Protocol Registration Receipt
03/06/2014

Grantor: CDER IND/IDE Number: 102,175 Serial Number:

Open-label Study to Evaluate the Safety, PK, and PD of MEK Inhibitor GSK1120212 in Subjects With Relapsed or Refractory Leukemias

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT00920140

Purpose

MEK111759 is a dose-escalation, Phase I/II, open-label study to determine the recommended dose and regimen for the orally administered MEK inhibitor GSK1120212 in subjects with relapsed or refractory leukemias. The recommended dose and regimen will be selected based on the safety, pharmacokinetic, and pharmacodynamic profiles. This study will identify the maximum tolerated and recommended Phase II doses using a dose-escalation procedure. Dose escalations will continue based on predefined parameters until a maximum tolerated dose is established. In Phase II, the clinical efficacy of GSK1120212 in subjects with relapsed or refractory leukaemias (AML, MDS or CMML) will be determined.

Condition	Intervention	Phase
Cancer	Drug: GSK1120212	Phase 2

Study Type: Interventional

Study Design: Treatment, Single Group Assignment, Open Label, Non-Randomized

Official Title: An Open-Label, Dose-Escalation, Phase I/II Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics, and Clinical Activity of the MEK Inhibitor GSK1120212 in Subjects With Relapsed or Refractory Leukemias

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Number of Participants With Any Adverse Event (AE) or Serious Adverse Event (SAE) by Dose [Time Frame: From the start of the study drug until the final study visit (up to approximately 407 days)] [Designated as safety issue: No]

  An AE is any untoward medical occurrence in a participant (par.) or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, or is an event of possible drug-induced liver injury. Refer to the general Adverse AE/SAE module for a complete list of AEs and SAEs.
- Number of Participants With a Change From Baseline Grade to Grade 3 and 4 for the Indicated Hematology Parameters by Dose [Time Frame: From the start of the study drug until the final study visit (up to approximately 407 days)] [Designated as safety issue: No]

  Hematology and clinical chemistry data were summarized according to National Cancer Institutes (NCI) Common Terminology Criteria for Adverse Events (CTCAE) grade, version 3.0. Grade 1, Mild; Grade 2, Moderate; Grade 3, Severe; Grade 4, Life-threatening or disabling; Grade 5, Death. Data are presented for only those parameters for which an increase to Grade 3 or Grade 4 occurred. Hematology tests where the toxicity grade is defined by NCI-CTCAE includes hemoglobin, international normalized ratio (INR), lymphocytes, total neutrophils, platelet count, and partial thromboplastin time (PTT). Participants with missing baseline grades were assumed to have a baseline grade of 0. Only those participants (par.) with laboratory values for worst-case on-therapy (defined as the worst shift that occurred at any time during the treatment period) are presented.
- Number of Participants With a Change From Baseline Grade to Grade 3 and 4 for the Indicated Clinical Chemistry Parameters by Dose [Time Frame: From the start of the study drug until the final study visit (up to approximately 407 days)] [Designated as safety issue: No]

  Hematology and clinical chemistry data were summarized according to NCI-CTCAE grade, version 3.0. Grade 1, Mild; Grade 2, Moderate; Grade 3, Severe; Grade 4, Life-threatening or disabling; Grade 5, Death. Data are presented for only those parameters for which an increase to Grade 3 or Grade 4 occurred. Clinical chemistry tests where the toxicity grade is defined by NCI-CTCAE includes albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase (AST), total bilirubin, calcium, creatinine, glucose, bicarbonate, potassium, magnesium, sodium, and phosphorus. Participants with missing Baseline grades were assumed to have a Baseline grade of 0. Only those participants (par.) with laboratory values for worst-case on-therapy are presented.
- Number of Participants With a Change From Baseline in Heart Rate by Dose [Time Frame: From the start of the study drug until the final study visit (up to

approximately 407 days)] [Designated as safety issue: No]

Change from Baseline in heart rate is categorized as decrease to <60 beats per minute (bpm), change to normal or no change, and increase to >100 bpm. Participants with a missing Baseline value are assumed to have a normal Baseline value. Participants are counted twice if the participant heart rate value decreased to <60 bpm and increased to >100 bpm post-baseline. Only those participants (par.) with heart rate values for worst-case on-therapy are presented.

- Number of Participants With a Change From Baseline in Systolic and Diastolic Blood Pressure by Dose [Time Frame: From the start of the study drug until the final study visit (up to approximately 407 days)] [Designated as safety issue: No]

  Change from Baseline in systolic blood pressure (SBP) is categorized as: Grade 0 (<120 millimeters of mercury [mmHg]), Grade 1 (120-139 mmHg), Grade 2 (140-159 mmHg), and Grade 3/4 (>=160 mmHg). Change from Baseline in diastolic blood pressure (DBP) is categorized as: Grade 0 (<80 mmHg), Grade 1 (80-89 mmHg), Grade 2 (90-99 mmHg), and Grade 3/4 (>=100 mmHg). An increase is defined as an increase in the CTCAE grade relative to the Baseline grade. Participants with missing Baseline values are assumed to have a Baseline value of grade 0. Only those participants (par.) with blood pressure values for worst-case on-therapy are presented.
- Number of Participants With a Change From Baseline in Temperature by Dose [Time Frame: From the start of the study drug until the final study visit (up to approximately 407 days)] [Designated as safety issue: No]

  Change from Baseline in temperature is categorized as a decrease to <=35 degrees celsius (C), change to normal or no change, and increase to >=38 degrees C. Participants with a missing Baseline value are assumed to have a normal Baseline value. Participants (par.) are counted twice if the participant temperature value decreased to <=35 degrees C and increased to >=38 degrees C post-Baseline. Only those participants with temperature values for worst-case on-therapy are presented.
- Number of Participants With an Investigator-assessed Best Response (Achieving Complete Response [CR], Marrow CR, Partial Response [PR], Complete Response Without Platelet Recovery [CRp] or Morphologic Leukaemia-free State[MLFS]) by Cohort [Time Frame: From the start of the study drug until the final study visit (up to approximately 407 days)] [Designated as safety issue: No]

  Overall response rate (ORR=CR+CRp+Marrow CR+MLFS+PR) was calculated from the investigator's assessment of response recorded within the first eight weeks of treatment. CR includes complete remission. Complete remission is a state in which the participant must be free of all symptoms related to leukemia and have an absolute neutrophil count >=1 x 10^9/L, platelet count >=100 x 10^9/L, and normal marrow differential (<=5% blasts). PR includes partial remission. Partial remission is a state in which the participant has a CR with 6 to 25% abnormal cells in the marrow or 50% decrease in bone marrow blasts. CRp is as per CR but platelet count <100 x 10^9/L. MLFS is a state in which the participant has a normal marrow differential (<5% blasts), neutrophil, and platelet counts are not considered.

Secondary Outcome Measures:

- AUC(0-24), AUC(0-t), and AUC(0-tau) of GSK1120212 in Part 1 [Time Frame: Cycle 1 Day 1 and Cycle 1 Day 15] [Designated as safety issue: No]

  Area under the concentration-time (AUC) curve from time zero (pre-dose) to 24 hours (AUC[0-24]) for Cycle 1 Day 1 (C1D1), from time zero to the last time of a quantifiable concentration (AUC[0-t]) for C1D1 and Cylce 1 Day 15 (C1D15) and AUC curve over the dosing interval AUC[0-tau] for C1D15 were measured. Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 minutes [min] before study drug administration) and at 0.5 hour (h), 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).

- Cmin and Cmax of GSK1120212 in Part 1 [Time Frame: Cycle 1 Day 1 and Cycle 1 Day 15] [Designated as safety issue: No]

  Cmax is defined as the maximum observed concentration of GSK1120212 and was measured for C1D1 and C1D15. Cmin is defined as the minimal observed concentration of GSK1120212 and was measured for C1D15. Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 min before study drug administration) and at 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).
- t1/2 at C1D1 and t1/2 Effective (Eff.) at C1D15 of GSK1120212 in Part 1 [Time Frame: Cycle 1 Day 1 (t1/2) and Cycle 1 Day 15 (t1/2eff)] [Designated as safety issue: No]

  t1/2 is defined as terminal phase half-life, which is the time required for the amount of the drug in the body to decrease by half and was measured for C1D1. t1/2eff. is defined as the effective half-life and was measured for C1D15. Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 min before study drug administration) and at 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).
- Tmax of GSK1120212 in Part 1 [Time Frame: Cycle 1 Day 1 and Cycle 1 Day 15] [Designated as safety issue: No]

  Tmax is defined as the time to reach the observed maximum concentration and was measured for C1D1 and C1D15. Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 min before study drug administration) and at 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).
- Accumulation Ratio (AR) of GSK1120212 in Part 1 [Time Frame: Cycle 1 Day 1 and Cycle 1 Day 15] [Designated as safety issue: No]

  AR is the ratio of the Day 15 AUC0-tau (0 hour to last dose interval) and Day 1 AUC0-tau (AUCtau C1D15/AUCtau C1D1). Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 min before study drug administration) and at 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).
- Ctau of GSK1120212 in Part 2 [Time Frame: C1D15, C2D1, C3D1, C4D1, C5D1, C6D1, C7D1, C8D1, C9D1, C10D1, C11D1 and C12D1] [Designated as safety issue: No]

  Ctau is the pre-dose (trough) concentration at the end of the dosing interval and was measured for Cycle 1 Day 15 (C1D15), Cycle 2 Day 1(C2D1), Cylce 3 Day 1 (C3D1), Cycle 4 Day 1 (C4D1), Cycle 5 Day 1 (C5D1), Cycle 6 Day 1 (C6D1), Cycle 7 Day 1 (C7D1), Cycle 8 Day 1 (C8D1), Cycle 9 Day 1 (C9D1), Cycle 10 Day 1 (C10D1), Cycle 11 Day 1 (C11D1) and Cycle 12 Day 1 (C12D1). Blood samples for PK analysis were collected pre-dose (i.e., no later than 15 min prior to dosing).
- Overall Survival by Cohort [Time Frame: From the start of the study drug until the final study visit (up to approximately 407 days)] [Designated as safety issue: No]

  Overall survival is defined as the time from the start of study treatment (GSK1120212) until death due to any cause. For the analysis of overall survival, the last date of known contact was used for those participants who had not died at the time of analysis; such participants were considered censored.

Enrollment: 97
Study Start Date: May 2011
Study Completion Date: April 2013
Primary Completion Date: April 2013

Arms	Assigned Interventions
Experimental: Phase I The proposed treatment schedule of GSK1120212 is continuous daily dosing. At the initiation of dosing, a loading dose will be given prior to starting continuous dosing (maintenance dose). Alterations to the dose and schedule will be based on emerging PK, PD, and tolerability data. The goal will be to define a regimen that is well tolerated and provides adequate PK and PD. This will be the recommended Phase II schedule.	Drug: GSK1120212 Starting dose based on GSK protocol MEK111054 and then dose escalation based on Dose Limiting Toxicities per protocol.
Experimental: Phase II A dose determined by Phase I to further evaulate the safety profile, PK, PD, and clinical activity of GSK1120212.	Drug: GSK1120212 Dose will be maximum tolerated dose based on Phase I results.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both

Inclusion Criteria:

- Phase I
- Written informed consent provided.
- 18 years old or older.
- Subjects must have relapsed/refractory leukemias for which no standard therapies are anticipated to result in a durable remission. Subjects with poor-risk myelodysplasia (MDS) and chronic melomonocytic leukemia (CMML) are also eligible. Relapsed/refractory leukemias include acute non-lymphocytic leukemia (AML), acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), or chronic myelogenous leukemia (CML) in blast crisis. Subjects with agnogenic myeloid metaplasia (AMM) are also eligible. Subjects with a haematological malignancy associated with human immunodeficiency virus

(HIV) infection or solid organ transplant are NOT eligible.
- Subjects who have previously received an autologous stem cell transplant are allowed if a minimum of three months has elapsed from the time of transplant (T0) and the subject has recovered from transplant-associated toxicities prior to the first dose of GSK1120212.
- Subjects with a history of allogeneic stem cell transplant are eligible for study participation provided the following eligibility criteria are met: transplant was greater than 100 days prior to study enrolment, subject has not taken immunosuppressive medications (per protocol) for at least 1 month, no signs or symptoms of graft versus host disease other than Grade 1 skin involvement, no active infection, subject meets the remainder of the eligibility criteria outlined in this protocol.
- Eastern Cooperative Oncology Group (ECOG) performance status of less than or equal to 2.
- Life expectancy of at least four weeks.
- Able to swallow and retain oral medication.
- Male subjects must agree to use one of the contraception methods listed in the protocol.
- Female subjects must be of non-childbearing potential as listed in the protocol or using a contraception method listed in the protocol.
- Calcium Phosphate Product less than or equal to 4.0 mmol (squared)/L (squared) or 50mg (squared)/dL (squared).
- Subjects must have adequate organ function as specified in the protocol.
- Phase II
- Confirmed diagnosis of one of the following: Relapsed or refractory acute myeloid leukemia (AML), Secondary AML including AML arising from antecedent hematologic diseases (e.g., myelodysplastic syndrome, myeloproliferative disorders, or therapyrelated AML), CMML, or MDS.

Cohorts 1: RAS Positive AML/MDS Cohort 2: Wild Type AML/MDS/CMML Cohort 3: RAS Positive CMML

Exclusion Criteria:

- Phase I
- Currently receiving cancer therapy as specified in the protocol.
- Received corticosteroids or imatinib within 24h of GSK1120212 administration.
- Received gemtuzumab ozogamicin (myelotarg) within two weeks of GSK1120212 adminstration.
- Received an investigational anti-cancer drug within four weeks or five half-lives, whichever is shorter of GSK1120212 administration, as specified in the protocol.
- Received major surgery, radiotherapy, or immunotherapy within four weeks of GSK1120212 administration.
- Received chemotherapy regimens with delayed toxicity within the last four weeks (six weeks for prior nitrosourea or mitomycin C). Received chemotherapy regimens given continuously or on a weekly basis with limited potential for delayed toxicity within the last two weeks.
- Received a MEK inhibitor.
- Current use of a prohibited medication per protocol.
- Current use of warfarin. Low molecular weight heparin and prophylactic low-dose warfarin are permitted per protocol.
- Presence of active gastrointestinal disease or other condition that will interfere significantly with the absorption, distribution, metabolism, or excretion of drugs.
- History of RVO.

- Visible retinal pathology as assessed by ophthalmologic exam that is considered a risk factor for retinal vein thrombosis.
- Intraocular pressure greater than 21mm Hg as measured by tonography.
- Psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol.
- Condition that in the investigator's opinion would jeopardize compliance with the protocol.
- Symptomatic or untreated central nervous system involvement by the hematologic malignancy, including primary CNS lymphoma. Subjects who were previously treated for CNS involvement, and are asymptomatic without anti-epileptic medications for at least two months are eligible.
- Evidence of severe or uncontrolled systemic diseases (e.g., unstable or uncompensated respiratory, hepatic, renal, or cardiac disease).
- Unresolved toxicity greater than Grade 1 from previous anti-cancer therapy except alopecia (if applicable) unless agreed to by a GSK Medical Monitor and the investigator.
- QTc interval greater than 480 msecs.
- History of acute coronary syndromes (including unstable angina), coronary angioplasty or stenting within the past 24 weeks.
- Class II, III, or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system.
- Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to the study drug, dimethyl sulfoxide (DMSO), or excipients (See Section 3.10). (To date there are no known FDA approved drugs chemically related to GSK1120212).
- Pregnant or lactating female.
- Unwillingness or inability to follow the procedures outlined in the protocol.

Contacts and Locations

Locations

United States, Alabama

GSK Investigational Site

Birmingham, Alabama, United States, 35249

United States, California

GSK Investigational Site

Duarte, California, United States, 91010

GSK Investigational Site

Los Angeles, California, United States, 90095

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San Francisco, California, United States, 94143

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Chicago, Illinois, United States, 60611

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Investigators

Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Responsible Party:	GlaxoSmithKline
Study ID Numbers:	111759
Health Authority:	United States: Food and Drug Administration

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Study Results

Participant Flow

Pre-Assignment Details

This is a Phase I/II study. Phase I is a dose escalation phase in participants with relapsed or refractory leukaemias to identify the recommended dose of GSK1120212 for Phase II. Phase II further evaluates the safety and efficacy of the recommended dose.

Reporting Groups

	Description
GSK1120212 < 2 mg OD	Participants with relapsed or refractory leukemias received either GSK1120212 3 milligrams (mg) loading dose (LD) followed by 1 mg once daily (OD) (3/1 mg LD/OD), or 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.
Cohort 1: AML/MDS With RAS Mutation	Participants with relapsed or refractory acute myeloid leukemia (AML) or myelodysplasia (MDS) with rat sarcoma (RAS) mutation received GSK1120212 2 mg OD as a continuous dose.
Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Participants with relapsed or refractory AML or MDS or chronic myelomonocytic leukemia (CMML) with RAS wild type (wt) or unknown mutation received GSK1120212 2 mg OD as a continuous dose.
Cohort 3: CMML With RAS Mutation	Participants with relapsed or refractory CMML with RAS mutation received GSK1120212 2 mg OD as a continuous dose.

Phase 1 (Dose Escalation)

	GSK1120212 < 2 mg OD	GSK1120212 2 mg OD	Cohort 1: AML/MDS With RAS Mutation	Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Cohort 3: CMML With RAS Mutation
Started	5	9	0	0	0
Completed	0	0	0	0	0
Not Completed	5	9	0	0	0
Adverse Event	3	3	0	0	0
Lack of Efficacy	2	4	0	0	0
Withdrawal by Subject	0	2	0	0	0

Phase 2

	GSK1120212 < 2 mg OD	GSK1120212 2 mg OD	Cohort 1: AML/MDS With RAS Mutation	Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Cohort 3: CMML With RAS Mutation
Started	0	0	50	22	11
Completed	0	0	0	0	0
Not Completed	0	0	50	22	11
Adverse Event	0	0	14	2	3
Lack of Efficacy	0	0	29	14	5
Lost to Follow-up	0	0	0	1	0
Physician Decision	0	0	3	3	2
Withdrawal by Subject	0	0	4	2	1

Baseline Characteristics

Reporting Groups

	Description
GSK1120212 <2 mg OD	Participants with relapsed or refractory leukemias received either GSK1120212 3 milligrams (mg) loading dose (LD) followed by 1 mg once daily (OD) (3/1 mg LD/OD), or 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.
Cohort 1: AML/MDS With RAS Mutation	Participants with relapsed or refractory AML or MDS with RAS mutation received GSK1120212 2 mg OD as a continuous dose.
Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Participants with relapsed or refractory AML or MDS or CMML with RAS wt or unknown mutation received GSK1120212 2 mg OD as a continuous dose.
Cohort 3: CMML With RAS Mutation	Participants with relapsed or refractory CMML with RAS mutation received GSK1120212 2 mg OD as a continuous dose.

Baseline Measures

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD	Cohort 1: AML/MDS With RAS Mutation	Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Cohort 3: CMML With RAS Mutation	Total
Number of Participants	5	9	50	22	11	97
Age, Continuous [units: Years] Mean (Standard Deviation)	70.4 (15.71)	60.2 (15.86)	65.6 (10.71)	59.6 (18.89)	67.7 (6.87)	64.2 (13.69)
Gender, Male/Female						

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD	Cohort 1: AML/MDS With RAS Mutation	Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Cohort 3: CMML With RAS Mutation	Total
[units: Participants]						
Female	4	2	22	7	6	41
Male	1	7	28	15	5	56
Race/Ethnicity, Customized [units: Participants]						
African American/African Heritage	1	0	5	2	0	8
White - White/Caucasian/European Heritage	4	9	40	18	9	80
Asian - Central/South Asian Heritage	0	0	0	1	1	2
Asian - Japanese Heritage	0	0	1	0	0	1
Asian - South East Asian Heritage	0	0	0	1	0	1
Missing	0	0	4	0	1	5

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants With Any Adverse Event (AE) or Serious Adverse Event (SAE) by Dose
Measure Description	An AE is any untoward medical occurrence in a participant (par.) or

	clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, or is an event of possible drug-induced liver injury. Refer to the general Adverse AE/SAE module for a complete list of AEs and SAEs.
Time Frame	From the start of the study drug until the final study visit (up to approximately 407 days)
Safety Issue?	No

Analysis Population Description

All Treated Population: all participants who received at least one dose of study medication. Safety data was evaluated based on this population. One Phase 2 par. was incorrectly dosed (received <2 mg [0.5 mg]); thus, 6 par. receiving GSK1120212 <2 mg OD were analyzed.

Reporting Groups

	Description
GSK1120212 <2 mg OD	Participants with relapsed or refractory leukemias received either GSK1120212 3 mg LD followed by 1 mg OD (3/1 mg LD/OD), or 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	6	91
Number of Participants With Any Adverse		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Event (AE) or Serious Adverse Event (SAE) by Dose [units: Participants]		
Any AE	6	91
Any SAE	2	64

2. Primary Outcome Measure:

Measure Title	Number of Participants With a Change From Baseline Grade to Grade 3 and 4 for the Indicated Hematology Parameters by Dose
Measure Description	Hematology and clinical chemistry data were summarized according to National Cancer Institutes (NCI) Common Terminology Criteria for Adverse Events (CTCAE) grade, version 3.0. Grade 1, Mild; Grade 2, Moderate; Grade 3, Severe; Grade 4, Life-threatening or disabling; Grade 5, Death. Data are presented for only those parameters for which an increase to Grade 3 or Grade 4 occurred. Hematology tests where the toxicity grade is defined by NCI-CTCAE includes hemoglobin, international normalized ratio (INR), lymphocytes, total neutrophils, platelet count, and partial thromboplastin time (PTT). Participants with missing baseline grades were assumed to have a baseline grade of 0. Only those participants (par.) with laboratory values for worst-case on-therapy (defined as the worst shift that occurred at any time during the treatment period) are presented.
Time Frame	From the start of the study drug until the final study visit (up to approximately 407 days)
Safety Issue?	No

Analysis Population Description

All Treated Population (ATP). Only those par. available at the specified time points were analyzed. Different par. may have been analyzed for different parameters; the overall number analyzed reflects everyone in the ATP. One Phase 2 par. was incorrectly dosed (received <2 mg [0.5 mg]); thus, 6 par. receiving GSK1120212 <2 mg OD were analyzed.

Reporting Groups

	Description
GSK1120212 <2 mg OD	Participants with relapsed or refractory leukemias received either GSK1120212 3 mg LD followed by 1 mg OD (3/1 mg LD/OD), or 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	6	91
Number of Participants With a Change From Baseline Grade to Grade 3 and 4 for the Indicated Hematology Parameters by Dose [units: Participants]		
Hemoglobin (Low), Grade 3, n=6, 91	3	28
Hemoglobin (Low), Grade 4, n=6, 91	0	7
INR (High), Grade 3, n=6, 75	0	0
INR (High), Grade 4, n=6, 75	0	0
Lymphocytes (Low), Grade 3, n=6, 90	0	12
Lymphocytes (Low), Grade 4, n=6, 90	0	7

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Total Neutrophils (Low), Grade 3, n=6, 89	1	4
Total Neutrophils (Low), Grade 4, n=6, 89	1	21
Platelet count (Low), Grade 3, n=6, 91	0	5
Platelet count (Low), Grade 4, n=6, 91	1	28
PTT (High), Grade 3, n=5, 75	0	1
PTT (High), Grade 4, n=5, 75	0	0
White Blood Cell count (Low), Grade 3, n=6, 91	1	13
White Blood Cell count (Low), Grade 4, n=6, 91	0	15

3. Primary Outcome Measure:

Measure Title	Number of Participants With a Change From Baseline Grade to Grade 3 and 4 for the Indicated Clinical Chemistry Parameters by Dose
Measure Description	Hematology and clinical chemistry data were summarized according to NCI-CTCAE grade, version 3.0. Grade 1, Mild; Grade 2, Moderate; Grade 3, Severe; Grade 4, Life-threatening or disabling; Grade 5, Death. Data are presented for only those parameters for which an increase to Grade 3 or Grade 4 occurred. Clinical chemistry tests where the toxicity grade is defined by NCI-CTCAE includes albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase (AST), total bilirubin, calcium, creatinine, glucose,

	bicarbonate, potassium, magnesium, sodium, and phosphorus. Participants with missing Baseline grades were assumed to have a Baseline grade of 0. Only those participants (par.) with laboratory values for worst-case on-therapy are presented.
Time Frame	From the start of the study drug until the final study visit (up to approximately 407 days)
Safety Issue?	No

Analysis Population Description

All Treated Population (ATP). Only those par. available at the specified time points were analyzed. Different par. may have been analyzed for different parameters; the overall number analyzed reflects everyone in the ATP. One Phase 2 par. was incorrectly dosed (received <2 mg [0.5 mg]); thus, 6 par. receiving GSK1120212 <2 mg OD were analyzed.

Reporting Groups

	Description
GSK1120212 <2 mg OD	Participants with relapsed or refractory leukemias received either GSK1120212 3 mg LD followed by 1 mg OD (3/1 mg LD/OD), or 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	6	91
Number of Participants With a Change From Baseline Grade to Grade 3 and 4 for the Indicated Clinical Chemistry Parameters by Dose		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
[units: Participants]		
Albumin (Low), Grade 3, n=6, 90	0	9
Albumin (Low), Grade 4, n=6, 90	0	0
Alkaline Phosphatase (High), Grade 3, n=6, 89	0	2
Alkaline Phosphatase (High), Grade 4, n=6, 89	0	0
Alanine Amino Transferase (High), Grade 3, n=6, 89	0	6
Alanine Amino Transferase (High), Grade 4, n=6, 89	0	1
AST (High), Grade 3, n=6, 86	0	5
AST (High), Grade 4, n=6, 86	0	2
Total Bilirubin (High), Grade 3, n=6, 89	0	3
Total Bilirubin (High), Grade 4, n=6, 89	0	0
Calcium (hypercalcemia), Grade 3, n=6, 91	0	0
Calcium (hypercalcemia), Grade 4, n=6, 91	0	0
Calcium (hypocalcemia), Grade 3, n=6, 91	0	8
Calcium (hypocalcemia), Grade 4, n=6, 91	0	2
Creatinine (High), Grade 3, n=6, 91	0	0

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Creatinine (High), Grade 4, n=6, 91	0	0
Glucose (hyperglycemia), Grade 3, n=6, 91	0	7
Glucose (hyperglycemia), Grade 4, n=6, 91	0	0
Glucose (hypoglycemia), Grade 3, n=6, 91	0	0
Glucose (hypoglycemia), Grade 4, n=6, 91	0	0
Bicarbonate (Low), Grade 3, n=5, 82	0	0
Bicarbonate (Low), Grade 4, n=5, 82	0	0
Potassium (hyperkalemia), Grade 3, n=6, 91	0	1
Potassium (hyperkalemia), Grade 4, n=6, 91	0	0
Potassium (hypokalemia), Grade 3, n=6, 91	0	7
Potassium (hypokalemia), Grade 4, n=6, 91	0	0
Magnesium (hypermagnesemia), Grade 3, n=6, 88	0	3
Magnesium (hypermagnesemia), Grade 4, n=6, 88	0	0
Magnesium (hypomagnesemia), Grade 3, n=6, 88	0	0

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Magnesium (hypomagnesemia), Grade 4, n=6, 88	0	0
Sodium (hypernatremia), Grade 3, n=6, 91	0	0
Sodium (hypernatremia), Grade 4, n=6, 91	0	0
Sodium (hyponatremia), Grade 3, n=6, 91	2	9
Sodium (hyponatremia), Grade 4, n=6, 91	0	0
Phosphorus, Grade 3, n=6, 88	0	5
Phosphorus, Grade 4, n=6, 88	0	1

4. Primary Outcome Measure:

Measure Title	Number of Participants With a Change From Baseline in Heart Rate by Dose
Measure Description	Change from Baseline in heart rate is categorized as decrease to <60 beats per minute (bpm), change to normal or no change, and increase to >100 bpm. Participants with a missing Baseline value are assumed to have a normal Baseline value. Participants are counted twice if the participant heart rate value decreased to <60 bpm and increased to >100 bpm post-baseline. Only those participants (par.) with heart rate values for worst-case on-therapy are presented.
Time Frame	From the start of the study drug until the final study visit (up to approximately 407 days)

Safety Issue?	No

Analysis Population Description

All Treated Population (ATP). Only those par. available at the specified time points were analyzed. Different par. may have been analyzed for different parameters; the overall number analyzed reflects everyone in the ATP. One Phase 2 par. was incorrectly dosed (received <2 mg [0.5 mg]); thus, 6 par. receiving GSK1120212 <2 mg OD were analyzed.

Reporting Groups

	Description
GSK1120212 <2 mg OD	Participants with relapsed or refractory leukemias received either GSK1120212 3 mg LD followed by 1 mg OD (3/1 mg LD/OD), or 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	6	91
Number of Participants With a Change From Baseline in Heart Rate by Dose [units: Participants]		
Decrease to <60, n=6, 90	0	10
No Change, n=6, 90	4	67
Increase to >100, n=6, 90	2	19

5. Primary Outcome Measure:

Measure Title	Number of Participants With a Change From Baseline in Systolic and Diastolic Blood Pressure by Dose
Measure Description	Change from Baseline in systolic blood pressure (SBP) is categorized as: Grade 0 (<120 millimeters of mercury [mmHg]), Grade 1 (120-139 mmHg), Grade 2 (140-159 mmHg), and Grade 3/4 (>=160 mmHg). Change from Baseline in diastolic blood pressure (DBP) is categorized as: Grade 0 (<80 mmHg), Grade 1 (80-89 mmHg), Grade 2 (90-99 mmHg), and Grade 3/4 (>=100 mmHg). An increase is defined as an increase in the CTCAE grade relative to the Baseline grade. Participants with missing Baseline values are assumed to have a Baseline value of grade 0. Only those participants (par.) with blood pressure values for worst-case on-therapy are presented.
Time Frame	From the start of the study drug until the final study visit (up to approximately 407 days)
Safety Issue?	No

Analysis Population Description

All Treated Population (ATP). Only those par. available at the specified time points were analyzed. Different par. may have been analyzed for different parameters; the overall number analyzed reflects everyone in the ATP. One Phase 2 par. was incorrectly dosed (received <2 mg [0.5 mg]); thus, 6 par. receiving GSK1120212 <2 mg OD were analyzed.

Reporting Groups

	Description
GSK1120212 <2 mg OD	Participants with relapsed or refractory leukemias received either GSK1120212 3 mg LD followed by 1 mg OD (3/1 mg LD/OD), or 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	6	91
Number of Participants With a Change From Baseline in Systolic and Diastolic Blood Pressure by Dose [units: Participants]		
DBP, Increase to Grade 1, n=6, 90	1	23
DBP, Increase to Grade 2, n=6, 90	1	13
DBP, Increase to Grade 3/4, n=6, 90	0	4
SBP, Increase to Grade 1, n=6, 90	0	16
SBP, Increase to Grade 2, n=6, 90	2	19
SBP, Increase to Grade 3/4, n=6, 90	1	13

6. Primary Outcome Measure:

Measure Title	Number of Participants With a Change From Baseline in Temperature by Dose
Measure Description	Change from Baseline in temperature is categorized as a decrease to <=35 degrees celsius (C), change to normal or no change, and increase to >=38 degrees C. Participants with a missing Baseline value are assumed to have a normal Baseline value. Participants (par.) are counted twice if the participant temperature value decreased to <=35 degrees C and increased to >=38 degrees C post-Baseline. Only those participants with temperature values for worst-case on-therapy are presented.
Time Frame	From the start of the study drug until the final study visit (up to approximately 407 days)

Safety Issue?	No

Analysis Population Description

All Treated Population (ATP). Only those par. available at the specified time points were analyzed. Different par. may have been analyzed for different parameters; the overall number analyzed reflects everyone in the ATP. One Phase 2 par. was incorrectly dosed (received <2 mg [0.5 mg]); thus, 6 par. receiving GSK1120212 <2 mg OD were analyzed.

Reporting Groups

	Description
GSK1120212 <2 mg OD	Participants with relapsed or refractory leukemias received either GSK1120212 3 mg LD followed by 1 mg OD (3/1 mg LD/OD), or 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	6	91
Number of Participants With a Change From Baseline in Temperature by Dose [units: Participants]		
Decrease to <=35, n=6, 90	0	4
No Change, n=6, 90	4	76
Increase to >=38, n=6, 90	2	12

7. Primary Outcome Measure:

Measure Title	Number of Participants With an Investigator-assessed Best Response (Achieving Complete Response [CR], Marrow CR, Partial Response [PR], Complete Response Without Platelet Recovery [CRp] or Morphologic Leukaemia-free State[MLFS]) by Cohort
Measure Description	Overall response rate (ORR=CR+CRp+Marrow CR+MLFS+PR) was calculated from the investigator's assessment of response recorded within the first eight weeks of treatment. CR includes complete remission. Complete remission is a state in which the participant must be free of all symptoms related to leukemia and have an absolute neutrophil count >=1 x 10^9/L, platelet count >=100 x 10^9/L, and normal marrow differential (<=5% blasts). PR includes partial remission. Partial remission is a state in which the participant has a CR with 6 to 25% abnormal cells in the marrow or 50% decrease in bone marrow blasts. CRp is as per CR but platelet count <100 x 10^9/L. MLFS is a state in which the participant has a normal marrow differential (<5% blasts), neutrophil, and platelet counts are not considered.
Time Frame	From the start of the study drug until the final study visit (up to approximately 407 days)
Safety Issue?	No

Analysis Population Description

Efficacy Population: all participants included in the All Treated Population who had received at least one dose of 2 mg of study drug in Phase 2. The number of participants for the Cohort 2: AML/MDS/CMML with RAS wt/Unknown treatment group is equal to the 8 participants from Phase 1 plus the 22 participants from Phase 2 (total of 30).

Reporting Groups

	Description
Cohort 1: AML/MDS With RAS Mutation	Participants with relapsed or refractory AML or MDS with RAS mutation received GSK1120212 2 mg OD as a continuous dose.

	Description
Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Participants with relapsed or refractory AML or MDS or CMML with RAS wt or unknown mutation received GSK1120212 2 mg OD as a continuous dose.
Cohort 3: CMML With RAS Mutation	Participants with relapsed or refractory CMML with RAS mutation received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	Cohort 1: AML/MDS With RAS Mutation	Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Cohort 3: CMML With RAS Mutation
Number of Participants Analyzed	50	30	11
Number of Participants With an Investigator-assessed Best Response (Achieving Complete Response [CR], Marrow CR, Partial Response [PR], Complete Response Without Platelet Recovery [CRp] or Morphologic Leukaemia-free State[MLFS]) by Cohort [units: Participants]			
CR	4	0	1
CRp	1	0	1
Marrow CR	1	0	1
MLFS	3	0	0
PR	1	1	0
ORR	10	1	3

8. Secondary Outcome Measure:

Measure Title	AUC(0-24), AUC(0-t), and AUC(0-tau) of GSK1120212 in Part 1
Measure Description	Area under the concentration-time (AUC) curve from time zero (pre-dose) to 24 hours (AUC[0-24]) for Cycle 1 Day 1 (C1D1), from time zero to the last time of a quantifiable concentration (AUC[0-t]) for C1D1 and Cylce 1 Day 15 (C1D15) and AUC curve over the dosing interval AUC[0-tau] for C1D15 were measured. Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 minutes [min] before study drug administration) and at 0.5 hour (h), 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).
Time Frame	Cycle 1 Day 1 and Cycle 1 Day 15
Safety Issue?	No

Analysis Population Description

Pharmacokinetic Population: all participants included in the All Treated Population for whom a PK sample was obtained and analyzed. Only participants with data available at the indicated time points were analyzed.

Reporting Groups

	Description
GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	Participants with relapsed or refractory leukemias received either GSK1120212 0.5 mg OD or 3/1 mg LD/OD as a continuous dose.
GSK1120212 1 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	GSK1120212 1 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	3	2	9
AUC(0-24), AUC(0-t), and AUC(0-tau) of GSK1120212 in Part 1 [units: nanograms*hour/milliliter] Geometric Mean (Geometric Coefficient of Variation)			
C1D1, AUC(0-24), n=3, 2, 9	77.6 (25.1%)	29.4 (5.2%)	28.0 (51.0%)
C1D1, AUC(0-t), n=3, 2, 9	77.6 (25.1%)	29.4 (5.2%)	28.0 (51.0%)
C1D15, AUC(0-t), n=2, 2, 8	172 (18.4%)	155 (61.9%)	298 (58.8%)
C1D15, AUC(0-tau), n=2, 2, 8	170 (17.2%)	241 (5.6%)	330 (34.6%)

9. Secondary Outcome Measure:

Measure Title	Cmin and Cmax of GSK1120212 in Part 1
Measure Description	Cmax is defined as the maximum observed concentration of GSK1120212 and was measured for C1D1 and C1D15. Cmin is defined as the minimal observed concentration of GSK1120212 and was measured for C1D15. Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 min before study drug administration) and at 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).
Time Frame	Cycle 1 Day 1 and Cycle 1 Day 15
Safety Issue?	No

Analysis Population Description

Pharmacokinetic Population. Only participants with data available at the indicated time points were analyzed.

Reporting Groups

	Description
GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	Participants with relapsed or refractory leukemias received either GSK1120212 0.5 mg OD or 3/1 mg LD/OD as a continuous dose.
GSK1120212 1 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	GSK1120212 1 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	3	2	9
Cmin and Cmax of GSK1120212 in Part 1 [units: nanograms per milliliter (ng/mL)] Geometric Mean (Geometric Coefficient of Variation)			
C1D1, Cmax, n=3, 2, 9	7.67 (27.6%)	3.69 (35.5%)	3.27 (93.2%)
C1D15, Cmax , n=2, 2, 8	12.3 (19.4%)	15.1 (15.6%)	18.7 (36.1%)
C1D15, Cmin, n=2, 2, 8	4.79 (6.6%)	8.50 (19.4%)	10.8 (36.8%)

10. Secondary Outcome Measure:

Measure Title	t1/2 at C1D1 and t1/2 Effective (Eff.) at C1D15 of

	GSK1120212 in Part 1
Measure Description	t1/2 is defined as terminal phase half-life, which is the time required for the amount of the drug in the body to decrease by half and was measured for C1D1. t1/2eff. is defined as the effective half-life and was measured for C1D15. Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 min before study drug administration) and at 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).
Time Frame	Cycle 1 Day 1 (t1/2) and Cycle 1 Day 15 (t1/2eff)
Safety Issue?	No

Analysis Population Description

Pharmacokinetic Population. Only participants with data available at the indicated time points were analyzed.

Reporting Groups

	Description
GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	Participants with relapsed or refractory leukemias received either GSK1120212 0.5 mg OD or 3/1 mg LD/OD as a continuous dose.
GSK1120212 1 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	GSK1120212 1 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	3	2	9
t1/2 at C1D1 and t1/2 Effective (Eff.) at C1D15 of GSK1120212 in Part 1 [units: Hours] Geometric Mean (Geometric Coefficient of Variation)			
C1D1, t1/2, n=3, 1, 8	33.5 (43.7%)	25.0 (NA%) [1]	37.0 (76.2%)
C1D15, t1/2 eff., n=2, 2, 8	96.41 (18.1%)	128 (11.6%)	174 (80.3%)

[1] There is only one participant in this cohort so dispersion can not be calculated.

11. Secondary Outcome Measure:

Measure Title	Tmax of GSK1120212 in Part 1
Measure Description	Tmax is defined as the time to reach the observed maximum concentration and was measured for C1D1 and C1D15. Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 min before study drug administration) and at 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).
Time Frame	Cycle 1 Day 1 and Cycle 1 Day 15
Safety Issue?	No

Analysis Population Description

Pharmacokinetic Population. Only participants with data available at the indicated time points were analyzed.

Reporting Groups

	Description
GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	Participants with relapsed or refractory leukemias received either GSK1120212 0.5 mg OD or 3/1 mg LD/OD as a continuous dose.
GSK1120212 1 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	GSK1120212 1 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	3	2	9
Tmax of GSK1120212 in Part 1 [units: Hours] Median (Full Range)			
C1D1, tmax, n=3, 2, 9	2.0 (1.00 to 3.00)	1.25 (1.00 to 1.50)	3.0 (0.50 to 5.00)
C1D15, tmax, n=2, 2, 8	1.75 (1.50 to 2.00)	2.25 (1.00 to 3.50)	3.0 (1.00 to 24.00)

12. Secondary Outcome Measure:

Measure Title	Accumulation Ratio (AR) of GSK1120212 in Part 1
Measure Description	AR is the ratio of the Day 15 AUC0-tau (0 hour to last dose interval)

	and Day 1 AUC0-tau (AUCtau C1D15/AUCtau C1D1). Blood samples for PK analysis were taken on Day 1 and Day 15 (within 30 min before study drug administration) and at 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, and 24 h post-dose. All other PK sampling were done pre-dose (i.e., within 30 min before study drug administration).
Time Frame	Cycle 1 Day 1 and Cycle 1 Day 15
Safety Issue?	No

Analysis Population Description

Pharmacokinetic Population. Only participants with data available at the indicated time points were analyzed.

Reporting Groups

	Description
GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	Participants with relapsed or refractory leukemias received either GSK1120212 0.5 mg OD or 3/1 mg LD/OD as a continuous dose.
GSK1120212 1 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	GSK1120212 1 mg OD	GSK1120212 2 mg OD
Number of Participants Analyzed	2	2	8
Accumulation Ratio (AR) of GSK1120212 in Part 1	6.32 (16.5%)	8.19 (10.8%)	11.1 (76.5%)

	GSK1120212 0.5 mg OD/ 3/1 mg LD/OD	GSK1120212 1 mg OD	GSK1120212 2 mg OD
[units: Ratio] Geometric Mean (Geometric Coefficient of Variation)			

13. Secondary Outcome Measure:

Measure Title	Ctau of GSK1120212 in Part 2
Measure Description	Ctau is the pre-dose (trough) concentration at the end of the dosing interval and was measured for Cycle 1 Day 15 (C1D15), Cycle 2 Day 1(C2D1), Cylce 3 Day 1 (C3D1), Cycle 4 Day 1 (C4D1), Cycle 5 Day 1 (C5D1), Cycle 6 Day 1 (C6D1), Cycle 7 Day 1 (C7D1), Cycle 8 Day 1 (C8D1), Cycle 9 Day 1 (C9D1), Cycle 10 Day 1 (C10D1), Cycle 11 Day 1 (C11D1) and Cycle 12 Day 1 (C12D1). Blood samples for PK analysis were collected pre-dose (i.e., no later than 15 min prior to dosing).
Time Frame	C1D15, C2D1, C3D1, C4D1, C5D1, C6D1, C7D1, C8D1, C9D1, C10D1, C11D1 and C12D1
Safety Issue?	No

Analysis Population Description

Pharmacokinetic Population. Only participants with data available at the indicated time points were analyzed.

Reporting Groups

	Description
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	GSK1120212 2 mg OD
Number of Participants Analyzed	75
Ctau of GSK1120212 in Part 2 [units: nanograms per milliliter (ng/mL)] Geometric Mean (Geometric Coefficient of Variation)	
C1D15, n=72	10.8 (63.8%)
C2D1, n=57	9.34 (78.9%)
C3D1, n=38	10.0 (64.9%)
C4D1, n=21	9.17 (99.9%)
C5D1, n=10	12.05 (37.4%)
C6D1, n=6	9.73 (44.8%)
C7D1, n=6	8.94 (55.0%)
C8D1, n=5	6.01 (222.3%)
C9D1, n=3	11.3 (30.7%)
C10D1, n=2	5.01 (73.9%)
C11D1, n=1	2.01 (NA%) [1]
C12D1, n=1	0.644 (NA%) [2]

[1] There is only one participant in this cohort so dispersion can not be calculated.

[2] There is only one participant in this cohort so dispersion can not be calculated.

14. Secondary Outcome Measure:

Measure Title	Overall Survival by Cohort
Measure Description	Overall survival is defined as the time from the start of study treatment (GSK1120212) until death due to any cause. For the analysis of overall survival, the last date of known contact was used for those participants who had not died at the time of analysis; such participants were considered censored.
Time Frame	From the start of the study drug until the final study visit (up to approximately 407 days)
Safety Issue?	No

Analysis Population Description

Efficacy Population. The number of participants for the Cohort 2: AML/MDS/CMML with RAS wt/Unknown treatment group is equal to the 8 participants from Phase 1 plus the 22 participants from Phase 2 (total of 30).

Reporting Groups

	Description
Cohort 1: AML/MDS With RAS Mutation	Participants with relapsed or refractory AML or MDS with RAS mutation received GSK1120212 2 mg OD as a continuous dose.
Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Participants with relapsed or refractory AML or MDS or CMML with RAS wt or unknown mutation received GSK1120212 2 mg OD as a continuous dose.
Cohort 3: CMML With RAS Mutation	Participants with relapsed or refractory CMML with RAS mutation received GSK1120212 2 mg OD as a continuous dose.

Measured Values

	Cohort 1: AML/MDS With RAS Mutation	Cohort 2: AML/MDS/CMML With RAS wt/Unknown	Cohort 3: CMML With RAS Mutation
Number of Participants Analyzed	50	30	11
Overall Survival by Cohort [units: Months] Median (90% Confidence Interval)	4.9 (4.0 to 5.7)	3.0 (1.8 to 7.4)	14.5 (8.6 to NA) [1]

[1] Due to the high censoring rate, the upper bound of the 95% CI cannot be calculated.

Reported Adverse Events

Reporting Groups

	Description
GSK1120212 <2 mg OD	Participants with relapsed or refractory leukemias received either GSK1120212 3 mg LD followed by 1 mg OD (3/1 mg LD/OD), or 1 mg OD as a continuous dose.
GSK1120212 2 mg OD	Participants with relapsed or refractory leukemias received GSK1120212 2 mg OD as a continuous dose.

Time Frame

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study drug until the final study visit (up to approximately 407 days).

Additional Description

SAEs and non-serious AEs were collected in members of the All treated Population, comprised of all participants (par.) who received at least one dose of study medication. One Phase 2 par. was incorrectly dosed (received <2 mg [0.5 mg]); thus, 6 par. receiving GSK1120212 <2 mg OD were analyzed. .

Serious Adverse Events

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Total # participants affected/at risk	2/6 (33.33%)	64/91 (70.33%)
Blood and lymphatic system disorders		
Anaemia † [A]		
# participants affected/at risk	0/6 (0%)	4/91 (4.4%)
# events		
Disseminated intravascular coagulation † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Febrile bone marrow aplasia † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Febrile neutropenia † [A]		
# participants affected/at risk	0/6 (0%)	15/91 (16.48%)
# events		
Leukocytosis † [A]		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# participants affected/at risk	0/6 (0%)	2/91 (2.2%)
# events		
Neutropenia † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Pancytopenia † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Cardiac disorders		
Acute myocardial infarction † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Atrial fibrillation † [A]		
# participants affected/at risk	0/6 (0%)	3/91 (3.3%)
# events		
Atrioventricular block † [A]		
# participants affected/at	0/6 (0%)	1/91 (1.1%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
risk		
# events		
Cardiac arrest † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Cardio-respiratory arrest † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Left ventricular dysfunction † [A]		
# participants affected/at risk	0/6 (0%)	2/91 (2.2%)
# events		
Left ventricular failure † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Mitral valve incompetence † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Myocardial infarction † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Gastrointestinal disorders		
Diarrhoea † [A]		
# participants affected/at risk	0/6 (0%)	3/91 (3.3%)
# events		
Gastrointestinal haemorrhage † [A]		
# participants affected/at risk	0/6 (0%)	4/91 (4.4%)
# events		
Ileus paralytic † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Nausea † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Oesophagitis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Stomatitis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Vomiting † [A]		
# participants affected/at risk	0/6 (0%)	3/91 (3.3%)
# events		
General disorders		
Asthenia † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Mucosal inflammation † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Pyrexia † [A]		
# participants affected/at risk	0/6 (0%)	3/91 (3.3%)
# events		
Immune system disorders		
Graft versus host disease in intestine † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Infections and infestations		
Bacteraemia † [A]		
# participants affected/at risk	0/6 (0%)	4/91 (4.4%)
# events		
Bacterial sepsis † [A]		
# participants affected/at risk	0/6 (0%)	2/91 (2.2%)
# events		
Cellulitis † [A]		
# participants affected/at	0/6 (0%)	4/91 (4.4%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
risk		
# events		
Clostridium difficile colitis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Cystitis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Device related infection † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Enterococcal bacteraemia † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Epiglottitis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Escherichia bacteraemia † [A]		
# participants affected/at risk	0/6 (0%)	2/91 (2.2%)
# events		
Lobar pneumonia † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Lung infection † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Neutropenic sepsis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Oral infection † [A]		
# participants affected/at risk	0/6 (0%)	2/91 (2.2%)
# events		
Periorbital cellulitis † [A]		
# participants affected/at	0/6 (0%)	1/91 (1.1%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
risk		
# events		
Pharyngitis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Pneumonia † [A]		
# participants affected/at risk	1/6 (16.67%)	17/91 (18.68%)
# events		
Pneumonia fungal † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Pseudomonas infection † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Pyelonephritis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Sepsis † [A]		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# participants affected/at risk	0/6 (0%)	7/91 (7.69%)
# events		
Septic shock † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Staphylococcal bacteraemia † [A]		
# participants affected/at risk	0/6 (0%)	2/91 (2.2%)
# events		
Staphylococcal infection † [A]		
# participants affected/at risk	0/6 (0%)	3/91 (3.3%)
# events		
Staphylococcal sepsis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Streptococcal bacteraemia † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Urinary tract infection † [A]		
# participants affected/at risk	1/6 (16.67%)	4/91 (4.4%)
# events		
Zygomycosis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Injury, poisoning and procedural complications		
Femoral neck fracture † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Transfusion reaction † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Investigations		
Blood culture positive † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Metabolism and nutrition disorders		
Decreased appetite † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Musculoskeletal and connective tissue disorders		
Neck mass † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Nervous system disorders		
Cerebral haemorrhage † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Cerebrovascular accident † [A]		
# participants affected/at	0/6 (0%)	3/91 (3.3%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
risk		
# events		
Convulsion † [A]		
# participants affected/at risk	0/6 (0%)	3/91 (3.3%)
# events		
Extrapyramidal disorder † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Tremor † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Psychiatric disorders		
Delirium † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Mental status changes † [A]		
# participants affected/at risk	0/6 (0%)	2/91 (2.2%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Renal and urinary disorders		
Renal failure acute † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Respiratory, thoracic and mediastinal disorders		
Epistaxis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Hypoxia † [A]		
# participants affected/at risk	0/6 (0%)	2/91 (2.2%)
# events		
Pleural effusion † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Skin and subcutaneous tissue disorders		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Acute febrile neutrophilic dermatosis † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Rash † [A]		
# participants affected/at risk	0/6 (0%)	2/91 (2.2%)
# events		
Subcutaneous emphysema † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Vascular disorders		
Hypotension † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		
Ischaemia † [A]		
# participants affected/at risk	0/6 (0%)	1/91 (1.1%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Total # participants affected/at risk	6/6 (100%)	90/91 (98.9%)
Blood and lymphatic system disorders		
Anaemia † [A]		
# participants affected/at risk	2/6 (33.33%)	18/91 (19.78%)
# events		
Febrile neutropenia † [A]		
# participants affected/at risk	3/6 (50%)	4/91 (4.4%)
# events		
Leukocytosis † [A]		
# participants affected/at risk	1/6 (16.67%)	1/91 (1.1%)
# events		
Thrombocytopenia † [A]		
# participants affected/at risk	3/6 (50%)	14/91 (15.38%)
# events		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Cardiac disorders		
Arrhythmia †[A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Cardiomyopathy †[A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Left ventricular dysfunction †[A]		
# participants affected/at risk	1/6 (16.67%)	7/91 (7.69%)
# events		
Pericardial effusion †[A]		
# participants affected/at risk	1/6 (16.67%)	2/91 (2.2%)
# events		
Tachycardia †[A]		
# participants affected/at risk	1/6 (16.67%)	7/91 (7.69%)
# events		
Eye disorders		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Glaucoma † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Vision blurred † [A]		
# participants affected/at risk	2/6 (33.33%)	13/91 (14.29%)
# events		
Gastrointestinal disorders		
Abdominal pain † [A]		
# participants affected/at risk	0/6 (0%)	11/91 (12.09%)
# events		
Abdominal pain upper † [A]		
# participants affected/at risk	1/6 (16.67%)	1/91 (1.1%)
# events		
Constipation † [A]		
# participants affected/at risk	1/6 (16.67%)	12/91 (13.19%)
# events		
Diarrhoea † [A]		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# participants affected/at risk	5/6 (83.33%)	43/91 (47.25%)
# events		
Gastrointestinal haemorrhage †[A]		
# participants affected/at risk	1/6 (16.67%)	2/91 (2.2%)
# events		
Gingival bleeding †[A]		
# participants affected/at risk	2/6 (33.33%)	3/91 (3.3%)
# events		
Haemorrhoidal haemorrhage †[A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Haemorrhoids †[A]		
# participants affected/at risk	0/6 (0%)	5/91 (5.49%)
# events		
Nausea †[A]		
# participants affected/at risk	3/6 (50%)	24/91 (26.37%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Oral pain † [A]		
# participants affected/at risk	1/6 (16.67%)	4/91 (4.4%)
# events		
Rectal ulcer † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Stomatitis † [A]		
# participants affected/at risk	0/6 (0%)	7/91 (7.69%)
# events		
Upper gastrointestinal haemorrhage † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Vomiting † [A]		
# participants affected/at risk	2/6 (33.33%)	18/91 (19.78%)
# events		
General disorders		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Asthenia †[A]		
# participants affected/at risk	0/6 (0%)	6/91 (6.59%)
# events		
Chills †[A]		
# participants affected/at risk	0/6 (0%)	5/91 (5.49%)
# events		
Fatigue †[A]		
# participants affected/at risk	2/6 (33.33%)	22/91 (24.18%)
# events		
Mucosal inflammation †[A]		
# participants affected/at risk	0/6 (0%)	9/91 (9.89%)
# events		
Oedema peripheral †[A]		
# participants affected/at risk	3/6 (50%)	21/91 (23.08%)
# events		
Pain †[A]		
# participants affected/at risk	1/6 (16.67%)	2/91 (2.2%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Pyrexia † [A]		
# participants affected/at risk	3/6 (50%)	21/91 (23.08%)
# events		
Swelling † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Hepatobiliary disorders		
Hyperbilirubinaemia † [A]		
# participants affected/at risk	0/6 (0%)	6/91 (6.59%)
# events		
Infections and infestations		
Cellulitis † [A]		
# participants affected/at risk	0/6 (0%)	8/91 (8.79%)
# events		
Enterococcal infection † [A]		
# participants affected/at risk	1/6 (16.67%)	2/91 (2.2%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Gingivitis † [A]		
# participants affected/at risk	1/6 (16.67%)	1/91 (1.1%)
# events		
Herpes simplex † [A]		
# participants affected/at risk	1/6 (16.67%)	1/91 (1.1%)
# events		
Pneumonia † [A]		
# participants affected/at risk	1/6 (16.67%)	11/91 (12.09%)
# events		
Staphylococcal infection † [A]		
# participants affected/at risk	1/6 (16.67%)	6/91 (6.59%)
# events		
Urinary tract infection † [A]		
# participants affected/at risk	2/6 (33.33%)	10/91 (10.99%)
# events		
Vulval cellulitis † [A]		
# participants affected/at	1/6 (16.67%)	0/91 (0%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
risk		
# events		
Injury, poisoning and procedural complications		
Contusion † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Fall † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Investigations		
Activated partial thromboplastin time prolonged † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Alanine aminotransferase increased † [A]		
# participants affected/at risk	0/6 (0%)	21/91 (23.08%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Aspartate aminotransferase increased † [A]		
# participants affected/at risk	2/6 (33.33%)	19/91 (20.88%)
# events		
Blood alkaline phosphatase increased † [A]		
# participants affected/at risk	1/6 (16.67%)	4/91 (4.4%)
# events		
Blood glucose increased † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Blood potassium increased † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Brain natriuretic peptide increased † [A]		
# participants affected/at risk	1/6 (16.67%)	1/91 (1.1%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Prothrombin time prolonged † [A]		
# participants affected/at risk	1/6 (16.67%)	1/91 (1.1%)
# events		
Metabolism and nutrition disorders		
Decreased appetite † [A]		
# participants affected/at risk	2/6 (33.33%)	10/91 (10.99%)
# events		
Dehydration † [A]		
# participants affected/at risk	0/6 (0%)	8/91 (8.79%)
# events		
Hyperglycaemia † [A]		
# participants affected/at risk	1/6 (16.67%)	4/91 (4.4%)
# events		
Hyperkalaemia † [A]		
# participants affected/at risk	1/6 (16.67%)	3/91 (3.3%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Hyperphosphataemia † [A]		
# participants affected/at risk	2/6 (33.33%)	0/91 (0%)
# events		
Hyperuricaemia † [A]		
# participants affected/at risk	0/6 (0%)	6/91 (6.59%)
# events		
Hypoalbuminaemia † [A]		
# participants affected/at risk	2/6 (33.33%)	10/91 (10.99%)
# events		
Hypocalcaemia † [A]		
# participants affected/at risk	1/6 (16.67%)	9/91 (9.89%)
# events		
Hypokalaemia † [A]		
# participants affected/at risk	1/6 (16.67%)	13/91 (14.29%)
# events		
Hypomagnesaemia † [A]		
# participants affected/at	1/6 (16.67%)	11/91

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
risk		(12.09%)
# events		
Hyponatraemia † [A]		
# participants affected/at risk	4/6 (66.67%)	8/91 (8.79%)
# events		
Hypouricaemia † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Musculoskeletal and connective tissue disorders		
Arthralgia † [A]		
# participants affected/at risk	1/6 (16.67%)	2/91 (2.2%)
# events		
Coccydynia † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Muscle spasms † [A]		
# participants affected/at	2/6 (33.33%)	3/91 (3.3%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
risk		
# events		
Musculoskeletal stiffness † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Myalgia † [A]		
# participants affected/at risk	2/6 (33.33%)	0/91 (0%)
# events		
Nervous system disorders		
Dizziness † [A]		
# participants affected/at risk	1/6 (16.67%)	4/91 (4.4%)
# events		
Headache † [A]		
# participants affected/at risk	2/6 (33.33%)	10/91 (10.99%)
# events		
Presyncope † [A]		
# participants affected/at	1/6 (16.67%)	1/91 (1.1%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
risk		
# events		
Syncope † [A]		
# participants affected/at risk	0/6 (0%)	5/91 (5.49%)
# events		
Psychiatric disorders		
Anxiety † [A]		
# participants affected/at risk	0/6 (0%)	6/91 (6.59%)
# events		
Insomnia † [A]		
# participants affected/at risk	1/6 (16.67%)	1/91 (1.1%)
# events		
Renal and urinary disorders		
Dysuria † [A]		
# participants affected/at risk	1/6 (16.67%)	1/91 (1.1%)
# events		
Haematuria † [A]		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# participants affected/at risk	0/6 (0%)	5/91 (5.49%)
# events		
Proteinuria † [A]		
# participants affected/at risk	2/6 (33.33%)	5/91 (5.49%)
# events		
Renal failure acute † [A]		
# participants affected/at risk	1/6 (16.67%)	4/91 (4.4%)
# events		
Respiratory, thoracic and mediastinal disorders		
Cough † [A]		
# participants affected/at risk	0/6 (0%)	11/91 (12.09%)
# events		
Dyspnoea † [A]		
# participants affected/at risk	0/6 (0%)	11/91 (12.09%)
# events		
Epistaxis † [A]		
# participants affected/at	1/6 (16.67%)	13/91

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
risk		(14.29%)
# events		
Oropharyngeal pain † [A]		
# participants affected/at risk	0/6 (0%)	7/91 (7.69%)
# events		
Pulmonary oedema † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Skin and subcutaneous tissue disorders		
Alopecia † [A]		
# participants affected/at risk	1/6 (16.67%)	1/91 (1.1%)
# events		
Dry skin † [A]		
# participants affected/at risk	2/6 (33.33%)	8/91 (8.79%)
# events		
Erythema † [A]		
# participants affected/at risk	1/6 (16.67%)	2/91 (2.2%)

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
# events		
Exfoliative rash † [A]		
# participants affected/at risk	1/6 (16.67%)	0/91 (0%)
# events		
Petechiae † [A]		
# participants affected/at risk	0/6 (0%)	6/91 (6.59%)
# events		
Pruritus † [A]		
# participants affected/at risk	1/6 (16.67%)	7/91 (7.69%)
# events		
Rash † [A]		
# participants affected/at risk	0/6 (0%)	24/91 (26.37%)
# events		
Vascular disorders		
Haematoma † [A]		
# participants affected/at risk	1/6 (16.67%)	2/91 (2.2%)
# events		

	GSK1120212 <2 mg OD	GSK1120212 2 mg OD
Hypotension † [A]		
# participants affected/at risk	3/6 (50%)	7/91 (7.69%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Limitations and Caveats:

Results Point of Contact:

Name/Official Title: GSK Response Center

Organization: GlaxoSmithKline

Phone: 866-435-7343

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