Statistical Analysis Plan: I5B-MC-JGDQ

An Open-Label, Multicenter, Phase 1a/1b Study of Olaratumab (LY3012207) Plus Pembrolizumab (MK3475) in Patients with Advanced or Metastatic Soft Tissue Sarcoma (STS) who have Failed Standard Treatments

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Approval Date: 15 Feb 2017

1. Statistical Analysis Plan: I5B-MC-JGDQ: An Open-Label, Multicenter, Phase 1a/1b Study of Olaratumab (LY3012207) Plus Pembrolizumab (MK3475) in Patients with Advanced or Metastatic Soft Tissue Sarcoma (STS) who have Failed Standard Treatments

Olaratumab (LY3012207)

This Phase 1 study is an open-label, multicenter, nonrandomized, noncomparative, dose-escalation study followed by cohort expansion of intravenous LY3012207 plus intravenous pembrolizumab (MK3475) in patients with advanced or metastatic soft tissue sarcoma who have failed standard treatments.

Eli Lilly and Company
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Protocol I5B-MC-JGDQ
Phase 1

Statistical Analysis Plan electronically signed and approved by Lilly on date provided below.

Approval Date: 15-Feb-2017 GMT

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3. Revision History

SAP Version 1 was approved prior to the first visit when a subject receives study drug or other protocol intervention.

4. Study Objectives

4.1. Phase 1a: Dose Escalation

4.1.1. Primary Objective

The primary objective of the Phase 1a portion of the study is to confirm the safety and tolerability of the combination of olaratumab plus pembrolizumab in patients with unresectable locally advanced or metastatic STS who have failed standard treatments.

4.1.2. Secondary Objectives

The secondary objectives of the Phase 1a portion of the study are:

- To characterize the pharmacokinetics (PK) and pharmacodynamics (PD) of olaratumab when administered in combination with pembrolizumab
- To determine the immunogenicity of olaratumab when administered in combination with pembrolizumab
- To document any antitumor activity of olaratumab when administered in combination with pembrolizumab as assessed by:
    - Objective response rate (ORR) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 and immune-related RECIST (irRECIST)
    - Disease control rate (DCR) using RECIST v1.1 and irRECIST
    - Duration of response (DOR) using RECIST v1.1 and irRECIST
    - Progression-free survival (PFS) using RECIST v1.1 and irRECIST
    - Overall survival (OS)

4.2. Phase 1b: Dose Expansion

4.2.1. Primary Objective

The primary objective of the Phase 1b portion of the study is to confirm the safety and tolerability of the combination of olaratumab plus pembrolizumab at the recommended dose in patients with unresectable locally advanced or metastatic STS who have failed standard treatments.

4.2.2. Secondary Objectives

The secondary objectives of the Phase 1b portion of the study are:

- To document any antitumor activity of olaratumab when administered in combination with pembrolizumab as assessed by:
    - ORR using RECIST v1.1 and irRECIST

- DCR using RECIST v1.1 and irRECIST
- DOR using RECIST v1.1 and irRECIST
- PFS using RECIST v1.1 and irRECIST
- OS

- To characterize the PK and PD of olaratumab when administered in combination with pembrolizumab
- To determine the immunogenicity of olaratumab when administered in combination with pembrolizumab

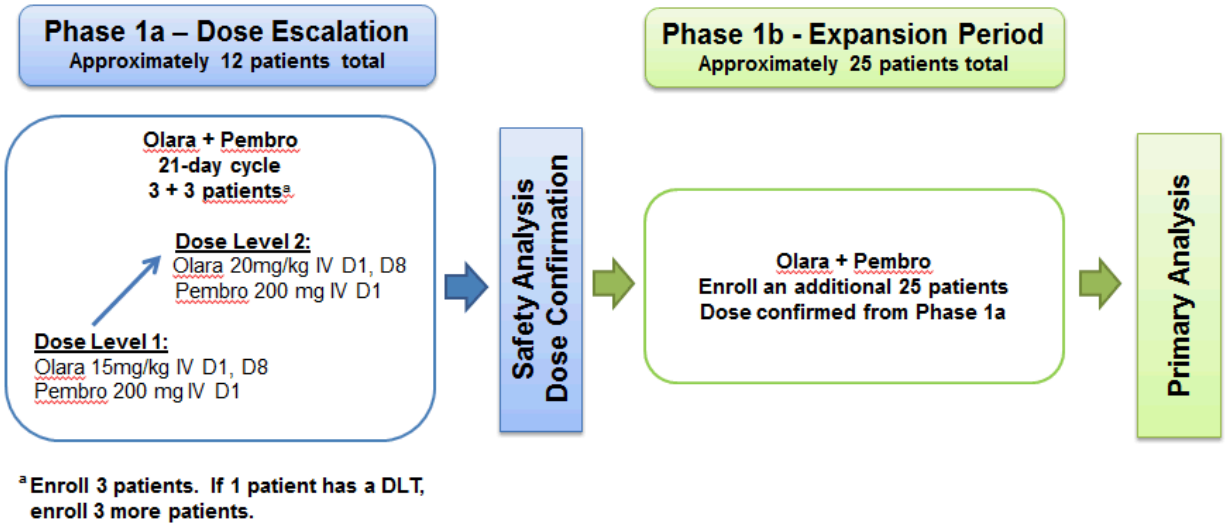
5. Study Design

5.1. Summary of Study Design

Study JGDQ is an open-label, multicenter, nonrandomized, Phase 1a/1b dose-escalation study followed by cohort expansion of intravenous olaratumab plus pembrolizumab in patients with advanced or metastatic STS who have failed standard treatments.

In the Phase 1a dose-escalation portion of the study, eligible patients will receive olaratumab 15 mg/kg (starting dose) or 20 mg/kg on Day 1 and Day 8 plus pembrolizumab 200 mg IV (fixed dose) on Day 1 of a 21-day cycle. Patients will enroll patients in a 3+3 fashion until dose-limiting toxicity (DLT) is observed or the maximum tolerated dose is achieved. Patients in any cohort who do not complete Cycle 1 treatment for reasons other than a DLT will be replaced. A minimum of 6 patients will be enrolled to the highest tolerated dose arm in Phase 1a.

Upon determination of recommended dose for olaratumab combinations, an expansion cohort in the Phase 1b portion of the study will open. Eligible patients will receive the recommended Phase 1b dose of olaratumab plus pembrolizumab according to a 21-day cycle.



5.2. Determination of Sample Size

In Phase 1a portion of the study, up to approximately 12 patients may be treated and evaluated in order to determine the recommended dose for the Phase 1b portion (recommended Phase 1b dose; RP1bD). In the Phase 1b portion, approximately 25 patients will be enrolled. Further details on the sample size determination are provided in the protocol.

6. A Priori Statistical Methods

6.1. General Considerations

Statistical analysis of this study will be the responsibility of Eli Lilly and Company.

The interpretation of the study results will be the responsibility of the investigator with the Lilly CRP/CRS, pharmacokineticist, and statistician. The CRP/CRS and statistician will also be responsible for the appropriate conduct of an internal review for both the final study report and any study-related material to be authorized by Lilly for publication.

All data summaries and figures will be split by treatment dose. Sponsor standard TFLs and supporting programs and software (e.g. TAFFY, BEACH) will be utilized for all analyses where a suitable standard exists. Data derivations in this SAP are defined based upon current sponsor reporting standards at the time of writing, and may be updated at the time of analysis in order to maintain accordance with the most current sponsor standards at that time.

In general, continuous variables will be presented using the mean, standard deviation (SD), coefficient of variation, median, minimum, maximum and number of patients with an observation (n). For categorical variables, the population size (N), the number of patients with events (n) and the percentage of patients with events are usually reported.

The following populations will be defined for this study:

Safety population: will include all enrolled patients who received any quantity of study treatment, regardless of their eligibility for the study. The safety evaluation will be performed based on the first dose of study treatment a patient actually received. The safety population will be used for all dosing/exposure, safety and efficacy analyses.

Pharmacokinetic population: will include all enrolled patients who received at least 1 dose of study treatment and have at least 1 postbaseline evaluable PK sample.

CCI [redacted]

The following data handling conventions will be used in the analysis.

Term	Definition or Rule
Relative Study Day	If assessment is on or after date of first dose then (date of assessment) – (date of first study drug dose) +1
	If assessment precedes first dose of drug then (date of assessment) – (date of first study drug dose)
	There is no study day 0. Study day 1 is the date of first dose and study day -1 is the day before the first dose.
Cycle Day	If assessment is on or after date of first dose in cycle then (date of assessment) – (date of first study drug dose in cycle) +1
	There is no cycle day 0. Cycle day 1 is the date of first dose in that cycle.
Baseline	For change from baseline analyses, baseline value is defined as the last reported measure on or before the first dose date (prior to the dose administration), unless otherwise specified.
Entered	Patients who have signed the informed consent document directly.
Enrolled	Patients who have been assigned to study treatment
Safety analysis set	Patients who have been enrolled and received at least one dose of any study drug.
Screen Failures	Patients who have signed informed consent, do not meet eligibility criteria and are not enrolled.

6.2. Adjustments for Covariates

Given the small sample size for each tumor type and treatment, no formal analysis investigating the impact of covariates is planned. Exploratory analyses may be performed on safety or efficacy measures to adjust for factors that may affect outcomes.

6.3. Handling of Dropouts or Missing Data

Missing data, except for dates, will not be imputed. They will be kept as missing in the data analyses, except for dates when used in calculations of relative study day, for which sponsor reporting standards will be utilized for imputation rules, defined as: Missing start days will be replaced with 1 and missing day/month with 01 JAN. Missing end days will be replaced with the last day of the month, and missing day/month with 31 DEC, or date of death if this occurs prior to the proposed imputation date. The imputation rule may be updated at the time of study reporting if necessary to maintain accordance with most recent sponsor standards. Partial dates should be reported in all listings and not the imputed date.

For time-to-event endpoints, the method for handling missing data will be censoring. Patients that withdrew from the study without progression will be censored at the date of the last tumor assessment. Additional sensitivity analyses may be conducted applying different censoring rules if data warrant and will follow sponsor defined standards.

6.4. Multicenter Studies

Given the small number of patients for each tumor type and treatment, patients across all sites will be grouped together for analysis purposes.

6.5. Multiple Comparisons/Multiplicity

No formal hypothesis testing is planned for this study. Thus, there will be no adjustments for multiplicity.

6.6. Use of an "Efficacy Subset" of Patients

Analyses of disposition will use all patients entered in to the study. All other analyses for this study, including efficacy analyses, will utilize the safety analysis set, defined as all enrolled patients who have received at least one dose of any study drug. Analyses will be reported according to patient's treatment.

6.7. Patient Disposition

All patient discontinuations will be documented, and the extent of each patient's participation in the study will be reported. If known, a reason for their discontinuation from both study treatment and study will be given. A detailed description of patient disposition will be provided. It will include a summary of the number and percentage of patients entered into the study, and treated as well as number and percentage of patients completing the study, or discontinuing (overall and by reason for discontinuation). A listing of primary reasons for study treatment discontinuation will also be provided according to each treatment.

6.8. Patient Characteristics

Patient characteristics will include a summary of the following:

- Patient demographics [including age, sex, screening height and weight, race, ethnicity, and screening body mass index (BMI)] will be reported.
- Baseline disease characteristics including ECOG status, initial pathological diagnosis, disease stage, histopathological diagnosis grade.

Other patient characteristics will be summarized as deemed appropriate.

6.9. Treatment Compliance

Treatment compliance will not be calculated since Olaratumab and Pembrolizumab are administered intravenously.

6.10. Concomitant Therapy

All medications will be coded to the generic preferred name according to the current World Health Organization (WHO) drug dictionary. All concomitant medications listings will include both the term reported in CRF and the WHO dictionary term and if concomitant medication use is due to an adverse event (AE), the associated AE will also be listed.

Prior anti-cancer systemic therapy, radiotherapy and surgery will be summarized. Summaries will include the reason, type of therapy, number of prior regimens and drug name. Prior therapies will also be listed, including the patients response to prior therapy.

Anti-cancer systemic therapy, radiotherapy or surgery that occurs post discontinuation of study treatment is captured separately from concomitant medication as the existence of such

therapies can lead to censoring of time to event endpoints. Patients that received post discontinuation therapies will be listed and summarized.

6.11. Efficacy Analyses

6.11.1. Efficacy Definitions

The following definitions for efficacy endpoints will be used:

Overall response rate (ORR) is the proportion of patients who achieved a complete response (CR) or partial response (PR) out of all patients treated. Tumor responses will be measured and recorded using the appropriate guidelines [RECIST 1.1 (Eisenhauer et al. 2009].

Best response is determined as the best response recorded from start of study treatment until PD or recurrence.

Disease Control Rate (DCR) is the proportion of patients who achieved a best response of complete response (CR), partial response (PR) or stable disease (SD) out of all patients treated.

Immune-related objective response rate (irORR) is defined as the proportion of treated patients achieving a best overall response of PR or CR per irRECIST, particularly, the best overall response by irRECIST closely related to confirmed response by RECIST. Immune-related ORR further captures responses after unconfirmed PD and does not require confirmation. For example:

- If the best response by RECIST v.1.1 is CR, then the best response by irRECIST is CR.
- If the best response by RECIST v.1.1 is PR, SD, or PD, the best response by irRECIST is the best response over the initial assessment (prior to PD by RECIST v.1.1) and the confirmation stage.

Overall, the best response by irRECIST should be the same or better than the best response by RECIST v.1.1 criteria. In addition, patients who do not have any postbaseline tumor response assessments for any reason are considered non-evaluable and will be included in the denominator when calculating the response rate.

Immune-related disease control rate (irDCR) is defined as the proportion of treated patients achieving a best overall response of CR, PR or SD per irRECIST.

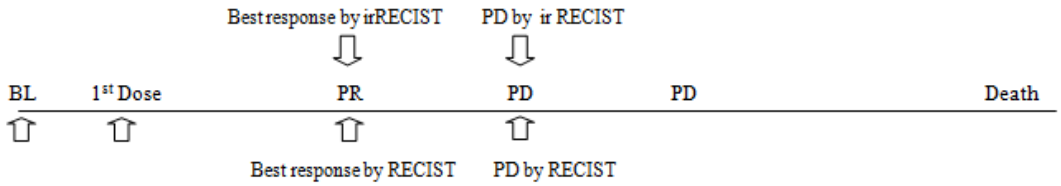
Duration of Response will be calculated for ORR and is defined only for responders (ie. CRs and PRs). It is measured from the date of first evidence of a confirmed response to the date of first progression of disease or the date of death due to any cause, whichever is earlier. For each patient who is not known to have died or to have had a progression of disease as of the data-inclusion cut-off date, duration of response will be censored at the date of last objective response assessment prior to the date of any subsequent systemic anticancer therapy.

Duration of Stable Disease will be calculated only for patients with best response of stable disease, CR or PR. It is measured from the date of start of treatment to the date of first progression of disease or the date of death due to any cause, whichever is earlier. For each patient who is not known to have died or to have had a progression of disease as of the data-inclusion cut-off date, duration of stable disease will be censored at the date of last objective response assessment prior to the date of any subsequent systemic anticancer therapy.

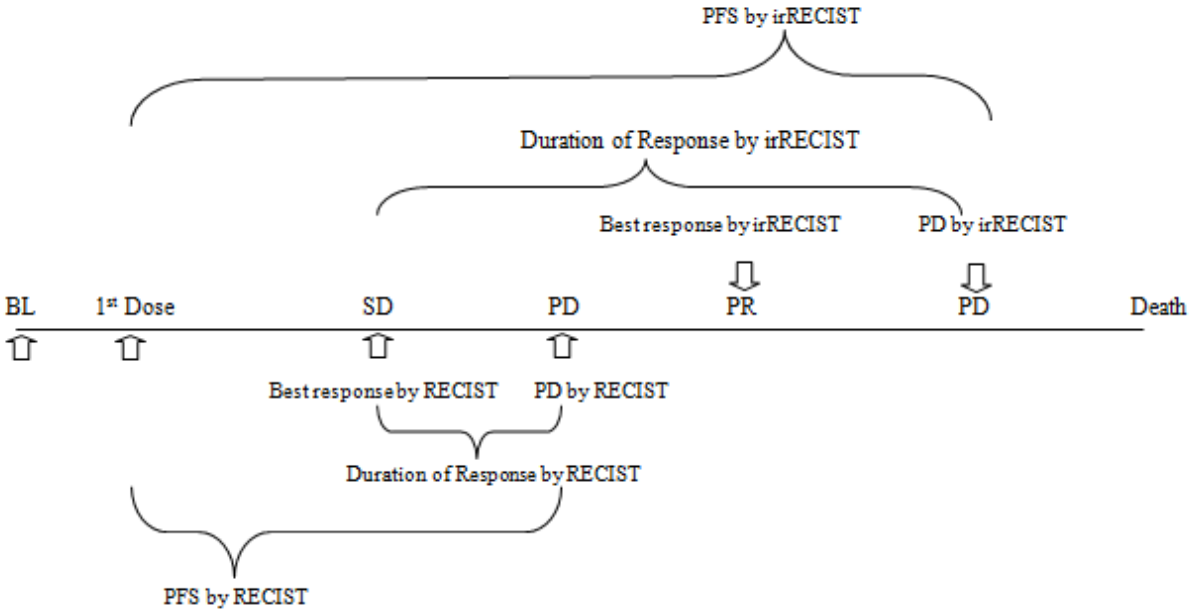
Duration of response by irRECIST is defined from the date of first documented irCR or irPR (responder) to the date of irPD or the date of death due to any cause, whichever is earlier.

Graphic Example:

Scenario 1: The initial PD is confirmed at the next scan (consecutive PD). The efficacy variables by irRECIST and RECIST are the same.



Scenario 2: The initial PD is not confirmed at the next scan (non-consecutive PD). The efficacy variables by irRECIST and RECIST v.1.1 are different.



In addition, the best response after initial PD may be listed. Other efficacy analysis based on irRECIST may be performed for exploratory analysis.

Change in tumor size will be assessed in each patient with measurable disease using radiographic imaging. Tumor size is the sum of the tumor measurements for target lesions at each tumor evaluation. Change in tumor size is defined as the percent change in tumor size from

the baseline evaluation to the minimum post-dose evaluation. Other definitions of CTS may be explored (including specific time points, and AUC formulations).

Progression-free survival (PFS) time is defined as the time from the date of start of study treatment to the first date of PD (symptomatic or objective) or death due to any cause, whichever occurs first. For patients who are not known to have died or progressed as of the data-inclusion cut-off date, PFS time will be censored at the date of the last objective progression-free disease assessment prior to the date of any subsequent systemic anticancer therapy.

Immune-related progression-free survival (irPFS) is defined as the date from the treatment started date to the time of PD assessed by irRECIST.

- If the initial PD is confirmed, then the date of immune-related (ir)PD is the initial PD date by RECIST v.1.1.
- If the initial PD is unconfirmed, then the date of irPD is the date of second PD.

6.11.2. Efficacy Analyses

Reported lesion data (target/ non-target), investigator assessment of response, duration of response/stable disease, PFS and OS will be listed for all patients.

Efficacy data will be summarized according to treatment. If data warrant, efficacy analyses of ORR and irORR will also be presented separately for each sarcoma histology and treatment.

The following efficacy summaries will be provided:

- ORR, DCR, irORR and irDCR will be presented with exact 95% CI.
- Time to event endpoints including PFS, DOR, irPFS, irDOR and OS will be summarized descriptively using the Kaplan-Meier method. Survival curves will be used to summarize the data. If data are sufficiently mature, medians will be reported with the 95% CIs. In addition, for each time-to-event variable, survival rates at adequate time points will be reported (for example, 3, 6, and 12 months).
- Change in tumor size over time will be presented graphically using line plots. Minimum change in tumor size will be presented using a waterfall plot.

6.12. Bioanalytical and Pharmacokinetic/Pharmacodynamic Methods

Unless stated otherwise, the Lilly pharmacokineticist will be responsible for the PK and PK/PD analyses and will be detailed separately in a PK/PD analysis plan.

Serum olaratumab concentrations at different time points will be summarized by descriptive statistics. Additional analyses utilizing the population pharmacokinetic approach may also be conducted if deemed appropriate.

PK and PD data will be analyzed with appropriate standard nonlinear analytic software. Pharmacokinetic parameter estimates for olaratumab will be calculated by standard noncompartmental methods of analysis.

The primary parameters for analysis will be maximum concentration (C_{max}) and area under the concentration-time curve ($AUC_{[0\text{-}tlast]}$, $AUC_{[0\text{-}\infty]}$) of olaratumab. Other noncompartmental parameters, such as time of half-life ($t_{1/2}$), apparent clearance (CL/F), and apparent volume of distribution (V/F) may be reported. Additional exploratory analyses will be performed if warranted by data and other validated pharmacokinetic software programs (for example, NONMEM) may be used if appropriate and approved by Global Pharmacokinetic management. The version of any software used for the analysis will be documented and the program will meet the Lilly requirements of software validation.

6.13. Safety Analyses

All safety summaries and analyses will be based upon the safety analysis set. Safety data will be listed and summarized with patient counts and percentages in each treatment arm. Details of the analyses are described in the following sections.

6.13.1. Extent of Exposure

A summary of exposure will be provided for each study drug, including cycle received, cumulative dose and duration of therapy, for all treatment patients per treatment arm and total.

A summary of dose intensity will be provided for each study drug, for all treatment patients per treatment arm and total. Percent dose intensity is calculated as:
100 x (actual cumulative dose taken (mg) / planned cumulative dose (mg))

Note that planned dose is the same as actual dose if there are no dose modification or cycle delays.

A summary of dose adjustments will be provided for each study drug, including dose omissions, dose reductions and cycle delays, and the corresponding reasons for dose adjustment, for all patients per treatment arm and total. If the reason for dose modification is due to an AE, the associated AE will be provided.

A Napoleon plot of treatment duration, treatment received and reason for discontinuation will be provided.

6.13.2. Adverse Events

A listing of all AEs by patient will be presented. This listing will include patient number, AE (reported term and preferred term [PT]), event start and end dates, CTCAE grade, relationship to study drug/procedure, seriousness, and outcome. A listing of serious AEs (SAEs) will be produced using the similar format.

An overall summary will be provided for AEs. The number and percent of evaluable patients will be summarized by treatment for each category below. The summary will provide counts for all AEs, and AEs related to study treatment.

- Patients with at least one treatment-emergent AE (TEAE)
- Patients with at least one grade 3 or 4 TEAE

- Patients with at least one SAE
- Patients who discontinued due to AE
- Patients who discontinued due to SAE
- Patients who died due to AE on study treatment
- Patients who died due to AE within 30 days of discontinuation from study treatment

Treatment-emergent adverse events (TEAE) are defined as follows:

- Any event that first occurred or worsened in severity after baseline, based on the CT LLT term and CTCAE severity grade. This means that any episode of the same AE with the same grade as at baseline that starts after the first dose of study treatment will not be defined as treatment-emergent, even if now considered drug related.
- Or any pre-existing condition [PEC] (emerged prior to signing the informed consent) or any AE (emerged after signing the informed consent) for which the outcome of the AE is ongoing at the time of first dose but has increased in severity (CTCAE grade) following the start of study treatment, regardless of causality.

As per Lilly's standard operating procedures, all "related", "probably related," "possibly related," or "does not know" AEs and SAEs will be defined as related to study drug.

MedDRA v16.1 (or higher) will be used when reporting AEs by MedDRA terms. TEAEs will be summarized by System Organ Class [SOC] and by decreasing frequency of PT within SOC.

TEAEs will be summarized by CTCAE grade, including the total for maximum Grade 3 and 4, and Grade 3, 4 and 5. These summaries will be provided for events regardless of study drug causality, and repeated for events deemed by the investigator to be related to study medication.

Dose-limiting toxicities (DLTs) and DLT-equivalent toxicities will be listed for all patients on therapy. Dose escalation phase 1a will be driven by safety using a 3+3 scheme.
Medical history and PECs will be listed for each patient.

6.13.3. Deaths, Other Serious Adverse Events, and Other Notable Adverse Events

All deaths in this study, including the reasons for death, will be listed by treatment. The reasons for death will be also summarized separately for on-therapy, within 30 days of last dose of study drug and during the long term follow-up including the specific AE preferred term if reason for death is AE.

Serious AEs will be summarized for each treatment by decreasing frequency of PT within SOC. The summary will be provided for events regardless of study drug causality, and repeated for events deemed by the investigator to be related to study medication.

AEs of special interest for Olaratumab include Infusion-Related Reactions and will be summarized and listed separately in accordance with similar analyses across Olaratumab studies.

Events of clinical interest (ECI) for Pembrolizumab will be summarized and listed separately. ECIs for Pembrolizumab include:

1) An overdose of pembrolizumab that is not associated with clinical symptoms or abnormal laboratory values. An overdose will be defined as ≥1000 mg (5 times the protocol-specified dose).
2) An elevated AST or ALT laboratory value that is greater than or equal to 3X the upper limit of normal (ULN) and an elevated total bilirubin laboratory value that is greater than or equal to 2X the ULN, and at the same time, an alkaline phosphatase laboratory value that is less than 2X the ULN, as determined by way of protocol-specific laboratory testing or unscheduled laboratory testing

6.13.4. Clinical Laboratory Evaluation

All laboratory results will be reviewed using Spotfire to assess changes over time. Key findings may be summarized in tables and/or illustrated graphically using line plots over time or box plots for example, as deemed appropriate.

Any abnormal results of clinical laboratory tests will be listed for all patients on therapy and where appropriate the calculated CTCAE grades using CTCAE v4.0 (or higher) will be given.

CTCAE grades will also be summarized for laboratory parameters where CTCAE grades are available by cohort/dose level.

6.13.5. Vital Signs and Other Physical Findings

All vital sign results will be reviewed using Spotfire to assess changes over time. Key findings may be summarized in tables and/or illustrated graphically using line plots over time or box plots for example, as deemed appropriate.

6.13.6. Immunogenicity

Immunogenicity data for Olaratumab will be summarized by dose. If warranted, evaluation of immunogenicity and AEs may be conducted. A listing will be provided of all available immunogenicity data. Additionally, a listing of immunogenicity data from those patients with at least one positive ADA at any time point will be provided. The frequency of patients with at least one positive ADA assessment, and frequency of patients who develop ADA after a negative baseline assessment will be provided.

6.14. Protocol Violations

All clinically relevant programmable protocol deviations will be listed by pre-determined categories (e.g. inclusion/exclusion criteria, non-compliance with protocol procedures, drug dosage/intervention, use of excluded treatments, informed consent/assent process, continuing after meeting withdrawal criteria, or other). Programmable protocol deviations will be documented in a separate trial issue management plan.

6.16. Interim Analyses and Data Monitoring

Because this is a dose-finding study, data will be reviewed on a cohort-by-cohort basis during the Phase 1a portion of the study. The purpose of these cohort-by-cohort reviews is to evaluate the safety data at each dose level and determine if a DLT has been observed. The investigators and the Lilly study team will make the determination regarding dose escalation based upon their review of the safety and tolerability data as described in this protocol.

For the Phase 1b portion of the study, 2 interim analyses may be planned. The first will occur once all patients enrolled in the cohort have completed or had the opportunity to complete approximately 3 months of treatment; the second will occur once all patients enrolled in the cohort have completed or had the opportunity to complete approximately 6 months of treatment. The intent of these interim analyses is to evaluate preliminary antitumor activity. The interim analyses may also be combined with ongoing trial-level safety review or annual safety review for annual safety update reporting. No independent data monitoring committee will be required for this study.

This study will be considered complete (that is, the scientific evaluation will be complete (study completion) after the last patient discontinues treatment with pembrolizumab. It is expected that at that time enough data will have been obtained to assess the primary objective and the secondary objectives and allow the creation of a clinical study report. All data defined in the protocol will continue to be collected from patients who remain on treatment in the continued

access period. These data may be reported separately and analyses on all patients including these data may not be performed.

6.17. Annual Report Analyses

The following reports are needed for the Development Safety Update Report (DSUR):

1. Estimated cumulative patient exposure
2. Cumulative exposure to investigational drug, by demographic characteristics for ongoing unblinded clinical trials and completed clinical trials
3. Exposure information for ongoing clinical trials and clinical trials that completed during the reporting period
4. Listing of patients who died during the DSUR period
5. Discontinuations due to adverse event during the DSUR Period.

For guidance on creation of these reports, see the DSUR collaboration site (http://lillynetcollaboration.global.lilly.com/sites/GMRS_GPS/Surv/dsur/default.aspx?PageView=Shared)

6.18. Clinical Trial Registry Analyses

Additional analyses will be performed for the purpose of fulfilling the Clinical Trial Registry (CTR) requirements. Analyses provided for the CTR requirements include the following:

Summary of adverse events, provided as a dataset which will be converted to an XML file. Both Serious Adverse Events and 'Other' Adverse Events are summarized: by treatment group, by MedDRA preferred term.

- An adverse event is considered 'Serious' whether or not it is a treatment emergent adverse event (TEAE).
- An adverse event is considered in the 'Other' category if it is both a TEAE and is not serious. For each Serious AE and 'Other' AE, for each term and treatment group, the following are provided:
    - the number of participants at risk of an event
    - the number of participants who experienced each event term
    - the number of events experienced.
- Consistent with www.ClinicalTrials.gov requirements, 'Other' AEs that occur in fewer than 5% of patients/subjects in every treatment group may not be included if a 5% threshold is chosen (5% is the minimum threshold).
- AE reporting is consistent with other document disclosures for example, the CSR, manuscripts, and so forth.

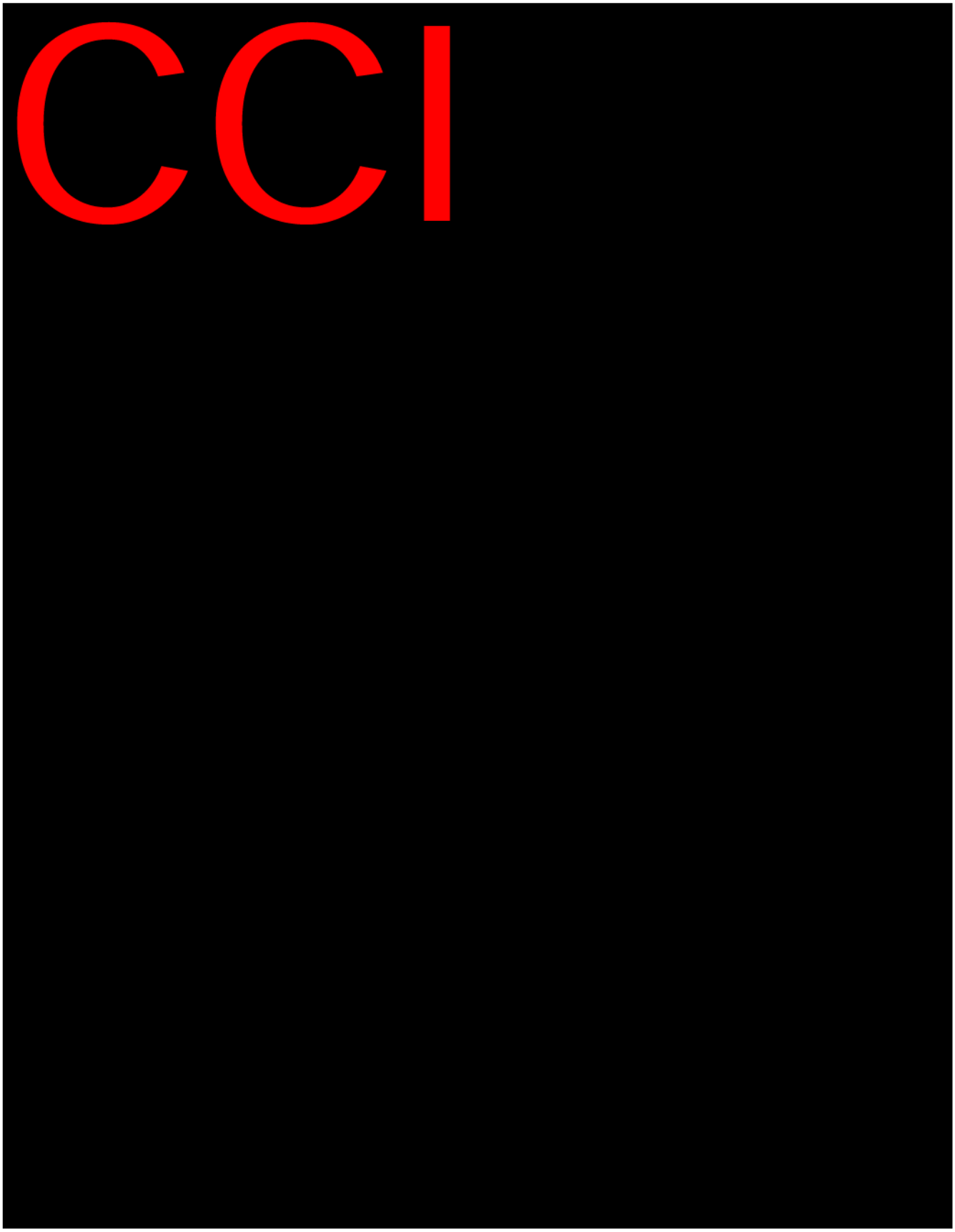
Analyses provided for the EudraCT requirements include the following:

- Summary of AEs, provided as a dataset which will be converted to an XML file, in accordance with EudraCT requirements.
- Categorical breakdown of age across the entire study, represented planned and actual number of patients for the following age groups: infants and toddlers (28 days-23 months), children (2-11 years), adolescents (12-17 years), adults (18-64 years, 65-84 years and 85 years and over).

For the purpose of CTR/ EudraCT reporting, patients who have died, or are still in the study but off treatment, at primary DBL will be considered a completer. Those that withdrew consent for all procedures, including follow-up, or were lost to follow up, will be considered as early discontinuers. Patients who remain on treatment will be counted as continuing treatment.

7. References

Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, Rubinstein L, Shankar L, Dodd L, Kaplan R, Lacombe D, Verweij J. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer*. 2009;45(2):228-247.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