Statistical Analysis Plan J1L-AM-JZGA (1)

A Phase 1, Open-Label Dose Escalation First-in-Human Study to Evaluate the Tolerability, Safety, Maximum Tolerated Dose, Preliminary Clinical Activity, and Pharmacokinetics of AM0010 in Patients with Advanced Solid Tumors

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1. A Phase 1, Open-Label Dose Escalation First-in-Human Study to Evaluate the Tolerability, Safety, Maximum Tolerated Dose, Preliminary Clinical Activity, and Pharmacokinetics of AM0010 in Patients with Advanced Solid Tumors

(AM0010, pegilodecakin, LY3500518)

This is a US only, multicenter, Phase 1, open-label dose escalation first-in-human study to evaluate the tolerability, safety , maximum tolerated dose. Preliminary clinical activity, and pharmacokinetics of AM0010 in patients with advanced solid tumors.

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Protocol J1L-AM-JZGA
Phase 1/1b

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

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3. Revision History

Statistical analysis plan (SAP) Version 1 was approved before final data base lock.

4. Study Objectives

4.1. Primary:

- To characterize the safety, tolerability, Maximum Tolerated Dose (MTD), and pharmacokinetics (PK) of AM0010 after daily subcutaneous (SC) administrations in patients with advanced solid tumors as monotherapy or in combination with chemotherapy or immunotherapy. AM0010 is also known as pegilodecakin and the internal Lilly identifier is LY3500518 and hereafter is used exchangably.

4.2. Secondary:

- To measure the objective tumor response
    - In ragiolographically measureable disease by immune related Response Criteria (irRC)
    - progression in bone in patients with metastatic castration-resistant prostate cancer (CRPC) by Prostate Cancer Working Group 2 (PCWG2)
    - or according to tumor evaluation criteria best suitable and accepted for the tumor type evaluated
- To evaluate the formation of anti-AM0010 antibodies

4.3. Exploratory:

- To investigate biomarkers for patient stratification and treatment response, including genetic analysis, serum chemokines and tumor antigen specific immune responses such as antibody and T cell responses as surrogates for antitumor activity of AM0010

5. Study Design

5.1. Summary of Study Design

This is a first-in-human, open-label, dose escalation study to evaluate the safety, tolerability, and preliminary clinical efficacy of AM0010 in patients with advanced solid tumors dosed daily SC.

The study will be done in 10 parts (A, B, C, D, E, F, G, H, I, and J) each with 2 phases (Escalation and Expansion). In some dose parts showing preliminary evidence for clinical efficacy of AM0010 in the primary escalation and expansion cohorts, the clinical efficacy of AM0010 will be further evaluated in selected patient populations. The AM0010 Dose Schedule is presented in Table JZGA.5.1 and further details about each study part can be found below.

Part A: In the Dose Escalation Phase the dose of AM0010 will be escalated to evaluate the safety, tolerability, PK, and MTD for patients with advanced solid tumors. In the Expansion Phase at least one cohort of 10-15 patients will be enrolled at a previously evaluated safe dose to expand the number of patients for additional safety, PK and pharmacodynamic (PD) analysis, and to establish a recommended dose for Phase 2/3.

Part B: In the Dose Escalation Phase the dose of AM0010 will be escalated in combination with Carboplatin or Cisplatin and Paclitaxel or Docetaxel chemotherapy to evaluate the safety, tolerability, PK, and MTD for patients with advanced solid tumors. In the Expansion Phase at least one cohort of 10-15 patients will be enrolled at a previously evaluated safe dose to expand the number of patients for additional safety, PK and PD analysis, and to establish a recommended dose for Phase 2/3.

Part C: In the Dose Escalation Phase the dose of AM0010 will be escalated in combination with FOLFOX chemotherapy to evaluate the safety, tolerability, PK, and MTD for patients with advanced solid tumors. In the Expansion Phase at least one Cohort of 10 – 15 patients will be enrolled at a previously evaluated safe dose of AM0010 in combination with FOLFOX to expand the number of patients for additional safety, PK and PD analysis, and to establish a recommended dose for Phase 2/3.

Part D: In the Dose Escalation Phase the dose of AM0010 will be escalated in combination with gemcitabine and nab-paclitaxel chemotherapy to evaluate the safety, tolerability, PK, and MTD for patients with advanced solid tumors. In the Expansion Phase Cohorts of 10 – 15 patients may be enrolled at a previously evaluated safe dose of AM0010 in combination with gemcitabine and nab-paclitaxel to expand the number of patients for additional safety, PK and PD analysis and to establish a recommended dose for Phase 2/3.

Part E: In the Dose Escalation Phase the dose of AM0010 will be escalated in combination with capecitabine chemotherapy to evaluate the safety, tolerability, PK, and MTD for patients with advanced solid tumors. In the Expansion Phase Cohorts of 10 – 15 patients may be enrolled at a previously evaluated safe dose of AM0010 in combination with capecitabine to expand the

number of patients for additional safety, PK and PD analysis, and to establish a recommended dose for Phase 2/3.

Part F: In the Dose Escalation Phase the dose of AM0010 will be escalated in combination with paclitaxel chemotherapy to evaluate the safety, tolerability, PK, and MTD for patients with advanced solid tumors. In the Expansion Phase Cohorts of 10 – 15 patients may be enrolled at a previously evaluated safe dose of AM0010 in combination with paclitaxel to expand the number of patients for additional safety, PK and PD analysis, and to establish a recommended dose for Phase 2/3.

Part G: In the Dose Escalation Phase the dose of AM0010 will be escalated in combination with pazopanib to evaluate the safety, tolerability, PK, and MTD for patients with advanced solid tumors. In the Expansion Phase at least one Cohort of 10 – 15 patients will be enrolled at a previously evaluated safe dose to expand the number of patients for additional safety, PK and PD analysis, and to establish a recommended dose for Phase 2/3.

Part H: In the Dose Escalation Phase, the dose of AM0010 will be escalated in combination with Pembrolizumab to evaluate the safety, tolerability, PK, and MTD for patients with immune sensitive advanced solid tumors. In the Expansion Phase at least one Cohort of 10 – 20 patients will be enrolled at a previously evaluated safe dose of AM0010 in combination with pembrolizumab to expand the number of patients for additional safety, PK and PD analysis, and to establish a recommended dose for Phase 2/3.

Part I: In the Dose Escalation Phase, the dose of AM0010 will be escalated in combination with nivolumab to evaluate the safety, tolerability, PK, and MTD for patients with immune sensitive advanced solid tumors. In the Expansion Phase, two cohorts, one of Non-small cell lung carcinoma (NSCLC) patients and another one of Renal Cell Carcinoma (RCC) patients will be enrolled. 30 patients each will be enrolled at a previously evaluated safe dose of AM0010 in combination with nivolumab to expand the number of patients for additional safety, PK and PD analysis, and to establish a recommended dose for Phase 2/3.

Part J: In the Dose Escalation Phase, the dose of AM0010 will be escalated in combination with gemcitabine and carboplatin to evaluate the safety, tolerability, PK, and MTD for patients with advanced solid tumors. In the Expansion Phase, at least one Cohort of 10 – 20 patients will be enrolled at a previously evaluated safe dose of AM0010 in combination with gemcitabine and carboplatin to expand the number of patients for additional safety, PK and PD analysis, and to establish a recommended dose for Phase 2/3.

If preliminary evidence for clinical efficacy of AM0010 is observed in the primary escalation or expansion cohorts, the clinical efficacy of AM0010 will be further evaluated in selected clinical indications.

Table JZGA.5.1. AM0010 Dose Schedule

Part A AM0010 Dose Escalation Phase- Monotherapy			
Dose Cohort	**Number of Patients**	**AM0010 Dose (µg/kg), daily**	**AM0010 qd (until irPD)**
1	3 – 6	1	No additional therapy
2	3 – 6	2.5	
3	3 – 6	5	
4	3 – 6	10	
5	3 – 6	20	
Optional*	3 – 6	40	
Expansion**	10–15	Previously evaluated, safe dose in combination therapy	
Part B AM0010 Dose Escalation Phase + Platinum/Taxane			
Dose Cohort	**Number of Patients**	**AM0010 Dose (µg/kg), daily**	**Platinum Taxane q21d x 5 (or x6) AM0010 qd (until irPD)**
1	3 – 6	2.5	Day 1 of every 21 day cycle Carboplatin or Cisplatin And Paclitaxel or Docetaxel
2	3 – 6	5	
3	3 – 6	10	
4	3 – 6	20	
Optional*	3 – 6	40	
Expansion**	10–15	Previously evaluated, safe dose in combination therapy	
Part C AM0010 Dose Escalation Phase + FOLFOX			
Dose Cohort	**Number of Patients**	**AM0010 Dose (µg/kg) daily**	**FOLFOX q14d x 12 AM0010 qd (until irPD)**
1	3 – 6	2.5	Day 1, 2 of every 14 day cycle.
2	3 – 6	5	
3	3 – 6	10	
4	3 – 6	20	
Optional*	3 – 6	40	
Expansion**	10–15	Previously evaluated, safe dose in combination therapy	

Part D AM0010 Dose Escalation Phase + Gemcitabine / nab-paclitaxel

Dose Cohort	Number of Patients	AM0010 Dose (µg/kg) daily	Gemcitabine / nab-paclitaxel q7d x 3 / 28 day cycle (until irPD) AM0010 qd (until irPD)
1	3–6	5	Day 1, 8, 15 of each 28 Day cycle
2	3–6	10	
3*	3–6	20	
Expansion**	10–15	Previously evaluated, safe dose in combination therapy	

Part E AM0010 Dose Escalation Phase + Capecitabine

Dose Cohort	Number of Patients	AM0010 Dose (µg/kg) daily	Capecitabine bid x 2 weeks (until irPD) AM0010 qd (until irPD)
1	3–6	10	Day 1-14 of every 21 day cycle
2	3–6	20	
Expansion**	10–15	Previously evaluated, safe dose in combination therapy	

Part F AM0010 Dose Escalation Phase + Paclitaxel

Dose Cohort	Number of Patients	AM0010 Dose (µg/kg) daily	Paclitaxel q7d x 3 / 28 day cycle (until irPD) AM0010 qd (until irPD)
1	3–6	10	Day 1, 8, 15 of every 28 day cycle.
2	3–6	20	
Expansion**	10–15	Previously evaluated, safe dose in combination therapy	

Part G AM0010 Dose Escalation Phase + Pazopanib

Dose Cohort	Number of Patients	AM0010 Dose (µg/kg) daily	Pazopanib qd (until irPD) AM0010 qd (until irPD)
1	3–6	10	Daily
2	3–6	20	
Expansion**	10–15	Previously evaluated, safe dose in combination therapy	

Part H AM0010 Dose Escalation Phase + anti PD-1 (Pembrolizumab)

Dose Cohort	Number of Patients	AM0010 Dose (µg/kg) daily	Pembrolizumab q3w (until irPD) AM0010 qd (until irPD)
1	3–6	10	Day 1 of every 21 day cycle
2*	3–6	20	
3	3 – 6	40	
Expansion**	10–20	Previously evaluated, safe dose in combination therapy	
Part I AM0010 Dose Escalation Phase + anti PD-1 (Nivolumab)			
Dose Cohort	**Number of Patients**	**AM0010 Dose (µg/kg) daily**	**Nivolumab q2w (until irPD) AM0010 qd (until irPD)**
1	3 – 6	20	Day 1 of every 14 day cycle
2	3 – 6	30	
Expansion**	10 – 20	Previously evaluated, safe dose in combination therapy	
Part J AM0010 Dose Escalation Phase + Gemcitabine & Carboplatin			
Dose Cohort	**Number of Patients**	**AM0010 Dose (µg/kg) daily**	**Gemcitabine & Carboplatin q7d x2 / 21 day cycle (until irPD) AM0010 qd (until irPD)**
1	3-6	10	Day 1 of every 21 day cycle
2	3-6	20	
Expansion**	10-20	Previously evaluated, safe dose in combination therapy	

*In the absence of dose limiting toxicities (DLTs) and continued clinical benefit, the dose may be further escalated, following a two-fold increase.

**Additional Cohorts may be enrolled based on emerging safety or PK data from the Dose Escalation Phase and Expansion Phase.

The schedule of assessments and procedures is provided in Appendices 1-10.

5.2. Determination of Sample Size

The exact number of patients required for this trial is dependent on the MTD and cannot be accurately predicted. This trial with AM0010 is expected to enroll at least 3 patients per cohort in Dose Escalation, depending upon the observation of DLTs. Fifteen additional patients will be enrolled at or below the MTD in every Dose Expansion Cohort, at the Sponsor's discretion, to evaluate further the safety, PK, and PD of AM0010. The cohort size of 15 excludes a 33% DLT rate if 2 or less patients experience a DLT in one of the indication specific expansion cohorts or expansion cohorts. An administrative decision to stop the trial may be made by the Sponsor at

any time. The sample size is based on practical considerations and is consistent for this type of study.

The study will initially enroll approximately 45 patients in each of the 3 initial Parts A–C for a total of approximately 135 patients. Six to 30 patients will be enrolled in the Dose Escalation Phases and 15 to 30 for each Expansion Phase (3 x 45 = 135).

Additional 2 expansion cohorts for further exploration and confirmation of safety and anti-tumor activity will enroll 20 to 30 patients to allow statistical relevant evaluation of toxicity and response rates compared to historical controls (2 x 30 = 60).

Enrollment of additional 5 parts (D – H) is anticipated to include a total of 105 patients. Up to 12 patients in dose escalation cohorts (5 parts x 12 = 60) followed by dose specific expansion cohorts of up to 15 patients in up to 3 parts (3 x 15 = 45). It is not anticipated that all parts of D–H will contain expansion cohorts (45 + 60 = 105).

Part I will enroll approximately 6 patients in thein the dose escalation portion and additional 30 patients in each of the 2 dose expansion phase (6 + 2 x 30 = 66).

Part J will enroll approximately 6 patients in the dose escalation portion and additional 20 to 30 patients in one dose expansion phase (6 + 20 = 26).

The total number of patients included in the study is therefore 392 (135 + 60 + 105 + 66 + 26 = 392).

Dose Escalation will continue until DLTs are observed in more than 33% of the patients in a cohort; the exact number of patients entering this trial can therefore not be accurately predicted. In the Dose Escalation Phase, at least 3 patients are enrolled per dose cohort; upon the observation of DLTs in one patient, an additional 3 patients will be enrolled at the same dose cohort. In the Dose Expansion Phase, 10 to 30 patients will be enrolled at or below the MTD at the Sponsor's discretion to expand on the safety, efficacy, and pharmacodynamics of AM0010.

The sample size is based on practical and statistical considerations and is consistent for this type of study. To detect an event which is expected to occur in more than 20% of a patient population, we intend to enroll a dose expansion cohort (DEC) of 10 patients.

To detect an event which is expected to occur in 10% of a patient population, we intend to enroll a DEC of 20 patients.

6. Study Endpoints

Primary:

- Incidence of adverse events (AEs), clinically relevant changes in laboratory values, electrocardiograms (ECGs), and vital signs
- PK parameters including the serum trough concentration (C_{min}), the maximal drug concentration (C_{max}), area under the curve of serum concentration over time (AUC), and half-life ($t_{1/2}$).

Secondary:

- Change in tumor burden measured by volumetric computed tomography (CT) or magnetic resonance imaging (MRI) according to irRC
- Progression in bone by bone scintigraphy according to PCWG2 for patients with metastatic CRPC
- Change in tumor evaluation criteria best suitable and accepted for the tumor type evaluated
- Treatment-emergent antidrug antibodies.

Exploratory:

- Biomarker analysis, including but not limited to whole blood DNA analysis for genetic predisposition, serum cyto- and chemokines, and antibodies directed against tumor associated antigens (TAA)
- Prevalence and expansion of TAA reactive T cells.

7. Analysis Populations

7.1. Safety Population

The Safety Population comprises all patients who received any amount of study drug(s) (AM0010 or chemotherapy or immunotherapy).

7.2. Evaluable Population

The Evaluable Population will be comprised of all patients who are enrolled without major protocol deviations, in the Safety Population, and have an adequate irRC tumor assessment (baseline assessment and at least one post-baseline assessment). Adequate tumor assessments are patients who are classified as either irSD, irCR, irPR, or irPD. Major protocol deviations will be identified based on review of all protocol deviations prior to database lock.

8. Definitions of Outcome Measures

8.1. Safety Outcomes

Safety will be assessed by analysis of the occurrence of AEs and serious adverse events (SAEs), as well as by clinically relevant changes in laboratory evaluations (serum chemistry, hematology), vital signs, ECGs, and physical examinations.

8.2. Clinical Response Outcomes

8.3. Immune Related Response Criteria

Tumor measurements will follow irRC guidelines (Wolchok, Hoos et al. 2009). Immune related Response Criteria outcomes will be determined by the investigator and will be specified on the electronic case report form (eCRF). The investigator will categorize the overall response as irCR, irPR, irSD, and irPD.

8.4. Prostate Cancer Working Group 2 Criteria in Bone

Metastatic prostate cancer will be evaluated by PCWG2 criteria for progression in bone (Scher, Halabi et al. 2008; Ryan, Smith et al. 2013). If any patients are enrolled and evaluated by PCWG2 criteria, these results will be listed.

9. Statistical Methods

9.1. Treatment Assignment

This is an open-label study and all patients will receive AM0010. In the Dose Escalation Phase of Parts A-J, patients will be assigned sequentially into cohorts of up to six patients per cohort. In other study parts, up to 3-6 patients are planned in each cohort. A total of 6 patients will be enrolled in each cohort in the event that a DLT is observed in one of the first 3 patients during the DLT assessment period (28 days). In the Expansion Phase of Parts A-C, patients will be assigned sequentially into cohorts of up to 15 patients per cohort. Additional expansion cohorts may be enrolled based on emerging safety, PK, PD data, and/or preliminary evidence of anti-tumor efficacy from the Dose Escalation Phase and the first Expansion Cohort.

9.2. Interim Analysis

Subsets of data from this study will be summarized and analyzed on a yearly basis for annual IND reporting requirements. Additional analyses may be produced to help plan future studies, produce publications, and to provide data for regulatory and other business needs.

9.3. Study Drug Regimen

The study drug regimen is defined as the combination of study drugs that the patient is exposed to during the study. All patients will be exposed to AM0010 and all patients (other than those enrolled in Part A) will be exposed to a combination of chemotherapy or immunotherapy drugs. Patients will be summarized based on their study drug regimens as specified in Table JZGA.9.1. If additional study drug regimens are added prior to the end of the study, they will be specified in the CSR. Since dose for study drugs may be adjusted during the study (e.g., AM0010, chemotherapy, immunotherapy dose adjustments), the dose cohort the patient was assigned at enrollment will be used to identify the study drug regimen for summarization purposes. Patients were assigned to one of the two doses in each dose cohort based on weight <80kg or weight ≥80kg. For reporting purposes, the following table will be used to map assigned dose cohort in µg/kg to mg.

Dose Cohort	1 µg/kg	2.5 µg/kg	5 µg/kg	10 µg/kg	20 µg/kg	40 µg/kg
Reporting Label	0.08 mg or 0.1 mg	0.2 mg or 0.25 mg	0.4 mg or 0.5 mg	0.8 mg or 1 mg	1.6 mg or 2 mg	3.2 mg or 4 mg

Table JZGA.9.1. Study Drug Regimens

Part	Study Drug Regimens	Possible LY3500518 (AM0010) Doses (µg/kg)
A	LY3500518 X[1]	1, 2.5, 5, 10, 20, 40
B	LY3500518 X[1] +Platinum/Taxane	2.5, 5, 10
C	LY3500518 X[1] + FOLFOX	2.5, 5,10
D	LY3500518 X[1] + Gemcitabine/nab-paclitaxel	5
E	LY3500518 X[1] + Capecitabine	10
F	LY3500518 X[1] + Paclitaxel	10
G	LY3500518 X[1] + Pazopanib	10
H	LY3500518 X[1] + Pembrolizumab	10, 20, 40
I	LY3500518 X[1] + Nivolumab	10, 20
J	LY3500518 X[1]+ Gemcitabine/Carboplatin	5, 10

[1] X is the dose of study drug in mg.

9.4. Comments on the Statistical Analyses

- All study data will be summarized by study part and AM0010 dose, unless otherwise specified.

  All study data will be summarized for patients with specific cancer types with ≥5 enrolled patients or subgroups within specified study parts including but not limited to:

  - Adenoid Cystic Carcinoma
  - Bladder Cancer
  - Castrate Resistant Prostate Cancer (CRPC)
  - Cholangiocarcinoma
  - Colorectal Carcinoma (CRC)
  - Gastric
  - Melanoma
  - Non-small Cell Lung Carcinoma (NSCLC)
  - Ovarian Cancer (epOC)
  - Pancreatic Carcinoma (PanC)
  - Renal Cell Carcinoma (RCC)
  - Squamous Cell Carcinoma Head and Neck (SCCH&N)
  - Triple Negative Breast Cancer (TNBC)
  - Chalangiocarcinoma

- Gastric
- Uveal Menaloma

Additional cancer types or subgroups may also be summarized and will be specified in the clinical study report (CSR). Unless otherwise specified, "study drug" refers to AM0010 and the combination of chemotherapy or immunotherapy within each study part.

- Continuous variables will be summarized using number (n), mean, standard deviation (SD), median, minimum, and maximum.
- Frequency counts and percentages will be reported for all categorical data.
- If a laboratory result is reported relative to a lower/upper range of detection for an assay, for example, "<10", the numeric portion of the result (10) will be used for statistical analyses and the full result, including any symbols, will be provided in the patient listings.
- Study Day 1 is defined as the first day of study drug administration. The day prior to the first dose of study drug is Study Day -1; there is no Study Day 0.
- For all clinical assessments performed prior to the date of the first study drug administration, Study Day will be calculated as the date of the assessment minus the date of the first dose of study drug. For all clinical assessments performed on or after the date of the first dose of study drug, Study Day will be calculated as the date of the assessment minus the date of the first dose of study drug, plus one.
- For AEs, Study Day will be calculated as the date of onset of the AE minus the date of the first dose of study drug, plus one.
- For prior medications, Study Day will be calculated as the start date of the medication minus the date of the first dose of study drug.
- For concomitant medications and prior medications taken on the same day as the first dose of study drug or thereafter, Study Day will be calculated as the start date of the medication minus the date of the first dose of study drug, plus one.
- Version 9.4 (or higher) of SAS statistical software package will be used to provide all summaries, listings, figures and statistical analyses.

9.5. Study Visits

9.5.1. Summarized Visits

For table summaries of ECGs, laboratory assessments, vital signs, Eastern Cooperative Oncology Group (ECOG), and serum tumor marker results, unless otherwise specified in Section 10.7 only data from the following visits will be summarized:

- Baseline (assessment closest to but prior to study drug administration on Day 1)
- Cycle 2, Day1
- Cycle 3, Day 1
- End of Treatment (EOT)
- Follow-up: 30 days after EOT

9.5.2. Study Visit Derivation

Some visits will be derived as identified in in Step 1 below for presentation in tabular presentations. Additionally, since some study assessments can occur between 1 and 3 days prior to the scheduled visit, Step 2 below will identify how to identify assessments for summarization purposes.

Step 1

When patients in Parts A, B, and C were initially enrolled, visit names in the study database were identified using days (e.g., Day 29, Day 365). The database was later updated to reflect protocol amendments and visits were subsequently identified by both cycles and days (e.g., Cycle 1 Day 1, Cycle 2 Day 8). All dates in the study database will be programmatically assigned visit names for summarization based on the following rules:

- In Part A, some patients visits are identified in the study database with days only and some patient visits are identified with cycle and days. For patients with visits with cycles and days, the study database identifies Cycle 2 Day1 begins as beginning on Day 57 with subsequent 28 day cycles. All patient visits in Part A will be programmatically converted to 28 day cycles with Cycle 2 Day 1 starting on Day 29 for summarization purposes. Note that Part A is daily monotherapy with AM0010, and cycles are used to describe visits even though the study drug administration is daily.
- In Part B, if a visit is identified with a cycle and a day within the study database, then that visit identifier will be used. However, if the study visit name does not include cycle information, then the visit cycle and day will be determined using dates from the Platinum/Taxane drug administration dataset. If corresponding dates are not available in

the Platinum/Taxane drug administration dataset, the visit cycle and day will be derived using the available dates in the Platinum/Taxane drug administration dataset.

- Similar to Part B, in Part C all study visits within the database will be associated with a Cycle and Day using the visit dates and visit names in the Folfox dataset for summarization purposes. However, although the Folfox cycle length is 14 days, the database and protocol identify Day 15 as "Cycle 1 Day 15" instead of "Cycle 2 Day 1". For this reason, visits will be renamed in Part C as follows for summarization purposes:
    - Cycle 1 Day 15 will be renamed as Cycle 2 Day 1
    - Cycle 2 Day 1 (typically occurs on Day 29) will be renamed as Cycle 3 Day 1
    - Cycle 3 Day 1 (typically occurs on Day 43) will be renamed as Cycle 4 Day 1
    - Etc.
- The study database contains visits labeled as Day 113/EOT. If a visit is identified as Day 113/EOT in the study database, then the date of this visit will be compared with the End of Treatment date identified from the End of Treatment eCRF. If the dates match, then the Day 113/EOT visit will be relabeled as an EOT visit. If the dates do not match or if an EOT visit date is not available from the EOT eCRF, then the visit will be reclassified as described above for Parts A, B, and C.
- In all study parts, continuing visits and follow-up visits will not be renamed.
- In Parts D-J, the visits as identified in the eCRF will be used for summarization purposes. All visit identifiers in Parts D-J include both Cycles and Days.

Step 2

Any data collected at the on the first day of a cycle (e.g., Cycle 2 Day 1, Cycle 3 Day 1) can be collected between 1 and 3 days prior to the scheduled visit.

After reclassifying visits as described in Step 1, any visits within 3 days prior to Day 1 of the cycle but prior to study drug administration on the scheduled visit day will be identified. The visit that occurs closest to the scheduled visit date will be summarized.

For example, if blood for safety laboratory assessments is collected both 1 and 2 days prior to the Cycle 2 Day 1 visit date, but no blood for safety labs is collected prior to drug administration on the Cycle 2 Day 1 date, then the values collected one day prior to Cycle 2 Day 1 will be summarized as Cycle 2 Day 1 values.

9.6. Handling of Missing Data

Missing data are handled as follows:

- Unless otherwise specified, missing values for individual data points will remain as missing. Missing values will not be imputed and only observed values will be used in data analyses and presentations.

- Where individual data points are missing, categorical data will be summarized based on reduced denominators (i.e., only patients with available data will be included in the denominators).

10. Statistical Summaries

10.1. Patient Disposition

The number of patients treated and the number of patients with ≥1 -baseline adequate tumor assessments will be summarized by Part, Phase (Escalation, Expansion, and both combined), and dose cohort. An adequate tumor assessment includes classification of the scan into: irCR, irPR, irSD, or irPD. In addition, the number of patients discontinuing from study drugs, discontinuing from the study, the reasons for discontinuation from study drugs and the study, and the number of deaths will be summarized by Part, by Phase (Escalation, Expansion, and both combined), and dose cohort as well as by cancer type/subgroup, phase, and dose cohort. .

Duration of treatment will be determined based on the date of the last dose of study drug(s) minus the start date of study drug, plus one.

10.2. Protocol Deviations

Protocol deviations maybe summarized or listed if needed.

10.3. Demographics and Baseline Characteristics

Descriptive statistics for continuous variables (age, height, weight, and body mass index [BMI]), and frequency counts and percentages for categorical demographics variables (age group, sex, race, ethnicity, and number of previous cancer therapies) will be summarized in the Safety Population. Age will be based on the date of informed consent (date of informed consent minus the date of birth, in years). The summarized age groups include: 18 to <45, 45 - <65, ≥65, and ≥75 years of age. Body mass index will be calculated by dividing weight (kg) by height squared (m^2).

Disease characteristics including diagnosis, site of disease at time of diagnosis, duration since diagnosis in years, and initial and current TNM stage will be summarized. Baseline ECOG performance status will also be presented in the Safety Population. The duration since diagnosis will be calculated as the time from diagnosis to the first dose of study drug.

Medical history terms will be summarized by the number and percentage of patients reporting each medical history body in the Safety Population.

10.4. AM0010 and Chemotherapy/Immunotherapy Exposure

10.4.1. AM0010 Exposure

Duration of AM0010 treatment (in weeks) will be summarized in the Safety Population. Duration of AM0010 treatment will be calculated as follows: [(date of last dose – date of first dose) +1]/7. The number and percentage of patients who received AM0010 for ≤4 weeks, >4- ≤8 weeks, >8- ≤12 weeks, and >12 weeks, as well as descriptive statistics of the number of days of AM0010 treatment (n, mean, standard deviation, minimum, median, and maximum) will be presented. The number and percentage of patients with at least AM0010 one dose interruption

≥7 consecutive days and at least one dose interruption ≥14 consecutive days will be summarized. Summary statistics of the duration of dose interruptions and the total number of interruptions will be presented. If the dose is interrupted on multiple consecutive days, then this is considered a single dose interruption. For patients with multiple dose interruptions, the mean duration of dose interruptions will be calculated and for all patients with dose interruptions, the mean duration of dose interruptions will be summarized.

The total amount of AM0010 (sum of all doses in mg) administered will also be presented. AM0010 is dispensed in CCI [redacted]. Treatment compliance is defined as the number of doses actually received (without regard to dose reduction) divided by the number of doses expected for the time period between the dates of the first and last doses of AM0010 drug (× 100). Patients are expected to receive one dose administered daily by SC injection for the duration of the study. Dose intentensity will be summarized as well.

For pancreatic cancer patients, number of patients who started dosing schedule of 5 days on 2 days off will be summarized.

10.4.2. Chemotherapy/Immunotherapy Exposure

For Parts B-J, Chemotherapy/immunotherapy exposure will be summarized by part and study drug regimen (Table JZGA.9.1). Since study therapy can be altered during the study, a patient will be summarized based on the chemotherapy/immunotherapy regimen identified at the beginning of the study.

For each patient, the following will be summarized using summary statistics:

- Duration of combination therapy (days)
- Number of cycles
- Number of chemotherapy/immunotherapy dose adjustments
- AM0010 cumulative dose (mg) while on combination therapy
- Duration of AM0010 maintenance (days)
- Cumulative Dose for each chemotherapy drug (Parts C, H, and I only)

The duration of AM0010 maintenance therapy is defined the number of days from the last dose of chemotherapy/immunotherapy + X days to the last dose of AM0010 study drug, where X is the cycle length. A dose is considered adjusted if any of the chemotherapy or immunotherapies is identified as dose reduced, dose interrupted, missed, delayed, or incomplete based on the drug administration eCRF.

In addition the number and percentage of patients with the following will be summarized:

- 1, 2, 3, 4, etc. treatment cycles
- At least one dose reduction
- At least one Dose Adjustments

In addition, the reasons for dose reductions and dose adjustments will be summarized. If a patient has multiple dose adjustments or dose reductions during the study, then the patient will be counted only once for the number of dose adjustments or reductions, but each unique reason for an adjustment or reduction will be summarized.

10.5. Concomitant Medications

The World Health Organization (WHO) drug dictionary will be used to classify prior and concomitant medications by therapeutic class. A prior medication is defined as any medication taken prior to the date of the first dose of study drug. A concomitant medication is defined as any medication taken on or after the date of the first dose of study drug through the follow-up visit, including continuing medications and medications with missing stop dates.

Concomitant medications will be summarized in a table by Anatomical Therapeutic Chemical (ATC) code level 3 and preferred term in the Safety Population. Patients receiving the same medication more than once will be counted only once for a particular medication class and medication.

10.6. Pharmacokinetics

Pegilodecakin observed concentrations will be summarized by descriptive statistics. Additional analysis utilizing the population PK approach may also be conducted if deemed appropriate and summarized in a separate report.

10.7. Safety Analyses

All safety analyses will be conducted in the Safety Population.

10.7.1. Adverse Events

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 16.1 and later. The Investigator will classify the severity of an adverse event using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE, Version 4.03) and will determine the relationship to study drug for each AE. All AEs will be summarized by part and dose.

A treatment emergent adverse event (TEAE) is defined as any AE that begins between the day of first dose and 30 days after treatment discontinuation (or up to any time if serious and related to study treatment), or any pre-existing condition that increases in CTCAE grade between the day of first dose and 30 days after treatment discontinuation (or up to any time if serious and related to study treatment). The number and percentage of patients reporting a TEAE will be tabulated by system organ class (SOC) and preferred term (PT). The number and percentage of patients

reporting a TEAE related to study drug will be tabulated by SOC and PT as well as by SOC, PT, and severity grade. The number and percentage of patients reporting a serious TEAE and a serious related TEAE will be tabulated separately by SOC and PT. Related AEs include those related to either AM0010 or study chemotherapy or immunotherapy.

For all analyses of TEAEs, if the same AE (based on PT) is reported for the same patient more than once, the AE is counted only once for that PT and at the highest severity grade, and strongest relationship to study drug.

The following TEAE/SAE outputs will be produced:

a. overview of TEAEs
b. summary of TEAEs by PTs (all grade and grade ≥3)
c. summary of TEAEs by SOC and PT (all grade and grade ≥3)
d. summary of TEAEs by PT and Maximum Grade
e. listing of SAEs
f. summary of SAEs by SOC and PT (all grade and grade ≥3)
g. listing of TEAEs leading to study treatment discontinuation

Summaries b, c, d, and f will be produced for the related TEAEs/SAEs

10.7.2. Deaths

All death on study will be listed along with the cause of death.

10.7.3. Consolidated AEs

Given the high level of granularity of the MedDRA dictionary, clinically identical or synonymous PTs reported under different terms in the database, in addition to being reported separately, will also be consolidated in a separate summary. The list of consolidated AE categories will be reported in the clinical study report.

10.7.4. Immune-mediated AE

Potential immune-mediated AE, such as colitis, pneumontitis, endocrine and hepatic events will be summarized.

10.7.5. AE of Special Interest

Adverse events of special interest (AESIs) are AEs thought to be potentially associated with the study treatment. Therefore, aggregate or single AE terms including additional medical interventions for identifying for AEs possibly associated with the investigational drug were developed.

Adverse events of special interest are listed in the Investigator's Brochure. The MedDRA PTs that are grouped under each of the AESI terms will be provided.

10.7.6. Clinical Laboratory Evaluations

Hematology and chemistry laboratory values will be graded according to CTCAE v4.03. The laboratory grade will be summarized for selected post-baseline visits. The selected post-baseline visits include Cycle 1 Day 1, Cycle 2 Day 1, Cycle 3 Day 1, EOT, and Follow-up. The worst post-baseline grade will be summarized.

In addition, the following summaries/analyses will be performed: hemoglobin, platelets, erythrocytes, and reticulocytes count up to 12 weeks from the start of study.

10.7.7. ECG Parameters

At pre-dose on Day 1, three separate ECGs will be performed. Electrocardiograms collected at pre-dose on Day 1 will be considered baseline ECGs (for continuous measures, e.g., QT and PR interval, the mean of the 3 values will be used as the baseline value).

The QTc interval corrected with Bazett (QTcB) and the QT interval corrected with Fridericia (QTcF) will be calculated as follows: $QTcB = QT / (60/HR)^{1/2}$ and $QTcF=QT/(60/HR)^{1/3}$, where HR= Heart Rate.

Descriptive statistics for QRS interval, PR interval, QT interval, QTcB, QTcF, and the change from baseline at selected post-baseline visits will also be summarized for patients in the Safety population. Change from baseline will be calculated for each patient at the specified visit as the value at the specified visit minus the baseline value. The summarized visits include Baseline, EOT, Follow-up, as well data collected on the first day of each cycle for a maximum of 6 months. Since the cycle length is different within each study Part, Day 1 data will be summarized through Cycle 7 Day 1 for Parts A, D, F, G (28 day cycles), through Cycle 9 Day 1 for Parts B, E, H, and J (21 day cycles), and through Cycle 13 Day 1 for Parts C and I (14 day cycles). In addition, the maximum post-baseline and minimum post-baseline values will be summarized.

10.7.8. ECOG Performance Status

Shift table of ECOG score from baseline to selected post-baseline visits will be provided in the Safety Population. The summarized visits include Baseline, Cycle 2 Day 1, Cycle 3 Day 1, Cycle 6 Day 1, Cycle 12 Day 1, EOT, and Follow-up. The maximum post-baseline shift from baseline will also be summarized.

10.7.9. Vital Signs

Descriptive statistics for heart rate, diastolic blood pressure, systolic blood pressure, pulse rate, respiratory rate, and temperature and changes from baseline at selected post-baseline visits will be summarized in the Safety Population. The selected visits include Baseline, Cycle 2 Day 1, Cycle 3 Day 1, EOT, and Follow-up. Change from baseline will be calculated for each patient at the specified visit as the value at the specified visit minus the baseline value. Baseline is defined as the last assessment prior to the first dose of study drug. In addition, the maximum post-baseline and minimum post-baseline values will be summarized.

10.8. Efficacy Analyses

All analyses specified in this section will be conducted in the Safety Population and will be repeated in in the Evaluable Population as well. All analyses will be conducted in Part A (monotherapy) by dose cohort and also by Part and dose for patients with the cancer types or subgroups identified in Section 9.4.

10.8.1. Clinical Response

Assessment of clinical response will be performed according to the irRC based on investigator's assessment. The overall best response will be tabulated. The overall best clinical response will identified from the following list which are ordered from best to worst: irCR, irPR, irSD, irPD.

In addition, Disease Control Rate and the Overall Response rate will be summarized and exact 95% confidence intervals will be calculated. Disease Control Rate = irCR + irPR + irSD and Overall Response Rate = irCR + irPR.

The time to response will be provided for patients with a post-baseline response (irCR or irPR) and will be presented using summary statistics. The time to response will be calculated from the first dose of study drug to the date that the criteria for irSD, irPR, or irSD was achieved.

Kaplan-Meier analyses of duration of response and progression-free survival will also be provided.

Duration of response will be calculated only for patients with a response and is defined as the time from the date the patient first meets the criteria for irCR or irPR to the date the patient progresses (irPD via scan or clinical progression as indicated by the study investigator on the disposition eCRF) or dies. For each patient that is not known to have progressed or died, duration of response will be censored at the date that the subject was last known to be alive and progression-free. For patients with both clinical progression and irPD (via scan) with different dates, the earlier date will be used for analyses. Since clinical progression is indicated on the Disposition eCRF and the date of the disposition event is not recorded in the eCRF, the date of the last clinical evaluation or last treatment date, whichever is later, will be used as the date of clinical progression.

Progression-free survival is defined as the time from the first dose of AM0010 to the date of disease progression (categorized as irPD according to irRC or clinical progression as indicated by the investigator) or death from any cause, whichever comes first. For each patient that is not known to have progressed or died, duration of progression-free survival will be censored at the date that the subject was last known to be alive and progression-free. For patients with both clinical progression and irPD (via scan) with different dates, the earlier date will be used for analyses. Since clinical progression is indicated on the Disposition eCRF and the date of the disposition event is not recorded in the eCRF, the date of the last clinical evaluation or treatment end date, whichever is later, will be used as the date of clinical progression. If irPD is recorded, but is not confirmed at a subsequent visit and is followed by tumor response of irCR, irSD, or

irPR at a later date, the single case or irPD is not considered disease progression for analysis purposes. However, a single irPD that is not followed by additional tumor assessments is considered disease progression.

10.8.2. Overall Survival

Survival time will be defined as the time from first dose of AM0010 until the date of death or censoring. Subjects alive at the time of the end of the study are censored at the last known date alive. Overall survival will be summarized using Kaplan-Meier methods and Kaplan-Meier curves will be presented.

10.8.3. Additional Exploratory Analyses

All efficacy analyses may be explored with respect to:

- PD-1 status in NSCLC patients
- TMB level in NSCLC patients
- Patients with or without prior PD-1 exposure (Pembrolizumab or Nivolumab)

10.9. Immunogenicity Analysis

The Treatment Emergent (TE) anti-drug-antibodies (ADA) evaluable population will be defined within the Safety Population as those patients with both a baseline ADA test result and a postbaseline ADA test result. As a proportion of the TE ADA evaluable population, the number and frequency of the following will be tabulated by treatment group: TE ADA+ patients, and TE ADA+ patients with detected higher-tier assay results. Included in the same tabulation will be, as a proportion of the TE ADA evaluable population, the number and frequency of patients with ADA present at baseline, as well as patients with detected higher-tier assay results at baseline.

A summary will be provided of the number and percentage of patients who receive AM0010 reporting specific TEAEs (overall and by PT) by patient TE ADA status (TE ADA+, TE ADA-, TE ADA Inconclusive, Patient not evaluable for TE ADA). The PT will be ordered by decreasing frequency in the TE ADA+ status group. The specific TEAE of interest are events in any one of the MedDRA Anaphylactic reactions Standardized MedDRA Query (SMQ), Hypersensitivity SMQ, Angioedema SMQ, Injection site reactions High Level Term (HLT), or Infusion site reactions HLT.

Additional immunogenicity analyses, to be presented in a standalone immunogenicity report in context with other studies of AM0010, will be described in a separate SAP.

11. References

Ryan CJ, Smith MR, de Bono JS, Molina A, Logothetis CJ, de Souza P, Fizazi K, Mainwaring P, Piulats JM, Ng S, Carles J, Mulders PF, Basch E, Small EJ, Saad F, Schrijvers D, Van Poppel H, Mukherjee SD, Suttmann H, Gerritsen WR, Flaig TW, George DJ, Yu EY, Efstathiou E, Pantuck A, Winquist E, Higano CS, Taplin ME, Park Y, Kheoh T, Griffin T, Scher HI, Rathkopf DE, and C.A. Investigators. Abiraterone in metastatic prostate cancer without previous chemotherapy. *N Engl J Med.* 2013;368(2):138-148.

Scher HI, Halabi S, Tannock I, Morris M, Sternberg CN, Carducci MA, Eisenberger MA, Higano C, Bubley GJ, Dreicer R, Petrylak D, Kantoff P, Basch E, Kelly WK, Figg WD, Small EJ, Beer TM, Wilding G, Martin A, Hussain M, and Prostate Cancer Clinical Trials Working. Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group. *J Clin Oncol*. 2008;26(7):1148-1159.

Wolchok JD, Hoos A, O'Day S, Weber JS, Hamid O, Lebbe C, Maio M, Binder M, Bohnsack O, Nichol G, Humphrey R, and Hodi FS. Guidelines for the evaluation of immune therapy activity in solid tumors: immune-related response criteria. *Clin Cancer Res.* 2009;15(23):7412-7420.

12. Appendices

Appendix 1. CTCAE V4.03 Laboratory value Grades

Laboratory Test	Grade 1	Grade 2	Grade 3	Grade 4
Chemistry				
Sodium (high)	>ULN – 150 mmol/L	>150-155 mmol/L	>155-160 mmol/L	>160 mmol/L
Sodium (low)	<LLN – 130 mmol/L	NA	<130-120 mmol/L	<120 mmol/L
Potassium (high)	>ULN – 5.5 mmol/L	>5.5 - 6.0 mmol/L	>6.0-7.0 mmol/L	>7.0 mmol/L
Potassium (low)		<LLN – 3.0 mmol/L	<3.0 – 2.5 mmol/L	<2.5 mmol/L
Chloride	Use normal ranges			
Bicarbonate	Use normal ranges			
Glucose Hypoglycemia	<LLN – 55 mg/dL <LLN – 3.0 mmol/L	<55-40 mg/dL <3.0 – 2.2 mmol/L	<40-30 mg/dL <2.2-1.7 mmol/L	<30 mg/dL <1.7 mmol/L
Cholesterol	>ULN – 300 mg/dl; >ULN – 7.75 mmol/L	>300 – 400 mg/dL; >7.75 – 10.34 mmol/L	>400 – 500 mg/dL >10.34 – 12.92 mmol/L	>500 mg/dL >12.92 mmol/L
HDL-C	Use normal ranges			
LDL-C	Use normal ranges			
BUN/Urea	Use normal ranges			
Creatinine Increased	>1-1.5 x baseline >ULN – 1.5 ULN	>1.5 – 3.0 x baseline >1.5-3.0 x ULN	>3.0 baseline >3.0-6.0 x ULN	>6.0 x ULN
LDH	Use normal ranges			
Alanine aminotransferase (ALT) increased	>ULN – 3.0 x ULN	>3.0 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN
Aspartate aminotransferase (AST) increased	>ULN – 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN
Gamma-glutamyltransferase (GGT) increased	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Alkaline phosphatase	>ULN – 2.5 ULN	>2.5 – 5.0 ULN	>5.0 – 20.0 x ULN	>20.0 x ULN

Laboratory Test	Grade 1	Grade 2	Grade 3	Grade 4
increased				
Total bilirubin increased	>ULN – 1.5 X ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN
Total protein	Use normal ranges			
Albumin Hypoalbuminemia	<LLN – 3 g/dL <LLN – 30 g/L	<3-2 g/dL <30-20 g/L	<2 g/dL <20 g/L	
Corrected Serum Calcium Hypercalcemia	>ULN – 11.5 mg/dL >ULN-2.9 mmol/L	>11.5-12.5 mg/dL >2.9-3.1 mmol/l	>12.5-13.5 mg/dL >3.1-3.4 mmol/L	>13.5 mg/dL >3.4 mmol/L
Magnesium (low) Hypomagnesemia	<LLN – 1.2 mg/dL <LLN -0.5 mmol/L	<1.2 – 0.9 mg/dL <0.5 – 0.4 mmol/L	<0.9-0.7 mg/dL <0.4-0.3 mmol/L	<0.7 mg/dL <0.3 mmol/L
Magnesium (high) Hypermagnesemia	>ULN – 3.0 mg/dL >ULN -1.23 mmol/L	NA	>3.0-8.0 mg/dL >1.23-3.30 mmol/L	>8.0 mg/dL >3.30 mmol/L
Iron	Use normal ranges			
Phosphatase	Use normal ranges			
Creatine Phosphokinase Increased	>ULN – 2.5 x ULN	>2.5 x ULN – 5 x ULN	>5 x ULN – 10 x ULN	>10 x ULN
Pancreatic lipase increased	>ULN – 1.5xULN	>1.5 – 2.0 x ULN	>2.0-5.0 ULN	>5.0 x ULN
Pancreatic amylase	Use normal ranges			
Hematology				
RBC Count	Use normal ranges			
WBC Count decreased	<LLN – 3000/mm3 <LLN-3.0 x 10^9/L	<3000-2000/mm3 <3.0-2.0 x 10^9/L	<2000-1000/mm3 <2.0-1.0 x 10^9/L	<1000/mm3 <1.0 x 10^9/L
Hemoglobin increased	Increase in >0-2 gm/dL above ULN or above baseline if baseline is above ULN	Increase in >2-4 gm/dL above ULN or above baseline if baseline is above ULN	Increase in >4 gm/dL above ULN or above baseline if baseline is above ULN	
Hemoglobin (low) Anemia	<LLN – 10.0 g/dL <LLN – 6.2 mmol/L	<10.0-8.0 g/dL <6.2-4.9 mmol/L	<8.0 g/dL <4.9 mmol/L	

Laboratory Test	Grade 1	Grade 2	Grade 3	Grade 4
Hematocrit	Use normal ranges			
Platelet count decreased	<LLN – 75,000/mm3 <LLN – 75.0 x 10^9/L	<75,000-50,000/mm3 <75.0-50.0 x 10^9/L	<50,000-25,000/mm3 <50.0 – 25.0 x 10^9/L	<25,000/mm3 <25.0 x 10^9/L
ANC	Use normal ranges			
Neutrophil count decreased	<LLN – 1500/mm3 <LLN – 1.5 x 10^9/L	<1500-1000/mm3 <1.5-1.0 x 10^9/L	<1000-500/mm3 <1.0-0.5 x 10^9/L	<500/mm3 <0.5 x 10^9/L
Lymphocyte count decreased	<LLN – 8000/mm3 <LLN – 0.8 10^9/L	<800-500/mm3 <0.8-0.5 x 10^9/L	<500-200/mm3 <0.5-0.2 x 10^9/L	<200/mm3 <0.2 x 10^9/L
Lymphocyte count increased		>4000/mm3-20,000/mm3	>20,000/mm3	
Monocytes	Use normal ranges			
Eosinophils	Use normal ranges			
aPTT	>ULN – 1.5 x ULN >1.5-2.5 ULN >2.5 x ULN			

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