Name of Sponsor/Company: Astellas Pharma Inc.		
Name of Finished Product: Not applicable		
Name of Active Ingredient: ASP0113		

SYNOPSIS

Title of Study: An Open Phase 2 Trial to Evaluate Safety of a Therapeutic Vaccine, ASP0113, in Recipients Undergoing Allogeneic Hematopoietic Cell Transplant (HCT)

Investigators/Coordinating Investigator: [redacted]

Study Centers: 3 sites in Japan

Publication Based on the Study: No publications based on the results of this study were available at the time this report was approved.

Study Period:

Study Initiation Date (Date of First Enrollment): 20 Jun 2013

Study Completion Date (Date of Last Evaluation): 19 Jan 2015

Phase of Development: Phase 2

Objectives:

The primary objective of this study was to evaluate the safety and tolerability of ASP0113 in recipients undergoing allogeneic HCT. The secondary objective was to evaluate the occurrence of cytomegalovirus (CMV) viremia in recipients undergoing allogeneic HCT inoculated with ASP0113.

Methodology:

- This study was a phase 2, open-label, multicenter study primarily to evaluate the safety and tolerability of ASP0113 in subjects undergoing allogeneic HCT.
- The subjects were CMV-seropositive or CMV-seronegative HCT recipients. Seronegative recipients scheduled to receive transplantation from a CMV-seronegative donor were not enrolled.
- ASP0113 is a vaccine containing 2.5 mg/mL each of 2 plasmids encoding glycoprotein B (gB) and phosphoprotein 65 (pp65) formulated with CRL1005 poloxamer and benzalkonium chloride (BAK).
- ASP0113 was dosed as 1 mL intramuscularly 5 times, on days −14 to −3, 14 to 40, 60 ± 5, 90 ± 10, and 180 ± 10, counting from the transplantation (stem cell transfusion) day (day 0). The first dose of the study drug was administered on the conditioning day (within 24 hours prior to starting conditioning) and before starting chemotherapy and radiotherapy. The second dose was administered on day 14 or soon thereafter. Each dose of the study drug was administered only if the platelet count was at least 50,000/mm^3 (spontaneous or after platelet transfusion) and there were no medical contraindications for intramuscular injection. Platelet counts obtained within 3 days prior to study drug administration were used. Subjects were observed for 6 months thereafter.

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- The CMV plasma viral loads were measured periodically through 1 year post-transplant. The viral load testing (CMV antigenemia test and quantitative polymerase chain reaction [PCR]) was performed at the central laboratory weekly (± 2 days) during days 0 to 100, every other week (± 3 days) during days 101 to 180, and once a month (± 5 days) during days 181 to 365. Viral load of subjects in whom CMV-specific antiviral therapy had been initiated was tested by the central laboratory at least once a week until the antiviral therapy ended, after which the prescribed measurement schedule was resumed. Pre-emptive therapy could be started based on the central laboratory assessment and the subject's clinical condition.
- Local and systemic reactogenicity was evaluated 60 minutes after each injection. Local reactogenicity was evaluated a total of 9 times, namely, at 60 minutes after each injection, on the 7 consecutive days following the injection and 10 to 14 days after the injection. When the subject could not be examined for the assessments on each of the 7 consecutive days following an injection, these assessments were done by the subject and reported to the site via the subject diary. When reactogenicity was reported as an adverse event (AE), the safety assessment was continued until resolution of all signs and symptoms or until the subject was medically stable.
- All AEs were collected from the consent day through 1 year post transplant (End of Study).
- To evaluate safety after the ASP0113 inoculations, the Safety Review Board was chartered to identify any safety concerns specific to Japanese patients.

Number of Patients (Planned, Enrolled and Analyzed):

Planned: 8 subjects

Enrolled: 10 subjects

Analyzed: 9 subjects

Diagnosis and Main Criteria for Inclusion:

Inclusion Criteria

A subject was eligible for the study if all of the following applied:

1. Written informed consent form had been obtained from subject.
2. Subject was at least 20 years of age at the time of consent.
3. Subject was scheduled to undergo either of the following HCTs.
   - Sibling Donor Transplant − 7/8 human-leukocyte antigen (HLA)-A, -B, -C, -DRB1 match utilizing high resolution deoxyribonucleic acid (DNA) typing or high- or low-resolution 8/8 match
   - Unrelated Donor Transplant − 7/8 or 8/8 HLA-A, -B, -C, -DRB1 match utilizing high resolution DNA typing
4. Subject had one of the following underlying diseases:

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- Acute myelocytic leukemia (AML), with or without a history of myelodysplastic syndrome (MDS), in first or second complete remission or in early relapse (< 20% blasts in bone marrow with no circulating blasts in peripheral blood and no extramedullary leukemia)
- Acute lymphoblastic leukemia (ALL) in first or second complete remission
- Acute undifferentiated leukemia (AUL) in first or second complete remission
- Acute biphenotypic leukemia in first or second complete remission
- Chronic myelocytic leukemia (CML) in either chronic or accelerated phase
- Chronic lymphatic leukemia (CLL)
- One of the following MDS(s) defined by the following:
  Refractory anemia, refractory anemia with ringed sideroblasts, refractory cytopenia with multilineage dysplasia, refractory cytopenia with multilineage dysplasia and ringed sideroblasts, refractory anemia with excess blasts-1 (5-10% blasts), refractory anemia with excess blasts-2 (10-20% blasts), MDS, unclassified, MDS associated with isolated del (5q), chronic myelomonocytic leukemia (CMML)
- Primary or secondary myelofibrosis without leukemic transformation, except if Dynamic International Prognostic Scoring System (DIPSS) category of high risk or intermediate risk-2
- Lymphoma (including Hodgkin's) with chemosensitive disease (≥ 50% response to chemotherapy)

5. Subject was scheduled to receive an allogeneic peripheral blood stem cell transplant (PBSCT) or bone marrow transplant (BMT) for the treatment of the hematologic disorders in Inclusion Criterion 4.
6. Male subject and their partners who were of childbearing potential had to use condoms or diaphragms for contraception from Screening through 90 days after the last inoculation.
7. Male subject was not allowed to donate sperm from Screening through 90 days after the last inoculation.
8. Female subject had to be either:
   - Of non-childbearing potential
     post-menopausal (defined as at least 1 year without any menses) prior to Screening, or documented surgically sterile at least 1 month prior to Screening (e.g., bilateral oophorectomy or hysterectomy)
   - Or, if of childbearing potential
     had to have a negative urine pregnancy test at Screening, and had to use condoms or diaphragms for contraception from Screening through 90 days after the last inoculation.
9. Female subject was not allowed to be breastfeeding from Screening through 90 days after the last inoculation.
10. Female subject was not allowed to donate ova from Screening through 90 days after the last inoculation.
11. Subject was willing to comply with the protocol.
12. Subject agreed not to participate in another interventional study while on treatment. New regimens of approved chemotherapeutic or conditioning drugs were allowed.

Exclusion Criteria

A subject was excluded from participation if any of the following applied:

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1. Subject had active CMV disease or infection or had received treatment for CMV within 90 days prior to transplant.
2. Subject had planned CMV prophylactic therapy with antiviral drugs or CMV-specific immunoglobulins from Screening to the day 365 Visit.
3. Subject had a modified hematopoietic cell transplant comorbidity index (HCT-CI) score ≥ 3.
4. Subject had been positive for human immunodeficiency virus (HIV), hepatitis B virus surface (HBs) antigen, or hepatitis C virus (HCV)-ribonucleic acid (RNA) when tested within 60 days prior to Screening.
5. Donor CMV serostatus was unknown.
6. Subject had received any of the following substances or treatments:
   - T cell depletion of donor cell product
   - Alemtuzumab within 60 days prior to transplant, including conditioning regimen, or subjects in whom treatment with alemtuzumab was planned at any time from 60 days prior to through 1 year post-transplant.
   - Administration of a CMV vaccine, including any prior exposure to ASP0113
7. Subject had received an allogeneic stem cell transplant within 1 year prior to transplant (subjects who had received a prior autologous transplant were allowed).
8. Subject had a co-existing malignancy in addition to the malignancy being treated for the study or the subject had a history of any other malignancy (within the past 5 years prior to Screening) except non-metastatic basal or squamous cell carcinoma that had been successfully treated or cancer in situ of the cervix uteri that had been handled by local surgery.
9. Subject had an unstable medical or psychiatric condition, including a history of illicit drug(s) or alcohol abuse that the investigator believed would interfere with protocol requirements.
10. Subject had had an allergic reaction to any component of the vaccine or aminoglycoside antibiotics (kanamycin and the like used for the vaccine production).
11. Subject had participated in any interventional clinical study or had been treated with any investigational research products within 30 days prior to Screening. (Investigational research products were considered those products that had not been approved for any indication in Japan. New regimens of approved chemotherapeutic drugs or conditioning drugs were allowed.)
12. Subject was CMV-seronegative and scheduled to receive a transplant from a CMV-seronegative donor.
13. Subject had received a prior allogeneic HCT and had residual chronic graft-versus-host disease (GVHD).
14. Other subjects considered ineligible by the investigator/sub-investigator.

Test Product, Dose and Mode of Administration, Batch Numbers:

Test drug: ASP0113 is a vaccine containing 2.5 mg/mL each of 2 plasmids encoding gB and pp65 formulated with CRL1005 poloxamer and BAK. ASP0113 is a milky white injection containing 1.3 mL of plasmid mixture at a concentration of 5 mg/mL in a 2-mL vial.

Lot number, [redacted] was used in the study.

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Mode of administration: 1 mL of ASP0113 was administered intramuscularly in the deltoid muscle, using a needle and syringe, alternating sides with each dose if possible.

Duration of Treatment (or Duration of Study, if applicable):

Subjects received 5 injections of ASP0113 over an approximate 6-month period. Subjects were observed for 6 months from the last injection.

Reference Product, Dose and Mode of Administration, Batch Numbers: Not applicable.

Criteria for Evaluation:

Safety

- AEs (according to Common Terminology Criteria for Adverse Events [NCI-CTCAE] v. 4.03)
- Local reactogenicity signs and symptoms using both the NCI-CTCAE v. 4.03 grading scale and the protocol-specified reactogenicity scale
- Laboratory assessments
- Vital signs
- Physical examination

Other Variables

- Incidence of CMV viremia
  - CMV plasma viral load ≥ 1000 copies/mL as assessed by the central laboratory
- CMV-specific antiviral therapy
  - Therapeutic intervention for CMV plasma viral load ≥ 1000 copies/mL as assessed by the central laboratory throughout 1 year post-transplant
- CMV end organ disease (e.g., CMV pneumonia, CMV gastrointestinal disease, CMV hepatitis)
- Maximum grade of acute GVHD or maximum chronic GVHD score
- Moderate to severe secondary infections
- Mortality
- Relapse of primary disease
- Rejection
- Failure to engraft
- Time to engraftment
- Time to platelet recovery

Statistical Methods:

Safety Variables

The safety analysis set (SAF) consisted of all subjects who received at least 1 dose of the study drug.

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- AEs

  Medical Dictionary for Regulatory Activities (MedDRA) version 16.0 was used to summarize AEs by system organ class (SOC) and preferred term (PT).

  Overview tables were provided for the number and percentage of subjects and the number of events with treatment-emergent AEs (TEAEs); TEAEs with NCI-CTCAE Grade = 3, 4, 5 and ≥ 3; serious TEAEs; TEAEs leading to permanent discontinuation of study drug; TEAEs leading to death; TEAEs associated with local reactogenicity event; TEAEs for infection; TEAEs associated with a CMV disease event; and TEAEs for infection other than a CMV disease event. Drug-related TEAEs were presented in a similar way.

  The number and percentage of subjects with TEAEs, as classified by SOC and PT, were summarized for TEAEs, drug-related TEAEs, serious TEAEs, drug-related serious TEAEs, all TEAEs excluding serious AEs, TEAEs associated with a CMV disease event, drug-related TEAEs associated with a CMV disease event, TEAEs for infection other than a CMV disease event, and drug-related TEAEs for infection other than a CMV disease event. The number and percentage of subjects with TEAEs and drug-related TEAEs, as classified by SOC and PT, were also summarized by NCI-CTCAE Grade.

- Laboratory Assessments and Vital Signs

  The baseline visit was screening for quantitative clinical laboratory variables (hematology and biochemistry), and prior to the first injection of study drug for vital signs (systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate, temperature and weight).

  Quantitative clinical laboratory variables and vital signs, and a within-subject change (calculated as the post-baseline measurement minus the baseline measurement) were summarized using mean, standard deviation, minimum, maximum and median at each visit.

  Results were presented graphically using spaghetti plot.

  Listings were prepared by subject.

  Frequency tabulations for categorical data for laboratory assessments were presented.

- Local Reactogenicity Assessments

  Local reactogenicity assessments (pain, tenderness, erythema/redness and induration/swelling) were summarized using frequency tables by visit.

Other Variables

Listings by subject were prepared of the data on occurrence and date of onset of CMV antigenemia and other variables.

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Summary of Results/Conclusions:

Population:

A total of 10 subjects provided informed consent [Figure 1]. Among them, 1 subject discontinued before the first dose of the study drug. The remaining 9 subjects received the study drug. Of these, 3 subjects completed the study, and 6 subjects discontinued the study. The primary reasons for discontinuation were progressive disease (3 subjects, 33.3%), and AE, death and physician's decision (1 subject, 11.1%, each) [Table 1].

All 9 subjects who received at least 1 dose of the study drug were included in the SAF.

Demographics and Other Baseline Characteristics:

Of the 9 subjects who received the study drug, 4 subjects were men (44.4%) and 5 subjects were women (55.6%) [Table 2]. The mean age was 46.0 years, the mean height was 163.48 cm, the mean weight was 56.57 kg and the mean body mass index was 20.93 kg/m^2.

Safety Results:

Overview of TEAEs, summary of TEAEs occurring in at least 2 subjects and summary of serious TEAEs are presented in [Table 3], [Table 4] and [Table 5], respectively.

- One subject died during this study, but the death was not considered drug-related, nor was it associated with CMV disease event; it was due to relapse of primary disease.
- The incidence of serious TEAEs was 100.0% (9/9 subjects). No drug-related serious TEAEs were reported.
- No TEAEs leading to permanent discontinuation of the study drug were reported.
- The incidence of TEAEs was 100.0% (9/9 subjects), and that of drug-related TEAEs was 66.7% (6/9 subjects).
- The incidences of TEAEs with NCI-CTCAE Grade 3, 4 and 5 were 100.0% (9/9 subjects), 100.0% (9/9 subjects) and 11.1% (1/9 subjects), respectively. One subject (11.1%) had a drug-related TEAE with NCI-CTCAE Grade 3 (injection site erythema). No drug-related TEAEs with NCI-CTCAE Grade ≥ 4 were reported.
- The incidence of TEAEs associated with a local reactogenicity event; that is local skin reaction was 55.6% (5/9 subjects), and that of drug-related TEAEs associated with a local reactogenicity event; that is local skin reaction was 55.6% (5/9 subjects). One severe event of erythema/redness was reported in 1 subject, but the severe erythema/redness persisted only for 1 day and resolved without treatment.
- The incidences of infection was 88.9% (8/9 subjects) including TEAEs associated with a CMV disease event (77.8% [7/9 subjects]) and infection other than a CMV disease event (88.9% [8/9 subjects]), none of these events were considered drug-related. All of the TEAEs associated with a CMV disease event

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(cytomegalovirus viraemia, none of which developed CMV end organ disease) were Grade 1 of the Maximum Severity Grading of Infection, except in 1 subject (Grade 2).

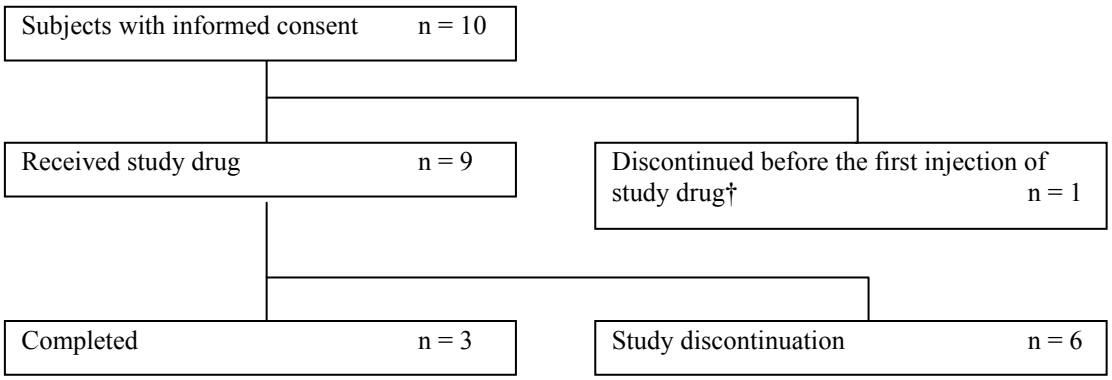
- TEAEs classified in MedDRA SOC investigations with NCI-CTCAE Grade ≥ 3 were platelet count decreased, white blood cell count decreased, lymphocyte count decreased, amylase increased and weight decreased; no laboratory abnormalities reported as a TEAE classified in MedDRA SOC investigations were considered drug-related. In no subjects were either alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) > 3 x upper limit of normal (ULN) and Total Bilirubin > 2 x ULN or ALT and/or AST > 20 x ULN or Total Bilirubin ≥ 10 x ULN observed.
- The incidence of CMV viremia with a CMV plasma viral load ≥ 1000 copies/mL as assessed by the central laboratory was 55.6% (5/9 subjects). There were 7 subjects (77.8%) who had taken CMV-specific antiviral therapy throughout the study; none of them initiated the CMV-specific antiviral therapy for a CMV plasma viral load ≥ 1000 copies/mL as assessed by the central laboratory.
- No CMV end organ disease was reported.
- Acute GVHD was reported in 7 subjects (77.8%); maximum grade of acute GVHD was Grade II for 5 subjects (55.6%) and Grade I for 2 subjects (22.2%). Chronic GVHD was reported in 2 subjects (22.2%); maximum Chronic GVHD Global Score was severe and mild in 1 subject (11.1%) each.
- Moderate to severe secondary infections were reported in 4 subjects (44.4%).
- Relapse of primary disease was reported in 5 subjects (55.6%), but none of these events were considered drug-related.
- No graft rejection was reported.
- No graft failure was reported. The time to engraftment was 12 to 35 days after transplantation.
- The time to platelet recovery was 24 to 193 days after transplantation.
- The Safety Review Board was held 3 times during this trial and concluded that no safety concerns specific to Japanese patients were identified.

CONCLUSIONS:

ASP0113 vaccine containing 2.5 mg/mL each of 2 plasmids encoding gB and pp65 formulated with CRL1005 poloxamer and BAK administered to recipients of allogeneic HCT appeared to be safe and well tolerated.

Date of Report: 13 Jul 2015

Figure 1 Disposition of Subjects



† Subjects who signed informed consent but discontinued before the first injection of the study drug were screen failures. One subject ([redacted]) was a screen failure whose primary reason for screen failure was inclusion criterion #4 (Appendix 13.2.1.1)

Source: Table 12.1.1.1, Table 12.1.1.3

Table 1 Subject Disposition

Category	Total
Subjects with informed consent	10
Discontinued before the first injection of study drug†	1
Subjects who received study drug	9
Study discontinuation‡	6 (66.7%)
Adverse event§¶	1 (11.1%)
Death	1 (11.1%)
Progressive disease¶	3 (33.3%)
Physician decision	1 (11.1%)

n (%). The denominator was the number of subjects who received the study drug.

† Subjects who signed informed consent but discontinued before the first injection of the study drug were screen failures.

‡ Only the primary end of study reason was collected.

§ Subject [redacted] had local reactogenicity of grade ≥ 3 [Appendix 13.2.1.2], which occurred after the last dose (dose 5) [Appendix 13.2.8.4], and was not counted as a TEAE leading to discontinuation of the study drug.

¶ One subject in AE and 3 subjects in progressive disease discontinued as they met discontinuation criteria.

Source: Table 12.1.1.1, Table 12.1.1.3

Table 2 Demographic Characteristics

Parameter	Category/statistic	ASP0113 (N = 9)
Sex	Male	4 (44.4%)
	Female	5 (55.6%)
Age (years)	Mean (SD)	46.0 (10.5)
	Median	48.0
	Min - Max	22 - 61
Race	Asian	9 (100.0%)
	Others	0
Height at Screening (cm)	Mean (SD)	163.48 (8.46)
	Median	158.70
	Min - Max	154.7 - 176.4
Weight prior to injection of dose 1 (kg)	Mean (SD)	56.57 (12.88)
	Median	56.70
	Min - Max	38.0 - 73.9
BMI prior to injection of dose 1 (kg/m^2)	Mean (SD)	20.93 (3.11)
	Median	21.96
	Min - Max	15.3 - 23.9
Primary diagnosis	Acute myeloid leukemia	3 (33.3%)
	Acute lymphoblastic leukemia	4 (44.4%)
	Acute undifferentiated leukemia	0
	Acute biphenotypic leukemia	0
	Chronic myelogenous leukemia	0
	Chronic lymphocytic leukemia	0
	Myelodysplastic syndrome	1 (11.1%)
	Primary or secondary myelofibrosis without leukemic transformation except if Dynamic International Prognostic Scoring System Category of high or intermediate -2.	0
	Lymphoma (including Hodgkin's) with chemosensitive disease (greater than or equal to 50% response to chemotherapy).	1 (11.1%)
Cytomegalovirus antibody IgG at screening	Negative	1 (11.1%)
	Positive	8 (88.9%)
HIV-1/2 antibody at Screening	Negative	9 (100.0%)
	Positive	0
Hepatitis B surface antigen at Screening	Negative	9 (100.0%)
	Positive	0
Hepatitis C virus RNA at Screening	Negative	9 (100.0%)
	Positive	0
Type of tansplant	Bone marrow	7 (77.8%)
	Peripheral blood stem cells	2 (22.2%)
HLA DNA typing	7/8	3 (33.3%)
	8/8	6 (66.7%)
Transplant between related donor and recipient	No	6 (66.7%)
	Yes	3 (33.3%)
Donor-recipient cytomegalovirus antibody IgG at transplant	Negative-positive	2 (22.2%)
	Positive-negative	1 (11.1%)
	Positive-positive	6 (66.7%)
Modified HCT-CI score at Screening	Mean (SD)	0.2 (0.4)
	Median	0.0
	Min - Max	0 - 1
Conditioning regimen	Myeloablative conditioning regimen	7 (77.8%)
	Non-myeloablative (reduced-intensity) conditioning regimen	2 (22.2%)

Footnotes continued on next page

Safety Analysis Set (SAF): all subjects who received at least 1 dose of the study drug.

BMI: body mass index, DNA: deoxyribonucleic acid, HCT-CI: hematopoietic cell transplant comorbidity index, HIV: human immunodeficiency virus, HLA: human-leukocyte antigen, IgG: immunoglobulin G, RNA: ribonucleic acid

Source: Table 12.1.2, Table 12.1.4

Table 3 Overview of Treatment-Emergent Adverse Events: SAF

	ASP0113 (N = 9)	
	n (%)	**number of events**
TEAEs	9 (100.0%)	272
Drug-related† TEAEs	6 (66.7%)	23
TEAEs with NCI-CTCAE Grade = 3	9 (100.0%)	69
Drug-related† TEAEs with NCI-CTCAE Grade = 3	1 (11.1%)	1
TEAEs with NCI-CTCAE Grade = 4	9 (100.0%)	28
Drug-related† TEAEs with NCI-CTCAE Grade = 4	0	0
TEAEs with NCI-CTCAE Grade = 5	1 (11.1%)	1
Drug-related† TEAEs with NCI-CTCAE Grade = 5	0	0
TEAEs with NCI-CTCAE Grade ≥ 3	9 (100.0%)	98
Drug-related† TEAEs with NCI-CTCAE Grade ≥ 3	1 (11.1%)	1
Serious TEAEs	9 (100.0%)	31
Drug-related† serious TEAEs	0	0
TEAEs leading to discontinuation of the study drug	0	0
Drug-related† TEAEs leading to discontinuation of the study drug	0	0
Death	1 (11.1%)	1
Drug-related† death	0	0
TEAEs associated with a local reactogenicity event	5 (55.6%)	19
Drug-related† TEAEs associated with a local reactogenicity event	5 (55.6%)	19
Infection	8 (88.9%)	32
Drug-related† infection	0	0

Safety Analysis Set (SAF): all subjects who received at least 1 dose of the study drug.

NCI-CTCAE: Common Terminology Criteria for Adverse Events, TEAE: treatment-emergent adverse event

† Drug-related: possible or probable, as assessed by the investigator, or records where relationship was missing.

Source: Table 12.6.1.1

Table 4 Summary of Treatment-Emergent Adverse Events Occurring in at Least 2 Subjects (Preferred Term)

MedDRA version 16.0 System Organ Class Preferred Term	ASP0113 (N = 9)	
	TEAEs	Drug-related TEAEs†
Overall	**9 (100.0%)**	**6 (66.7%)**
Blood and lymphatic system disorders	**9 (100.0%)**	**0**
Anaemia	8 (88.9%)	0
Febrile neutropenia	8 (88.9%)	0
Leukopenia	2 (22.2%)	0
Lymphopenia	2 (22.2%)	0
Thrombocytopenia	2 (22.2%)	0
Gastrointestinal disorders	**9 (100.0%)**	**0**
Constipation	3 (33.3%)	0
Diarrhoea	9 (100.0%)	0
Haemorrhoids	2 (22.2%)	0
Nausea	4 (44.4%)	0
Oral disorder	3 (33.3%)	0
Proctalgia	2 (22.2%)	0
Stomatitis	6 (66.7%)	0
Vomiting	6 (66.7%)	0
General disorders and administration site conditions	**9 (100.0%)**	**6 (66.7%)**
Injection site pain	2 (22.2%)	2 (22.2%)
Oedema	3 (33.3%)	0
Oedema peripheral	2 (22.2%)	0
Pyrexia	5 (55.6%)	3 (33.3%)
Tenderness	2 (22.2%)	2 (22.2%)
Hepatobiliary disorders	**2 (22.2%)**	**0**
Hepatic function abnormal	2 (22.2%)	0
Immune system disorders	**8 (88.9%)**	**0**
Acute graft versus host disease	6 (66.7%)	0
Chronic graft versus host disease	2 (22.2%)	0
Hypogammaglobulinaemia	3 (33.3%)	0
Infections and infestations	**7 (77.8%)**	**0**
Bacteraemia	3 (33.3%)	0
Cytomegalovirus viraemia	7 (77.8%)	0
Skin infection	2 (22.2%)	0
Investigations	**8 (88.9%)**	**0**
Blood creatinine increased	2 (22.2%)	0
Lymphocyte count decreased	3 (33.3%)	0
Platelet count decreased	7 (77.8%)	0
White blood cell count decreased	7 (77.8%)	0
Metabolism and nutrition disorders	**9 (100.0%)**	**1 (11.1%)**
Decreased appetite	6 (66.7%)	0
Hyperglycaemia	2 (22.2%)	0
Hypokalaemia	5 (55.6%)	0
Hypomagnesaemia	5 (55.6%)	0
Malnutrition	2 (22.2%)	0
Musculoskeletal and connective tissue disorders	**3 (33.3%)**	**0**
Back pain	3 (33.3%)	0

Table continued on next page

MedDRA version 16.0 System Organ Class Preferred Term	ASP0113 (N = 9)	
	TEAEs	Drug-related TEAEs†
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**5 (55.6%)**	**0**
Acute lymphocytic leukaemia recurrent	2 (22.2%)	0
Nervous system disorders	**8 (88.9%)**	**0**
Headache	8 (88.9%)	0
Psychiatric disorders	**5 (55.6%)**	**0**
Insomnia	4 (44.4%)	0
Sleep disorder	2 (22.2%)	0
Skin and subcutaneous tissue disorders	**8 (88.9%)**	**3 (33.3%)**
Erythema	2 (22.2%)	2 (22.2%)
Rash	6 (66.7%)	1 (11.1%)
Vascular disorders	**5 (55.6%)**	**0**
Hypertension	5 (55.6%)	0

Safety Analysis Set (SAF): all subjects who received at least 1 dose of the study drug.

n (%)

TEAE: treatment-emergent adverse event

† Drug-related: possible or probable, as assessed by the investigator, or records where relationship is missing.

Source: Table 12.6.1.2

Table 5 Summary of Serious Treatment-Emergent Adverse Events

MedDRA version 16.0 System Organ Class Preferred Term	ASP0113 (N = 9)	
	TEAEs	Drug-related TEAEs†
Overall	**9 (100.0%)**	**0**
Blood and lymphatic system disorders	**2 (22.2%)**	**0**
Leukopenia	1 (11.1%)	0
Lymphopenia	2 (22.2%)	0
Thrombocytopenia	2 (22.2%)	0
Infections and infestations	**1 (11.1%)**	**0**
Pneumocystis jiroveci pneumonia	1 (11.1%)	0
Investigations	**8 (88.9%)**	**0**
Amylase increased	1 (11.1%)	0
Lymphocyte count decreased	3 (33.3%)	0
Platelet count decreased	7 (77.8%)	0
White blood cell count decreased	7 (77.8%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**5 (55.6%)**	**0**
Acute lymphocytic leukaemia recurrent	2 (22.2%)	0
Chronic myelomonocytic leukaemia	1 (11.1%)	0
Leukaemia recurrent	1 (11.1%)	0
Non-Hodgkin's lymphoma recurrent	1 (11.1%)	0

Safety Analysis Set (SAF): all subjects who received at least 1 dose of the study drug.

n (%)

TEAE: treatment-emergent adverse event

† Drug-related: possible or probable, as assessed by the investigator, or records where relationship was missing.

Source: Table 12.6.1.5