 14.1.3.16
Prior and Concomitant Medications
Safety Population

ATC Class [1] Preferred Name	Placebo (N=xx)	Tarextumab (N=xx)
Subjects Receiving any Prior or Concomitant Medications	xx (xx.x%)	xx (xx.x%)
ATC Class 1		
Preferred Name 1.1	xx (xx.x%)	xx (xx.x%)
Preferred Name 1.2	xx (xx.x%)	xx (xx.x%)
Preferred Name 1.3	xx (xx.x%)	xx (xx.x%)
ATC Class 2		
Preferred Name 2.1	xx (xx.x%)	xx (xx.x%)
Preferred Name 2.2	xx (xx.x%)	xx (xx.x%)
Preferred Name 2.3	xx (xx.x%)	xx (xx.x%)
ATC Class 3		
Preferred Name 3.1	xx (xx.x%)	xx (xx.x%)
Preferred Name 3.2	xx (xx.x%)	xx (xx.x%)
Preferred Name 3.3	xx (xx.x%)	xx (xx.x%)

Note: At each level of summation (overall, ATC class and preferred name), subjects reporting more than one medication are counted only once.

[1] ATC Class and Preferred Name are coded according to the WHO Drug Dictionary Enhanced (version March 1, 2014).

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.2.1.1
Overall Survival
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)
Total Follow-Up Time (person-years) [1]	xxx.x	xxx.x
Number of Subjects who Died	xx (xx.x%)	xx (xx.x%)
Number of Subjects who did not Die (Censored)	xx (xx.x%)	xx (xx.x%)
Hazard [2]	0.xx	0.xx
Kaplan-Meier Estimates: Quartiles [95% C.I.] (days)		
25th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
50th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
75th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
Kaplan-Meier Estimate (# at risk) [SE]		
180 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
360 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
540 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
720 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
Range (Subjects who Died) (days)	xxx, xxx	xxx, xxx
Range (All Subjects) (days)	xxx, xxx	xxx, xxx
Hazard Ratio [95% C.I.] [3]		x.xx [x.xx,x.xx]
P-value [3]		0.xxx

Note: Overall Survival = Date of Documentation of Death – Randomization Date + 1. Subjects who had not experienced death by their last contact date were censored at that time. Subjects lacking data after randomization who do not die have their event time censored on the date of randomization with duration of 1 day. For detailed event and censoring rules, refer to protocol section 13.5.4 and SAP section 8.6. C.I. = Confidence Interval. SE = Standard Error.
[1] Sum of all individual follow-up times in days divided by 365.25.
[2] Number of deaths / total follow-up time.
[3] Hazard ratio, 95% C.I. and p-value from Cox proportional hazards model with main effects for treatment, platinum choice and prior treatment modality.

Programmer notes: (a) repeat this table using the per-protocol population

Table 14.2.1.3
Overall Survival for Subjects Receiving Cisplatin
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)
Platinum Choice [1]		
Cisplatin	xx (xx.x%)	xx (xx.x%)
Carboplatin	xx (xx.x%)	xx (xx.x%)
Total Follow-Up Time (person-years) [2]	xxx.x	xxx.x
Number of Subjects who Died	xx (xx.x%)	xx (xx.x%)
Number of Subjects who did not Die (Censored)	xx (xx.x%)	xx (xx.x%)
Hazard [3]	0.xx	0.xx
Kaplan-Meier Estimates: Quartiles [95% C.I.] (days)		
25th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
50th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
75th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
Kaplan-Meier Estimate (# at risk) [SE]		
180 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
360 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
40 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
720 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
Range (Subjects who Died) (days)	xxx, xxx	xxx, xxx
Range (All Subjects) (days)	xxx, xxx	xxx, xxx
Hazard Ratio [95% C.I.] [4]		x.xx [x.xx,x.xx]
P-value [4]		0.xxx

Note: Overall Survival = Date of Documentation of Death – Randomization Date + 1. Subjects who had not experienced death by their last contact date were censored at that time. Subjects lacking data after randomization who do not die have their event time censored on the date of randomization with duration of 1 day. For detailed event and censoring rules, refer to protocol section 13.5.4 and SAP section 8.6. C.I. = Confidence Interval. SE = Standard Error.

[1] Analyses presented in this table include only subjects who received cisplatin. Percentages below the first set of rows are based on subjects who received cisplatin.

[2] Sum of all individual follow-up times in days divided by 365.25.

[3] Number of deaths / total follow-up time.

[4] Hazard ratio, 95% C.I. and p-value from Cox proportional hazards model with main effects for treatment and prior treatment modality.

Programmer notes: (a) repeat this table using the per-protocol population

OncoMed Pharmaceuticals, Inc.
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Table 14.2.1.5
Overall Survival for Subjects Receiving Carboplatin
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)
Platinum Choice [1]		
Cisplatin	xx (xx.x%)	xx (xx.x%)
Carboplatin	xx (xx.x%)	xx (xx.x%)
Total Follow-Up Time (person-years) [2]	xxx.x	xxx.x
Number of Subjects who Died	xx (xx.x%)	xx (xx.x%)
Number of Subjects who did not Die (Censored)	xx (xx.x%)	xx (xx.x%)
Hazard [3]	0.xx	0.xx
Kaplan-Meier Estimates: Quartiles [95% C.I.] (days)		
25th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
50th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
75th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
Kaplan-Meier Estimate (# at risk) [SE]		
180 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
360 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
540 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
720 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
Range (Subjects who Died) (days)	xxx, xxx	xxx, xxx
Range (All Subjects) (days)	xxx, xxx	xxx, xxx
Hazard Ratio [95% C.I.] [4]		x.xx [x.xx,x.xx]
P-value [4]		0.xxx

Note: Overall Survival = Date of Documentation of Death – Randomization Date + 1. Subjects who had not experienced death by their last contact date were censored at that time. Subjects lacking data after randomization who do not die have their event time censored on the date of randomization with duration of 1 day. For detailed event and censoring rules, refer to protocol section 13.5.4 and SAP section 8.6. C.I. = Confidence Interval. SE = Standard Error.
[1] Analyses presented in this table include only subjects who received carboplatin. Percentages below the first set of rows are based on subjects who received carboplatin.
[2] Sum of all individual follow-up times in days divided by 365.25.
[3] Number of deaths / total follow-up time.
[4] Hazard ratio, 95% C.I. and p-value from Cox proportional hazards model with main effects for treatment and prior treatment modality.

Programmer notes: (a) repeat this table using the per-protocol population

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Table 14.2.1.7
Overall Survival – Impact of Biomarker Expression
ITT Population

	Model Coefficients (SE) [1]		Hazard Ratio [95% Confidence Interval] [1]		
Biomarker	Treatment	Treatment x Biomarker Interaction	At 25th Percentile	At 50th Percentile	At 75th Percentile
Notch3	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes1	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey2	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey1	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes6	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]

[1] Coefficients, hazard ratios and 95% confidence intervals are from Cox proportional hazards models with effects for treatment, biomarker and treatment-by-biomarker interaction. A separate model was used for each biomarker.

Programmer notes: (a) repeat this table using the per-protocol population

Table 14.2.1.9
Overall Survival – Impact of Notch3 Expression in Subjects with High/Low Notch Pathway Markers
ITT Population

			Model Coefficients (SE) [1]		Hazard Ratio [95% Confidence Interval] [1]		
Biomarker	Biomarker Level	n	Treatment	Treatment x Notch3	At Notch3 25th Percentile	At Notch3 50th Percentile	At Notch3 75th Percentile
N3RPI [2]	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes1	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey2	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey1	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes6	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]

[1] Coefficients, hazard ratios and 95% confidence intervals are from Cox proportional hazards models with effects for treatment, Notch3 and treatment-by-Notch3 interaction. A separate model was used for each biomarker.
[2] N3RPI is the Notch3-related PFS Index; N3RPI = –0.569*HES6*NOTCH3 +1.076*HES1*HES6*NOTCH3

Programmer notes: (a) repeat this table using the per-protocol population

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.2.2.1
Progression-Free Survival – Primary Analysis
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)
Total Follow-Up Time (person-years) [1]	xxx.x	xxx.x
Number of Subjects with Disease Progression or Death	xx (xx.x%)	xx (xx.x%)
Number of Subjects who did not Progress or Die (Censored)	xx (xx.x%)	xx (xx.x%)
Hazard [2]	0.xx	0.xx
Kaplan-Meier Estimates: Quartiles [95% C.I.] (days)		
25th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
50th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
75th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
Range (Subjects who Progressed or Died) (days)	xxx, xxx	xxx, xxx
Range (All Subjects) (days)	xxx, xxx	xxx, xxx
Hazard Ratio [95% C.I.] [3]		x.xx [x.xx,x.xx]
P-value [4]		0.xxx

Note: PFS= Date of Documentation of Death/Progression – Randomization Date + 1. Subjects who had not experienced death or progression by their last contact were censored at the time of their last radiographic response assessment. Subjects lacking a radiographic response assessment after randomization who do not progress or die have their event time censored on the date of randomization with duration of 1 day. For detailed event and censoring rules refer to protocol section 13.5.1 and SAP section 8.1. C.I. = Confidence Interval.
[1] Sum of all individual follow-up times in days divided by 365.25.
[2] Number of Subjects with Disease Progression or Death/ Total Follow-up Time (Person-years).
[3] Hazard ratio and 95% C.I. from Cox proportional hazards model with main effects for treatment, platinum choice and prior treatment modality.
[4] P-value for treatment effect from stratified log rank test using platinum choice and prior treatment modality as stratification factors.

Programmer notes: (a) repeat this table using the per-protocol population

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.2.2.3
Progression-Free Survival During Combination Chemotherapy
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)
Total Follow-Up Time (person-years) [1]	xxx.x	xxx.x
Number of Subjects with Disease Progression or Death	xx (xx.x%)	xx (xx.x%)
Number of Subjects who did not Progress or Die (Censored) [2]	xx (xx.x%)	xx (xx.x%)
Hazard [3]	0.xx	0.xx
Kaplan-Meier Estimates: Quartiles [95% C.I.] (days)		
25th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
50th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
75th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
Range (Subjects who Progressed or Died) (days)	xxx, xxx	xxx, xxx
Range (All Subjects) (days)	xxx, xxx	xxx, xxx
Hazard Ratio [95% C.I.] [4]		x.xx [x.xx,x.xx]
P-value [5]		0.xxx

Note: PFS= Date of Documentation of Death/Progression – Randomization Date + 1. Subjects who had not experienced death or progression by their last contact were censored at the time of their last radiographic response assessment. Subjects lacking a radiographic response assessment after randomization who do not progress or die have their event time censored on the date of randomization with duration of 1 day. For detailed event and censoring rules refer to protocol section 13.5.1 and SAP section 8.1. C.I. = Confidence Interval.
[1] Sum of all individual follow-up times in days divided by 365.25.
[2] The same censoring mechanisms used in the primary analysis of PFS were employed here. Additionally, for this analysis, a subject's PFS was censored 35 days (the scheduled time for 1 treatment cycle plus 7 days) following his or her last dose of etoposide or platinum.
[3] Number of Subjects with Disease Progression or Death/ Total Follow-up Time (Person-years).
[4] Hazard ratio and 95% C.I. from Cox proportional hazards model with main effects for treatment, platinum choice and prior treatment modality.
[5] P-value for treatment effect from stratified log rank test using platinum choice and prior treatment modality as stratification factors.

Programmer notes: (a) repeat this table using the per-protocol population

Table 14.2.2.5
Progression-Free Survival – Impact of Biomarker Expression
ITT Population

	Model Coefficients (SE) [1]		Hazard Ratio [95% Confidence Interval] [1]		
Biomarker	Treatment	Treatment x Biomarker Interaction	At 25th Percentile	At 50th Percentile	At 75th Percentile
Notch3	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes1	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey2	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey1	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes6	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]

[1] Coefficients, hazard ratios and 95% confidence intervals are from Cox proportional hazards models with effects for treatment, biomarker and treatment-by-biomarker interaction. A separate model was used for each biomarker.

Programmer notes: (a) repeat this table using the per-protocol population

Table 14.2.2.7
Progression-Free Survival – Impact of Notch3 Expression in Subjects with High/Low Notch Pathway Markers
ITT Population

			Model Coefficients (SE) [1]		Hazard Ratio [95% Confidence Interval] [1]		
Biomarker	Biomarker Level	n	Treatment	Treatment x Notch3	At Notch3 25th Percentile	At Notch3 50th Percentile	At Notch3 75th Percentile
N3RPI [2]	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes1	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey2	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey1	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes6	High	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
	Low	xx	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]

[1] Coefficients, hazard ratios and 95% confidence intervals are from Cox proportional hazards models with effects for treatment, Notch3 and treatment-by-Notch3 interaction. A separate model was used for each biomarker.
[2] N3RPI is the Notch3-related PFS Index; N3RPI = –0.569*HES6*NOTCH3 +1.076*HES1*HES6*NOTCH3

Programmer notes: (a) repeat this table using the per-protocol population

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.2.2.9
Progression-Free Survival – Sensitivity Analysis
Per-Protocol Population

	Placebo (N=xx)	Tarextumab (N=xx)
Total Follow-Up Time (person-years) [1]	xxx.x	xxx.x
Number of Subjects with Disease Progression or Death	xx (xx.x%)	xx (xx.x%)
Number of Subjects who did not Progress or Die (Censored)	xx (xx.x%)	xx (xx.x%)
Hazard [2]	0.xx	0.xx
Kaplan-Meier Estimates: Quartiles [95% C.I.] (days)		
25th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
50th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
75th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
Range (Subjects who Progressed or Died) (days)	xxx, xxx	xxx, xxx
Range (All Subjects) (days)	xxx, xxx	xxx, xxx
Hazard Ratio [95% C.I.] [3]		x.xx [x.xx,x.xx]
P-value [4]		0.xxx

Note: PFS= Date of Documentation of Death/Progression – Randomization Date + 1. Subjects who had not experienced death or progression by their last contact were censored at the time of their last radiographic response assessment. Subjects lacking a radiographic response assessment after randomization who do not progress or die have their event time censored on the date of randomization with duration of 1 day. For detailed event and censoring rules refer to protocol section 13.5.1 and SAP section 8.1. C.I. = Confidence Interval.
[1] Sum of all individual follow-up times in days divided by 365.25.
[2] Number of Subjects with Disease Progression or Death/ Total Follow-up Time (Person-years).
[3] Hazard ratio and 95% C.I. from Cox proportional hazards model with treatment as the only explanatory variable.
[4] P-value for treatment effect from unstratified log rank test.

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.2.3.1
Landmark Survival at 180, 360, 540 and 720 Days
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)	P-Value
Survival (# at risk) [SE] [1]			
180 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]	0.xxx
360 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]	0.xxx
540 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]	0.xxx
720 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]	0.xxx

[1] Landmark survival p-values from independent Z tests.

Programmer notes: (a) repeat this table using the per-protocol population

Table 14.2.4.1
Summary Assessment of Tumor Length (mm)
ITT Population

	Placebo (N=xx)			Tarextumab (N=xx)		
	Result	Change from Baseline	Percent Change	Result	Change from Baseline	Percent Change
Baseline Sum of Longest Diameters (SLD)						
n	xx			xx		
Mean (SD)	xx.x (xx.xx)			xx.x (xx.xx)		
95% C.I.	[xx.x, xx.x]			[xx.x, xx.x]		
Median	xx			xx		
25th, 75th Percentile	xx, xx			xx, xx		
Min, Max	xx, xx			xx, xx		
Cycle-3, Day-1 Sum of Longest Diameters (SLD)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
95% C.I.	[xx.x, xx.x]	[xx.x, xx.x]	[xx.x, xx.x]	[xx.x, xx.x]	[xx.x, xx.x]	[xx.x, xx.x]
Median	xx	xx	xx	xx	xx	xx
25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
ANCOVA p-values [1,2]					0.xxx	0.xxx
Cycle-5, Day-1 Sum of Longest Diameters (SLD)						
[*etcetera*]	[⋮]	[⋮]	[⋮]	[⋮]	[⋮]	[⋮]

Note: tumor length is calculated as the sum of the longest diameters (SLD) for the target lesions. SD = Standard Deviation; LS = Least Squares; SE = Standard Error; C.I. = Confidence Interval.
[1] The difference between the follow-up and baseline SLD (e.g., $SLD_{C3D1} - SLD_{baseline}$) is the dependent variable in the ANCOVA model for change from baseline. Treatment, platinum choice (cisplatin versus carboplatin) and prior treatment modality (WBRT or PCI) will be categorical factors in the model, and $SLD_{baseline}$ will be included as a continuous covariate.
[2] The log of the ratio of follow-up to baseline SLD (e.g., log [$SLD_{C3D1}/SLD_{baseline}$]) is the dependent variable in the ANCOVA model for percent change. Treatment, platinum choice and prior treatment modality will be categorical factors in the model, and log [$SLD_{baseline}$] will be included as a continuous covariate.

Programmer notes: (a) repeat this table using the per-protocol population

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.2.4.3
Rate of Change in Total Tumor Length at Progression
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)
SLD at Nadir		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
SLD at Progression		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Rate of SLD Change from Nadir to Progression (%/day) [1]		
N	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
P-value [2]		0.xxx

Note: SLD = Sum of Longest Diameters (i.e., total tumor length for target lesions as defined by RECIST criteria [version 1.1]).
[1] Rate of Change in SLD at progression = 100 x (SLD at Progression – SLD at Nadir) / SLD at Nadir / (number of days between nadir and progression).
[2] P-value for treatment effect from ANOVA model with treatment, platinum choice and prior treatment modality as categorical independent variables.

Programmer notes: (a) repeat this table using the per-protocol population

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.2.4.5
Rate of Change from Total Tumor Length at Baseline
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)
SLD at Baseline		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
SLD at Cycle 3, Day 1		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Rate of SLD Change from Baseline to Cycle 3, Day 1Assessment (%/day) [1]		
N	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
P-value [2]		0.xxx

Note: SLD = Sum of Longest Diameters (i.e., total tumor length for target lesions as defined by RECIST criteria [version 1.1]).
[1] Rate of Change in SLD from baseline to CxD1 = 100 x (SLD at CxD1 – SLD at Baseline) / SLD at Baseline / (number of days between baseline and CxD1 assessment).
[2] P-value for treatment effect from ANOVA model with treatment, platinum choice and prior treatment modality as categorical independent variables.

Programmer notes: (a) add rows for (i) SLD at Cycle 5, Day 1 and (ii) Rate of SLD Change from Baseline to Cycle 5, Day 1Assessment; (b) repeat this table using the per-protocol population

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.2.5.1
Best Overall Tumor Response Based on Investigator Assessment
ITT Population

	Placebo (N=xx)		Tarextumab (N=xx)	
	Response Rate	95% C.I.[2]	Response Rate	95% C.I.[2]
Best Overall Tumor Response [1]				
Complete Response (CR)	xx.x (xx.x%)	[xx.x, xx.x]	xx.x (xx.x%)	[xx.x, xx.x]
Partial Response (PR)	xx.x (xx.x%)	[xx.x, xx.x]	xx.x (xx.x%)	[xx.x, xx.x]
Stable Disease (SD)	xx.x (xx.x%)	[xx.x, xx.x]	xx.x (xx.x%)	[xx.x, xx.x]
Progressive Disease (PD)	xx.x (xx.x%)	[xx.x, xx.x]	xx.x (xx.x%)	[xx.x, xx.x]
Not Evaluable (NE)	xx.x (xx.x%)	[xx.x, xx.x]	xx.x (xx.x%)	[xx.x, xx.x]
No Post-Baseline Tumor Assessment Collected	xx.x (xx.x%)	[xx.x, xx.x]	xx.x (xx.x%)	[xx.x, xx.x]
Overall Response Rate (CR or PR)	xx.x (xx.x%)		xx.x (xx.x%)	[xx.x, xx.x]
Odds Ratio (Tarextumab/Placebo) [3]			x.xx	
P-value [3]			0.xxx	

[1] Tumor response based on RECIST criteria (version 1.1).
[2] Two-sided exact 95% C.I..
[3] Odds ratio and p-value from logistic regression model including treatment, platinum choice and prior treatment modality as independent variables.

Programmer notes: (a) repeat this table using the per-protocol population

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.2.5.3
Best Overall Tumor Response Based on Investigator Assessment – Impact of Biomarker Expression
ITT Population

	Model Coefficients (SE) [1]		Odds Ratio [95% Confidence Interval] [1]		
Biomarker	Treatment	Treatment x Biomarker Interaction	At 25th Percentile	At 50th Percentile	At 75th Percentile
Notch3	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes1	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey2	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hey1	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]
Hes6	xx.x (xx.x)	xx.x (xx.x)	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]	x.xx [x.xx,xx.xx]

[1] Coefficients, odds ratio and 95% confidence interval from logistic regression models with effects for treatment, biomarker and treatment-by-biomarker interaction. A separate model was used for each biomarker.

Programmer notes: (a) repeat this table using the per-protocol population

Table 14.2.6.1
Duration of Response
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)
Number of Subjects with Objective Response (CR or PR)	xx	xx
Total Follow-Up Time (person-years) [1]	xxx.x	xxx.x
Number of Responders with Disease Progression or Death	xx (xx.x%)	xx (xx.x%)
Number of Responders who did not Progress or Die (Censored)	xx (xx.x%)	xx (xx.x%)
Hazard [2]	0.xx	0.xx
Kaplan-Meier Estimates: Quartiles [95% C.I.] (days)		
25th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
50th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
75th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
Range (Responders who Progressed or Died) (days)	xx.x – xx.x	xx.x – xx.x
Range (All Responders) (days)	xx.x – xx.x	xx.x – xx.x
Hazard Ratio [95% C.I.] [3]		x.xx [x.xx,x.xx]
P-value [2]		0.xxx

Note: For this table summary, Responders are those subjects who experienced an Objective Response.
Note: Analyses presented in this table include only subjects who achieved a CR or PR. Percentages below the first row are based on subjects who achieved a CR or PR.
Note: Duration of Response = Date of Documentation of Death/Progression – Date of First Partial (PR) or Complete Response (CR) + 1. Responders who had not experienced death or progression by their last contact were censored at the time of their last radiographic response assessment. Responders lacking a radiographic response assessment after first response who do not progress or die have their event time censored on the date of first response with duration of 1 day. For detailed event and censoring rules refer to protocol section 13.5.3 and SAP section 8.4. C.I. = Confidence Interval.
[1] Sum of all individual follow-up times in days divided by 365.25.
[2] Number of Subjects with Disease Progression or Death/ Total Follow-up Time (Person-years).
[3] Hazard ratio, 95% C.I. and p-value from Cox proportional hazards model with main effects for treatment, platinum choice and prior treatment modality.

Programmer notes: Percentages displayed to be based on number of subjects with an objective response.

Programmer notes: (a) repeat this table using the per-protocol population

Table 14.2.7.1
Sites of Progression
ITT Population

	Placebo (N=xx)	Tarextumab (N=xx)
Subjects with Progressive Disease [1]	xx (xx.x%)	xx (xx.x%)
Progression based on…		
New Lesion	xx (xx.x%)	xx (xx.x%)
Existing Lesion	xx (xx.x%)	xx (xx.x%)
Chi-Square p-value [2]		0.xxx
Site of Progression		
Progression of existing lesion	xx (xx.x%)	xx (xx.x%)
Liver	xx (xx.x%)	xx (xx.x%)
Lung	xx (xx.x%)	xx (xx.x%)
Lymph Node	xx (xx.x%)	xx (xx.x%)
[...]	[⋮]	[⋮]
More than one new lesion	xx (xx.x%)	xx (xx.x%)
Chi-Square p-value [3]		0.xxx

[1] Analyses presented in this table include only subjects who had progressive disease during the study. Percentages below the first row are based on subjects who had progressive disease on study.
[2] Hypothesis 1 is equivalent distributions of manner of disease progression (new lesion or progression of existing lesion).
[3] Hypothesis 2 is equivalent distributions of site of progression with progression of an existing lesion grouped in a single category (i.e., regardless of site).

Programmer notes: (a) repeat this table using the per-protocol population

OncoMed Pharmaceuticals, Inc.
59R5-003 (Phase 2)

Table 14.3.1.1
Overall Summary of Treatment-Emergent Adverse Events (TEAEs)
Safety Population

	Placebo (N=xx)	Tarextumab (N=xx)
Subjects Reporting at Least One TEAE	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One TEAE	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One TEAE Related to Study Drug [1]	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One TEAE Related to Etoposide	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One TEAE Related to Platinum Therapy	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Serious TEAE	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Serious TEAE Related to Study Drug [1]	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Serious TEAE Related to Etoposide	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Serious TEAE Related to Platinum Therapy	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Grade 3 or Higher TEAE	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Grade 4 or Higher TEAE	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Delay/Interruption of Study Drug [1]	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Delay/Interruption of Etoposide	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Delay/Interruption of Platinum Therapy	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Dose Reduction of Study Drug [1]	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Dose Reduction of Etoposide	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Dose Reduction of Platinum Therapy	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Withdrawal of Study Drug [1]	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Withdrawal of Etoposide	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Withdrawal of Platinum Therapy	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE with Outcome of Death	xx (xx.x%)	xx (xx.x%)
Maximum CTCAE Severity Grade [2]		
Grade 1	xx (xx.x%)	xx (xx.x%)
Grade 2	xx (xx.x%)	xx (xx.x%)
Grade 3	xx (xx.x%)	xx (xx.x%)
Grade 4	xx (xx.x%)	xx (xx.x%)
Grade 5	xx (xx.x%)	xx (xx.x%)

[1] Study drug = tarextumab or placebo.
[2] CTCAE = Common Terminology Criteria for Adverse Events (version 4.02). Subjects with more than one TEAE are counted only once at the highest CTCAE severity grade across all TEAEs.

Table 14.3.1.2
Treatment-Emergent Adverse Events (TEAEs) by System Organ Class and Preferred Term
Safety Population

System Organ Class / Preferred Term	Placebo (N=xx)	Tarextumab (N=xx)
Subjects Reporting at Least One Qualifying TEAE	xx (xx.x%)	xx (xx.x%)
System Organ Class 1	xx (xx.x%)	xx (xx.x%)
Preferred Term 1.1	xx (xx.x%)	xx (xx.x%)
Preferred Term 1.2	xx (xx.x%)	xx (xx.x%)
Preferred Term 1.3	xx (xx.x%)	xx (xx.x%)
[*etcetera*]	[⋮]	[⋮]
System Organ Class 2	xx (xx.x%)	xx (xx.x%)
Preferred Term 2.1	xx (xx.x%)	xx (xx.x%)
Preferred Term 2.2	xx (xx.x%)	xx (xx.x%)
Preferred Term 2.3	xx (xx.x%)	xx (xx.x%)
[*etcetera*]	[⋮]	[⋮]

Note: At each level of summation (overall, system organ class, preferred term), subjects reporting more than one adverse event are counted only once.

Programmer notes: (a) primary sort order is descending SOC frequency under tarextumab, secondary sort order is descending PT frequency under tarextumab; (b) duplicate this table for the following TEAE subsets making the necessary changes to the table's title – (i) TEAEs related to study drug, (ii) TEAEs related to etoposide, (iii) TEAEs related to platinum therapy, (iv) serious TEAEs, (v) serious TEAEs related to study drug, (vi) serious TEAEs related to etoposide, (vii) serious TEAEs related to platinum therapy, (viii) TEAEs leading to delay/interruption of study drug, (ix) TEAEs leading to delay/interruption of etoposide, (x) TEAEs leading to delay/interruption of platinum therapy, (xi) TEAEs leading to dose reduction of study drug, (xii) TEAEs leading to dose reduction of etoposide, (xiii) TEAEs leading to dose reduction of platinum therapy, (xiv) TEAEs leading to withdrawal of study drug, (xv) TEAEs leading to withdrawal of etoposide, (xvi) TEAEs leading to withdrawal of platinum therapy, (xvii) TEAEs leading to discontinuation of study drug, (xviii) TEAEs with outcome of death

Table 14.3.1.6
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Severity Grade
Safety Population

System Organ Class / Preferred Term	Placebo (N=)						Tarextumab (N=)					
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
Subjects Reporting at Least One Qualifying TEAE	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
System Organ Class 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.												
.												
System Organ Class 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.												
.												

Note: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Life Threatening; Grade 5 = Fatal.
At each level of summation (overall, system organ class, and preferred term), subjects reporting more than one qualifying event are counted only once at the highest CTCAE severity grade.

Programmer notes: (a) primary sort order is descending SOC frequency under tarextumab, secondary sort order is descending PT (total) frequency under tarextumab (total frequency [i.e., sum of frequencies for grades 1 through 5] even though total frequency is not displayed in table); (b) duplicate this table for the following TEAE subsets making the necessary changes to the table's title – (i) TEAEs related to study drug, (ii) TEAEs related to etoposide, (iii) TEAEs related to platinum therapy, (iv) serious TEAEs, (v) serious TEAEs related to study drug, (vi) serious TEAEs related to etoposide, (vii) serious TEAEs related to platinum therapy

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Table 14.3.1.10
Treatment-Emergent Adverse Events by Preferred Term
Safety Population

Preferred Term	Placebo (N=xx)	Tarextumab (N=xx)
Subjects Reporting at Least One Qualifying TEAE	xx (xx.x%)	xx (xx.x%)
Preferred Term 1	xx (xx.x%)	xx (xx.x%)
Preferred Term 2	xx (xx.x%)	xx (xx.x%)
Preferred Term 3	xx (xx.x%)	xx (xx.x%)
Preferred Term 4	xx (xx.x%)	xx (xx.x%)
Preferred Term 5	xx (xx.x%)	xx (xx.x%)
Preferred Term 6	xx (xx.x%)	xx (xx.x%)
[*etcetera*]	[⋮]	[⋮]

Note: At each level of summation (overall and preferred term), subjects reporting more than one qualifying event are counted only once.

Programmer notes: (a) primary sort order is descending PT frequency under tarextumab; (b) duplicate this table for the following TEAE subsets making the necessary changes to the table's title – (i) TEAEs related to study drug, (ii) TEAEs related to etoposide, (iii) TEAEs related to platinum therapy, (iv) serious TEAEs, (v) serious TEAEs related to study drug, (vi) serious TEAEs related to etoposide, (vii) serious TEAEs related to platinum therapy, (viii) TEAEs leading to delay/interruption of study drug, (ix) TEAEs leading to delay/interruption of etoposide, (x) TEAEs leading to delay/interruption of platinum therapy, (xi) TEAEs leading to dose reduction of study drug, (xii) TEAEs leading to dose reduction of etoposide, (xiii) TEAEs leading to dose reduction of platinum therapy, (xiv) TEAEs leading to withdrawal of study drug, (xv) TEAEs leading to withdrawal of etoposide, (xvi) TEAEs leading to withdrawal of platinum therapy, (xvii) TEAEs leading to discontinuation of study drug, (xviii) TEAEs with outcome of death

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Table 14.3.4.1
Hematology
Safety Population

Laboratory Parameter	Time Point	Placebo (N=xx) Result	Placebo (N=xx) Change from Baseline	Tarextumab (N=xx) Result	Tarextumab (N=xx) Change from Baseline
Hemoglobin (g/dL)	Baseline [1]				
	n	xx		xx	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx		xx	
	25th, 75th Percentile	xx, xx		xx, xx	
	Min, Max	xx, xx		xx, xx	
	Maximum Post-Baseline				
	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx	xx
	25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Minimum Post-Baseline				
	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx	xx
	25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Last Observation Post-Baseline				
	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx	xx
	25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Hematocrit (%)	Baseline [1]				
[*etcetera*]	[⋮]	[⋮]	[⋮]	[⋮]	[⋮]

[1] Baseline is defined as the last non-missing value prior to first dose of study drug.

Programmer notes: (a) continue for all remaining hematology parameters; (b) duplicate table for (i) serum chemistry, (ii) coagulation tests (PT, aPTT and INR)

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Table 14.3.4.2
Hematology – Shift from Baseline
Safety Population

Laboratory Parameter	Shift from Baseline [1]	Placebo (N=)	Tarextumab (N=)
Hemoglobin (g/dL)	Low or Normal to Any High Post-Baseline	n (%)	n (%)
	Normal or High to Any Low Post-Baseline	n (%)	n (%)
	Low or Normal to Last Observation High Post-Baseline	n (%)	n (%)
	Normal or High to Last Observation Low Post-Baseline	n (%)	n (%)
Hematocrit (%)			
….			

[1] Baseline is defined as the last non-missing value prior to first dose of study drug.

Programmer notes: (a) continue for all remaining hematology parameters; (b) duplicate table for (i) serum chemistry, (ii) coagulation tests (PT, aPTT and INR)

Table 14.3.4.3
Hematology – Range Change Abnormal – High
Safety Population

Laboratory Parameter	Placebo (N=xx)	Tarextumab (N=xx)
Hemoglobin (g/dL)		
n	xx (xx.x%)	xx (xx.x%)
Any Post-Baseline [1]		
Grade 4	xx (xx.x%)	xx (xx.x%)
Grade 3	xx (xx.x%)	xx (xx.x%)
Grade 2	xx (xx.x%)	xx (xx.x%)
Grade 1	xx (xx.x%)	xx (xx.x%)
Last Observation Post-Baseline		
Grade 4	xx (xx.x%)	xx (xx.x%)
Grade 3	xx (xx.x%)	xx (xx.x%)
Grade 2	xx (xx.x%)	xx (xx.x%)
Grade 1	xx (xx.x%)	xx (xx.x%)
Platelets (x10^9/L)		
[*etcetera*]	[⋮]	[⋮]

[1] Subjects are counted only once using their highest post-baseline CTCAE severity grade. Only patients who have an increase in CTCAE grade severity from baseline are considered for counts of Grades 1 through 4. Subjects who have a baseline result and at least one post-baseline result for a particular analyte are considered when determining percentages, regardless of whether the patient had a CTCAE grade counted for the analyte.

Programmer notes: (a) continue for all remaining hematology parameters with CTCAE severity grading criteria; (b) duplicate table for (i) serum chemistry, (ii) coagulation tests (PT, aPTT and INR)

Table 14.3.4.13
Urinalysis – Shift from Baseline
Safety Population

Laboratory Parameter	Time Point	Placebo (N=)	Tarextumab (N=)
Protein	n		
	Any Post-Baseline		
	Absent to Present	n (%)	n (%)
	Last Observation Post-Baseline		
	Absent to Present	n (%)	n (%)
Glucose	n		
	Any Post-Baseline		
	Absent to Present	n (%)	n (%)
	Last Observation Post-Baseline		
	Absent to Present	n (%)	n (%)
pH	n		
	Any Post-Baseline		
	Low or Normal to High	n (%)	n (%)
	Normal or High to Low	n (%)	n (%)
	Last Observation Post-Baseline		
	Low or Normal to High	n (%)	n (%)
	Normal or High to Low	n (%)	n (%)
Specific Gravity			
…			

[1] Baseline is defined as the last non-missing value prior to first dose of study drug.

Table 14.3.4.14
Vital Signs
Safety Population

Parameter	Time Point	Placebo (N=xx) Result	Placebo (N=xx) Change from Baseline	Tarextumab (N=xx) Result	Tarextumab (N=xx) Change from Baseline
Systolic Blood Pressure (mmHg)	Baseline [1]				
	n	xx		xx	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx		xx	
	25th, 75th Percentile	xx, xx		xx, xx	
	Min, Max	xx, xx		xx, xx	
	Maximum Post-Baseline				
	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx	xx
	25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Minimum Post-Baseline				
	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx	xx
	25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Last Observation Post-Baseline				
	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx	xx
	25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Diastolic Blood Pressure (mmHg)	Baseline [1]				
[*etcetera*]	[⋮]	[⋮]	[⋮]	[⋮]	[⋮]

[1] Baseline is defined as the last non-missing value prior to first dose of study drug.

Programmer notes: (a) continue for all vital sign parameters (systolic and diastolic blood pressures, pulse, body temperature and respiration rate)

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Table 14.3.4.15
Vital Signs – Range Change Abnormal (RCA)
Safety Population

Vital Signs Parameter	Placebo (N=xx)	Tarextumab (N=xx)
n	xx	xx
Any Post-Baseline		
High [1]		
Temperature	xx (xx.x%)	xx (xx.x%)
Pulse Rate	xx (xx.x%)	xx (xx.x%)
Respiratory Rate	xx (xx.x%)	xx (xx.x%)
SBP	xx (xx.x%)	xx (xx.x%)
DBP	xx (xx.x%)	xx (xx.x%)
Low [1]		
Temperature	xx (xx.x%)	xx (xx.x%)
Pulse Rate	xx (xx.x%)	xx (xx.x%)
Respiratory Rate	xx (xx.x%)	xx (xx.x%)
SBP	xx (xx.x%)	xx (xx.x%)
DBP	xx (xx.x%)	xx (xx.x%)
Last Post-Baseline Visit		
High[1]		
Temperature	xx (xx.x%)	xx (xx.x%)
Pulse Rate	xx (xx.x%)	xx (xx.x%)
Respiratory Rate	xx (xx.x%)	xx (xx.x%)
SBP	xx (xx.x%)	xx (xx.x%)
DBP	xx (xx.x%)	xx (xx.x%)
Low[1]		
Temperature	xx (xx.x%)	xx (xx.x%)
Pulse Rate	xx (xx.x%)	xx (xx.x%)
Respiratory Rate	xx (xx.x%)	xx (xx.x%)
SBP	xx (xx.x%)	xx (xx.x%)
DBP	xx (xx.x%)	xx (xx.x%)

Note: SBP=Systolic Blood Pressure. DBP=Diastolic Blood Pressure. Normal Range Temperature: 36.6°C to 37.3°C. Normal Range SBP: 90-120 mmHg. Normal Range DBP: 60-80 mmHg. Normal Range Respiratory Rate: 12-18 breaths per minute. Normal Range Pulse Rate: 60-100 beats per minute.
[1] Each subject is represented once by their worst change. A range change can be either a change in a vital sign parameter value from baseline low or normal to post-baseline high or a change from baseline high or normal to post-baseline low. A subject can be included in both 'High' and 'Low' categories if applicable.

Table 14.3.4.16
12-Lead Electrocardiogram (ECG)
Safety Population

Parameter	Time Point	Placebo (N=xx) Result	Placebo (N=xx) Change from Baseline	Tarextumab (N=xx) Result	Tarextumab (N=xx) Change from Baseline
QRS Duration (msec)	Baseline [1]				
	n	xx		xx	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx		xx	
	25th, 75th Percentile	xx, xx		xx, xx	
	Min, Max	xx, xx		xx, xx	
	Maximum Post-Baseline				
	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx	xx
	25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Minimum Post-Baseline				
	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx	xx
	25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Last Observation Post-Baseline				
	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx	xx
	25th, 75th Percentile	xx, xx	xx, xx	xx, xx	xx, xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
PR Interval (msec) [*etcetera*]	Baseline [1] [⋮]	[⋮]	[⋮]	[⋮]	[⋮]

[1] Baseline is defined as the last non-missing value prior to first dose of study drug.

Programmer notes: (a) continue for all electrocardiogram parameters (QRS duration, PR interval, QTc Interval)

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Table 14.3.4.17
12-Lead Electrocardiogram (ECG) – Range Change Abnormal
Safety Population

ECG Parameter	Placebo (N=xx)	Tarextumab (N=xx)
n	xx	xx
Any Post-Baseline		
High [1]		
QRS Duration (msec)	xx (xx.x%)	xx (xx.x%)
PR Interval (msec)	xx (xx.x%)	xx (xx.x%)
QTc Interval (msec)	xx (xx.x%)	xx (xx.x%)
Low [1]		
QRS Duration (msec)	xx (xx.x%)	xx (xx.x%)
PR Interval (msec)	xx (xx.x%)	xx (xx.x%)
QTc Interval (msec)	xx (xx.x%)	xx (xx.x%)
Last Observation Post-Baseline		
High[1]		
QRS Duration (msec)	xx (xx.x%)	xx (xx.x%)
PR Interval (msec)	xx (xx.x%)	xx (xx.x%)
QTc Interval (msec)	xx (xx.x%)	xx (xx.x%)
Low[1]		
QRS Duration (msec)	xx (xx.x%)	xx (xx.x%)
PR Interval (msec)	xx (xx.x%)	xx (xx.x%)
QTc Interval (msec)	xx (xx.x%)	xx (xx.x%)

Note: Reference ranges: QRS duration 80-100 msec; PR interval 120-200 msec; QTc interval ≤430 msec (males), ≤450 msec (females).
[1] Each subject is represented once by their worst change. A range change can be either a change in an ECG parameter value from baseline low or normal to post-baseline high or a change from baseline high or normal to post-baseline low. A subject can be included in both 'High' and 'Low' categories if fits both categories.

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Table 14.3.4.18
12-Lead Electrocardiogram (ECG) – QTc Interval
Safety Population

Time Point	Placebo (N=xx)	Tarextumab (N=xx)
Baseline [1]		
<480	xx (xx.x%)	xx (xx.x%)
480-500 msec	xx (xx.x%)	xx (xx.x%)
>500 msec	xx (xx.x%)	xx (xx.x%)
Worst (Maximum) Post-Baseline		
<480	xx (xx.x%)	xx (xx.x%)
480-500 msec	xx (xx.x%)	xx (xx.x%)
>500 msec	xx (xx.x%)	xx (xx.x%)
Last Observation Post-Baseline		
<480	xx (xx.x%)	xx (xx.x%)
480-500 msec	xx (xx.x%)	xx (xx.x%)
>500 msec	xx (xx.x%)	xx (xx.x%)

[1]Baseline is defined as the last non-missing value prior to first dose of study drug.

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Table 14.3.4.19
12-Lead Electrocardiogram (ECG) – Overall Interpretation
Safety Population

Time Point	Placebo (N=)	Tarextumab (N=)
Baseline [1]		
n	n	n
Normal	n (%)	n (%)
Abnormal NCS	n (%)	n (%)
Abnormal CS	n (%)	n (%)
Worst Post-Baseline		
n	n	n
Normal	n (%)	n (%)
Abnormal NCS	n (%)	n (%)
Abnormal CS	n (%)	n (%)
Last Observation Post-Baseline		
n	n	n
Normal	n (%)	n (%)
Abnormal NCS	n (%)	n (%)
Abnormal CS	n (%)	n (%)

Note: NCS = Not clinically significant, CS = Clinically significant. Percentages are based on the number of subjects with a non-missing response at each visit.
[1] Baseline is defined as the last non-missing value prior to first dose of study drug.

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Table 14.3.4.20
12-Lead Electrocardiogram (ECG) – Overall Interpretation Shift from Baseline
Safety Population

Baseline [1]	Most Extreme Post-Baseline	Placebo (N=xx)	Tarextumab (N=xx)
Normal	Normal	xx (xx.x%)	xx (xx.x%)
	Abnormal - Not Clinically Significant	xx (xx.x%)	xx (xx.x%)
	Abnormal - Clinically Significant	xx (xx.x%)	xx (xx.x%)
Abnormal - Not Clinically Significant	Normal	xx (xx.x%)	xx (xx.x%)
	Abnormal - Not Clinically Significant	xx (xx.x%)	xx (xx.x%)
	Abnormal - Clinically Significant	xx (xx.x%)	xx (xx.x%)
Abnormal - Clinically Significant	Normal	xx (xx.x%)	xx (xx.x%)
	Abnormal - Not Clinically Significant	xx (xx.x%)	xx (xx.x%)
	Abnormal - Clinically Significant	xx (xx.x%)	xx (xx.x%)

[1] Baseline is defined as the last non-missing value prior to first dose of study drug.

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Table 14.3.4.21
ECOG Performance Status
Safety Population

Performance Status Score [1]	Placebo (N=xx)	Tarextumab (N=xx)
Baseline [2]		
n	xx	xx
0	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)
5	xx (xx.x%)	xx (xx.x%)
Maximum Post-Baseline		
n	xx	xx
0	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)
5	xx (xx.x%)	xx (xx.x%)
Minimum Post-Baseline		
n	xx	xx
0	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)
5	xx (xx.x%)	xx (xx.x%)
Last Observation Post-Baseline		
n	xx	xx
0	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)
5	xx (xx.x%)	xx (xx.x%)

Note: Percentages are based on the number of patients with a non-missing response at each visit.
[1] For complete definitions of each activity status code, reference Appendix D of the clinical protocol.
[2] Baseline is defined as the last non-missing value prior to first dose of study drug.

Table 14.3.4.22
ECOG Performance Status – Shift from Baseline
Safety Population

	Placebo (N=) Baseline [2]		Tarextumab (N=) Baseline [2]	
Performance Status Score [1]	0	1	0	1
Maximum Post-Baseline				
n	n	n	n	n
0	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)
Minimum Post-Baseline				
n	n	n	n	n
0	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)

[1] For complete definitions of each activity status code, reference Appendix D of the clinical protocol.
[2] Baseline is defined as the last non-missing value prior to first dose of study drug.

Programming note: Continue for Last Observation Post-Baseline.
Programming note: Add additional baseline columns as needed.

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59R5-003 (Phase 2)

Table 14.3.4.23
Anti-Tarextumab Antibodies
Immunogenicity Population

Time Point	Tarextumab (N=xx)
Any Positive Sample During Study	xx (xx.x%)
Cycle 1, Day 1	
Positive	xx (xx.x%)
Negative	xx (xx.x%)
Viable Sample Not Available	xx (xx.x%)
Cycle 3, Day 1	
Positive	xx (xx.x%)
Negative	xx (xx.x%)
Viable Sample Not Available	xx (xx.x%)
Cycle 5, Day 1	
Positive	xx (xx.x%)
Negative	xx (xx.x%)
Viable Sample Not Available	xx (xx.x%)
Treatment Termination	
Positive	xx (xx.x%)
Negative	xx (xx.x%)
Viable Sample Not Available	xx (xx.x%)

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Table 14.3.4.24
Impact of Anti-Tarextumab Antibodies on Progression-Free Survival
Immunogenicity Population

	Tarextumab (N=xx)	
	Anti-Tarextumab Antibody Negative (N=xx)	Anti-Tarextumab Antibody Positive (N=xx)
Total Follow-Up Time (person-years) [1]	xxx.x	xxx.x
Number of Subjects with Disease Progression or Death	xx (xx.x%)	xx (xx.x%)
Number of Subjects who did not Progress or Die (Censored)	xx (xx.x%)	xx (xx.x%)
Hazard [2]	0.xx	0.xx
Kaplan-Meier Estimates: Quartiles [95% C.I.] (days)		
25th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
50th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
75th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
Range (Subjects who Progressed or Died) (days)	xxx, xxx	xxx, xxx
Range (All Subjects) (days)	xxx, xxx	xxx, xxx
Hazard Ratio [95% C.I.] [3]		x.xx [x.xx,x.xx]
P-value [4]		0.xxx

Note: PFS= Date of Documentation of Death/Progression – Randomization Date + 1. Subjects who had not experienced death or progression by their last contact were censored at the time of their last radiographic response assessment. Subjects lacking a radiographic response assessment after randomization who do not progress or die have their event time censored on the date of randomization with duration of 1 day. For detailed event and censoring rules refer to protocol section 13.5.1 and SAP section 8.1. C.I. = Confidence Interval.
[1] Sum of all individual follow-up times in days divided by 365.25.
[2] Number of Subjects with Disease Progression or Death/ Total Follow-up Time (Person-years).
[3] Hazard ratio and 95% C.I. from Cox proportional hazards model with main effects for anti-tarextumab antibody status (positive or negative).
[4] P-value for treatment effect from unstratified log rank test.

Programmer notes: (a) percentages are based on the numbers of subjects who are antibody negative and antibody positive, not on the number of subjects receiving tarextumab

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Table 14.3.4.25
Impact of Anti-Tarextumab Antibodies on Overall Survival
Immunogenicity Population

	Tarextumab (N=xx)	
	Anti-Tarextumab Antibody Negative (N=xx)	Anti-Tarextumab Antibody Positive (N=xx)
Total Follow-Up Time (person-years) [1]	xxx.x	xxx.x
Number of Subjects who Died	xx (xx.x%)	xx (xx.x%)
Number of Subjects who did not Die (Censored)	xx (xx.x%)	xx (xx.x%)
Hazard [2]	0.xx	0.xx
Kaplan-Meier Estimates: [95% C.I.] (days)		
25th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
50th Percentile (Median)	xxx [xxx,xxx]	xxx [xxx,xxx]
75th Percentile	xxx [xxx,xxx]	xxx [xxx,xxx]
Kaplan-Meier Estimate (# at risk) [SE]		
180 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
360 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
540 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
720 Days	0.xx (xx) [x.xx]	0.xx (xx) [x.xx]
Range (Subjects who Died) (days)	xxx, xxx	xxx, xxx
Range (All Subjects) (days)	xxx, xxx	xxx, xxx
Hazard Ratio [95% C.I.] [3]		x.xx [x.xx,x.xx]
P-value [4]		0.xxx

Note: Overall Survival = Date of Documentation of Death – Randomization Date + 1. Subjects who had not experienced death by their last contact date were censored at that time. Subjects lacking data after randomization who do not die have their event time censored on the date of randomization with duration of 1 day. For detailed event and censoring rules refer to protocol section 13.5.4 and SAP section 8.6. C.I. = Confidence Interval. SE = Standard Error.
[1] Sum of all individual follow-up times in days divided by 365.25.
[2] Number of Subjects who Died/ Total Follow-up Time (Person-years).
[3] Hazard ratio and 95% C.I. from Cox proportional hazards model with main effects for anti-tarextumab antibody status (positive or negative).
[4] P-value for treatment effect from unstratified log rank test.

Programmer notes: (a) percentages are based on the numbers of subjects who are antibody negative and antibody positive, not on the number of subjects receiving tarextumab

Table 14.3.4.26
Overall Summary of Impact of Anti-Tarextumab Antibodies on Treatment-Emergent Adverse Events (TEAEs)
Immunogenicity Population

	Tarextumab (N=xx)	
	Anti-Tarextumab Antibody Negative (N=xx)	Anti-Tarextumab Antibody Positive (N=xx)
Subjects Reporting at Least One TEAE	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Serious TEAE	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Serious TEAE Related to Tarextumab	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Serious TEAE Related to Etoposide	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Serious TEAE Related to Platinum Therapy	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Grade 3 or Higher TEAE	xx (xx.x%)	xx (xx.x%)
Subjects Reporting at Least One Grade 4 or Higher TEAE	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Delay/Interruption of Tarextumab	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Delay/Interruption of Etoposide	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Delay/Interruption of Platinum Therapy	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Dose Reduction of Tarextumab	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Dose Reduction of Etoposide	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Dose Reduction of Platinum Therapy	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Withdrawal of Tarextumab	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Withdrawal of Etoposide	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE Leading to Withdrawal of Platinum Therapy	xx (xx.x%)	xx (xx.x%)
Subjects Reporting TEAE with Outcome of Death	xx (xx.x%)	xx (xx.x%)
Maximum CTCAE Severity Grade [1]		
Grade 1	xx (xx.x%)	xx (xx.x%)
Grade 2	xx (xx.x%)	xx (xx.x%)
Grade 3	xx (xx.x%)	xx (xx.x%)
Grade 4	xx (xx.x%)	xx (xx.x%)
Grade 5	xx (xx.x%)	xx (xx.x%)

[1]CTCAE = Common Terminology Criteria for Adverse Events (version 4.02). Subjects with more than one TEAE are counted only once at the highest CTCAE severity grade across all TEAEs.

Programmer notes: (a) percentages are based on the numbers of subjects who are antibody negative and antibody positive, not on the number of subjects receiving tarextumab

Table 14.3.4.27
Impact of Anti-Tarextumab Antibodies Treatment-Emergent Adverse Events (TEAEs)
Safety Population

	Tarextumab (N=xx)	
Preferred Term	Anti-Tarextumab Antibody Negative (N=xx)	Anti-Tarextumab Antibody Positive (N=xx)
Subjects Reporting at Least One TEAE	xx (xx.x%)	xx (xx.x%)
Preferred Term 1	xx (xx.x%)	xx (xx.x%)
Preferred Term 2	xx (xx.x%)	xx (xx.x%)
Preferred Term 3	xx (xx.x%)	xx (xx.x%)
Preferred Term 4	xx (xx.x%)	xx (xx.x%)
Preferred Term 5	xx (xx.x%)	xx (xx.x%)
Preferred Term 6	xx (xx.x%)	xx (xx.x%)
[*etcetera*]	[⋮]	[⋮]

Note: At each level of summation (overall and preferred term), subjects reporting more than one qualifying event are counted only once.

Programmer notes: (a) percentages are based on the numbers of subjects who are antibody negative and antibody positive, not on the number of subjects receiving tarextumab

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Table 14.3.5.1
Study Drug Exposure – Tarextumab/Placebo
Safety Population

	Placebo (N=xx)	Tarextumab (N=xx)
Treatment Cycles		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Number of Infusions Administered		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Total Dose Administered (mg) [1]		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Duration of Treatment (days) [2]		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Dose Intensity		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx

[1] Placebo exposure is summarized in tarextumab-equivalent units (i.e., the number of milligrams of tarextumab the placebo "replaced" during treatment-blinded dosing).
[2] Duration of treatment = number of days from the first dose (Day 1) until the last dose.

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Table 14.3.5.2
Dosing Compliance – Tarextumab/Placebo
Safety Population

	Placebo (N=xx)	Tarextumab (N=xx)
Dosing Compliance (%) [1]		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
0% to <20% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
20% to <40% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
40% to <60% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
60% to <80% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
80% to <100% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
100% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
Number of Missed Doses	xx	xx
Reason for Missed Dose		
Adverse Event	xx	xx
Other	xx	xx
Number of Delayed Doses	xx	xx
Reason for Delayed Dose		
Adverse Event	xx	xx
Other	xx	xx
Number of Reduced Doses	xx	xx
Reason for Reduced Dose		
Adverse Event	xx	xx
Other	xx	xx

[1] Dosing compliance = (number of doses administered) / number of planned doses x 100.

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Table 14.3.5.3
Study Drug Exposure – Etoposide
Safety Population

	Placebo (N=xx)	Tarextumab (N=xx)
Treatment Cycles		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Number of Infusions Administered		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Total Dose Administered (mg)		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Duration of Treatment (days) [1]		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Dose Intensity		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx

[1] Duration of treatment = number of days from the first dose (Day 1) until the last dose.

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Table 14.3.5.4
Dosing Compliance – Etoposide
Safety Population

	Placebo (N=xx)	Tarextumab (N=xx)
Dosing Compliance [1]		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
0% to <20% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
20% to <40% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
40% to <60% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
60% to <80% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
80% to <100% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
100% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
Number of Missed Doses	xx	xx
Reason for Missed Dose		
Adverse Event	xx	xx
Other	xx	xx
Number of Delayed Doses	xx	xx
Reason for Delayed Dose		
Adverse Event	xx	xx
Other	xx	xx

[1] Dosing compliance = (number of doses administered) / number of planned doses.

Table 14.3.5.5
Study Drug Exposure – Cisplatin
Safety Population

	Placebo (N=xx)	Tarextumab (N=xx)
Platinum Therapy [1]		
Cisplatin	xx (xx.x%)	xx (xx.x%)
Carboplatin	xx (xx.x%)	xx (xx.x%)
Treatment Cycles		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Number of Infusions Administered		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Total Dose Administered (mg)		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Duration of Treatment (days) [2]		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
Dose Intensity		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx

[1] Analyses presented in this table include only subjects who received cisplatin as their platinum therapy. Percentages below the first set of rows are based on subjects who received cisplatin.
[2] Duration of treatment = number of days from the first dose (Day 1) until the last dose.

Programmer notes: (a) produce the same table replacing "cisplatin" with "carboplatin" in the title and footnote

Table 14.3.5.6
Dosing Compliance – Cisplatin
Safety Population

	Placebo (N=xx)	Tarextumab (N=xx)
Dosing Compliance [1]		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx
25th, 75th Percentile	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx
0% to <20% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
20% to <40% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
40% to <60% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
60% to <80% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
80% to <100% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
100% Dosing Compliance	xx (xx.x%)	xx (xx.x%)
Number of Missed Doses	xx	xx
Reason for Missed Dose		
Adverse Event	xx	xx
Other	xx	xx
Number of Delayed Doses	xx	xx
Reason for Delayed Dose		
Adverse Event	xx	xx
Other	xx	xx

[1] Dosing compliance = (number of doses administered) / number of planned doses.

Programmer notes: (a) produce the same table replacing "cisplatin" with "carboplatin" in the title

APPENDIX C. FIGURE SHELLS

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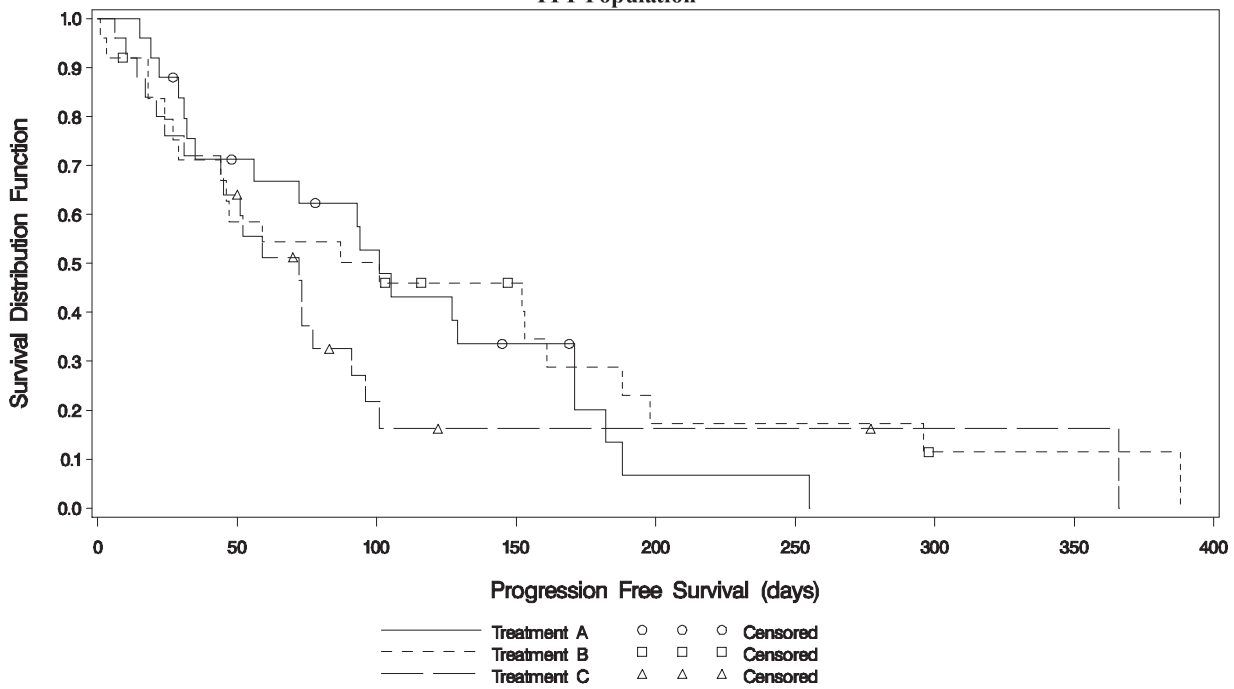
Figure 14.2.1.1
Overall Survival
ITT Population



Programmer notes: (a) replace "Treatment A" with "Placebo"; (b) replace "Treatment B" with "Tarextumab"; (c) include "at risk" counts beneath the x-axis (see secondary figure mock below); (d) delete "Treatment C"; (e) duplicate figure using per-protocol population and all gene-expression subsets of the ITT population; (f) duplicate figure for progression-free survival using the ITT population; (f) duplicate figure for overall survival using the per-protocol population and all gene-expression subsets of the ITT population

Secondary figure mock showing format for "at risk" summary:

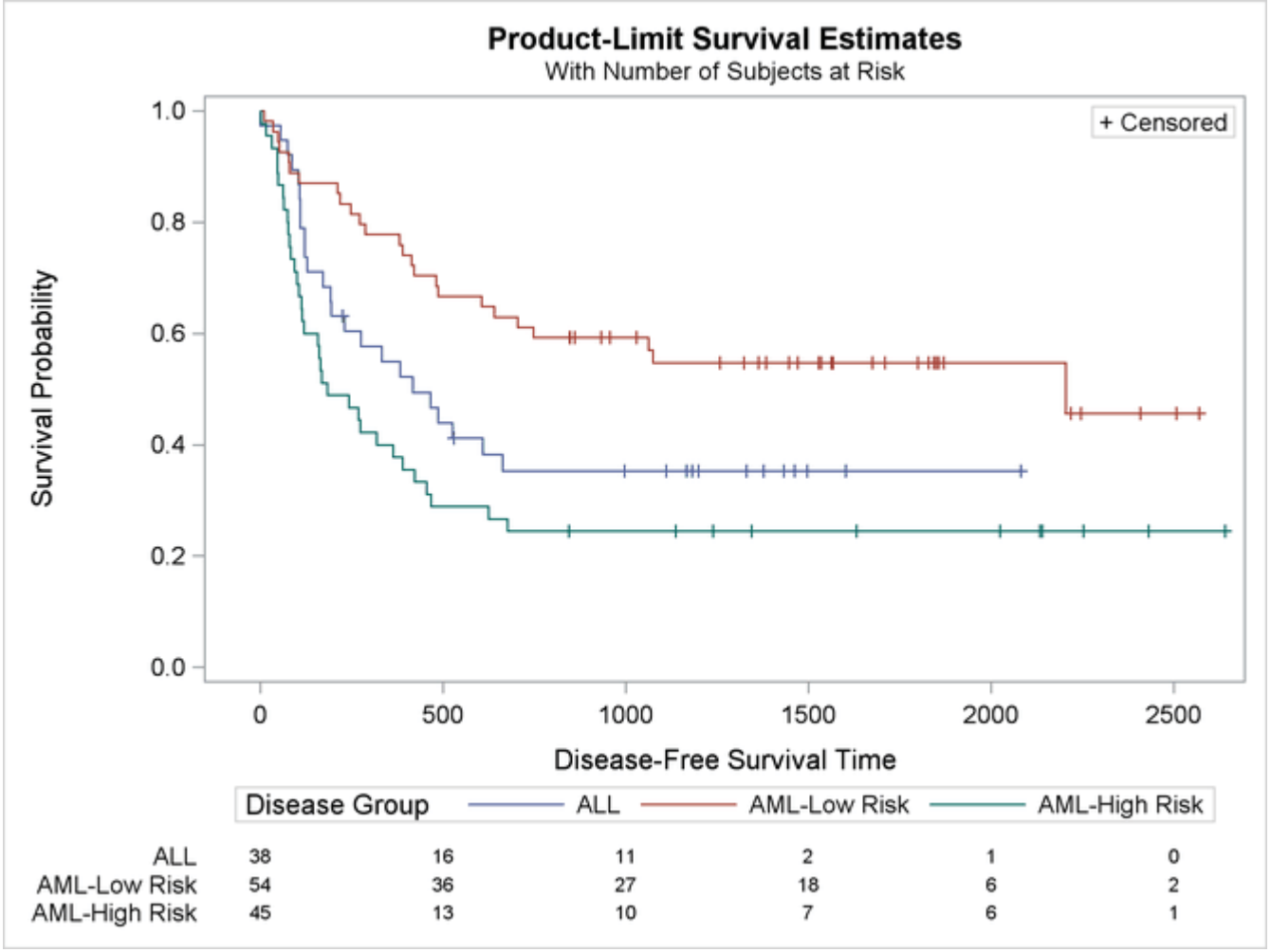


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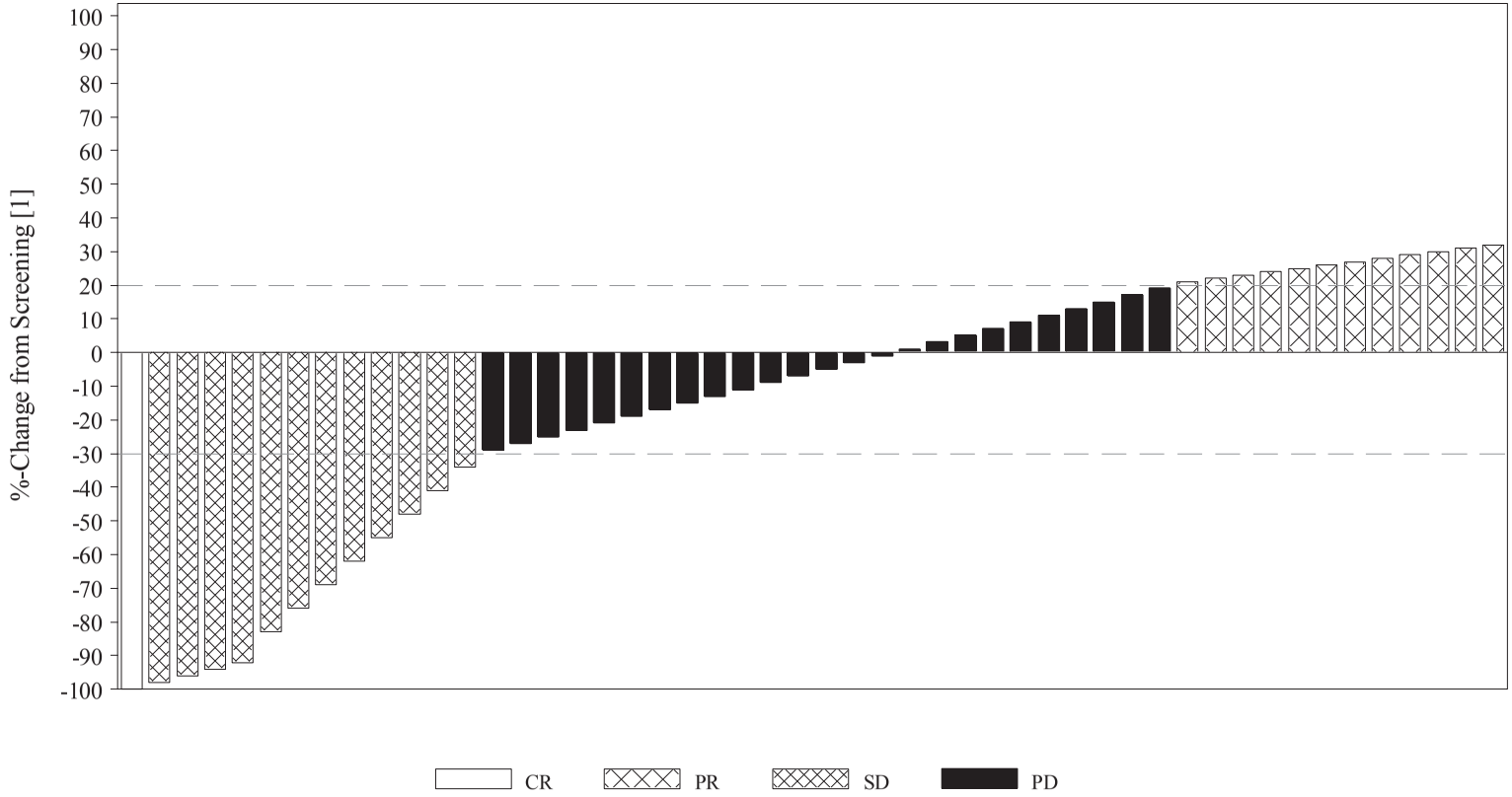
Figure 14.2.4.1
Waterfall Plot of Best Percentage Change from Baseline Total Tumor Length
ITT Population



Programmer notes: (a) replace "screening" in the y-axis label with "Baseline"; (b) delete the footnote marker "[1]" from the y-axis label; (c) duplicate figure using per-protocol population

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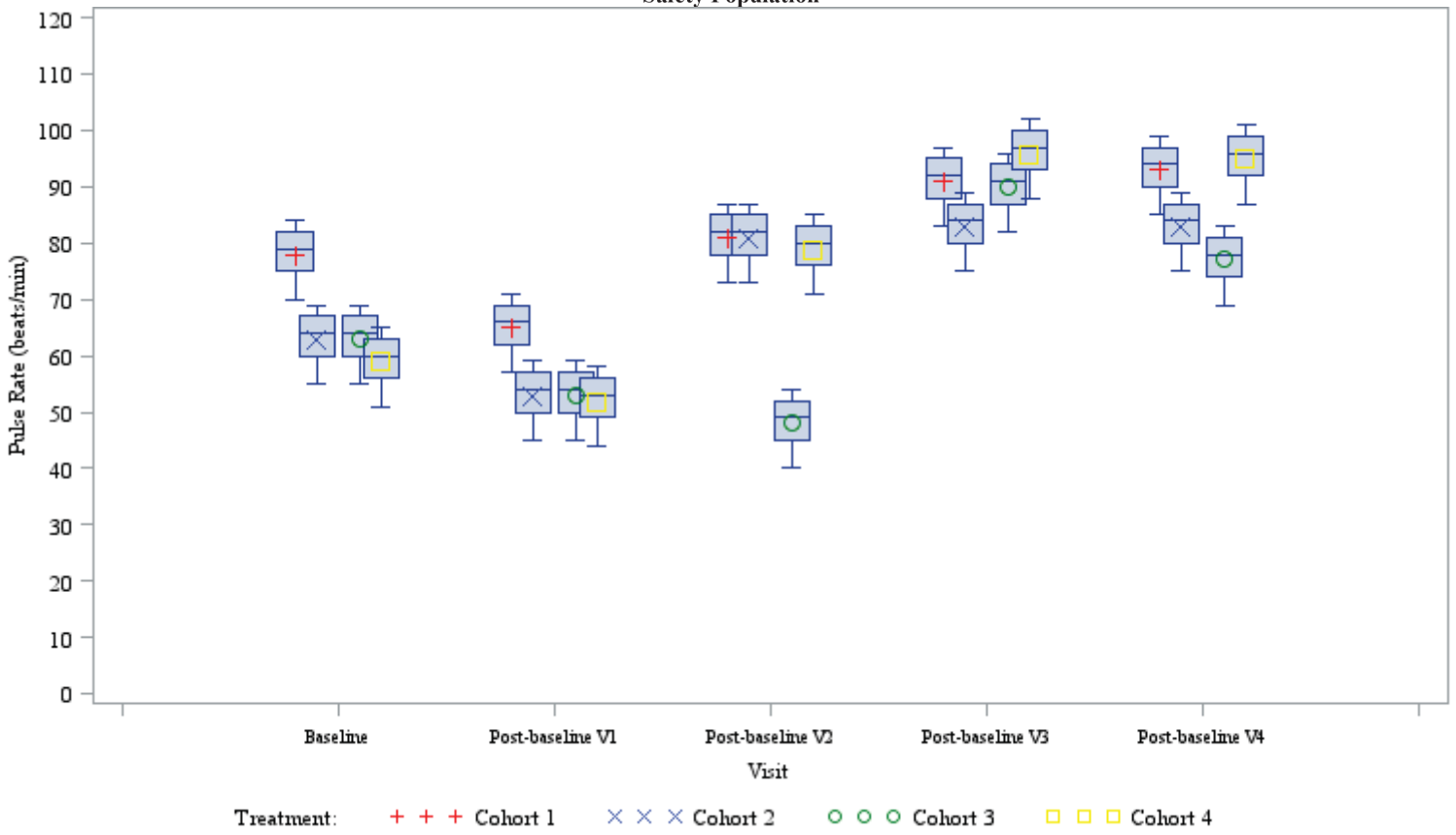
Figure 14.3.4.63
Box Plot of Pulse Rate by Visit
Safety Population



Programmer notes: (a) replace "Cohort 1" with "Placebo"; (b) replace "Cohort 2" with "Tarextumab"; (c) delete "Cohort 3" and "Cohort 4"; (d) duplicate figure for all clinical laboratory, vital sign and ECG parameters (see Planned Tables, Figures and Listings [Appendix A] for complete list); (e) duplicate all figures for "Box Plot of Change from Baseline Parameter *by Visit" – remember to (i) remove the "Baseline" marker from the x-axis and (ii) replace the y-axis label "*Parameter *(*unit*)" with "Change from Baseline* Parameter *(*unit*)"*

APPENDIX D. LISTING SHELLS

Listing 16.2.1.1
Subject Disposition

Treatment Group	Subject ID	ITT Population	Per-Protocol Population	Safety Population	Immuno-genicity Population	Pharmaco-kinetic Population	Treatment Start Date	Treatment End Date	Primary Reason for Ending Study Treatment	Study Exit Date	Primary Reason for Study Exit
Placebo | Tarextumab	003-xxx-xxx	Y | N	Y | N	Y | N	Y | N	Y | N	ddmmmyyyy	ddmmmyyyy	Lost to follow-up | Withdrawal of consent/Patient decision | Death | Adverse Event #xx: Adverse Event term | Disease Progression | Investigator decision based on patient's best interest Study Terminated by OncoMed | Other: Other term	ddmmmyyyy	Death | Lost to Follow-Up | Study Terminated by OncoMed | Withdrawal by Subject | Other: Other term

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Listing 16.2.1.2
Informed Consent

Treatment Group	Subject ID	Informed Consent Date	Randomization Date	Consented to Optional Tumor Biopsy	If Yes, Date Optional Tumor Biopsy Consent Date	Consented to Optional Pharmacogenomics Blood Sample	If Yes, Optional Pharmaco-genomics Blood Sample Consent Date	Consented to DNA Testing on Blood Sample	If Yes, DNA Testing on Blood Sample Consent Date	Consented to DNA Testing on Tumor Tissue Sample	If Yes, DNA Testing on Tumor Tissue Consent Date
Placebo | Tarextumab	003-xxx-xxx	ddmmmyyyy	ddmmmyyyy	Yes | No	ddmmmyyyy	Yes | No	ddmmmyyyy	Yes | No	ddmmmyyyy	Yes | No	ddmmmyyyy

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Listing 16.2.2.1
Major Protocol Deviations

Treatment Group	Subject ID	Protocol Deviation Description	Deviation Code
Placebo | Tarextumab	003-xxx-xxx	Description	xx-Deviation Code

Listing 16.2.3.1
Inclusion/Exclusion Criteria

Treatment Group	Subject ID	Protocol Version Date	Did the subject meet all eligibility criteria?	Criteria Type	Criterion Number	Reason Not Met
Placebo | Tarextumab	003-xxx-xxx	ddmmmyyyy	Ye s | No	Inclusion | Exclusion | None	xx	Reason

Programmer notes: (a) all subjects should be listed; (b) Display "None" for Criteria Type as appropriate

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Listing 16.2.4.1
Demographics and Baseline Characteristics
Part 1 of 2

Treatment Group	Subject ID	Date of Birth	Age (years)[1]	Sex	If Female, Child-Bearing Potential?	Race	Ethnicity
Placebo | Tarextumab	003-xxx-xxx	ddmmmyyyy	xx.x	Male | Female	Yes | No	American Indian or Alaska Native | Asian | Black or African American | Native Hawaiian or Other Pacific Islander | White	Hispanic or Latino | Not Hispanic or Latino

<second part of listing>

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Listing 16.2.4.1
Demographics and Baseline Characteristics
Part 2 of 2

Treatment Group	Subject ID	Height (cm)	Weight (kg)	Body Mass Index [2] (mg/m^2)	ECOG	Smoking History	If Ex-Smoker or Current Smoker, number of pack years	If Ex-Smoker, Stop Date
Placebo | Tarextumab	003-xxx-xxx	xxx	xx.x	x.xx	0 | 1 | 2	Never Smoked | Ex Smoker | Current Smoker	xx	ddmmmyyyy

[1] Age at time informed consent was signed.
[2] BMI (kg/m^2) = weight (kg) / [height (cm)]^2.

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Listing 16.2.4.2
Medical/Surgical History

Treatment Group	Subject ID	Any past and/or concomitant diseases or past surgeries?	Description of Medical Condition/Event	Onset Date	End Date	Ongoing/ Resolved
Placebo | Tarextumab	003-xxx-xxx	Yes | No	Description	ddmmmyyyy	ddmmmyyyy	Ongoing | Resolved

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Listing 16.2.4.3
Extensive Small Cell Lung Cancer History

Treatment Group	Subject ID	Date of Diagnosis (Study Day)	Months Since Diagnosis	Histological/ Cytological Type	Anatomical Location of Primary Cancer	Number of Sites of Disease at Study Entry	Sites of Disease at Study Entry
Placebo | Tarextumab	003-xxx-xxx	ddmmmyyyy (xx)	xx	Small Cell Only | Mixed Type | Other: Other term	Right Upper Lung | Right Lower Lung | Middle of Right Lung | Left Upper Lung | Other: Other term	x	Bone | Brain: Symptomatic/ Asymptomatic | Pleura | Adrenal Gland | Lymph Nodes: Specify Lymph Nodes | Other Nodes: Other location

Programmer notes: (a) for Sites of Disease at Study Entry, list all that apply

Listing 16.2.4.4
Prior Surgery for Lung Cancer

Treatment Group	Subject ID	Prior Surgery for Lung Cancer	Surgery Date	Description of Surgery	Location of Surgery
Placebo | Tarextumab	003-xxx-xxx	Yes | No	ddmmmyyyy	Description	Location

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Listing 16.2.4.5
Prior Radiotherapy for Lung Cancer

Treatment Group	Subject ID	Prior Radiotherapy for Lung Cancer	Start Date	End Date	Site of Treatment	Total cGY
Placebo | Tarextumab	003-xxx-xxx	Yes | No	ddmmmyyyy	ddmmmyyyy	Site of Treatment	xx | Unknown

Listing 16.2.4.6
Baseline Gene Expression

Treatment Group	Subject ID	Notch3 Expression	Hes1 Expression	Hey1 Expression	Hey2 Expression	Hes6 Expression
Placebo | Tarextumab	003-xxx-xxx	Yes | No	Yes | No	Yes | No	Yes | No	Yes | No

Listing 16.2.4.7
FFPE Tissue Sample
Part 1 of 2

		Archival Tissue				
Treatment Group	Subject ID	Sample submitted?	Biopsy Date (Study Day)	Date of Submission to OncoMed (Study Day)	Anatomical Location	Location Description
Placebo | Tarextumab	003-xxx-xxx	Yes | No	ddmmmyyyy (xx)	ddmmmyyyy (xx)	Liver | Lymph Nodes | Peritoneum | Chest Wall | Abdomen | Pelvis | Breast | Skin | Kidney | Lung | Other: *Other organ*	Description

[1] If archival tissue was not submitted.

<second part of listing>

Listing 16.2.4.7
FFPE Tissue Sample
Part 2 of 2

		Fresh Tumor Core Biopsies				
Treatment Group	Subject ID	Biopsies Performed?[1]	Biopsies Date (Study Day)	Date of Submission to OncoMed (Study Day)	Anatomical Location	Location Description
Placebo | Tarextumab	003-xxx-xxx	Yes | No	ddmmmyyyy (xx)	ddmmmyyyy (xx)	Liver | Lymph Nodes | Peritoneum | Chest Wall | Abdomen | Pelvis | Breast | Skin | Kidney | Lung | Other: *Other organ*	Description

[1] If archival tissue was not submitted.

Listing 16.2.4.8
Prior and Concomitant Medications

Treatment Group	Subject ID	Verbatim Term // Preferred Name // ATC Class[1]	Start Date (Study Day)	End Date (Study Day)	Route	Indication
Placebo | Tarextumab	003-xxx-xxx	Verbatim Term // Preferred Name // ATC Class	ddmmmyyyy (xx)	ddmmmyyyy (xx) | Ongoing	Inhalation | Intra-arterial | Intralesional | Intramuscular | Intraocular | Intraperitoneal | Intravenous | Nasal | Oral | Rectal | Subcutaneous | Topical | Transdermal | Vaginal | Other: Other term	Medical History #xx: MH term | Adverse Event #xx: AE term | Other: Other term

[1] ATC Class and Preferred Name are coded using WHO Drug Dictionary Enhanced (version March 1, 2014).

Listing 16.2.4.9
Concomitant Procedures

Treatment Group	Subject ID	Any Concomitant Procedures?	Procedure	Anatomical Location	Start Date (Study Day)	End Date (Study Day)	Indication
Placebo | Tarextumab	003-xxx-xxx	Yes | No	Procedure	Location	ddmmmyyyy (xx)	ddmmmyyyy (xx)	Medical History #xx: MH term | Adverse Event #xx: AE term | Other: Other term

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Listing 16.2.5.1
Study Drug Infusion
Part 1 of 3: Infusion Administration

Treatment Group	Subject ID	Visit	Infusion Performed?	If Infusion Was Not Performed, Specify Reason	If AE, Specify	Date of Infusion (Study Day)	Infusion Start / Stop Times	Intended Dose Per Protocol (mg)	What Weight Was Used to Calculate Dose?	Infusion Dose (mg)
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Adverse Event | Other: Other term	AE term	ddmmmyyyy (xx)	xx:xx / xx:xx	xx.xx	Weight at Current Visit | Weight at Baseline | Other: Other term	xxxx

<second part of listing>

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Listing 16.2.5.1
Study Drug Infusion
Part 2 of 3: Infusion Reduced or Delayed

			Dose Reduced			Infusion Delayed		
Treatment Group	Subject ID	Visit	Dose reduced since last infusion?	Specify Reason	If AE, Specify	Infusion Delayed?	Specify Reason	If AE, Specify
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Adverse Event | Other: Other term	AE term	Yes | No	Adverse Event | Other: Other term	AE term

<third part of listing on next page>

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Listing 16.2.5.1
Study Drug Infusion
Part 3 of 3: Infusion Interrupted or Restarted

			Infusion Interrupted			Restart after Interruption				Total Dose
Treatment Group	Subject ID	Visit	Infusion Interrupted?	Specify Reason	If AE, Specify	Infusion Restarted?	Start / Stop Times	Dose (mg)	Completed After Restart	Administered (mg)
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Adverse Event | Other: Other term	AE term	Yes | No	xx:xx / xx:xx	xxxx	Infusion was completed | Infusion was interrupted again	xxxx

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Listing 16.2.5.2
Etoposide Infusion
Part 1 of 3: Infusion Administration

Treatment Group	Subject ID	Visit	Infusion Performed?	If Infusion Was Not Performed, Specify Reason	If AE, Specify	Date of Infusion (Study Day)	Infusion Start / Stop Times	Intended Dose Per Protocol (mg)	What Weight Was Used to Calculate Dose?	BSA (m^2)	Actual Dose (mg)
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Adverse Event | Other: Other term	AE term	ddmmmyyyy (xx)	xx:xx / xx:xx	xx.xx	Weight at Current Visit | Weight at Baseline | Other: Other term	xx	xxxx

<second part of listing>

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Listing 16.2.5.2
Etoposide Infusion
Part 2 of 3: Infusion Reduced or Delayed

			Dose Reduced			Infusion Delayed		
Treatment Group	Subject ID	Visit	Dose reduced since last infusion?	Specify Reason	If AE, Specify	Infusion Delayed?	Specify Reason	If AE, Specify
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Adverse Event | Other: Other term	AE term	Yes | No	Adverse Event | Other: Other term	AE term

<third part of listing>

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Listing 16.2.5.2
Etoposide Infusion
Part 3 of 3: Infusion Interrupted or Restarted

			Infusion Interrupted			Restart after Interruption				
Treatment Group	Subject ID	Visit	Infusion Interrupted?	Specify Reason	If AE, Specify	Infusion Restarted?	Start / Stop Times	Dose (mg)	Completed After Restart	Total Dose Administered (mg)
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Adverse Event | Other: Other term	AE term	Yes | No	xx:xx / xx:xx	xxxx	Infusion was completed | Infusion was interrupted again	xxxx

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Listing 16.2.5.3
Platinum Therapy Infusion
Part 1 of 3: Infusion Administration

Treatment Group	Subject ID	Visit	Infusion Performed?	If Yes, Specify therapy	If Infusion Was Not Performed, Specify Reason	If AE, Specify	Date of Infusion (Study Day)	Infusion Start / Stop Times	Intended Dose Per Protocol	What Weight Was Used to Calculate Dose?	BSA (m^2)	GFR (mL/min/ 1.73 m^2)	Actual Dose (mg)
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Cisplatin | Carboplatin	Adverse Event | Other: Other term	AE term	ddmmmyyyy (xx)	xx:xx / xx:xx	xx.xx mg/m^2 | xx.xx mg/mL-min	Weight at Current Visit | Weight at Baseline | Other: Other term	xx	xx	xxxx

<second part of listing>

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Listing 16.2.5.3
Platinum Therapy Infusion
Part 2 of 3: Infusion Reduced or Delayed

			Dose Reduced			Infusion Delayed		
Treatment Group	Subject ID	Visit	Dose reduced since last infusion?	Specify Reason	If AE, Specify	Infusion Delayed?	Specify Reason	If AE, Specify
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Adverse Event | Other: Other term	AE term	Yes | No	Adverse Event | Other: Other term	AE term

<third part of listing>

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Listing 16.2.5.3
Platinum Therapy Infusion
Part 3 of 3: Infusion Interrupted or Restarted

			Infusion Interrupted			Restart after Interruption					
Treatment Group	Subject ID	Visit	Infusion Interrupted?	Specify Reason	If AE, Specify	Infusion Restarted?	Start / Stop Times	Dose (mg)	Completed After Restart	Total Dose Administered (mg)	Total Planned Dose (mg)
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Adverse Event | Other: Other term	AE term	Yes | No	xx:xx / xx:xx	xxxx	Infusion was completed | Infusion was interrupted again	xxxx	xxxx

Listing 16.2.5.4
Doses Delayed, Interrupted, Reduced and Not Administered

Treatment Group	Subject ID	Visit	Date (Study Day)	Dosing	Reason	Adverse Event/Other Reason
Placebo | Tarextumab	003-xxx-xxx	CYCLE X DAY X	Yes | No	Dose Delayed | Dose Interrupted | Dose Reduced | Not Administered	Adverse Event | Other	Adverse Event #xx: AE term | Other term

Note: This listing is sorted by Treatment, Dosing, Reason, and Subject.

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Listing 16.2.5.5
Pre-dose, Post-dose and Single PK Samples

Treatment Group	Subject ID	Visit	Was PK Sample Drawn?	Draw Date (Study Day)	Time Point	Draw Time
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	Pre-dose | Post-dose | [*blank*]	xx:xx

Listing 16.2.6.2
Tumor Evaluations – Target Lesions

Treatment Group	Subject ID	Visit	Was radiographic evaluation performed?	Date Performed (Study Day)	Location Number	Location	Location Description (Position within Organ)	Technique Used	Thickness of slice (mm)[1]	Longest Diameter (mm)[2]	Baseline Sum of Longest Diameters (mm)	Visit Sum of Longest Diameters (mm)	Percent Change from Baseline
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	1 | 2 | 3, etc.	Pancreas | Liver | Lymph Nodes | Peritoneum | Chest Wall | Abdomen | Pelvis | Breast | Skin | Kidney | Lung | Other: *Other location*	Position	MRI | Conventional CT | Spiral CT | PET CT | Bone Scan | Other: *Other technique*	xx.x	xx.x | Unable to Evaluate	[*blank*]	[*blank*]	[*blank*]
						⋮	⋮	⋮		⋮			
						Visit Summary	[*blank*]	[*blank*]		[*blank*]	xx.x	xx.x | NA	xx.x%

[1] If Spiral or Conventional CT Scan.
[2] If lymph node, short axis measurement is recorded.
Note: CT = Computed Tomography, NA = Not Applicable.

Programmer notes: (a) place a "Visit Summary" row following the last line for each time point; (b) leave blank the cells for Baseline Sum of Longest Diameters, Visit Sum of Longest Diameters, and Percent Change from Baseline in each row except for the Visit Summary row described in note (a)

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Listing 16.2.6.3
Tumor Evaluations – Non-target Lesions

Treatment Group	Subject ID	Visit	Was radiographic evaluation performed?	Date Performed (Study Day)	Location	Location Description (Position within Organ)	Technique Used	Lesion Status [1]
Placebo | Tarextumab	003-xxx-xxx	Baseline | Cycle x	Yes | No	ddmmmyyyy (xx)	Pancreas | Liver | Lymph Nodes | Peritoneum | Chest Wall | Abdomen | Pelvis | Breast | Skin | Kidney | Lung | Other: Other location	Position	MRI | Conventional CT | Spiral CT | PET CT | Bone Scan | Other: Other technique	CR | Non-CR/Non-PD | PD | Unable to Evaluate

[1] CR = complete response; PD = progressive disease

Listing 16.2.6.4
Tumor Evaluations – New Lesions

Treatment Group	Subject ID	Visit	Was radiographic evaluation performed?	Date Performed (Study Day)	Location	Location Description (Position within Organ)	Technique Used	Lesion Status [1]
Placebo | Tarextumab	003-xxx-xxx	Baseline | Cycle x	Yes | No	ddmmmyyyy (xx)	Pancreas | Liver | Lymph Nodes | Peritoneum | Chest Wall | Abdomen | Pelvis | Breast | Skin | Kidney | Lung | Bone | CNS | Other: Other location	Position	MRI | Conventional CT | Spiral CT | PET-CT | Bone Scan | X-Ray | Physical Exam | Other: Other technique	CR | Non-CR/Non-PD | PD | Unable to Evaluate

[1] CR = complete response; PD = progressive disease

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Listing 16.2.6.5
Tumor Assessments (RECIST Overall Response)

Treatment Group	Subject ID	Visit	Response Date (Study Day)	Target Lesion Response [1]	Target Lesion Response [1]	New Lesions	Overall Response Assessment [1]	If Overall Response is Progressive Disease, was it non-radiographic clinical progression?
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	ddmmmyyyy (xx)	CR | PR | SD | PD | Unable to Evaluate: *Reason* | Not Evaluated	No Lesions at Baseline | CR | PR | SD | PD | Unable to Evaluate: *Reason* | Not Evaluated	Yes | No	CR | PR | SD | PD | PD | Not Evaluated	Yes | No

[1] CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease

Listing 16.2.6.6
Derived Efficacy Data

		RECIST v1.1 Assessment		PFS[2]		OS[3]		DOR[4]	
Treatment Group	Subject ID	Best Tumor Response	Objective Response[1]	Censored	Days	Censored	Days	Censored	Days
Placebo | Tarextumab	003-xxx-xxx	CR | PR | SD | PD | NE	Yes | No	Yes | No	xxx	Yes | No	xxx	Yes | No	xxx

Note: CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; NE = Not Evaluated.
[1] Best response of CR or PR.
[2] Progression-Free Survival (PFS) = Date of Documentation of Death/Progression – Randomization Date + 1. Subjects who had not experienced death or progression by their last contact were censored at the time of their last radiographic response assessment. Subjects lacking a radiographic response assessment after randomization who do not progress or die have their event time censored on the date of randomization with duration of 1 day.
[3] Overall Survival (OS) = Date of Documentation of Death – Randomization Date + 1. Subjects who had not experienced death by their last contact were censored at the time. Subjects lacking data after randomization who do not die have their event time censored on the date of randomization with duration of 1 day.
[4] Duration of Response (DOR) = Date of Documentation of Death/Progression – Date of First Partial (PR) or Complete Response (CR) + 1. Patients who discontinue the study without disease progression or death while on study are censored on the date of the last on study tumor assessment documenting the absence of progressive disease. Patients lacking a tumor assessment after first dose who do not progress or die while on study have their event time censored on the date of first dose with duration of 1 day.

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Listing 16.2.21
End of Treatment

<table>
<tr><th></th><th></th><th colspan="3">Study Drug</th><th colspan="3">Etoposide</th><th colspan="3">Platinum Therapy</th></tr>
<tr><th>Treatment Group</th><th>Subject ID</th><th>Date of Last Dose (Study Day)</th><th>Primary Reason for Ending</th><th>Primary Associated AE</th><th>Date of Last Dose (Study Day)</th><th>Primary Reason for Ending</th><th>Primary Associated AE</th><th>Date of Last Dose (Study Day)</th><th>Primary Reason for Ending</th><th>Primary Associated AE</th></tr>
<tr><td>Placebo |
Tarextumab</td><td>003-xxx-xxx</td><td>ddmmmyyyy
(xx)</td><td>Lost to follow-up |
Withdrawal of consent/Patient Decision |
Death |
Adverse Event |
Disease progression |
Investigator decision based on patient's best interest |
Study Terminated by OncoMed |
Other: Other term</td><td>Adverse Event #xx: AE term</td><td>ddmmmyyyy
(xx)</td><td>Lost to follow-up |
Withdrawal of consent/Patient Decision |
Death |
Adverse Event |
Disease progression |
Investigator decision based on patient's best interest |
Study Terminated by OncoMed |
Other: Other term</td><td>Adverse Event #xx: AE term</td><td>ddmmmyyyy
(xx)</td><td>Lost to follow-up |
Withdrawal of consent/Patient Decision |
Death |
Adverse Event |
Disease progression |
Investigator decision based on patient's best interest |
Study Terminated by OncoMed |
Other: Other term</td><td>Adverse Event #xx: AE term</td></tr>
</table>

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Listing 16.2.7.1
Adverse Events
Part 1 of 2

Treatment Group	Subject ID	AE #	Verbatim Term // MedDRA Preferred Term // System Organ Class	Onset Date (Study Day)	End Date (Study Day)	On-going	Severity (CTCAE V4.02 Grade)	Treatment of Event	Infusion Reaction	Outcome	Caused Study Drug Discon-tinuation	Serious Event	Serious Event Type
Placebo |Tarextumab	003-xxx-xxx	xx	Verbatim Term // MedDRA Preferred Term // System Organ Class	ddmmmyyyy (xx)	ddmmmyyyy (xx)	Yes | No	x	None | Medication | Non-Drug Treatment | Hospitalization	Yes | No	Recovered/Resolved without Sequelae | Recovered/Resolved with Sequelae | Not Recovered/Not Resolved | Fatal | Unknown	Yes | No	Yes | No	Yes | No

<second part of listing>

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Listing 16.2.7.1
Adverse Events
Part 2 of 2

Treatment Group	Subject ID	AE #	Relationship to			Initial Action Taken with			Action Taken with		
			Tarextumab	Etoposide	Platinum Therapy	Tarextumab	Etoposide	Platinum Therapy	Tarextumab	Etoposide	Platinum Therapy
Placebo | Tarextumab	003-xxx-xxx	xx	Related | Not Related	Related | Not Related	Related | Not Related	None | Dose Reduced | Dose Delayed | Infusion Interrupted | Withdrawn | Not Applicable	None | Dose Reduced | Dose Delayed | Infusion Interrupted | Withdrawn | Not Applicable	None | Dose Reduced | Dose Delayed | Infusion Interrupted | Withdrawn | Not Applicable	None | Dose Reduced | Dose Delayed | Infusion Interrupted | Withdrawn | Not Applicable	None | Dose Reduced | Dose Delayed | Infusion Interrupted | Withdrawn | Not Applicable	None | Dose Reduced | Dose Delayed | Infusion Interrupted | Withdrawn | Not Applicable

Programmer notes: (a) Duplicate this listing to create Listing 16.2.7.3 of "Serious Adverse Events" and Listing 16.2.7.4 of "Adverse Events Leading to Study Drug Discontinuation"

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Listing 16.2.7.2
Deaths

Treatment Group	Subject ID	Date of Death (Study Day)	Cause of Death	Primary Associated AE
Placebo | Tarextumab	003-xxx-xxx	ddmmmyyyy (xx)	Adverse Event | Progressive Disease Unknown | Other: Other term	AE term

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Listing 16.2.8.1
Hematology
Part 1 of 2

Treatment Group	Subject ID	Visit	Sample collected?	Collection Date (Study Day)	Collection Time	Hemoglobin (g/dL)	Hematocrit (%)	Platelets ($x10^3$/uL)	RBC ($x10^6$/uL)	WBC ($x10^3$/uL)	ANC ($x10^3$/uL)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	xx:xx	xx.x[L/H, G1/G2/G3/G4]	xx.x	xx.x	xx.x	xx.x	xx.x

Note: RBC = Red Blood Cells, WBC = White Blood Cell, ANC = Absolute Neutrophil Count, ND = Not Done. L = Low, H = High, with respect to laboratory reference ranges. Grades are according to NCI Common Terminology Criteria Adverse Events (CTCAE) version 4.03

Programming notes: Display L/H, G1/G2/G3/G4/G5 for each lab test result, where applicable.

<second part of listing>

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Listing 16.2.8.1
Hematology
Part 2 of 2

Treatment Group	Subject ID	Visit	Sample collected?	Collection Date (Study Day)	Collection Time	Neutrophils (%)	Bands (%)	Lymphocytes (%)	Eosinophils (%)	Monocytes (%)	Basophils (%)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	xx:xx	xx.x[L/H, G1/G2/G3/G4]	xx.x	xx.x	xx.x	xx.x	xx.x

Note: RBC = Red Blood Cells, WBC = White Blood Cell, ANC = Absolute Neutrophil Count, ND = Not Done. L = Low, H = High, with respect to laboratory reference ranges. Grades are according to NCI Common Terminology Criteria Adverse Events (CTCAE) version 4.03

Programming notes: Display L/H, G1/G2/G3/G4/G5 for each lab test result, where applicable.

Listing 16.2.8.2
PT/INR and aPTT

Treatment Group	Subject ID	Visit	Sample collected?	Collection Date (Study Day)	Collection Time	Prothrombin Time (PT) (sec)	International Normalized Ratio (INR)	Activated Partial Thromboplastin Time (aPTT) (sec)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	xx:xx	xx.x[L/H, G1/G2/G3/G4]	xx.x	xx.x

Note: ND = Not Done. L = Low, H = High, with respect to laboratory reference ranges. Grades are according to NCI Common Terminology Criteria Adverse Events (CTCAE) version 4.03

Programming notes: Display L/H, G1/G2/G3/G4 for each lab test result, where applicable.

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Listing 16.2.8.3
Serum Chemistry
Part 1 of 2

Treatment Group	Subject ID	Visit	Sample collected?	Collection Date (Study Day)	Collection Time	Fasting for at least 6 hours?	Albumin (g/dL)	Alkaline Phosphatase (U/L)	Total Bilirubin (mg/dL)	Direct Bilirubin (mg/dL)	Bicarbonate (mEq/L)	Blood Urea Nitrogen (mg/dL)	Calcium (mg/dL)	Chloride (mEq/L)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	xx:xx	Yes | No	xx.x L/H, G1/G2/G3/G4	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x

Note: LDH = Lactic Dehydrogenase, ND = Not Done. L = Low, H = High, with respect to laboratory reference ranges. Grades are according to NCI Common Terminology Criteria Adverse Events (CTCAE) version 4.03

Programming notes: Display L/H, G1/G2/G3/G4/G5 for each lab test result, where applicable.

<second part of listing>

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Listing 16.2.8.3
Serum Chemistry
Part 2 of 2

Treatment Group	Subject ID	Visit	Sample collected?	Collection Date (Study Day)	Collection Time	Fasting for at least 6 hours?	Creatinine (mg/dL)	Blood Glucose (mg/dL)	LDH (U/L)	Magnesium (mg/dL)	Phosphorus (mg/dL)	Potassium (mEq/L)	Total Protein (g/dL)	AST (SGOT) (U/L)	ALT (SGPT) (U/L)	Sodium (mEq/L)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	xx:xx	Yes | No	xx.x L/H, G1/G2/G3/G4	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	

Note: LDH = Lactic Dehydrogenase, ND = Not Done. L = Low, H = High, with respect to laboratory reference ranges. Grades are according to NCI Common Terminology Criteria Adverse Events (CTCAE) version 4.03

Programming notes: Display L/H, G1/G2/G3/G4/G5 for each lab test result, where applicable.

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Listing 16.2.8.4
Urinalysis
Part 1 of 2

Treatment Group	Subject ID	Visit	Sample collected?	Collection Date (Study Day)	Collect-ion Time	Protein	Glucose	Ketones	Blood	Bilirubin	pH	Specific Gravity
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE 1 DAY 1	Yes | No	ddmmmyyyy (xx)	xx:xx	Negative | Positive: Trace/ 1+/ 2+/ 3+/ 4+/ Unknown | Not Done	Negative | Positive | Not Done	Negative | Positive | Not Done	Negative | Positive | Not Done	Negative | Positive | Not Done	x.x	x.xx

<second part of listing>

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Listing 16.2.8.4
Urinalysis
Part 2 of 2

Treatment Group	Subject ID	Visit	Sample collected?	Collection Date (Study Day)	Collection Time	Microscopic Exam Performed?	Bacteria	Casts	Crystals	RBC (cells/hpf)	WBC (cells/hpf)	Other test	Result (units)	Reference Range
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE 1 DAY 1	Yes | No	ddmmmyyyy (xx)	xx:xx	Yes | No	Absent | Present | Not Done	Absent | Present | Not Done	Absent | Present | Not Done	xx	xx	x.xx	xx units	xx-xx

Listing 16.2.8.5
Vital Signs

Treatment Group	Subject ID	Visit	Vital Signs Measured?	Date (Study Day)	Time	Temperature (°C)	Pulse Rate (beast/min)	Respiratory Rate (beats/min)	Blood Pressure (Systolic/ Diastolic) (mmHg)	Height (cm)	Weight (kg)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy	xx:xx	xx.x	xx	xx	xxx/xx	xxx.x	xx.x

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Listing 16.2.8.6
ECOG Performance Status

Treatment Group	Subject ID	Visit	ECOG Assessment Performed?	Assessment Date (Study Day)	Score[1]
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	x

[1] 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature (e.g., light housework, office work; 2 = Ambulatory and capable of all self-care, but unable to carry out any work activities. Up and about more than 50% of waking hour; 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hour; 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair; 5 = Dead.

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Listing 16.2.8.7
12-Lead ECG
Part 1 of 2

Treatment Group	Subject ID	Visit	Was ECG Performed?	Date of Assessment (Study Day)	PR Interval (msec)	QRS Duration (msec)	QTc Interval (msec)	QTc Interval Formula
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	xxx	xxx	xxx	Bazett | Fridericia

Note: MH = Medical History

<second part of listing>

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Listing 16.2.8.7
12-Lead ECG
Part 2 of 2

Treatment Group	Subject ID	Visit	Was ECG Performed?	Date of Assessment (Study Day)	Interpretation	If Abnormal, Describe Abnormality	If Abnormal, Clinically Significant?	Primary Associated AE	Primary Associated MH
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	Normal | Abnormal	Description	Yes | No	AE term	MH term

Note: MH = Medical History

Listing 16.2.8.8
Physical Examination

Treatment Group	Subject ID	Visit	Was Physical Exam Performed?	Date of Exam (Study Day)	Abnormal Findings?	If Abnormal, Clinically Significant?	If Yes, Primary MH	If Yes, Primary AE	If No, Description of Non-Clinically Significant Abnormality
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	Yes | No	Yes | No	MH term	AE term	Description

Note: MH = Medical History

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Listing 16.2.8.9
Optional Blood for Pharmacogenomics

Treatment Group	Subject ID	Visit	Was optional blood sample collected for pharmacogenomics?	PG Blood Date of Collection (Study Day)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)

Listing 16.2.8.10
CA 19-9 Tumor Marker

Treatment Group	Subject ID	Visit	Was the CA19-9 Tumor Marker Sample Collected?	Collection Date (Study Day)	Result (Units)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	xxxxx.x units

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Listing 16.2.8.11
Anti-Tarextumab Antibodies

Treatment Group	Subject ID	Visit	Was the Anti-Tarextumab Antibody Sample Collected?	Collection Date (Study Day)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)

Listing 16.2.8.12
Blood for Biomarkers

Treatment Group	Subject ID	Visit	Was Blood Sample for Plasma Biomarkers Collected?	Blood Sample for Plasma Biomarkers Collection Date (Study Day)	Was Blood Sample for mRNA Biomarkers Collected?	Blood Sample for mRNA Biomarkers Collection Date (Study Day)	Was Blood Sample for CTCs Collected?	Blood Sample for CTCs Collection Date (Study Day)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	Yes | No	ddmmmyyyy (xx)	Yes | No	ddmmmyyyy (xx)

Listing 16.2.8.13
Serum Pregnancy Test

Treatment Group	Subject ID	Visit	Was the Pregnancy Test performed?	If No, Specify Reason	Date of Assessment (Study Day)	Result
Placebo | Tarextumab	003-xxx-xxx	SCREENING | UNSCHEDULED	Yes | No	Prior Hysterectomy | Other Reason:	ddmmmyyyy (xx)	Positive | Negative

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Listing 16.2.8.14
Optional Tumor Core Biopsy

Treatment Group	Subject ID	Visit	Was an Optional Tumor Core Biopsy Sample Collected?	Date of Collection (Study Day)	Time of Collection	Location	Location Description (Position within Organ)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	ddmmmyyyy (xx)	xx:xx	Pancreas | Liver | Lymph | Nodes | Peritoneum | Chest Wall | Abdomen | Pelvis | Breast | Skin | Kidney | Lung | Other: Other organ	Description

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Listing 16.2.8.15
On Study PCI or WBRT (PCI)

			Prophylactic Cranial Irradiation (PCI)				Whole Brain Radiation [WBRT (PCI)]			
Treatment Group	Subject ID	Visit	Administered during study?	Total cGY	Start Date (Study Day)	Stop Date (Study Day)	Administered during study?	Total cGY	Start Date (Study Day)	Stop Date (Study Day)
Placebo | Tarextumab	003-xxx-xxx	SCREENING | CYCLE X DAY X	Yes | No	xx | Unknown	ddmmmyyyy (xx)	ddmmmyyyy (xx)	Yes | No	xx | Unknown	ddmmmyyyy (xx)	ddmmmyyyy (xx)

Listing 16.2.8.16
Follow-Up After Discontinuation of Study Treatment

Treatment Group	Subject ID	Visit	Was a Survival Follow-Up Done?	Date of Survival Assessment (Study Day)	Subject Status	Last Known Survival Date (Study Day)
Placebo | Tarextumab	003-xxx-xxx	X MONTH SURVIVAL FOLLOW-UP	Yes | No	ddmmmyyyy (xx)	Alive | Dead | Lost to Follow-Up	ddmmmyyyy (xx)

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Listing 16.2.17
Treatments and Procedures for Extensive Small Lung Cancer During Follow-Up Period
Part 1 of 3: Surgery

Treatment Group	Subject ID	Visit	Any surgeries for the treatment of lung cancer during follow-up period?	Surgery Description	Location	Surgery Date (Study Day)
Placebo | Tarextumab	003-xxx-xxx	X MONTH SURVIVAL FOLLOW-UP	Yes | No	Description	Location	ddmmmyyyy (xx)

<second part of listing>

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Listing 16.2.17
Treatments and Procedures for Extensive Small Lung Cancer During Follow-Up Period
Part 2 of 3: Radiotherapy

Treatment Group	Subject ID	Visit	Any radiotherapy for the treatment of lung cancer during follow-up period?	Site of Treatment	Total cGY	Start Date (Study Day)	Stop Date (Study Day)	Systemic Therapy?
Placebo | Tarextumab	003-xxx-xxx	X MONTH SURVIVAL FOLLOW-UP	Yes | No	Site	xx | Unknown	ddmmmyyyy (xx)	ddmmmyyyy (xx)	Yes | No

<third part of listing>

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Listing 16.2.17
Treatments and Procedures for Extensive Small Lung Cancer During Follow-Up Period
Part 3 of 3: Systemic Therapy

Treatment Group	Subject ID	Visit	Any systemic therapy for the treatment of lung cancer during follow-up period?	Regimen	Start Date (Study Day)	End Date (Study Day)
Placebo | Tarextumab	003-xxx-xxx	X MONTH SURVIVAL FOLLOW-UP	Yes | No	Regimen	ddmmmyyyy (xx)	ddmmmyyyy (xx)