



Clinical trial results:

An Open-label, Single-arm, Phase 2 Study to Evaluate Efficacy and Safety of Avapritinib (BLU-285), a Selective KIT Mutation-targeted Tyrosine Kinase Inhibitor, in Patients with Advanced Systemic Mastocytosis

Summary

EudraCT number	2017-004836-13
Trial protocol	NL GB NO DE DK ES PL FR AT IT
Global end of trial date	18 December 2024

Results information

Result version number	v1 (current)
This version publication date	02 January 2026
First version publication date	02 January 2026

Trial information

Trial identification

Sponsor protocol code	BLU-285-2202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03580655
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Blueprint Medicines Corporation
Sponsor organisation address	45 Sidney Street, Cambridge, MA, United States, 02139
Public contact	Medical Information, Blueprint Medicines Corporation, +31 85 064 4001, medinfoeurope@blueprintmedicines.com
Scientific contact	Medical Information, Blueprint Medicines Corporation, +31 85 064 4001, medinfoeurope@blueprintmedicines.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	18 December 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to determine adjudicated overall response rate (ORR) (complete remission [CR], complete remission with partial recovery of peripheral blood counts [CRh], partial remission [PR], or clinical improvement [CI]) based on modified international working group-myeloproliferative neoplasms research and treatment and European competence network on mastocytosis (mIWG-MRT-ECNM) consensus response criteria in participants with advanced systemic mastocytosis (AdvSM) treated with avapritinib.

Protection of trial subjects:

This trial was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2018
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	Canada: 1
Country: Number of subjects enrolled	United States: 45
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	107
EEA total number of subjects	52

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)	37
From 65 to 84 years	67
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The avapritinib group (N=107) includes all participants treated at a starting dose of 200 milligrams (mg) once daily (QD) (N=105) and 2 participants treated at a starting dose of 100 mg QD.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Avapritinib (100 mg)

Arm description:

Avapritinib was administered once daily as an immediate-release tablet, orally, in 28-day cycles.

Arm type	Experimental
Investigational medicinal product name	Avapritinib
Investigational medicinal product code	
Other name	BLU-285
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered as an immediate release tablet for oral administration.

Arm title	Avapritinib (200 mg)
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Arm description:

Avapritinib was administered once daily as an immediate-release tablet, orally, in 28-day cycles.

Arm type	Experimental
Investigational medicinal product name	Avapritinib
Investigational medicinal product code	
Other name	BLU-285
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered as an immediate release tablet for oral administration.

Number of subjects in period 1	Avapritinib (100 mg)	Avapritinib (200 mg)
Started	2	105
Received at Least 1 Dose of Study Drug	2	105
Response-evaluable	2	81
Pure Pathologic Response-evaluable	2	105

Completed	0	0
Not completed	2	105
Adverse event, serious fatal	1	33
Physician decision	-	5
Consent withdrawn by subject	-	19
Sponsor Decision	1	43
Participant Non-compliance	-	2
Intracranial Haemorrhage	-	1
Lost to follow-up	-	1
Disease Progression	-	1

Baseline characteristics

Reporting groups

Reporting group title	Avapritinib (100 mg)
Reporting group description:	
Avapritinib was administered once daily as an immediate-release tablet, orally, in 28-day cycles.	
Reporting group title	Avapritinib (200 mg)
Reporting group description:	
Avapritinib was administered once daily as an immediate-release tablet, orally, in 28-day cycles.	

Reporting group values	Avapritinib (100 mg)	Avapritinib (200 mg)	Total
Number of subjects	2	105	107
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	36	37
From 65-84 years	1	66	67
85 years and over	0	3	3
Sex: Female, Male			
Units:			
Female	1	44	45
Male	1	61	62
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	2	2
Not Hispanic or Latino	2	89	91
Unknown or Not Reported	0	14	14
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	2	89	91
More than one race	0	0	0
Unknown or Not Reported	0	15	15

End points

End points reporting groups

Reporting group title	Avapritinib (100 mg)
Reporting group description: Avapritinib was administered once daily as an immediate-release tablet, orally, in 28-day cycles.	
Reporting group title	Avapritinib (200 mg)
Reporting group description: Avapritinib was administered once daily as an immediate-release tablet, orally, in 28-day cycles.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description: All participants who received ≥ 1 dose of avapritinib.	
Subject analysis set title	Response-evaluable (RE) Population
Subject analysis set type	Full analysis
Subject analysis set description: All participants who received ≥ 1 dose of avapritinib, were deemed evaluable per mIWG-MRT-ECNM criteria at baseline as assessed by study steering committee review (SSC) and had 1 of the following conditions: ≥ 2 complete postbaseline bone marrow assessments and had been on study for ≥ 6 cycles; had an end of study visit.	
Subject analysis set title	Pure Pathologic Response-evaluable (PPRE) Population
Subject analysis set type	Full analysis
Subject analysis set description: All participants who received ≥ 1 dose of avapritinib and had 1 of the following conditions: ≥ 2 complete postbaseline bone marrow assessments and had been on study for ≥ 6 cycles; had an end of study visit.	
Subject analysis set title	Pharmacokinetic Population
Subject analysis set type	Sub-group analysis
Subject analysis set description: All participants who received ≥ 1 dose of avapritinib and had had >3 post-dose concentrations collected.	

Primary: ORR Based on mIWG-MRT-ECNM Response Criteria

End point title	ORR Based on mIWG-MRT-ECNM Response Criteria ^[1]
End point description: ORR was defined as percentage of participants with a confirmed best response of CR, CRh, PR, or CI by mIWG-MRT-ECNM criteria. The mIWG-MRT-ECNM criteria were based on findings from bone marrow biopsy and aspirate, and peripheral blood smear; bone marrow cytogenetics; other extracutaneous tissue biopsies (when available); liver and spleen imaging; and other clinical and laboratory parameters. Statistical test on binomial proportion of ORR against a null hypothesis of 28%, 1 sided alpha=0.025, gave $p < 0.0001$ (Wald test).	
End point type	Primary
End point timeframe: Baseline through Month 65	

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: Only descriptive statistics (percentage of participants plus confidence interval) are reported for this primary end point, as prespecified in the statistical analysis plan.

End point values	Response-evaluable (RE) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	83			
Units: Percentage of Participants				
number (confidence interval 95%)	73.5 (62.7 to 82.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Advanced Systemic Mastocytosis-Symptom Assessment Form (AdvSM-SAF) Total Symptom Score (TTS)

End point title	Mean Change From Baseline in Advanced Systemic Mastocytosis-Symptom Assessment Form (AdvSM-SAF) Total Symptom Score (TTS)
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End point description:

The AdvSM-SAF is a 10-item questionnaire that assesses eight symptoms specific to AdvSM. All eight symptoms are scored on a scale of 0 (absence of symptoms) to 10 (more severe symptoms) (up to 80 points maximum). Each symptom contributes to the TSS equally. The TSS was generated based on average scores for each 7-day period. An increase in score from 0 (no symptoms) to 80 (worst symptoms represents a worse symptoms outcome. Participants completed the AdvSM-SAF daily using an electronic diary (eDiary). Here, 'Number of Subjects Analyzed' signifies those participants evaluable for this end point at the specified time points. Each cycle is 28 days long.

End point type	Secondary
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End point timeframe:

Baseline up to Month 6 (Cycle 6, Day 1)

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	92			
Units: Score on a Scale				
arithmetic mean (standard deviation)	-6.40 (± 9.158)			

Statistical analyses

No statistical analyses for this end point

Secondary: ORR Based on mIWG-MRT-ECNM Response Criteria as Assessed by Local Investigator

End point title	ORR Based on mIWG-MRT-ECNM Response Criteria as Assessed by Local Investigator
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End point description:

Due to the complexity of response evaluation according to the mIWG-MRT-ECNM criteria, data analysis was not carried out. Summary-level data not available as data analysis was not performed.

End point type	Secondary
End point timeframe:	
Baseline through Month 48	

End point values	Response-evaluable (RE) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	0 ^[2]			
Units: Percentage of Participants				
number (confidence interval 95%)	(to)			

Notes:

[2] - Due to the complexity of response evaluation data analysis was not carried out.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)
End point description:	
DOR was defined as the time from initial documentation of a CI or better to the time of initial documentation of confirmed progressive disease (PD) or death due to any cause, whichever occurred first. For responders who had not progressed or died at the time of analysis, DOR was censored at the last response assessment that was stable disease (SD) or better. Here, 'Number of subjects analysed' signifies those participants with a confirmed best response of CR, CRh, PR, and CI by mIWG-MRT-ECNM criteria. '9999' = Values were non-estimable (insufficient number of participants with events).	
End point type	Secondary
End point timeframe:	
Baseline through Month 65	

End point values	Response-evaluable (RE) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: Months				
median (confidence interval 95%)	57.8 (46.1 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time-to-Response (TTR)

End point title	Time-to-Response (TTR)
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End point description:

TTR was defined as the time from first dose to the time of initial evaluation of clinical improvement (CI) or better. Here, 'Number of subjects analysed' signifies those participants with a confirmed best response of CR, CRh, PR and CI by mIWG-MRT-ECNM criteria.

End point type	Secondary
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End point timeframe:

Baseline through Month 65

End point values	Response-evaluable (RE) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: Months				
median (full range (min-max))	2.30 (0.3 to 20.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate

End point title	Objective Response Rate
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End point description:

The objective response rate was defined as the number of participants with a confirmed best response of morphologic complete remission (mCR), morphologic complete remission with partial recovery of peripheral blood counts (mCRh), or morphologic partial remission (mPR) by pure pathologic response (PPR) criteria. The PPR criteria are a modification of the mIWG-MRT-ECNM criteria that define deep responses where direct measure of the disease burden determined the response and focus on objective changes (bone marrow mast cell burden, serum tryptase, and complete blood count).

End point type	Secondary
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End point timeframe:

Baseline through Month 65

End point values	Pure Pathologic Response-evaluable (PPRE) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	107			
Units: Percentage of Participants				
number (confidence interval 95%)	73.8 (64.4 to 81.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)
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End point description:

PFS was defined as time from first dose to the time of initial documentation of confirmed PD or death due to any cause, whichever occurred first. Participants who had not progressed or died at the time of analysis were censored at the last response assessment that was SD or better. '9999' = Values were non-estimable (insufficient number of participants with events).

End point type	Secondary
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End point timeframe:

Baseline through Month 65

End point values	Response-evaluable (RE) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	83			
Units: Months				
median (confidence interval 95%)	51.3 (38.7 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

OS was defined as time from first dose to the time of death due to any cause. Participants who were known to be alive or are lost to follow-up were censored at the last time point they were known to be alive. '9999' = Values were non-estimable (insufficient number of participants with events).

End point type	Secondary
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End point timeframe:

Baseline through Month 65

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	107			
Units: Months				
median (confidence interval 95%)	61.6 (60.1 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate

End point title	Clinical Benefit Rate
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End point description:

The clinical benefit rate was defined as the percentage of participants with a confirmed best response of CR, CRh, PR, CI, and SD by mIWG-MRT-ECNM criteria.

End point type	Secondary
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End point timeframe:

Baseline through Month 65

End point values	Response-evaluable (RE) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	83			
Units: Percentage of Participants				
number (confidence interval 95%)	89.2 (80.4 to 94.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Bone Marrow Mast Cells

End point title	Percent Change From Baseline in Bone Marrow Mast Cells
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End point description:

Bone marrow biopsies and aspirates and peripheral blood smears were obtained for systemic mastocytosis response assessment according to mIWG-MRT-ECNM criteria. Here, 'Number of subjects analysed' signifies those participants evaluable for this end point at the specified timepoint. Each cycle is 28 days long.

End point type	Secondary
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End point timeframe:

Baseline up to Month 65

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	84			
Units: Percent Change				
arithmetic mean (standard deviation)				
Cycle 3, Day 1 (N=84)	-63.74 (± 39.445)			
Cycle 7, Day 1 (N=84)	-71.12 (± 35.602)			
Cycle 11, Day 1 (N=69)	-73.10 (± 49.885)			
Cycle 17, Day 1 (N=61)	-81.33 (± 32.377)			
Cycle 23, Day 1 (N=54)	-80.84 (± 29.283)			
Cycle 29, Day 1 (N=40)	-78.90 (± 29.181)			
Cycle 35, Day 1 (N=34)	-83.53 (± 28.316)			
Cycle 41, Day 1 (N=25)	-83.32 (± 21.374)			
Cycle 47, Day 1 (N=19)	-81.38 (± 21.656)			
Cycle 53, Day 1 (N=16)	-75.83 (± 29.094)			
Cycle 59, Day 1 (N=10)	-79.55 (± 21.921)			
Cycle 65, Day 1 (N=3)	-68.03 (± 26.781)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Serum Tryptase

End point title	Percent Change From Baseline in Serum Tryptase
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End point description:

Blood samples were collected to characterize the change in serum tryptase concentration during treatment with avapritinib. Here, 'Number of subjects analysed' signifies those participants evaluable for this end point at the specified timepoint. Each cycle is 28 days long.

End point type	Secondary
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End point timeframe:

Baseline up to Month 65

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	98			
Units: Percent Change				
arithmetic mean (standard deviation)				
Cycle 1, Day 15 (N=98)	-64.54 (± 41.191)			
Cycle 2, Day 1 (N=96)	-68.54 (± 42.091)			
Cycle 3, Day 1 (N=89)	-71.76 (± 40.023)			
Cycle 7, Day 1 (N=75)	-75.18 (± 45.822)			
Cycle 11, Day 1 (N=77)	-78.69 (± 36.038)			
Cycle 17, Day 1 (N=67)	-85.22 (± 26.070)			
Cycle 23, Day 1 (N=58)	-85.61 (± 30.510)			
Cycle 29, Day 1 (N=48)	-83.50 (± 40.716)			
Cycle 35, Day 1 (N=43)	-83.39 (± 45.603)			
Cycle 41, Day 1 (N=40)	-90.64 (± 14.206)			
Cycle 47, Day 1 (N=33)	-90.64 (± 12.581)			
Cycle 53, Day 1 (N=25)	-68.65 (± 85.482)			
Cycle 59, Day 1 (N=13)	-92.23 (± 6.8211)			
Cycle 65, Day 1 (N=5)	-82.01 (± 14.529)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in V-kit Hardy-Zuckerman 4 Feline Sarcoma Viral Oncogene Homolog Aspartate 816 Valine (KIT D816V) Mutation Burden

End point title	Percent Change From Baseline in V-kit Hardy-Zuckerman 4 Feline Sarcoma Viral Oncogene Homolog Aspartate 816 Valine (KIT D816V) Mutation Burden
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End point description:

Bone marrow aspirate and PB samples were collected to characterize the KIT D816V mutation allele fraction. Here, 'Number of subjects analysed' signifies those participants evaluable for this end point at the specified timepoint. Each cycle is 28 days long.

End point type	Secondary
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End point timeframe:

Baseline up to Month 65

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	97			
Units: Percent Change				
arithmetic mean (standard deviation)				
Cycle 1, Day 15 (N=92)	-14.65 (± 21.049)			
Cycle 2, Day 1 (N=87)	-41.68 (± 23.171)			
Cycle 3, Day 1 (N=97)	-54.32 (± 31.272)			
Cycle 7, Day 1 (N=85)	-65.46 (± 32.953)			
Cycle 11, Day 1 (N=85)	-67.77 (± 30.802)			
Cycle 17, Day 1 (N=72)	-77.25 (± 26.783)			
Cycle 23, Day 1 (N=63)	-77.09 (± 29.838)			
Cycle 29, Day 1 (N=52)	-80.97 (± 29.775)			
Cycle 35, Day 1 (N=39)	-81.93 (± 31.110)			
Cycle 41, Day 1 (N=41)	-85.31 (± 24.911)			
Cycle 47, Day 1 (N=31)	-81.76 (± 28.490)			
Cycle 53, Day 1 (N=25)	-76.27 (± 34.561)			
Cycle 59, Day 1 (N=10)	-64.42 (± 37.677)			
Cycle 65, Day 1 (N=5)	-47.58 (± 47.893)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Liver Volume by Imaging

End point title	Percent Change From Baseline in Liver Volume by Imaging
End point description: Assessment of liver volume was performed using serial imaging with magnetic resonance imaging (MRI). Response was defined as resolution of palpable hepatomegaly (CR). Here, 'Number of subjects analysed' signifies those participants evaluable for this end point at the specified timepoint. Each cycle is 28 days long.	
End point type	Secondary
End point timeframe: Baseline up to Month 65	

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: Percent Change				
arithmetic mean (standard deviation)				
Cycle 3, Day 1 (N=85)	-12.45 (± 10.103)			
Cycle 7, Day 1 (N=69)	-18.53 (± 12.376)			
Cycle 11, Day 1 (N=74)	-22.07 (± 11.603)			
Cycle 17, Day 1 (N=63)	-27.92 (± 11.949)			
Cycle 23, Day 1 (N=57)	-29.50 (± 12.983)			
Cycle 29, Day 1 (N=45)	-29.84 (± 13.588)			
Cycle 35, Day 1 (N=36)	-29.81 (± 16.764)			
Cycle 41, Day 1 (N=36)	-31.77 (± 16.694)			
Cycle 47, Day 1 (N=30)	-34.31 (± 13.973)			
Cycle 53, Day 1 (N=20)	-35.86 (± 14.147)			
Cycle 59, Day 1 (N=11)	-31.74 (± 18.020)			
Cycle 65, Day 1 (N=4)	-26.88 (± 21.594)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Spleen Volume by Imaging

End point title	Percent Change From Baseline in Spleen Volume by Imaging
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End point description:

Assessment of spleen volume was performed using serial imaging with MRI. Response was defined as ≥35% reduction in spleen volume (PR) or resolution of palpable splenomegaly (CR). Here, 'Number of subjects analysed' signifies those participants evaluable for this end point at the specified timepoint. Each cycle is 28 days long.

End point type	Secondary
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End point timeframe:

Baseline up to Month 65

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	84			
Units: Percent Change				
arithmetic mean (standard deviation)				
Cycle 3, Day 1 (N=84)	-28.47 (± 26.817)			
Cycle 7, Day 1 (N=67)	-35.77 (± 26.770)			
Cycle 11, Day 1 (N=73)	-38.71 (± 28.700)			
Cycle 17, Day 1 (N=62)	-47.53 (± 23.957)			
Cycle 23, Day 1 (N=56)	-44.89 (± 24.377)			
Cycle 29, Day 1 (N=44)	-44.30 (± 32.952)			
Cycle 35, Day 1 (N=36)	-45.00 (± 32.274)			
Cycle 41, Day 1 (N=36)	-51.33 (± 25.812)			
Cycle 47, Day 1 (N=30)	-52.45 (± 24.580)			
Cycle 53, Day 1 (N=20)	-42.85 (± 45.498)			
Cycle 59, Day 1 (N=11)	-40.35 (± 28.396)			
Cycle 65, Day 1 (N=4)	-40.27 (± 11.884)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in AdvSM-SAF Skin and Gastrointestinal Domain Scores at Month 10

End point title	Mean Change from Baseline in AdvSM-SAF Skin and Gastrointestinal Domain Scores at Month 10
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End point description:

The AdvSM-SAF is a 10-item questionnaire that assesses symptoms and functional domains specific to AdvSM. Eight symptoms are scored on a scale of 0 to 10 for severity and 2 symptoms (vomiting and diarrhoea) are scored for number of episodes. Skin and gastrointestinal domain scores were generated based on average scores for each 7-day period. An increase in score represents a worse symptoms outcome. Participants completed the AdvSM-SAF daily using an e-Diary. Here, 'Number of subjects analysed' signifies those participants evaluable for this end point at the specified time points.

End point type	Secondary
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End point timeframe:

Baseline, Month 10

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	93			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Skin Domain	-2.52 (± 5.362)			
Gastrointestinal Domain	-2.81 (± 5.172)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in AdvSM-SAF Individual Symptom Scores at Month 10

End point title	Mean Change from Baseline in AdvSM-SAF Individual Symptom Scores at Month 10
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End point description:

The AdvSM-SAF is a 10-item questionnaire that assesses symptoms and functional domains specific to AdvSM. Individual symptom scores are generated based on average scores for each 7-day period. Eight symptoms are scored on a scale of 0 to 10 for severity and 2 symptoms (vomiting and diarrhoea) are scored for number of episodes. An increase in score represents a worse symptoms outcome. Participants completed the AdvSM-SAF daily using an eDiary. Here, 'Number of subjects analysed' signifies those participants evaluable for this end point (at the specified time points).

End point type	Secondary
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End point timeframe:

Baseline, Month 10

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	93			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Fatigue	-1.12 (± 2.836)			
Spots	-0.80 (± 2.099)			
Itching	-0.94 (± 2.302)			
Flushing	-0.78 (± 2.351)			
Abdominal Pain	-1.51 (± 2.439)			
Nausea	-0.75 (± 1.723)			
Vomiting Severity	-0.03 (± 1.004)			
Diarrhoea Severity	-0.53 (± 1.970)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Global Impression of Symptom Severity (PGIS)

End point title	Change From Baseline in Patient's Global Impression of Symptom Severity (PGIS)
End point description: The PGIS is a single-item scale that assesses a participant's perception of disease symptoms at a point in time. Scores range from 0 to 4 points, with higher values representing worse symptom outcomes. It is widely used to evaluate a participant's overall sense of whether a treatment has been beneficial. Here, 'Number of subjects analysed' signifies those participants evaluable for this end point at the specified timepoint. Each cycle is 28 days long.	
End point type	Secondary
End point timeframe: Baseline up to Month 65	

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	87			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Cycle 1, Day 15 (N=87)	-0.7 (± 1.23)			
Cycle 2, Day 1 (N=82)	-0.9 (± 1.24)			
Cycle 3, Day 1 (N=85)	-1.0 (± 1.20)			
Cycle 5, Day 1 (N=73)	-1.0 (± 1.32)			
Cycle 7, Day 1 (N=71)	-1.1 (± 1.46)			
Cycle 9, Day 1 (N=65)	-1.3 (± 1.50)			
Cycle 11, Day 1 (N=67)	-1.3 (± 1.36)			
Cycle 14, Day 1 (N=56)	-1.4 (± 1.65)			
Cycle 17, Day 1 (N=56)	-1.5 (± 1.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)

End point title	Change From Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC
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End point description:

Quality of life was assessed using EORTC QLQ-C30, which is a 30-item questionnaire that includes 5 functional domains (physical, cognitive, role, emotional, and social) and a global health status scale. Twenty-eight questions are scored from 1 (not at all) to 4 (very much), while the other 2 are scored from 1 (very poor) to 7 (excellent). The calculated average is standardized using a linear transformation to a standardized scale of 0 to 100, with a decrease in score representing a decrease in quality of life. Here, 'Number of subjects analysed' signifies those participants evaluable for this end point at the specified timepoint. Each cycle is 28 days long.

End point type	Secondary
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End point timeframe:

Baseline up to Month 65

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	87			
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Cycle 1, Day 15 (N=87)	14.66 (± 23.397)			
Cycle 2, Day 1 (N=82)	14.33 (± 24.855)			
Cycle 3, Day 1 (N=85)	15.00 (± 28.516)			
Cycle 5, Day 1 (N=73)	14.04 (± 30.042)			
Cycle 7, Day 1 (N=71)	15.85 (± 30.575)			
Cycle 9, Day 1 (N=65)	17.95 (± 29.801)			
Cycle 11, Day 1 (N=67)	18.78 (± 28.179)			
Cycle 14, Day 1 (N=56)	22.32 (± 31.346)			
Cycle 17, Day 1 (N=57)	21.49 (± 29.207)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (C_{max}) of a Single Dose of Avapritinib

End point title	Maximum Plasma Concentration (C _{max}) of a Single Dose of Avapritinib
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End point description:

Blood samples were collected at specified timepoints. Results reported as nanograms/millilitre (ng/mL).

End point type	Secondary
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End point timeframe:

Up to 4 hours post dose on Day 1 of Cycle 1 (28 days/cycle)

End point values	Pharmacokinetic Population			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: ng/mL				
arithmetic mean (full range (min-max))	191 (191 to 191)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Treatment-emergent Adverse Events (TEAE)

End point title	Number of Participants Experiencing Treatment-emergent Adverse Events (TEAE)
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End point description:

A TEAE was defined as any adverse events that occurred between the first dose of a study drug through 30 days after the last dose of any study drug. A summary of all Serious Adverse Events and Non Serious Adverse Events regardless of causality is located in the 'Adverse Events' Section.

End point type	Secondary
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End point timeframe:

Baseline through Month 65

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	107			
Units: Participants	107			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation Between TSS and Serum Tryptase

End point title	Correlation Between TSS and Serum Tryptase
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End point description:

The change in baseline for AdvSM-SAF TSS was correlated with the change in baseline for serum tryptase. Spearman correlation coefficients were performed with corresponding scatter plots on change from baseline.

End point type	Secondary
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End point timeframe:

Baseline, Month 65

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	107			
Units: Spearman Coefficient				
number (not applicable)	0.1043			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 through Month 65

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Avapritinib
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Reporting group description:

Avapritinib was administered once daily as an immediate-release tablet, orally, in 28-day cycles.

Serious adverse events	Avapritinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	69 / 107 (64.49%)		
number of deaths (all causes)	34		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Papillary thyroid cancer			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bladder cancer			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angiosarcoma			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Angiodysplasia			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphangiectasia			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration			

site conditions			
Disease progression			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Pyrexia			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Thoracic haemorrhage			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary mass			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pneumothorax			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemothorax			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchial haemorrhage			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bipolar disorder			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Investigations			

Haemoglobin decreased			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic enzyme increased			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Procedural haemorrhage			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Procedural nausea			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Post procedural hypotension subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haematuria subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis radiation subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radiation proctitis subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Acute myocardial infarction			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	3 / 107 (2.80%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Atrial fibrillation			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery dissection			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Cognitive disorder			
subjects affected / exposed	4 / 107 (3.74%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			

subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Polyneuropathy			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorder			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dementia			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Haemorrhagic diathesis			

subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	3 / 107 (2.80%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Mast cell activation syndrome			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	4 / 107 (3.74%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dysphagia			

subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intra-abdominal haemorrhage			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Small intestinal obstruction			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatic fistula			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphangiectasia intestinal			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			

subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus paralytic			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis erosive			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Acute cholecystitis necrotic			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Budd-Chiari syndrome			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			

subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin lesion			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Hypertonic bladder			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Chronic kidney disease			
subjects affected / exposed	3 / 107 (2.80%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	3 / 107 (2.80%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	1 / 2		
Nephrolithiasis			
subjects affected / exposed	4 / 107 (3.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Obstructive nephropathy			

subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diverticulitis intestinal perforated			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	2 / 107 (1.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	3 / 107 (2.80%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	3 / 107 (2.80%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	4 / 107 (3.74%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
COVID-19			

subjects affected / exposed	4 / 107 (3.74%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	3 / 107 (2.80%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Fournier's gangrene				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Gastroenteritis astroviral				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				

subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Appendiceal abscess				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	2 / 107 (1.87%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 107 (1.87%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	2 / 107 (1.87%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	2 / 107 (1.87%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	2 / 107 (1.87%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Groin abscess				

subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intervertebral discitis				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Parapharyngeal space infection				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paraspinal abscess				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Septic endocarditis				
subjects affected / exposed	1 / 107 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Septic shock				

subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Spontaneous bacterial peritonitis			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stoma site cellulitis			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Submandibular abscess			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection bacterial			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			

subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 107 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 107 (0.93%)		
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	Avapritinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 107 (99.07%)		
Vascular disorders			
Flushing			
subjects affected / exposed	6 / 107 (5.61%)		
occurrences (all)	9		
Hypertension			
subjects affected / exposed	7 / 107 (6.54%)		
occurrences (all)	16		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	49 / 107 (45.79%)		
occurrences (all)	73		
Fatigue			
subjects affected / exposed	24 / 107 (22.43%)		
occurrences (all)	33		
Face oedema			
subjects affected / exposed	18 / 107 (16.82%)		
occurrences (all)	19		
Asthenia			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Swelling face</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oedema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>13 / 107 (12.15%)</p> <p>27</p> <p>9 / 107 (8.41%)</p> <p>11</p> <p>7 / 107 (6.54%)</p> <p>9</p> <p>6 / 107 (5.61%)</p> <p>6</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Pleural effusion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 107 (5.61%)</p> <p>6</p> <p>7 / 107 (6.54%)</p> <p>10</p> <p>12 / 107 (11.21%)</p> <p>38</p> <p>20 / 107 (18.69%)</p> <p>25</p>		
<p>Psychiatric disorders</p> <p>Confusional state</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 107 (5.61%)</p> <p>8</p> <p>9 / 107 (8.41%)</p> <p>9</p>		
<p>Investigations</p> <p>Blood alkaline phosphatase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood creatinine increased</p>	<p>17 / 107 (15.89%)</p> <p>22</p>		

subjects affected / exposed	16 / 107 (14.95%)		
occurrences (all)	19		
Blood bilirubin increased			
subjects affected / exposed	15 / 107 (14.02%)		
occurrences (all)	38		
Weight increased			
subjects affected / exposed	15 / 107 (14.02%)		
occurrences (all)	29		
Neutrophil count decreased			
subjects affected / exposed	14 / 107 (13.08%)		
occurrences (all)	85		
Platelet count decreased			
subjects affected / exposed	17 / 107 (15.89%)		
occurrences (all)	82		
White blood cell count decreased			
subjects affected / exposed	12 / 107 (11.21%)		
occurrences (all)	57		
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 107 (9.35%)		
occurrences (all)	15		
Gamma-glutamyltransferase increased			
subjects affected / exposed	9 / 107 (8.41%)		
occurrences (all)	16		
Alanine aminotransferase increased			
subjects affected / exposed	8 / 107 (7.48%)		
occurrences (all)	9		
Blood lactate dehydrogenase increased			
subjects affected / exposed	8 / 107 (7.48%)		
occurrences (all)	8		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	10 / 107 (9.35%)		
occurrences (all)	11		
Nervous system disorders			

Paraesthesia			
subjects affected / exposed	6 / 107 (5.61%)		
occurrences (all)	7		
Taste disorder			
subjects affected / exposed	8 / 107 (7.48%)		
occurrences (all)	9		
Disturbance in attention			
subjects affected / exposed	8 / 107 (7.48%)		
occurrences (all)	8		
Memory impairment			
subjects affected / exposed	10 / 107 (9.35%)		
occurrences (all)	12		
Dysgeusia			
subjects affected / exposed	10 / 107 (9.35%)		
occurrences (all)	13		
Dizziness			
subjects affected / exposed	13 / 107 (12.15%)		
occurrences (all)	16		
Headache			
subjects affected / exposed	16 / 107 (14.95%)		
occurrences (all)	23		
Cognitive disorder			
subjects affected / exposed	19 / 107 (17.76%)		
occurrences (all)	31		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	56 / 107 (52.34%)		
occurrences (all)	205		
Neutropenia			
subjects affected / exposed	25 / 107 (23.36%)		
occurrences (all)	131		
Leukopenia			
subjects affected / exposed	9 / 107 (8.41%)		
occurrences (all)	32		
Thrombocytopenia			

subjects affected / exposed	48 / 107 (44.86%)		
occurrences (all)	282		
Eye disorders			
Periorbital oedema			
subjects affected / exposed	46 / 107 (42.99%)		
occurrences (all)	79		
Eyelid oedema			
subjects affected / exposed	14 / 107 (13.08%)		
occurrences (all)	15		
Lacrimation increased			
subjects affected / exposed	8 / 107 (7.48%)		
occurrences (all)	9		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	38 / 107 (35.51%)		
occurrences (all)	62		
Nausea			
subjects affected / exposed	29 / 107 (27.10%)		
occurrences (all)	36		
Vomiting			
subjects affected / exposed	25 / 107 (23.36%)		
occurrences (all)	30		
Abdominal pain			
subjects affected / exposed	16 / 107 (14.95%)		
occurrences (all)	22		
Constipation			
subjects affected / exposed	16 / 107 (14.95%)		
occurrences (all)	20		
Dyspepsia			
subjects affected / exposed	9 / 107 (8.41%)		
occurrences (all)	10		
Ascites			
subjects affected / exposed	7 / 107 (6.54%)		
occurrences (all)	14		
Abdominal distension			

subjects affected / exposed	6 / 107 (5.61%)		
occurrences (all)	6		
Abdominal pain upper			
subjects affected / exposed	6 / 107 (5.61%)		
occurrences (all)	10		
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 107 (5.61%)		
occurrences (all)	6		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	7 / 107 (6.54%)		
occurrences (all)	10		
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	8 / 107 (7.48%)		
occurrences (all)	8		
Rash			
subjects affected / exposed	18 / 107 (16.82%)		
occurrences (all)	24		
Hair colour changes			
subjects affected / exposed	18 / 107 (16.82%)		
occurrences (all)	19		
Pruritus			
subjects affected / exposed	19 / 107 (17.76%)		
occurrences (all)	35		
Rash maculo-papular			
subjects affected / exposed	6 / 107 (5.61%)		
occurrences (all)	6		
Petechiae			
subjects affected / exposed	6 / 107 (5.61%)		
occurrences (all)	6		
Alopecia			
subjects affected / exposed	12 / 107 (11.21%)		
occurrences (all)	12		
Musculoskeletal and connective tissue disorders			

Neck pain subjects affected / exposed occurrences (all)	6 / 107 (5.61%) 6		
Bone pain subjects affected / exposed occurrences (all)	8 / 107 (7.48%) 9		
Back pain subjects affected / exposed occurrences (all)	9 / 107 (8.41%) 9		
Pain in extremity subjects affected / exposed occurrences (all)	14 / 107 (13.08%) 19		
Arthralgia subjects affected / exposed occurrences (all)	28 / 107 (26.17%) 45		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	20 / 107 (18.69%) 23		
Urinary tract infection subjects affected / exposed occurrences (all)	14 / 107 (13.08%) 33		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	7 / 107 (6.54%) 8		
Herpes zoster subjects affected / exposed occurrences (all)	6 / 107 (5.61%) 7		
Metabolism and nutrition disorders Hyperuricaemia subjects affected / exposed occurrences (all)	14 / 107 (13.08%) 19		
Hypophosphataemia subjects affected / exposed occurrences (all)	9 / 107 (8.41%) 11		
Hypomagnesaemia			

subjects affected / exposed	6 / 107 (5.61%)		
occurrences (all)	8		
Hypokalaemia			
subjects affected / exposed	8 / 107 (7.48%)		
occurrences (all)	13		
Hypocalcaemia			
subjects affected / exposed	7 / 107 (6.54%)		
occurrences (all)	10		
Folate deficiency			
subjects affected / exposed	6 / 107 (5.61%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2018	<ul style="list-style-type: none">- Based on new safety and efficacy data from Phase 1 study BLU 285-2101, starting dose of avapritinib was reduced from 300 mg QD to 200 mg QD- Dosing guidelines were updated to include information regarding dose reduction in the event of toxicity, with the lowest permitted dose being 50 mg QD- Exclusion criteria added to clarify participant eligibility requirements and confirmation of diagnosis- Option to use archival samples for bone marrow (BM) biopsy was removed- Intensive pharmacokinetics (PK) sampling in a subset of participants was removed- Clarification of the study steering SSC's adjudicated review process added- Study objectives and efficacy endpoints were updated to reflect that mean change from baseline in AdvSM-SAF TSS and mean change from baseline in AdvSM-SAF domain and individual symptom scores will be assessed, rather than mean percent reduction from baseline.
18 June 2019	<ul style="list-style-type: none">- Enrollment was expanded to include participants with AdvSM (aggressive systemic mastocytosis or systemic mastocytosis with an associated hematologic neoplasm) but lacking an evaluable C-finding at baseline in Cohort 2 based on SSC review- An interim analysis was added for efficacy- To manage thrombocytopenia and bleeding risk, participants with platelets < 25,000/microlitre (µL) at baseline were excluded from study, starting dose of avapritinib was changed to 100 mg for participants with 25,000 to 50,000/µL platelets, and the following was introduced: new dose modifications for severe thrombocytopenia, new precautions around concomitant coagulopathy, and use of antithrombotic and anticoagulant therapy and increased monitoring for risk factors and signs and symptoms of intracranial bleeding;- An exploratory objective of assessing platelet aggregation defects as potential mechanisms for bleeding events was added- Intensive PK sampling for a subset of up to 15 participants was added- Dose reduction to 25 mg QD daily is now permitted in the event of toxicity- Requirement for prolonged washout period prior to bone marrow assessment was removed for participants with PD
24 October 2019	<ul style="list-style-type: none">- To reduce the incidence of participants experiencing severe thrombocytopenia, the following changes were introduced:<ul style="list-style-type: none">* Participants with any degree of thrombocytopenia at Screening had to repeat a complete blood count (CBC) with differential twice before study drug initiation* Participants with platelets < 50,000/µL within 28 days before dosing or requiring platelet transfusion were excluded. Participants enrolled before Protocol Amendment 5 were allowed to continue on study if they benefited from treatment.* Dose modification guidance for thrombocytopenia was updated, CBC monitoring on study was increased to at least every cycle, and coagulation studies were updated to include fibrinogen and increased monitoring of coagulation.
28 February 2020	<ul style="list-style-type: none">- Participants who experienced intracranial bleeding had to permanently discontinue treatment- Inclusion criterion #5 was clarified. To be eligible in Cohort 1, participants had to have documented mast cell aggregates in BM and/or other extracutaneous organs and had to be willing to have follow-up biopsies of other affected organs.
21 April 2020	<ul style="list-style-type: none">- Definition of the RE population was clarified

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported