Clinical trial results:
A phase I/II, open-label, 2 arm study to investigate the safety, clinical activity, pharmacokinetics and pharmacodynamics of GSK2879552 administered alone or in combination with azacitidine, in adult subjects with IPSS-R high and very high risk myelodysplastic syndromes (MDS) previously treated with hypomethylating agents (HMA)

Summary

EudraCT number	2016-002294-35
Trial protocol	ES
Global end of trial date	18 December 2018

Results information

Result version number	v2 (current)
This version publication date	09 May 2019
First version publication date	01 March 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	205744

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 December 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Part I. To determine the recommended phase 2 dose (RP2D) of GSK2879552 administered alone and in combination with azacitidine in adult subjects with HR MDS previously treated with HMA.
Part II. To evaluate clinical activity after treatment with GSK2879552, alone or in combination with azacitidine, in adult subjects with HR MDS previously treated with HMA

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 July 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	5
EEA total number of subjects	2

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was an open-label, 2 arm study to evaluate the safety and clinical activity of GSK2879552 alone, or in combination with azacitidine in adult participants with myelodysplastic syndromes (MDS). The study was conducted in 3 centers among 2 countries.

Pre-assignment

Screening details:

Total 5 participants were included into Part 1 and received GSK2879552. The study was terminated during Part 1 and hence Part 2 was not conducted as the risk benefit in earlier studies do not favor continuation of this study.

Period 1

Period 1 title	Part 1: Dose Confirmation (Upto 2 years) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Part 1: GSK2879552

Arm description:

Participants in this monotherapy arm were administered with GSK2879552 0.5 milligrams or 2 milligrams oral capsules once a day as continuous daily dosing in each cycle (of 28 days) until disease progression during Part 1 of the study.

Arm type	Experimental
Investigational medicinal product name	GSK2879552
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

GSK2879552 was administered orally once a day as continuous daily dosing in each cycle (of 28 days) until disease progression.

Number of subjects in period 1	Part 1: GSK2879552
Started	5
Completed	0
Not completed	5
Adverse event, serious fatal	2
Study terminated by sponsor	3

Baseline characteristics

Reporting groups

Reporting group title	Part 1: GSK2879552

Reporting group description:

Participants in this monotherapy arm were administered with GSK2879552 0.5 milligrams or 2 milligrams oral capsules once a day as continuous daily dosing in each cycle (of 28 days) until disease progression during Part 1 of the study.

Reporting group values	Part 1: GSK2879552	Total	
Number of subjects	5	5	
Age categorical			
Part 1 data is presented as study was terminated during Part 1 and hence Part 2 was not initiated.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
99 indicates data was not available as study was terminated during Part 1 and hence Part 2 was not initiated. Only Part 1 data is presented.			
Units: years			
arithmetic mean	77.2		
standard deviation	± 5.07	-	
Sex: Female, Male			
Part 1 data is presented as study was terminated during Part 1 and hence Part 2 was not initiated.			
Units: Subjects			
Female	3	3	
Male	2	2	
Race, Customized			
Part 1 data is presented as study was terminated during Part 1 and hence Part 2 was not initiated.			
Units: Subjects			
White - White/Caucasian/European Heritage	5	5	

End points

End points reporting groups

Reporting group title	Part 1: GSK2879552

Reporting group description:

Participants in this monotherapy arm were administered with GSK2879552 0.5 milligrams or 2 milligrams oral capsules once a day as continuous daily dosing in each cycle (of 28 days) until disease progression during Part 1 of the study.

Subject analysis set title	Part 2: GSK2879552
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in this monotherapy arm were administered with GSK2879552 0.5 milligrams or 2 milligrams oral capsules once a day as continuous daily dosing in each cycle (of 28 days) until disease progression during Part 1 of the study.

Subject analysis set title	Part 2: GSK2879552+Azacitidine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Part 2 was to be initiated once Part 1 is completed and dose has been selected for GSK2879552 monotherapy and combination of azacitidine with GSK2879552. Treatment with GSK2879552 in this combination therapy arm was to be administered orally once a day at RP2D as continuous daily dosing in each cycle (of 28 days) until disease progression in Part 2 of the study. Azacitidine was to be administered at 75 milligram per meter^2 on Days 1-7 of each 28 day cycle by intravenous (IV) infusion or subcutaneous (SC) injection (route of administration: by physicians choice).

Subject analysis set title	Part 1: GSK2879552+Azacitidine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in this monotherapy arm were administered with GSK2879552 0.5 milligrams or 2 milligrams oral capsules once a day as continuous daily dosing in each cycle (of 28 days) until disease progression during Part 1 of the study. Participants were also received azacitidine on days 1 to 7 of 28 days cycle via IV or SC administration.

Primary: Part 1: Number of participants with any non-serious adverse event (non-SAE), serious AE (SAE), dose limiting toxicities (DLT), dose reductions or delays and withdrawals due to toxicities

End point title	Part 1: Number of participants with any non-serious adverse event (non-SAE), serious AE (SAE), dose limiting toxicities (DLT), dose reductions or delays and withdrawals due to toxicities[1]

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention or event associated with liver injury and impaired liver function were categorized as SAE. An event was considered a DLT if it occurred within the first 28 days of treatment, and met the DLT criteria unless it could be clearly established that the event was unrelated to treatment.

End point type	Primary

End point timeframe:

Up to 2 years

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[2]			
Units: Participants				
Non-SAEs	5			
SAEs	1			
DLT	0			
Dose reductions or delays	0			
Withdrawals due to toxicities	0			

Notes:

[2] - All Treated Subjects Population: All participants who received at least one dose of study treatment.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Platelets, neutrophils, monocytes, lymphocytes, leucocyte, eosinophils and basophils at indicated time-points

End point title	Part 1: Change from Baseline in Platelets, neutrophils, monocytes, lymphocytes, leucocyte, eosinophils and basophils at indicated time-points[3]

End point description:

Blood samples were collected from participants for evaluation of hematology parameters including platelets, neutrophils, monocytes, lymphocytes, leucocyte, eosinophils and basophils. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[4]			
Units: 10^9 cells per liter				
arithmetic mean (standard deviation)				
Platelets, Cycle 1, Day 1, n=5	-13.826 (± 16.2868)			
Platelets, Cycle 1, Day 7, n=5	-17.984 (± 15.7398)			
Platelets, Cycle 1, Day 15, n=4	-19.250 (± 8.2614)			
Platelets, Cycle 1, Day 22, n=3	-20.667 (± 14.3643)			
Platelets, Cycle 2, Day 1, n=3	-16.000 (± 18.7350)			
Platelets, Cycle 2, Day 7, n=3	-21.333 (± 28.3784)			

Platelets, Cycle 2, Day 15, n=3	-24.333 (± 15.3731)			
Platelets, Cycle 2, Day 22, n=3	-24.667 (± 19.3477)			
Platelets, Cycle 3, Day 1, n=3	-17.000 (± 14.1067)			
Platelets, Cycle 4, Day 1, n=2	-13.000 (± 4.2426)			
Platelets, Cycle 5, Day 1, n=1	-11.000 (± 99999)			
Neutrophils, Cycle 1, Day 1, n=5	-0.019 (± 0.1298)			
Neutrophils, Cycle 1, Day 7, n=5	0.035 (± 0.2058)			
Neutrophils, Cycle 1, Day 15, n=4	0.060 (± 0.3282)			
Neutrophils, Cycle 1, Day 22, n=3	0.100 (± 0.1732)			
Neutrophils, Cycle 2, Day 1, n=3	0.200 (± 0.3000)			
Neutrophils, Cycle 2, Day 7, n=3	0.300 (± 0.3606)			
Neutrophils, Cycle 2, Day 15, n=3	0.333 (± 0.3055)			
Neutrophils, Cycle 2, Day 22, n=3	0.267 (± 0.4041)			
Neutrophils, Cycle 3, Day 1, n=3	0.267 (± 0.3215)			
Neutrophils, Cycle 4, Day 1, n=2	0.650 (± 0.2121)			
Neutrophils, Cycle 5, Day 1, n=1	0.800 (± 99999)			
Monocytes, Cycle 1, Day 1, n=5	0.017 (± 0.1359)			
Monocytes, Cycle 1, Day 7, n=5	0.059 (± 0.0853)			
Monocytes, Cycle 1, Day 15, n=4	0.100 (± 0.0816)			
Monocytes, Cycle 1, Day 22, n=3	12.633 (± 21.7086)			
Monocytes, Cycle 2, Day 1, n=3	0.267 (± 0.2517)			
Monocytes, Cycle 2, Day 7, n=3	0.400 (± 0.6083)			
Monocytes, Cycle 2, Day 15, n=3	0.633 (± 0.7095)			
Monocytes, Cycle 2, Day 22, n=3	0.267 (± 0.2517)			
Monocytes, Cycle 3, Day 1, n=3	0.300 (± 0.1732)			
Monocytes, Cycle 4, Day 1, n=2	1.000 (± 0.1414)			
Monocytes, Cycle 5, Day 1, n=1	1.600 (± 99999)			
Lymphocytes, Cycle 1, Day 1, n=5	-0.036 (± 0.0924)			
Lymphocytes, Cycle 1, Day 7, n=5	0.008 (± 0.1761)			
Lymphocytes, Cycle 1, Day 15, n=4	-0.073 (± 0.0486)			
Lymphocytes, Cycle 1, Day 22, n=3	-0.033 (± 0.0577)			

Lymphocytes, Cycle 2, Day 1, n=3	-0.067 (± 0.1528)			
Lymphocytes, Cycle 2, Day 7, n=3	-0.033 (± 0.3055)			
Lymphocytes, Cycle 2, Day 15, n=3	0.033 (± 0.3786)			
Lymphocytes, Cycle 2, Day 22, n=3	0.033 (± 0.2082)			
Lymphocytes, Cycle 3, Day 1, n=3	-0.067 (± 0.3055)			
Lymphocytes, Cycle 4, Day 1, n=2	0.200 (± 0.0000)			
Lymphocytes, Cycle 5, Day 1, n=1	0.400 (± 99999)			
Leucocytes, Cycle 1, Day 1, n=5	-0.054 (± 0.1720)			
Leucocytes, Cycle 1, Day 7, n=5	0.154 (± 0.3257)			
Leucocytes, Cycle 1, Day 15, n=4	0.032 (± 0.3208)			
Leucocytes, Cycle 1, Day 22, n=3	0.267 (± 0.5132)			
Leucocytes, Cycle 2, Day 1, n=3	0.433 (± 0.7234)			
Leucocytes, Cycle 2, Day 7, n=3	0.700 (± 1.3748)			
Leucocytes, Cycle 2, Day 15, n=3	1.033 (± 1.4572)			
Leucocytes, Cycle 2, Day 22, n=3	0.633 (± 0.9292)			
Leucocytes, Cycle 3, Day 1, n=3	0.633 (± 0.9074)			
Leucocytes, Cycle 4, Day 1, n=2	2.000 (± 0.0000)			
Leucocytes, Cycle 5, Day 1, n=1	2.900 (± 99999)			
Eosinophils, Cycle 1, Day 1, n=5	-0.000 (± 0.0009)			
Eosinophils, Cycle 1, Day 7, n=5	0.016 (± 0.0252)			
Eosinophils, Cycle 1, Day 15, n=4	-0.008 (± 0.0150)			
Eosinophils, Cycle 1, Day 22, n=3	0.000 (± 0.0000)			
Eosinophils, Cycle 2, Day 1, n=3	0.000 (± 0.0000)			
Eosinophils, Cycle 2, Day 7, n=3	0.000 (± 0.0000)			
Eosinophils, Cycle 2, Day 15, n=3	0.000 (± 0.0000)			
Eosinophils, Cycle 2, Day 22, n=3	0.000 (± 0.0000)			
Eosinophils, Cycle 3, Day 1, n=3	0.000 (± 0.0000)			
Eosinophils, Cycle 4, Day 1, n=2	0.050 (± 0.0707)			
Eosinophils, Cycle 5, Day 1, n=1	0.100 (± 99999)			
Basophils, Cycle 1, Day 1, n=5	0.004 (± 0.0080)			
Basophils, Cycle 1, Day 7, n=5	0.017 (± 0.0323)			

Basophils, Cycle 1, Day 15, n=4	0.003 (± 0.0050)			
Basophils, Cycle 1, Day 22, n=3	0.000 (± 0.0000)			
Basophils, Cycle 2, Day 1, n=3	0.000 (± 0.0000)			
Basophils, Cycle 2, Day 7, n=3	0.000 (± 0.0000)			
Basophils, Cycle 2, Day 15, n=3	0.000 (± 0.0000)			
Basophils, Cycle 2, Day 22, n=3	0.000 (± 0.0000)			
Basophils, Cycle 3, Day 1, n=3	0.000 (± 0.0000)			
Basophils, Cycle 4, Day 1, n=2	0.050 (± 0.0707)			
Basophils, Cycle 5, Day 1, n=1	0.000 (± 99999)			

Notes:

[4] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Mean corpuscular volume (MCV) at indicated time-points

End point title	Part 1: Change from Baseline in Mean corpuscular volume (MCV) at indicated time-points[5]

End point description:

Blood samples were collected from participants for evaluation of hematology parameters including MCV. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available due to standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[6]			
Units: Femtoliter				
arithmetic mean (standard deviation)				
Cycle 1, Day 1, n=5	-0.280 (± 1.5450)			
Cycle 1, Day 7, n=4	-0.400 (± 1.9442)			
Cycle 1, Day 15, n=3	-0.267 (± 3.6679)			

Cycle 1, Day 22, n=3	0.400 (± 5.1730)			
Cycle 2, Day 1, n=3	1.667 (± 6.0003)			
Cycle 2, Day 7, n=3	3.500 (± 6.3592)			
Cycle 2, Day 15, n=3	2.933 (± 7.3528)			
Cycle 2, Day 22, n=3	2.900 (± 9.0000)			
Cycle 3, Day 1, n=3	2.700 (± 9.7370)			
Cycle 4, Day 1, n=2	6.750 (± 6.2933)			
Cycle 5, Day 1, n=1	8.500 (± 99999)			

Notes:

[6] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Mean corpuscular hemoglobin (MCH) at indicated time-points

End point title	Part 1: Change from Baseline in Mean corpuscular hemoglobin (MCH) at indicated time-points[7]

End point description:

Blood samples were collected from participants for evaluation of hematology parameters including MCH. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[8]			
Units: Picogram				
arithmetic mean (standard deviation)				
Cycle 1, Day 1, n=5	-1.100 (± 2.8679)			
Cycle 1, Day 7, n=4	-1.350 (± 3.3000)			
Cycle 1, Day 15, n=3	-0.100 (± 1.1358)			
Cycle 1, Day 22, n=3	0.067 (± 1.5308)			

Cycle 2, Day 1, n=3	0.833 (± 1.5177)			
Cycle 2, Day 7, n=3	1.067 (± 1.3796)			
Cycle 2, Day 15, n=3	0.900 (± 1.9672)			
Cycle 2, Day 22, n=3	0.767 (± 2.3798)			
Cycle 3, Day 1, n=3	0.933 (± 3.0665)			
Cycle 4, Day 1, n=2	1.950 (± 1.3435)			
Cycle 5, Day 1, n=1	2.200 (± 99999)			

Notes:

[8] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Mean corpuscular hemoglobin concentration (MCHC) and Hemoglobin (Hb) at indicated time-points

End point title	Part 1: Change from Baseline in Mean corpuscular hemoglobin concentration (MCHC) and Hemoglobin (Hb) at indicated time-points[9]

End point description:

Blood samples were collected from participants for evaluation of hematology parameters including MCHC and Hb. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[10]			
Units: Grams per liter				
arithmetic mean (standard deviation)				
MCHC, Cycle 1, Day 1, n=5	-10.400 (± 29.3053)			
MCHC, Cycle 1, Day 7, n=4	-12.500 (± 35.8190)			
MCHC, Cycle 1, Day 15, n=3	0.333 (± 2.0817)			
MCHC, Cycle 1, Day 22, n=3	0.000 (± 8.1854)			
MCHC, Cycle 2, Day 1, n=3	3.667 (± 6.6583)			

MCHC, Cycle 2, Day 7, n=3	-1.000 (± 12.4900)			
MCHC, Cycle 2, Day 15, n=3	0.000 (± 7.8102)			
MCHC, Cycle 2, Day 22, n=3	-2.000 (± 8.6603)			
MCHC, Cycle 3, Day 1, n=3	1.333 (± 6.0277)			
MCHC, Cycle 4, Day 1, n=2	-3.500 (± 9.1924)			
MCHC, Cycle 5, Day 1, n=1	-8.000 (± 99999)			
Hb, Cycle 1, Day 1, n=5	-2.000 (± 7.0000)			
Hb, Cycle 1, Day 7, n=5	-4.200 (± 11.3666)			
Hb, Cycle 1, Day 15, n=4	-5.000 (± 11.8040)			
Hb, Cycle 1, Day 22, n=3	2.000 (± 2.6458)			
Hb, Cycle 2, Day 1, n=3	-3.667 (± 12.5831)			
Hb, Cycle 2, Day 7, n=3	2.000 (± 13.4536)			
Hb, Cycle 2, Day 15, n=3	0.333 (± 16.5630)			
Hb, Cycle 2, Day 22, n=3	-3.000 (± 5.2915)			
Hb, Cycle 3, Day 1, n=3	-2.333 (± 7.2342)			
Hb, Cycle 4, Day 1, n=2	7.000 (± 4.2426)			
Hb, Cycle 5, Day 1, n=1	6.000 (± 99999)			

Notes:

[10] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Hematocrit at indicated time-points

End point title	Part 1: Change from Baseline in Hematocrit at indicated time-points[11]

End point description:

Blood samples were collected from participants for evaluation of hematology parameters including Hematocrit. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[12]			
Units: Proportion of red blood cells in blood				
arithmetic mean (standard deviation)				
Cycle 1, Day 1, n=5	0.001 (± 0.0334)			
Cycle 1, Day 7, n=5	-0.008 (± 0.0525)			
Cycle 1, Day 15, n=4	-0.018 (± 0.0401)			
Cycle 1, Day 22, n=3	0.007 (± 0.0100)			
Cycle 2, Day 1, n=3	-0.014 (± 0.0396)			
Cycle 2, Day 7, n=3	0.007 (± 0.0448)			
Cycle 2, Day 15, n=3	0.002 (± 0.0520)			
Cycle 2, Day 22, n=3	-0.009 (± 0.0206)			
Cycle 3, Day 1, n=3	-0.008 (± 0.0244)			
Cycle 4, Day 1, n=2	0.024 (± 0.0191)			
Cycle 5, Day 1, n=1	0.023 (± 99999)			

Notes:

[12] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in erythrocytes at indicated time-points

End point title	Part 1: Change from Baseline in erythrocytes at indicated time-points[13]

End point description:

Blood samples were collected from participants for evaluation of hematology parameters including erythrocytes. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[14]			
Units: 10^12 cells per Liter				
arithmetic mean (standard deviation)				
Cycle 1, Day 1, n=5	0.030 (± 0.3489)			
Cycle 1, Day 7, n=5	-0.058 (± 0.5363)			
Cycle 1, Day 15, n=4	-0.138 (± 0.3216)			
Cycle 1, Day 22, n=3	0.077 (± 0.0643)			
Cycle 2, Day 1, n=3	-0.193 (± 0.2558)			
Cycle 2, Day 7, n=3	-0.017 (± 0.2996)			
Cycle 2, Day 15, n=3	-0.063 (± 0.3402)			
Cycle 2, Day 22, n=3	-0.173 (± 0.1901)			
Cycle 3, Day 1, n=3	-0.160 (± 0.2425)			
Cycle 4, Day 1, n=2	0.060 (± 0.0141)			
Cycle 5, Day 1, n=1	0.000 (± 99999)			

Notes:

[14] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in percent reticulocytes at indicated time-points

End point title	Part 1: Change from Baseline in percent reticulocytes at indicated time-points[15]

End point description:

Blood samples were collected from participants for evaluation of hematology parameters including percent reticulocytes. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1) (each cycle of 28 days)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	1[16]			
Units: Percentage of reticulocytes				
arithmetic mean (standard deviation)				
Cycle 1, Day 7	0.000 (± 99999)			
Cycle 1, Day 22	-0.100 (± 99999)			
Cycle 2, Day 1	-0.100 (± 99999)			
Cycle 2, Day 7	0.000 (± 99999)			
Cycle 2, Day 15	0.000 (± 99999)			
Cycle 3, Day 1	-0.100 (± 99999)			
Cycle 4, Day 1	-0.100 (± 99999)			

Notes:

[16] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in blast/leukocytes at indicated time-points

End point title	Part 1: Change from Baseline in blast/leukocytes at indicated time-points[17]

End point description:

Blood samples were collected from participants for evaluation of hematology parameters including blast/leukocytes. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants.

End point type	Primary

End point timeframe:

Baseline and Day 1 of Cycle 1 (Cycle of 28 days)

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	1[18]			
Units: Ratio of blasts to leukocytes				
arithmetic mean (standard deviation)	0.000 (± 99999)			

Notes:

[18] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Alanine Aminotransferase (ALT), Alkaline phosphatase (ALP), Aspartate Aminotransferase (AST), Lactate dehydrogenase (LDH) and Gamma Glutamyl Transferase (GGT) at indicated time-points

End point title	Part 1: Change from Baseline in Alanine Aminotransferase (ALT), Alkaline phosphatase (ALP), Aspartate Aminotransferase (AST), Lactate dehydrogenase (LDH) and Gamma Glutamyl Transferase (GGT) at indicated time-points[19]

End point description:

Blood samples were collected from participants for evaluation of clinical chemistry parameters including ALT, ALP, AST, LDH and GGT. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. All Treated Subjects Population. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[20]			
Units: International unit per liter (IU/L)				
arithmetic mean (standard deviation)				
ALT, Cycle 1, Day 1, n=4	-10.000 (± 18.1292)			
ALT Cycle 1, Day 7, n=5	-3.000 (± 13.5093)			
ALT Cycle 1, Day 15, n=4	-6.250 (± 15.5000)			
ALT Cycle 1, Day 22, n=3	1.333 (± 15.1767)			
ALT Cycle 2, Day 1, n=3	3.000 (± 39.5095)			
ALT Cycle 3, Day 1, n=3	3.333 (± 42.0040)			
ALT Cycle 4, Day 1, n=2	33.000 (± 1.4142)			
ALT Cycle 5, Day 1, n=1	3.000 (± 99999)			
ALP, Cycle 1, Day 1, n=4	-4.750 (± 3.2016)			
ALP Cycle 1, Day 7, n=5	-6.800 (± 10.3053)			
ALP Cycle 1, Day 15, n=4	-4.250 (± 22.3961)			
ALP Cycle 1, Day 22, n=3	8.000 (± 21.6564)			
ALP Cycle 2, Day 1, n=3	23.667 (± 62.5007)			
ALP Cycle 3, Day 1, n=3	15.667 (± 31.3422)			

ALP Cycle 4, Day 1, n=2	18.500 (± 60.1041)			
ALP Cycle 5, Day 1, n=1	21.000 (± 99999)			
AST, Cycle 1, Day 1, n=4	-6.750 (± 14.8633)			
AST Cycle 1, Day 7, n=5	-3.200 (± 9.3381)			
AST Cycle 1, Day 15, n=4	-3.250 (± 17.6517)			
AST Cycle 1, Day 22, n=3	3.000 (± 27.5136)			
AST Cycle 2, Day 1, n=3	-0.333 (± 30.9246)			
AST Cycle 3, Day 1, n=3	-3.667 (± 38.5530)			
AST Cycle 4, Day 1, n=2	22.000 (± 21.2132)			
AST Cycle 5, Day 1, n=1	16.000 (± 99999)			
LDH, Cycle 1, Day 1, n=4	4.000 (± 90.9395)			
LDH Cycle 1, Day 7, n=5	-31.200 (± 47.2515)			
LDH Cycle 1, Day 15, n=3	4.000 (± 22.6053)			
LDH Cycle 1, Day 22, n=3	-12.000 (± 47.5710)			
LDH Cycle 2, Day 1, n=3	-18.333 (± 55.4106)			
LDH Cycle 3, Day 1, n=3	-20.667 (± 62.7402)			
LDH Cycle 4, Day 1, n=2	12.500 (± 3.5355)			
LDH Cycle 5, Day 1, n=1	11.000 (± 99999)			
GGT, Cycle 1, Day 1, n=1	-17.000 (± 99999)			
GGT Cycle 1, Day 7, n=2	-7.500 (± 9.1924)			
GGT Cycle 1, Day 22, n=1	0.000 (± 99999)			
GGT Cycle 2, Day 1, n=1	3.000 (± 99999)			
GGT Cycle 3, Day 1, n=1	8.000 (± 99999)			
GGT Cycle 4, Day 1, n=1	5.000 (± 99999)			

Notes:

[20] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Calcium, chloride, glucose, potassium, sodium, phosphate and urea nitrogen at indicated time-points

End point title	Part 1: Change from Baseline in Calcium, chloride, glucose, potassium, sodium, phosphate and urea nitrogen at indicated time-points[21]

End point description:

Blood samples were collected from participants for evaluation of clinical chemistry parameters including calcium, chloride, glucose, potassium, sodium, phosphate and urea nitrogen. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[22]			
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Calcium, Cycle 1, Day 1, n=3	-0.008 (± 0.0520)			
Calcium Cycle 1, Day 7, n=4	-0.075 (± 0.0535)			
Calcium Cycle 1, Day 15, n=3	-0.066 (± 0.0758)			
Calcium Cycle 1, Day 22, n=3	-0.033 (± 0.0624)			
Calcium Cycle 2, Day 1, n=3	-0.067 (± 0.0144)			
Calcium Cycle 3, Day 1, n=3	-0.183 (± 0.1523)			
Calcium Cycle 4, Day 1, n=2	-0.050 (± 0.0700)			
Calcium, Cycle 5, Day 1, n=1	-0.050 (± 99999)			
Chloride, Cycle 1, Day 1, n=4	-0.750 (± 0.5000)			
Chloride Cycle 1, Day 7, n=5	0.600 (± 4.3932)			
Chloride Cycle 1, Day 15, n=4	0.250 (± 2.5000)			
Chloride Cycle 1, Day 22, n=3	0.333 (± 1.1547)			
Chloride Cycle 2, Day 1, n=3	0.333 (± 1.5275)			
Chloride Cycle 3, Day 1, n=3	-0.333 (± 1.5275)			
Chloride Cycle 4, Day 1, n=2	0.000 (± 2.8284)			
Chloride, Cycle 5, Day 1, n=1	0.000 (± 99999)			
Glucose, Cycle 1, Day 1, n=4	0.527 (± 1.9147)			
Glucose Cycle 1, Day 7, n=5	-0.333 (± 1.5357)			
Glucose Cycle 1, Day 15, n=4	0.014 (± 0.7971)			

Glucose Cycle 1, Day 22, n=3	0.870 (± 0.9309)			
Glucose Cycle 2, Day 1, n=3	1.924 (± 2.1037)			
Glucose Cycle 3, Day 1, n=3	1.628 (± 2.8543)			
Glucose Cycle 4, Day 1, n=2	1.027 (± 1.2954)			
Glucose, Cycle 5, Day 1, n=1	1.110 (± 99999)			
Potassium, Cycle 1, Day 1, n=4	0.325 (± 0.5315)			
Potassium Cycle 1, Day 7, n=5	0.000 (± 0.4528)			
Potassium Cycle 1, Day 15, n=4	-0.025 (± 0.4272)			
Potassium Cycle 1, Day 22, n=3	0.067 (± 0.2887)			
Potassium Cycle 2, Day 1, n=3	0.067 (± 0.1528)			
Potassium Cycle 3, Day 1, n=3	-0.367 (± 0.3786)			
Potassium Cycle 4, Day 1, n=2	0.050 (± 0.0707)			
Potassium, Cycle 5, Day 1, n=1	0.500 (± 99999)			
Sodium, Cycle 1, Day 1, n=4	-1.750 (± 1.2583)			
Sodium Cycle 1, Day 7, n=5	-1.000 (± 2.2361)			
Sodium Cycle 1, Day 15, n=4	-2.000 (± 2.4495)			
Sodium Cycle 1, Day 22, n=3	-0.667 (± 2.0817)			
Sodium Cycle 2, Day 1, n=3	0.333 (± 0.5774)			
Sodium Cycle 3, Day 1, n=3	-1.000 (± 5.0000)			
Sodium Cycle 4, Day 1, n=2	-0.500 (± 2.1213)			
Sodium, Cycle 5, Day 1, n=1	0.000 (± 99999)			
Urea nitrogen, Cycle 1, Day 1, n=3	2.701 (± 2.3181)			
Urea nitrogen Cycle 1, Day 7, n=4	1.214 (± 3.4779)			
Urea nitrogen Cycle 1, Day 15, n=3	1.547 (± 3.3171)			
Urea nitrogen Cycle 1, Day 22, n=3	1.309 (± 3.8173)			
Urea nitrogen Cycle 2, Day 1, n=3	0.238 (± 2.1519)			
Urea nitrogen Cycle 3, Day 1, n=3	-1.190 (± 1.7610)			
Urea nitrogen Cycle 4, Day 1, n=2	-0.535 (± 1.2622)			
Urea nitrogen, Cycle 5, Day 1, n=1	-1.428 (± 99999)			
Phosphate, Cycle 1, Day 1, n=1	0.194 (± 99999)			
Phosphate Cycle 1, Day 7, n=2	-0.081 (± 0.1598)			

Phosphate Cycle 1, Day 22, n=1	-0.032 (± 99999)			
Phosphate Cycle 2, Day 1, n=1	0.194 (± 99999)			
Phosphate Cycle 3, Day 1, n=1	0.000 (± 99999)			
Phosphate Cycle 4, Day 1, n=1	0.032 (± 99999)			

Notes:

[22] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Albumin and Protein at indicated time points

End point title	Part 1: Change from Baseline in Albumin and Protein at indicated time points[23]

End point description:

Blood samples were collected from participants for evaluation of clinical chemistry parameters including Albumin and Protein. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[24]			
Units: G/L				
arithmetic mean (standard deviation)				
Albumin, Cycle 1, Day 1, n=4	-1.250 (± 2.2174)			
Albumin Cycle 1, Day 7, n=4	-1.250 (± 2.5000)			
Albumin Cycle 1, Day 15, n=3	-1.667 (± 1.5275)			
Albumin Cycle 1, Day 22, n=3	-1.333 (± 0.5774)			
Albumin Cycle 2, Day 1, n=3	-1.667 (± 2.0817)			
Albumin Cycle 3, Day 1, n=3	-6.000 (± 6.2450)			
Albumin Cycle 4, Day 1, n=2	0.000 (± 1.4142)			
Albumin Cycle 5, Day 1, n=1	1.000 (± 99999)			

Protein, Cycle 1, Day 1, n=4	-3.250 (± 3.8622)			
Protein Cycle 1, Day 7, n=5	-3.200 (± 4.3243)			
Protein Cycle 1, Day 15, n=4	-1.500 (± 4.4347)			
Protein Cycle 1, Day 22, n=3	-1.667 (± 1.1547)			
Protein Cycle 2, Day 1, n=3	-3.333 (± 5.8595)			
Protein Cycle 3, Day 1, n=3	-7.333 (± 6.8069)			
Protein Cycle 4, Day 1, n=2	-2.000 (± 2.8284)			
Protein Cycle 5, Day 1, n=1	0.000 (± 99999)			

Notes:

[24] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Partial Pressure Carbon Dioxide (pCO2) at indicated time points

End point title	Part 1: Change from Baseline in Partial Pressure Carbon Dioxide (pCO2) at indicated time points[25]

End point description:

Blood samples were collected from participants for evaluation of clinical chemistry parameters including pCO2. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline and Day 1 of Cycle 1 (cycle of 28 days)

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	1[26]			
Units: Kilopascal				
arithmetic mean (standard deviation)	0.173 (± 99999)			

Notes:

[26] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Systolic blood pressure (SBP) and diastolic

blood pressure (DBP) at indicated time-points

End point title	Part 1: Change from Baseline in Systolic blood pressure (SBP) and diastolic blood pressure (DBP) at indicated time-points[27]

End point description:

Vital signs including SBP and DBP were measured after resting for at least 5 minutes in a semi-supine position. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1 (Days 7, 15), Cycle 2 (Days 1), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[28]			
Units: Millimeters of mercury				
arithmetic mean (standard deviation)				
SBP, Cycle 1, Day 7, n=5	-10.2 (± 4.76)			
SBP, Cycle 1, Day 15, n=4	-13.5 (± 3.87)			
SBP, Cycle 2, Day 1, n=3	-4.7 (± 3.79)			
SBP, Cycle 3, Day 1, n=3	-3.7 (± 8.39)			
SBP, Cycle 4, Day 1, n=2	-5.0 (± 2.83)			
SBP, Cycle 5, Day 1, n=1	-6.0 (± 99999)			
DBP, Cycle 1, Day 7, n=5	-2.6 (± 8.62)			
DBP, Cycle 1, Day 15, n=4	-3.5 (± 4.04)			
DBP, Cycle 2, Day 1, n=3	-7.3 (± 10.02)			
DBP, Cycle 3, Day 1, n=3	2.7 (± 4.73)			
DBP, Cycle 4, Day 1, n=2	3.0 (± 7.07)			
DBP, Cycle 5, Day 1, n=1	-4.0 (± 99999)			

Notes:

[28] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in heart rate at indicated time-points

End point title	Part 1: Change from Baseline in heart rate at indicated time-points[29]

End point description:

Vital signs including heart rate was measured after resting for at least 5 minutes in a semi-supine position. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1 (Days 7, 15), Cycle 2 (Days 1), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[30]			
Units: Beats per minute				
arithmetic mean (standard deviation)				
Cycle 1, Day 7, n=5	4.8 (± 6.69)			
Cycle 1, Day 15, n=4	-2.5 (± 7.42)			
Cycle 2, Day 1, n=3	-6.3 (± 2.89)			
Cycle 3, Day 1, n=3	-1.0 (± 9.00)			
Cycle 4, Day 1, n=2	-2.0 (± 8.49)			
Cycle 5, Day 1, n=1	-1.0 (± 99999)			

Notes:

[30] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in respiratory rate at indicated time-points

End point title	Part 1: Change from Baseline in respiratory rate at indicated time-points[31]

End point description:

Vital signs including respiratory rate was measured after resting for at least 5 minutes in a semi-supine position. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1 (Days 7, 15), Cycle 2 (Days 1), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[32]			
Units: Breaths per minute				
arithmetic mean (standard deviation)				
Cycle 1, Day 7, n=5	-0.4 (± 1.14)			
Cycle 1, Day 15, n=4	-0.5 (± 1.00)			
Cycle 2, Day 1, n=3	-1.0 (± 1.00)			

Cycle 3, Day 1, n=3	-0.3 (± 1.53)			
Cycle 4, Day 1, n=2	-0.5 (± 0.71)			
Cycle 5, Day 1, n=1	-1.0 (± 99999)			

Notes:

[32] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in body temperature at indicated time-points

End point title	Part 1: Change from Baseline in body temperature at indicated time-points[33]

End point description:

Vital signs including body temperature was measured after resting for at least 5 minutes in a semi-supine position. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1 (Days 7, 15), Cycle 2 (Days 1), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[34]			
Units: Celsius				
arithmetic mean (standard deviation)				
Cycle 1, Day 7, n=5	0.14 (± 0.279)			
Cycle 1, Day 15, n=4	0.10 (± 0.216)			
Cycle 2, Day 1, n=3	0.27 (± 0.231)			
Cycle 3, Day 1, n=3	0.20 (± 0.300)			
Cycle 4, Day 1, n=2	0.10 (± 0.283)			
Cycle 5, Day 1, n=1	-0.20 (± 99999)			

Notes:

[34] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in electrocardiogram (ECG) mean heart rate at indicated time-points

End point title	Part 1: Change from Baseline in electrocardiogram (ECG) mean heart rate at indicated time-points[35]

End point description:

Single 12-lead ECG was obtained at designated time points during the study using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT, and corrected QT (QTc) intervals. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1 (Days 1,7), Cycle 2 (Days 1), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[36]			
Units: Beats per minute				
arithmetic mean (standard deviation)				
Cycle 1, Day 1, n=2	2.0 (± 2.83)			
Cycle 1, Day 7, n=5	-1.0 (± 11.94)			
Cycle 2, Day 1, n=3	-5.3 (± 5.51)			
Cycle 3, Day 1, n=3	2.3 (± 10.02)			
Cycle 4, Day 1, n=2	-3.0 (± 9.90)			
Cycle 5, Day 1, n=1	-7.0 (± 99999)			

Notes:

[36] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in ECG PR interval, QRS duration, QT interval, QTc corrected by Bazett's formula (QTcB) and QTc corrected by Fridericia's formula (QTcF) at indicated time-points

End point title	Part 1: Change from Baseline in ECG PR interval, QRS duration, QT interval, QTc corrected by Bazett's formula (QTcB) and QTc corrected by Fridericia's formula (QTcF) at indicated time-points[37]

End point description:

Single 12-lead ECG was obtained at designated time points during the study using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT, and QTc intervals. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1 (Days 1,7), Cycle 2 (Days 1), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[38]			
Units: Milliseconds				
arithmetic mean (standard deviation)				
PR interval, Cycle 1, Day 1, n=2	0.0 (± 0.00)			
PR interval, Cycle 1, Day 7, n=5	39.8 (± 88.34)			
PR interval, Cycle 2, Day 1, n=3	6.0 (± 9.17)			
PR interval, Cycle 3, Day 1, n=3	0.7 (± 8.08)			
PR interval, Cycle 4, Day 1, n=2	6.0 (± 14.14)			
PR interval, Cycle 5, Day 1, n=1	12.0 (± 99999)			
QRS duration, Cycle 1, Day 1, n=2	-1.0 (± 4.24)			
QRS duration, Cycle 1, Day 7, n=5	-17.2 (± 39.61)			
QRS duration, Cycle 2, Day 1, n=3	2.0 (± 2.00)			
QRS duration, Cycle 3, Day 1, n=3	3.3 (± 1.15)			
QRS duration, Cycle 4, Day 1, n=2	-1.0 (± 1.41)			
QRS duration, Cycle 5, Day 1, n=1	-8.0 (± 99999)			
QT interval, Cycle 1, Day 1, n=2	0.0 (± 0.00)			
QT interval, Cycle 1, Day 7, n=5	-5.6 (± 29.37)			
QT interval, Cycle 2, Day 1, n=3	24.7 (± 18.58)			
QT interval, Cycle 3, Day 1, n=3	2.0 (± 18.00)			
QT interval, Cycle 4, Day 1, n=1	-4.0 (± 99999)			
QT interval, Cycle 5, Day 1, n=1	14.0 (± 99999)			
QTcB interval, Cycle 1, Day 1, n=2	7.0 (± 9.90)			
QTcB interval, Cycle 1, Day 7, n=2	-35.5 (± 82.73)			
QTcF interval, Cycle 1, Day 1, n=2	4.5 (± 6.36)			
QTcF interval, Cycle 1, Day 7, n=5	-9.4 (± 38.12)			
QTcF interval, Cycle 2, Day 1, n=3	8.0 (± 5.57)			
QTcF interval, Cycle 3, Day 1, n=3	13.0 (± 18.52)			
QTcF interval, Cycle 4, Day 1, n=2	-6.0 (± 19.80)			
QTcF interval, Cycle 5, Day 1, n=1	-8.0 (± 99999)			

Notes:

[38] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of participants with abnormal findings during physical examination

End point title	Part 1: Number of participants with abnormal findings during physical examination[39]

End point description:

A complete physical examination included, at a minimum, assessment of the Cardiovascular, Respiratory, Gastrointestinal and Neurological systems. A brief physical examination included, at a minimum assessments of the skin, lungs, cardiovascular system, and abdomen (liver and spleen). This

analysis was planned but data was not captured in the database. Abnormal changes were captured as adverse events if they were clinically significant. This analysis was planned but data was not captured in the database.

End point type	Primary

End point timeframe:

Up to 2 years

Notes:

[39] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	0[40]			
Units: Participants				

Notes:

[40] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Percentage of participants with investigator-assessed best response assessed by Clinical Benefit Rate (CBR)

End point title	Part 2: Percentage of participants with investigator-assessed best response assessed by Clinical Benefit Rate (CBR)[41]

End point description:

CBR was defined as the percentage of participants achieving a confirmed Complete Remission (CR) or Partial Remission (PR) or Marrow Complete Remission (mCR) or confirmed Hematologic Improvement (HI) or Stable Disease (SD) prior to new anti-cancer therapy and crossover on the All Treated Subjects Population. Participants with Not Evaluable or missing response were to be treated as non-responders. International Working Group (IWG) criteria, 2006 was to be used to evaluate response. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Primary

End point timeframe:

Up to 2.5 years

Notes:

[41] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 2: GSK2879552+ Azacitidine	Part 1: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[42]	0[43]		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[42] - All Treated Subjects Population.

[43] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Percentage of participants with investigator-assessed best response assessed by Objective Response Rate (ORR)

End point title	Part 2: Percentage of participants with investigator-assessed best response assessed by Objective Response Rate (ORR)[44]

End point description:

Objective response rate was defined as the percentage of participants who achieved CR or PR or mCR or HI prior to new anti-cancer therapy on the All Treated Subjects Population. Participants with Not Evaluable or missing response were to be treated as non-responders. IWG criteria, 2006 was to be used to evaluate response. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Primary

End point timeframe:

Up to 2.5 years

Notes:

[44] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[45]	0[46]		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[45] - All Treated Subjects Population.

[46] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Change from Baseline in Total Bilirubin, Direct Bilirubin, Creatinine and urate at indicated time points

End point title	Part 1: Change from Baseline in Total Bilirubin, Direct Bilirubin, Creatinine and urate at indicated time points[47]

End point description:

Blood samples were collected from participants for evaluation of clinical chemistry parameters including Total Bilirubin, Direct Bilirubin, Creatinine and urate. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was calculated by subtracting post-dose value from Baseline value. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and Cycle 1(Days 1, 7, 15, 22), Cycle 2 (Days 1, 7, 15 ,22), Cycle 3 (Day 1), Cycle 4 (Day 1), Cycle 5 (Day 1) (each cycle of 28 days)

Notes:

[47] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are not statistical data to report.

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[48]			
Units: Micromoles per liter (umol/L)				
arithmetic mean (standard deviation)				
Total Bilirubin, Cycle 1, Day 1, n=4	-3.420 (± 5.4075)			
Total Bilirubin Cycle 1, Day 7, n=5	-1.094 (± 5.6580)			
Total Bilirubin Cycle 1, Day 15, n=4	0.128 (± 6.6278)			
Total Bilirubin Cycle 1, Day 22, n=3	-1.710 (± 2.9618)			
Total Bilirubin Cycle 2, Day 1, n=3	-2.850 (± 3.5596)			
Total Bilirubin Cycle 3, Day 1, n=3	0.000 (± 3.4200)			
Total Bilirubin Cycle 4, Day 1, n=2	-0.855 (± 3.6275)			
Total Bilirubin, Cycle 5, Day 1, n=1	-3.420 (± 99999)			
Direct Bilirubin, Cycle 1, Day 1, n=1	1.368 (± 99999)			
Creatinine, Cycle 1, Day 1, n=4	16.133 (± 25.5329)			
Creatinine Cycle 1, Day 7, n=5	4.066 (± 11.2271)			
Creatinine Cycle 1, Day 15, n=4	17.238 (± 17.4800)			
Creatinine Cycle 1, Day 22, n=3	23.279 (± 18.5500)			
Creatinine Cycle 2, Day 1, n=3	16.501 (± 16.6402)			
Creatinine Cycle 3, Day 1, n=3	15.912 (± 20.5613)			
Creatinine Cycle 4, Day 1, n=2	32.708 (± 8.7512)			
Creatinine, Cycle 5, Day 1, n=1	4.420 (± 99999)			
Urate, Cycle 1, Day 1, n=1	41.636 (± 99999)			
Urate Cycle 1, Day 7, n=2	5.948 (± 0.0000)			
Urate Cycle 1, Day 22, n=1	35.688 (± 99999)			
Urate Cycle 2, Day 1, n=1	65.428 (± 99999)			
Urate Cycle 3, Day 1, n=1	89.220 (± 99999)			
Urate Cycle 4, Day 1, n=1	59.480 (± 99999)			

Notes:

[48] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants with investigator-assessed best response assessed by Clinical Benefit Rate (CBR)

End point title	Part 1: Percentage of participants with investigator-assessed best response assessed by Clinical Benefit Rate (CBR)

End point description:

CBR was defined as the percentage of participants achieving a confirmed Complete Remission (CR) or Partial Remission (PR) or Marrow Complete Remission (mCR) or confirmed Hematologic Improvement (HI) or Stable Disease (SD) prior to new anti-cancer therapy and crossover on the All Treated Subjects Population. Participants with Not Evaluable or missing response were treated as non-responders. International Working Group (IWG) criteria, 2006 was used to evaluate response.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[49]			
Units: Percentage of Participants				
number (confidence interval 95%)	40 (5.3 to 85.3)			

Notes:

[49] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants with investigator-assessed best response assessed by Objective Response Rate (ORR)

End point title	Part 1: Percentage of participants with investigator-assessed best response assessed by Objective Response Rate (ORR)

End point description:

ORR was defined as the percentage of participants who achieved Complete Remission (CR) or Partial Remission (PR) or Marrow Complete Remission (mCR) or confirmed Hematologic Improvement (HI) prior to new anti-cancer therapy on the All Treated Subjects Population. Participants with Not Evaluable or missing response were treated as non-responders. International Working Group (IWG) criteria, 2006 was used to evaluate response.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[50]			
Units: Percentage of Participants				
number (confidence interval 95%)	20 (0.5 to 71.6)			

Notes:
[50] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Plasma concentration of GSK2879552

End point title	Part 1: Plasma concentration of GSK2879552

End point description:

Blood samples were collected at indicated time points to evaluate concentration of GSK2879552. Each Pharmacokinetic (PK) sample was collected as close as possible to the planned time relative to the dose (i.e., time zero) administered to the participant on PK days. PK Concentration Population consisted of all participants in the All Treated Subject Population for whom a blood samples for pharmacokinetics were obtained and analyzed. 99999 indicates data was not available as standard deviation could not be calculated due to insufficient number of participants. For Cycle 1, Day 1, pre-dose, all concentration values were less than the lower limit of quantification, therefore they have been imputed with 0 because they were so small. Hence, standard deviation was not calculated as it would result to "0" and would be misleading. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Cycle 1, Day 1: pre-dose, 0.5, 1, 3 hour; pre-dose on Days 2,4; Day 7: pre-dose, 0.5, 1, 3 hour; Day 15: pre-dose, 0.5-1 hour post-dose; pre-dose on Day 22; Cycle 2: pre-dose on Days 1, 7, 15, 22; Pre-dose on Day 1 of Cycles 3,4,5 (each cycle of 28 days)

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[51]			
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)				
Cycle 1, Day 1, pre-dose, n=5	0.00 (± 99999)			
Cycle 1, Day 1, 0.5 hour, n=4	11.79 (± 9.270)			
Cycle 1, Day 1, 1 hour, n=5	8.18 (± 4.830)			
Cycle 1, Day 1, 3 hour, n=5	6.40 (± 1.990)			
Cycle 1, Day 2, pre-dose, n=5	1.03 (± 0.409)			
Cycle 1, Day 4, pre-dose, n=5	1.87 (± 0.716)			
Cycle 1, Day 7, pre-dose, n=5	1.97 (± 0.553)			
Cycle 1, Day 7, 0.5 hour, n=5	9.58 (± 8.395)			
Cycle 1, Day 7, 1 hour, n=5	9.17 (± 4.4777)			
Cycle 1, Day 7, 3 hour, n=5	8.58 (± 3.595)			
Cycle 1, Day 15, pre-dose, n=3	2.00 (± 0.798)			
Cycle 1, Day 15, 0.5-1 hour, n=3	13.39 (± 0.798)			
Cycle 1, Day 22, pre-dose, n=3	1.89 (± 0.723)			
Cycle 2, Day 1, pre-dose, n=3	2.16 (± 0.843)			
Cycle 2, Day 7, pre-dose, n=3	1.81 (± 0.585)			

Cycle 2, Day 15, pre-dose, n=3	2.33 (± 1.135)			
Cycle 2, Day 22, pre-dose, n=3	2.11 (± 0.709)			
Cycle 3, Day 1, pre-dose, n=3	1.99 (± 0.802)			
Cycle 4, Day 1, pre-dose, n=2	1.63 (± 0.085)			
Cycle 5, Day 1, pre-dose, n=1	1.97 (± 99999)			

Notes:

[51] - PK Concentration Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Plasma concentration of Azacitidine

End point title	Part 1: Plasma concentration of Azacitidine

End point description:

Blood samples were to be collected at indicated time points to evaluate concentration of Azacitidine. Data was not collected due to blood samples were not collected as participants were not enrolled in GSK2879552 + Azacitidine arm due to early termination of the study.

End point type	Secondary

End point timeframe:

Cycle 1, Day 1: pre-dose, 0.5, 1, 3 hour; pre-dose on Days 2,4; Day 7: pre-dose, 0.5, 1, 3 hour; Day 15: pre-dose, 0.5-1 hour post-dose; pre-dose on Day 22; Cycle 2: pre-dose on Days 1, 7, 15, 22; Pre-dose on Day 1 of Cycles 3,4,5 (each cycle of 28 days)

End point values	Part 1: GSK2879552+ Azacitidine			
Subject group type	Subject analysis set			
Number of subjects analysed	0[52]			
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)	()			

Notes:

[52] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Duration of Response

End point title	Part 1: Duration of Response

End point description:

Duration of response is defined as the subset of participants (responders) who show a response (CR, mCR, PR, or HI), the time from first documented evidence of response until the first documented sign of disease progression or death. If no disease progression or death, the DOR was to be censored at last disease assessment. Data was not collected for this endpoint as DOR could not be calculated because of the early termination of the study did not allow for this endpoint to be observed.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	0[53]			
Units: Weeks				
median (confidence interval 95%)	(to)			

Notes:

[53] - All Treated Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Progression-free Survival

End point title	Part 1: Progression-free Survival

End point description:

Progression-free survival (PFS) is defined as the time from first treatment dose until the first documented sign of disease progression or death. If the participant missed more than one visit prior to the date of documented events, PFS was censored at the last adequate assessment prior to missing. Otherwise, if the participant did not have a documented date of events, PFS was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[54]			
Units: Weeks				
median (confidence interval 95%)	22.4 (4.3 to 22.4)			

Notes:

[54] - All Treated Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Overall Survival

End point title	Part 1: Overall Survival

End point description:

Overall survival (OS) is defined as the time from first treatment dose until death due to any reason. For the analysis of overall survival (OS), 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. 99999 indicates data was not available as the data and very small number of subjects do not allow meaningful calculation of the upper limit of 95% CI.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[55]			
Units: Weeks				
median (confidence interval 95%)	22.4 (16.4 to 99999)			

Notes:

[55] - All Treated Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Proportion of participants with disease progression to Acute Myeloblastic Leukemia (AML)

End point title	Part 1: Proportion of participants with disease progression to Acute Myeloblastic Leukemia (AML)

End point description:

The proportion of participants with disease progression to AML is defined as the percentage of participants experiencing AML on the All Treated Subjects Population.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[56]			
Units: Percentage of Participants	40			

Notes:

[56] - All Treated Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Time to AML progression

End point title	Part 1: Time to AML progression

End point description:

Time to AML progression is defined as the time from first treatment dose until AML progression or crossover if using the All Treated Subjects Population. For the analysis of time to AML, if the participant did not experience AML, time to AML was censored at the last treatment prior to the initiation of anti-cancer therapy or crossover.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[57]			
Units: Weeks				
median (confidence interval 95%)	22.4 (4.3 to 22.4)			

Notes:

[57] - All Treated Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of participants with documented platelet and red blood cell (RBC) transfusions per month

End point title	Part 1: Number of participants with documented platelet and red blood cell (RBC) transfusions per month

End point description:

Number of participants with documented platelet and RBC transfusions have been presented.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Part 1: GSK2879552			
Subject group type	Reporting group			
Number of subjects analysed	5[58]			
Units: Participants				
Platelets transfusion	5			
RBC transfusion	4			
RBC concentrated transfusion	1			

Notes:

[58] - All Treated Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of participants with any AEs and SAEs

End point title	Part 2: Number of participants with any AEs and SAEs

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention or event associated with liver injury and impaired liver function were categorized as SAE. All Treated Subject Population was defined as all participants who received at least one dose of study treatment. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[59]	0[60]		
Units: Participants				

Notes:

[59] - All Treated Subjects Population.

[60] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in Platelets, neutrophils, monocytes, lymphocytes, leucocyte, eosinophils and basophils at indicated time-points

End point title	Part 2: Change from Baseline in Platelets, neutrophils, monocytes, lymphocytes, leucocyte, eosinophils and basophils at indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of hematology parameters including platelets, neutrophils, monocytes, lymphocytes, leucocyte, eosinophils and basophils. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[61]	0[62]		
Units: 10^9 cells per liter				
arithmetic mean (standard deviation)	()	()		

Notes:

[61] - All Treated Subjects Population.

[62] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in MCV at indicated time-points

End point title	Part 2: Change from Baseline in MCV at indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of hematology parameters including MCV. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[63]	0[64]		
Units: Femtoliter				
arithmetic mean (standard deviation)	()	()		

Notes:

[63] - All Treated Subjects Population.

[64] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in MCH at indicated time-points

End point title	Part 2: Change from Baseline in MCH at indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of hematology parameters including MCH. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[65]	0[66]		
Units: Picogram				
arithmetic mean (standard deviation)	()	()		

Notes:

[65] - All Treated Subjects Population.

[66] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in MCHC and Hb at indicated time-points

End point title	Part 2: Change from Baseline in MCHC and Hb at indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of hematology parameters including MCHC and Hb. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[67]	0[68]		
Units: Grams per liter				
arithmetic mean (standard deviation)	()	()		

Notes:

[67] - All Treated Subjects Population.

[68] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in Hematocrit at indicated time-points

End point title	Part 2: Change from Baseline in Hematocrit at indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of hematology parameters including Hematocrit. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. All Treated Subjects Population. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[69]	0[70]		
Units: Proportion of red blood cells in blood				
arithmetic mean (standard deviation)	()	()		

Notes:

[69] - All Treated Subjects Population.

[70] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in erythrocytes at indicated time-points

End point title	Part 2: Change from Baseline in erythrocytes at indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of hematology parameters including erythrocytes. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. All Treated Subjects Population. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[71]	0[72]		
Units: 10^12 cells per Liter				
arithmetic mean (standard deviation)	()	()		

Notes:

[71] - All Treated Subjects Population.

[72] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in percent reticulocytes at indicated time-points

End point title	Part 2: Change from Baseline in percent reticulocytes at

	indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of hematology parameters including percent reticulocytes. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[73]	0[74]		
Units: Percentage of reticulocytes				
arithmetic mean (standard deviation)	()	()		

Notes:

[73] - All Treated Subjects Population.

[74] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in blast/leukocytes at indicated time-points

End point title	Part 2: Change from Baseline in blast/leukocytes at indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of hematology parameters including blast/leukocytes. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[75]	0[76]		
Units: Ratio of blasts to leukocytes				
arithmetic mean (standard deviation)	()	()		

Notes:

[75] - All Treated Subjects Population.

[76] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in ALT, ALP, AST, LDH and GGT at indicated time-points

End point title	Part 2: Change from Baseline in ALT, ALP, AST, LDH and GGT at indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of clinical chemistry parameters including ALT, ALP, AST, LDH and GGT. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[77]	0[78]		
Units: IU/L				
arithmetic mean (standard deviation)	()	()		

Notes:

[77] - All Treated Subjects Population.

[78] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in Calcium, chloride, glucose, potassium, sodium, phosphate and urea nitrogen at indicated time-points

End point title	Part 2: Change from Baseline in Calcium, chloride, glucose, potassium, sodium, phosphate and urea nitrogen at indicated time-points

End point description:

Blood samples were to be collected from participants for evaluation of clinical chemistry parameters including Calcium, chloride, glucose, potassium, sodium, phosphate and urea nitrogen. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[79]	0[80]		
Units: mmol/L				
arithmetic mean (standard deviation)	()	()		

Notes:

[79] - All Treated Subjects Population.

[80] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in Total Bilirubin, Direct Bilirubin, Creatinine and urate at indicated time points

End point title	Part 2: Change from Baseline in Total Bilirubin, Direct Bilirubin, Creatinine and urate at indicated time points

End point description:

Blood samples were to be collected from participants for evaluation of clinical chemistry parameters including Total Bilirubin, Direct Bilirubin, Creatinine and urate. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[81]	0[82]		
Units: umol/L				
arithmetic mean (standard deviation)	()	()		

Notes:

[81] - All Treated Subjects Population.

[82] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in Albumin and Protein at indicated time points

End point title	Part 2: Change from Baseline in Albumin and Protein at indicated time points

End point description:

Blood samples were to be collected from participants for evaluation of clinical chemistry parameters including Albumin and Protein. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[83]	0[84]		
Units: G/L				
arithmetic mean (standard deviation)	()	()		

Notes:

[83] - All Treated Subjects Population.

[84] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in pCO2 at indicated time points

End point title	Part 2: Change from Baseline in pCO2 at indicated time points

End point description:

Blood samples were to be collected from participants for evaluation of clinical chemistry parameters including pCO2. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[85]	0[86]		
Units: Kilopascal				
arithmetic mean (standard deviation)	()	()		

Notes:

[85] - All Treated Subjects Population.

[86] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in SBP and DBP at indicated time-points

End point title	Part 2: Change from Baseline in SBP and DBP at indicated time-points

End point description:

Vital signs including SBP and DBP were to be measured after resting for at least 5 minutes in a semi-supine position. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[87]	0[88]		
Units: Millimeters of mercury				
arithmetic mean (standard deviation)	()	()		

Notes:

[87] - All Treated Subjects Population.

[88] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in heart rate at indicated time-points

End point title	Part 2: Change from Baseline in heart rate at indicated time-points

End point description:

Vital signs including heart rate was to be measured after resting for at least 5 minutes in a semi-supine position. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. All Treated Subjects Population. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[89]	0[90]		
Units: Beats per minute				
arithmetic mean (standard deviation)	()	()		

Notes:

[89] - All Treated Subjects Population.

[90] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in respiratory rate at indicated time-points

End point title	Part 2: Change from Baseline in respiratory rate at indicated time-points

End point description:

Vital signs including respiratory rate was to be measured after resting for at least 5 minutes in a semi-supine position. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[91]	0[92]		
Units: Breaths per minute				
arithmetic mean (standard deviation)	()	()		

Notes:

[91] - All Treated Subjects Population.

[92] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in body temperature at indicated time-points

End point title	Part 2: Change from Baseline in body temperature at indicated time-points

End point description:

Vital signs including body temperature was to be measured after resting for at least 5 minutes in a semi-supine position. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[93]	0[94]		
Units: Celsius				
arithmetic mean (standard deviation)	()	()		

Notes:

[93] - All Treated Subjects Population.

[94] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in ECG mean heart rate at indicated time-points

End point title	Part 2: Change from Baseline in ECG mean heart rate at indicated time-points

End point description:

Single 12-lead ECG was to be obtained at designated time points during the study using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT, and QTc intervals. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[95]	0[96]		
Units: Beats per minute				
arithmetic mean (standard deviation)	()	()		

Notes:

[95] - All Treated Subjects Population.

[96] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in ECG PR interval, QRS duration, QT interval, QTcB and QTcF at indicated time-points

End point title	Part 2: Change from Baseline in ECG PR interval, QRS duration, QT interval, QTcB and QTcF at indicated time-points

End point description:

Single 12-lead ECG was to be obtained at designated time points during the study using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT, and QTc intervals. Baseline was defined as the value obtained prior to first dosing (Day 1). Change from Baseline was to be calculated by subtracting post-dose value from Baseline value. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Baseline and up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[97]	0[98]		
Units: Milliseconds				
arithmetic mean (standard deviation)	()	()		

Notes:

[97] - All Treated Subjects Population.

[98] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of participants with abnormal findings during physical examination

End point title	Part 2: Number of participants with abnormal findings during physical examination

End point description:

A complete physical examination included, at a minimum, assessment of the Cardiovascular, Respiratory, Gastrointestinal and Neurological systems. A brief physical examination included, at a minimum assessments of the skin, lungs, cardiovascular system, and abdomen (liver and spleen). Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[99]	0[100]		
Units: Participants				

Notes:

[99] - All Treated Subjects Population.

[100] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Plasma clearance (CL/F) of GSK2879552

End point title	Part 2: Plasma clearance (CL/F) of GSK2879552

End point description:

Blood samples were to be collected at indicated time points to evaluate CL/F of GSK2879552. Each PK sample was to be collected as close as possible to the planned time relative to the dose (i.e., time zero) administered to the participant on PK days. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Cycle 1, Day 1: pre-dose, 0.5, 1, 3 hour; pre-dose on Day 4; Day 7: pre-dose, 0.5, 1, 3 hour; Day 15: pre-dose, 0.5-1 hour post-dose; pre-dose on Day 22; Cycle 2: pre-dose on Days 1, 7, 15, 22; Pre-dose on Day 1 of Cycles 3 to 1 (each cycle of 28 days)

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[101]	0[102]		
Units: Liters per hour				
arithmetic mean (standard deviation)	()	()		

Notes:

[101] - PK Concentration Population.

[102] - PK Concentration Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Duration of Response

End point title	Part 2: Duration of Response

End point description:

Duration of response is defined as the time from first documented evidence of response until the first documented sign of disease progression or death. If no disease progression or death, the duration of response was to be censored at last disease assessment. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[103]	0[104]		
Units: Weeks				
median (confidence interval 95%)	(to)	(to)		

Notes:

[103] - All Treated Subjects Population.

[104] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Progression-free Survival

End point title	Part 2: Progression-free Survival

End point description:

Progression-free survival is defined as the time from first treatment dose until the first documented sign of disease progression or death. If the participant missed more than one visit prior to the date of documented events, PFS was to be censored at the last adequate assessment prior to missing. Otherwise, if the participant did not have a documented date of events, PFS was to be censored at the date of the last adequate assessment. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[105]	0[106]		
Units: Weeks				
median (confidence interval 95%)	(to)	(to)		

Notes:

[105] - All Treated Subjects Population.

[106] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Overall Survival

End point title	Part 2: Overall Survival

End point description:

Overall survival is defined as the time from first treatment dose until death due to any reason. For the analysis of overall survival, the last date of known contact was to be used for those participants who had not died at the time of analysis; such participants were to be considered censored. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[107]	0[108]		
Units: Weeks				
median (confidence interval 95%)	(to)	(to)		

Notes:

[107] - All Treated Subjects Population.

[108] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of participants with disease progression to AML

End point title	Part 2: Percentage of participants with disease progression to AML

End point description:

The percentage of participants experiencing AML on the All Treated Subjects Population was to be presented. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[109]	0[110]		
Units: Percentage of Participants				

Notes:

[109] - All Treated Subjects Population.

[110] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Time to AML progression

End point title	Part 2: Time to AML progression

End point description:

Time to AML progression is defined as the time from first treatment dose until AML progression or crossover if using the All Treated Subjects Population. For the analysis of time to AML, if the participant did not experience AML, time to AML was to be censored at the last treatment prior to the initiation of anti-cancer therapy or crossover. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[111]	0[112]		
Units: Weeks				
median (confidence interval 95%)	(to)	(to)		

Notes:

[111] - All Treated Subjects Population.

[112] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of participants with documented platelet and red blood cell (RBC) transfusions per month

End point title	Part 2: Number of participants with documented platelet and red blood cell (RBC) transfusions per month

End point description:

Number of participants with documented platelet and RBC transfusions were to be presented. Data was not collected for this endpoint as study was terminated during Part 1 and Part 2 was not initiated.

End point type	Secondary

End point timeframe:

Up to 2.5 years

End point values	Part 2: GSK2879552	Part 2: GSK2879552+ Azacitidine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[113]	0[114]		
Units: Participants				

Notes:

[113] - All Treated Subjects Population.

[114] - All Treated Subjects Population.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and Non-serious adverse events (Non-SAEs) were collected from the start of the study treatment up to Cycle 5 (each cycle of 28 days) in Part 1.

Adverse event reporting additional description:

SAEs and Non-SAEs were reported by treatment for the All Treated Subjects Population which comprised of all participants who received at least one dose of study treatment. Data is presented for Part 1 only as data was not collected in Part 2 due to the study was terminated during Part 1 only, and Part 2 was not initiated.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Part 1: GSK2879552

Reporting group description:

Participants in this monotherapy arm were administered with GSK2879552 0.5 milligrams or 2 milligrams oral capsules once a day as continuous daily dosing in each cycle (of 28 days) until disease progression during Part 1 of the study.

Serious adverse events	Part 1: GSK2879552		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transfusion reaction			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sinusitis			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Part 1: GSK2879552		
Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 5 (100.00%)		
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Oedema subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 3 / 5 (60.00%) 3 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Respiratory, thoracic and mediastinal disorders Dyspnoea exertional subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Insomnia	 1 / 5 (20.00%) 1 		

subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Investigations Weight decreased subjects affected / exposed occurrences (all) White blood cell count decreased subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 2		
Nervous system disorders Balance disorder subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Parosmia subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Increased tendency to bruise subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Dyspepsia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Gingival bleeding subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2		
Blood blister subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Eczema subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Back pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Infections and infestations Fungal infection subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Staphylococcal infection subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Fluid overload			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Tumour lysis syndrome			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 May 2017	Amendment No. 1: Addition of language to include a stopping rule that halts enrollment upon the occurrence of any encephalopathy, unless clearly attributable to central nervous system disease involvement or intercurrent illness. Minor clarifications, correction of typographical errors, reformatting of tables, administrative and grammatical changes to text and Time and Events tables/footnotes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported