



Clinical trial results:

Open-Label, Single Arm, Phase 3b, Multi-Center Study Evaluating the Impact of Venetoclax on the Quality of Life of Relapsed/Refractory Subjects with Chronic Lymphocytic Leukemia (CLL) (VENICE II)

Summary

EudraCT number	2016-001097-15
Trial protocol	HU PL BG
Global end of trial date	29 December 2021

Results information

Result version number	v1
This version publication date	06 January 2023
First version publication date	06 January 2023

Trial information

Trial identification

Sponsor protocol code	M15-889
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02980731
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road,, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.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	29 December 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this open-label, single-arm study was to evaluate the impact of venetoclax on the quality of life of participants including those with relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL; a type of cancer affecting the blood and the bone marrow) with or without the 17p deletion or TP53 mutation, including participants with an unknown status, as well as R/R CLL participants who had been previously treated with B-cell receptor inhibitor (BCRi) therapy. The starting dose of venetoclax was 20 mg once daily. The dose must have been gradually increased over a period of 5 weeks up to the daily dose of 400 mg. Participants may have continued receiving venetoclax for up to 2 years. After the treatment period, participants may have continued on into a 2-year follow-up period.

Protection of trial subjects:

The Investigator or his/her representative explained the nature of the study to the subject and answered all questions regarding this study. Prior to any study-related screening procedure being performed on the subject the informed consent statement was reviewed, signed and dated by the subject, the person who administered the informed consent, and any other signatories according to local requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 4
Country: Number of subjects enrolled	Australia: 57
Country: Number of subjects enrolled	Bulgaria: 14
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Mexico: 11
Country: Number of subjects enrolled	New Zealand: 23
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Russian Federation: 46
Country: Number of subjects enrolled	Taiwan: 16
Worldwide total number of subjects	210
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)	102
From 65 to 84 years	107
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants underwent screening procedures within 28 days prior to initial venetoclax administration, with the exception of the CT scan (or MRI if CT was medically contraindicated). A CT scan was accepted if previously performed within 35 days prior to venetoclax administration.

Period 1

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

Arms

Arm title	Venetoclax
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Arm description:

Venetoclax was administered orally once daily (QD) for a planned duration of up to 2 years or until disease progression; median time on treatment was 127 weeks. The starting dose was 20 mg daily, increasing over a period of 5 weeks up to the daily dose of 400 mg.

Arm type	Experimental
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	
Other name	ABT-199, VENCLEXTA, VENCPLYXTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Venetoclax tablets were to be taken orally once daily with a meal and water in the morning at approximately the same time each day. Tablets were to be swallowed whole and not chewed, crushed, or broken prior to swallowing.

Number of subjects in period 1	Venetoclax
Started	210
Completed	0
Not completed	210
Completed survival follow-up period	65
Death	63
Other, not specified	66
Study terminated by sponsor	4
Lost to follow-up	5
COVID-19 infection	1
Withdrawal by subject	6

Baseline characteristics

Reporting groups

Reporting group title	Venetoclax
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Reporting group description:

Venetoclax was administered orally once daily (QD) for a planned duration of up to 2 years or until disease progression; median time on treatment was 127 weeks. The starting dose was 20 mg daily, increasing over a period of 5 weeks up to the daily dose of 400 mg.

Reporting group values	Venetoclax	Total	
Number of subjects	210	210	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	63.9 ± 10.37	-	
Gender categorical Units: Subjects			
Female	69	69	
Male	141	141	
Race/Ethnicity Units: Subjects			
White	182	182	
Black or African American	1	1	
Asian	18	18	
American Indian or Alaska Native	8	8	
Native Hawaiian or other Pacific Islander	1	1	
Other	0	0	

End points

End points reporting groups

Reporting group title	Venetoclax
Reporting group description: Venetoclax was administered orally once daily (QD) for a planned duration of up to 2 years or until disease progression; median time on treatment was 127 weeks. The starting dose was 20 mg daily, increasing over a period of 5 weeks up to the daily dose of 400 mg.	

Primary: Mean Change from Baseline to Week 48 in Global Health Status/Quality of Life (GHS/QoL) subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change from Baseline to Week 48 in Global Health Status/Quality of Life (GHS/QoL) subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30) ^[1]
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a global health status/quality of life (GHS/QoL) scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the global health status/quality of life scale indicates a better level of functioning, and positive changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Primary
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End point timeframe:

Baseline, Week 48

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: A paired t-test of H_0 : mean difference (Week 48 - baseline) ≤ 5 versus H_1 : mean difference (Week 48 - baseline) > 5 was conducted, with $p=0.004$.

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	157 ^[2]			
Units: units on a scale				
arithmetic mean (standard deviation)	9.3 (\pm 20.11)			

Notes:

[2] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Global Health Status/Quality of Life (GHS/QoL) Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change From Baseline in Global Health Status/Quality of Life (GHS/QoL) Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a global health status/quality of life (GHS/QoL) scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the global health status/quality of life scale indicates a better level of functioning, and positive changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	199 ^[3]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=194	3.9 (± 17.65)			
Week 8, n=188	6.0 (± 20.67)			
Week 12, n=189	7.6 (± 20.13)			
Week 24, n=179	9.2 (± 20.29)			
Week 36, n=167	9.4 (± 19.45)			
Week 48, n=157	9.3 (± 20.11)			
Week 60, n=154	10.3 (± 21.83)			
Week 72, n=145	10.2 (± 23.87)			
Week 84, n=141	11.2 (± 20.96)			
Week 96, n=136	8.9 (± 20.92)			
Week 108, n=122	9.2 (± 19.97)			
Final visit, n=199	4.8 (± 23.58)			

Notes:

[3] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Physical Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change From Baseline in Physical Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a physical functioning scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the physical functioning scale indicates a better level of functioning, and positive changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[4]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	1.2 (± 12.86)			
Week 8, n=189	3.0 (± 16.16)			
Week 12, n=190	4.6 (± 15.89)			
Week 24, n=181	5.2 (± 16.90)			
Week 36, n=168	5.6 (± 15.59)			
Week 48, n=158	6.1 (± 16.30)			
Week 60, n=154	6.0 (± 17.73)			
Week 72, n=145	5.7 (± 18.47)			
Week 84, n=140	4.8 (± 15.04)			
Week 96, n=135	4.0 (± 17.18)			
Week 108, n=122	5.7 (± 16.43)			
Final visit, n=200	1.8 (± 20.52)			

Notes:

[4] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Role Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change From Baseline in Role Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a physical functioning scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the physical functioning scale indicates a better level of functioning, and positive changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[5]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	2.6 (± 22.75)			

Week 8, n=189	4.0 (± 28.31)			
Week 12, n=190	7.1 (± 28.60)			
Week 24, n=180	9.2 (± 26.85)			
Week 36, n=168	9.8 (± 26.70)			
Week 48, n=158	10.4 (± 26.10)			
Week 60, n=154	8.4 (± 27.63)			
Week 72, n=145	11.6 (± 31.01)			
Week 84, n=141	9.9 (± 27.38)			
Week 96, n=136	8.3 (± 31.23)			
Week 108, n=122	11.5 (± 28.03)			
Final visit, n=200	3.3 (± 33.29)			

Notes:

[5] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Emotional Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change From Baseline in Emotional Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including an emotional functioning scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the emotional functioning scale indicates a better level of functioning, and positive changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	199 ^[6]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=194	4.9 (± 16.30)			
Week 8, n=188	4.7 (± 16.96)			
Week 12, n=189	5.7 (± 17.11)			
Week 24, n=179	3.6 (± 17.62)			
Week 36, n=167	4.3 (± 17.08)			
Week 48, n=157	5.7 (± 17.64)			
Week 60, n=154	5.2 (± 18.79)			
Week 72, n=145	5.1 (± 18.54)			
Week 84, n=141	4.0 (± 17.95)			
Week 96, n=136	4.2 (± 19.95)			

Week 108, n=122	6.1 (± 20.18)			
Final visit, n=199	1.4 (± 21.78)			

Notes:

[6] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Cognitive Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change From Baseline in Cognitive Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a cognitive functioning scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the cognitive functioning scale indicates a better level of functioning, and positive changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	199 ^[7]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=194	2.3 (± 15.61)			
Week 8, n=188	4.2 (± 18.93)			
Week 12, n=189	4.3 (± 18.29)			
Week 24, n=179	3.4 (± 18.42)			
Week 36, n=167	3.8 (± 18.54)			
Week 48, n=157	3.7 (± 17.15)			
Week 60, n=154	4.1 (± 20.01)			
Week 72, n=145	4.7 (± 17.65)			
Week 84, n=141	3.5 (± 17.91)			
Week 96, n=136	1.1 (± 19.58)			
Week 108, n=122	5.6 (± 18.75)			
Final visit, n=199	2.3 (± 20.79)			

Notes:

[7] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Social Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change From Baseline in Social Functioning Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a social functioning scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the social functioning scale indicates a better level of functioning, and positive changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
End point timeframe:	Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	199 ^[8]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=194	2.2 (± 19.14)			
Week 8, n=188	5.5 (± 22.13)			
Week 12, n=189	6.6 (± 22.26)			
Week 24, n=179	7.2 (± 24.79)			
Week 36, n=167	8.6 (± 21.63)			
Week 48, n=157	9.9 (± 22.80)			
Week 60, n=154	9.2 (± 25.78)			
Week 72, n=145	9.7 (± 27.41)			
Week 84, n=141	8.7 (± 23.95)			
Week 96, n=136	8.2 (± 26.14)			
Week 108, n=122	11.7 (± 24.21)			
Final visit, n=199	3.4 (± 29.70)			

Notes:

[8] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Fatigue subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change from Baseline in Fatigue subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a fatigue scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the fatigue scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change,

and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
End point timeframe:	
Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit	

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[9]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-4.6 (± 18.63)			
Week 8, n=189	-7.7 (± 22.70)			
Week 12, n=190	-11.2 (± 24.66)			
Week 24, n=181	-10.9 (± 20.70)			
Week 36, n=168	-12.5 (± 23.21)			
Week 48, n=158	-12.9 (± 21.40)			
Week 60, n=154	-13.0 (± 22.79)			
Week 72, n=145	-13.8 (± 25.90)			
Week 84, n=140	-12.9 (± 23.49)			
Week 96, n=136	-10.7 (± 24.13)			
Week 108, n=122	-13.8 (± 22.69)			
Final visit, n=200	-7.5 (± 26.16)			

Notes:

[9] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Nausea and Vomiting Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change From Baseline in Nausea and Vomiting Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a nausea and vomiting scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the nausea and vomiting scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
End point timeframe:	
Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit	

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[10]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-0.2 (± 18.02)			
Week 8, n=189	0.4 (± 17.19)			
Week 12, n=190	-0.3 (± 18.50)			
Week 24, n=181	-1.5 (± 17.24)			
Week 36, n=168	-2.0 (± 16.19)			
Week 48, n=158	-0.6 (± 19.45)			
Week 60, n=154	-0.3 (± 15.42)			
Week 72, n=145	0.3 (± 17.40)			
Week 84, n=139	0.4 (± 18.00)			
Week 96, n=136	0.1 (± 17.15)			
Week 108, n=122	-1.1 (± 16.28)			
Final visit, n=200	-0.8 (± 17.58)			

Notes:

[10] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

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

End point title	Mean Change From Baseline in Pain Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a pain scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the pain scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[11]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-4.6 (± 21.05)			

Week 8, n=189	-2.9 (± 21.31)			
Week 12, n=190	-3.6 (± 22.56)			
Week 24, n=181	-4.1 (± 22.08)			
Week 36, n=168	-4.0 (± 22.43)			
Week 48, n=157	-4.6 (± 20.29)			
Week 60, n=154	-5.2 (± 23.46)			
Week 72, n=145	-4.7 (± 23.30)			
Week 84, n=141	-4.6 (± 22.10)			
Week 96, n=136	1.1 (± 25.35)			
Week 108, n=122	-3.4 (± 24.33)			
Final visit, n=200	-0.1 (± 26.50)			

Notes:

[11] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

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

End point title	Mean Change From Baseline in Dyspnea Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a dyspnea scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the dyspnea scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[12]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-3.7 (± 23.33)			
Week 8, n=189	-5.5 (± 26.62)			
Week 12, n=190	-7.7 (± 29.08)			
Week 24, n=181	-8.5 (± 26.56)			
Week 36, n=168	-8.3 (± 28.43)			
Week 48, n=157	-8.5 (± 27.19)			
Week 60, n=153	-8.5 (± 26.08)			
Week 72, n=145	-9.2 (± 31.30)			
Week 84, n=140	-9.3 (± 26.84)			
Week 96, n=136	-6.4 (± 28.55)			

Week 108, n=122	-10.9 (± 27.92)			
Final visit, n=200	-5.3 (± 29.60)			

Notes:

[12] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

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

End point title	Mean Change From Baseline in Insomnia Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including an insomnia scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the insomnia scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[13]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-6.5 (± 25.78)			
Week 8, n=189	-7.9 (± 30.39)			
Week 12, n=190	-9.1 (± 29.27)			
Week 24, n=181	-9.0 (± 27.19)			
Week 36, n=168	-8.3 (± 30.68)			
Week 48, n=158	-11.6 (± 25.77)			
Week 60, n=153	-10.2 (± 28.94)			
Week 72, n=145	-7.8 (± 29.40)			
Week 84, n=140	-9.5 (± 28.35)			
Week 96, n=136	-6.6 (± 29.76)			
Week 108, n=122	-10.7 (± 26.16)			
Final visit, n=200	-5.3 (± 30.52)			

Notes:

[13] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Appetite Loss Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change From Baseline in Appetite Loss Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including an appetite loss scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the appetite loss scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[14]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-3.4 (± 23.63)			
Week 8, n=189	-6.2 (± 24.85)			
Week 12, n=189	-6.0 (± 29.56)			
Week 24, n=181	-8.8 (± 27.36)			
Week 36, n=168	-8.1 (± 24.06)			
Week 48, n=158	-7.8 (± 24.14)			
Week 60, n=154	-5.6 (± 27.16)			
Week 72, n=145	-5.1 (± 27.59)			
Week 84, n=140	-6.9 (± 24.16)			
Week 96, n=136	-6.4 (± 27.07)			
Week 108, n=122	-9.3 (± 25.81)			
Final visit, n=200	-4.0 (± 30.36)			

Notes:

[14] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

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

End point title	Mean Change From Baseline in Constipation Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a constipation scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the constipation scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	199 ^[15]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=194	1.7 (± 17.87)			
Week 8, n=188	2.5 (± 21.38)			
Week 12, n=189	1.4 (± 20.58)			
Week 24, n=180	1.1 (± 18.61)			
Week 36, n=167	-0.8 (± 20.36)			
Week 48, n=156	-0.2 (± 18.35)			
Week 60, n=153	1.7 (± 20.52)			
Week 72, n=143	0.5 (± 18.97)			
Week 84, n=138	1.7 (± 19.45)			
Week 96, n=135	0.7 (± 20.55)			
Week 108, n=121	-0.8 (± 18.98)			
Final visit, n=199	1.2 (± 19.64)			

Notes:

[15] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

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

End point title	Mean Change From Baseline in Diarrhea Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a diarrhea scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the diarrhea scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	199 ^[16]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=194	-0.7 (± 20.63)			
Week 8, n=188	1.8 (± 21.45)			
Week 12, n=189	2.3 (± 22.30)			
Week 24, n=179	4.7 (± 21.42)			
Week 36, n=167	4.6 (± 21.62)			
Week 48, n=157	4.0 (± 21.13)			
Week 60, n=154	7.4 (± 27.01)			
Week 72, n=145	3.0 (± 25.74)			
Week 84, n=141	4.3 (± 23.18)			
Week 96, n=136	3.7 (± 22.47)			
Week 108, n=122	3.8 (± 21.51)			
Final visit, n=199	4.9 (± 23.30)			

Notes:

[16] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Financial Difficulties Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)

End point title	Mean Change From Baseline in Financial Difficulties Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)
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End point description:

EORTC QLQ-C30 is a 30-item participant self-report questionnaire composed of both multi-item and single scales, including a financial difficulties scale. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the financial difficulties scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
End point timeframe:	
Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit	

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	199 ^[17]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=194	-6.4 (± 20.07)			
Week 8, n=187	-4.6 (± 21.91)			
Week 12, n=189	-6.0 (± 24.54)			
Week 24, n=179	-7.3 (± 25.05)			
Week 36, n=167	-7.8 (± 23.70)			
Week 48, n=157	-8.9 (± 26.52)			
Week 60, n=153	-10.0 (± 25.96)			
Week 72, n=145	-8.5 (± 27.99)			
Week 84, n=141	-10.9 (± 23.06)			
Week 96, n=136	-8.6 (± 25.34)			
Week 108, n=122	-9.6 (± 24.04)			
Final visit, n=199	-6.5 (± 25.88)			

Notes:

[17] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Fatigue Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)

End point title	Mean Change From Baseline in Fatigue Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)
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End point description:

EORTC QLQ-CLL16 is comprised of 16 questions that address 5 domains of health-related quality of life important in CLL. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the fatigue scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
End point timeframe:	Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[18]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-6.3 (± 32.20)			

Week 8, n=189	-10.2 (± 38.11)			
Week 12, n=189	-13.9 (± 38.59)			
Week 24, n=181	-15.3 (± 37.96)			
Week 36, n=168	-16.3 (± 34.41)			
Week 48, n=158	-16.1 (± 35.41)			
Week 60, n=154	-14.5 (± 36.59)			
Week 72, n=145	-16.4 (± 36.85)			
Week 84, n=141	-17.4 (± 34.90)			
Week 96, n=136	-13.0 (± 35.18)			
Week 108, n=122	-19.8 (± 35.17)			
Final visit, n=200	-10.6 (± 41.71)			

Notes:

[18] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Treatment Side Effects Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)

End point title	Mean Change From Baseline in Treatment Side Effects Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)
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End point description:

EORTC QLQ-CLL16 is comprised of 16 questions that address 5 domains of health-related quality of life important in CLL. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the treatment side effects scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[19]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-2.6 (± 17.70)			
Week 8, n=189	-4.0 (± 17.84)			

Week 12, n=189	-4.8 (± 17.96)			
Week 24, n=181	-7.5 (± 18.46)			
Week 36, n=168	-7.8 (± 18.03)			
Week 48, n=158	-7.5 (± 19.19)			
Week 60, n=154	-6.3 (± 19.41)			
Week 72, n=145	-6.3 (± 18.73)			
Week 84, n=141	-6.8 (± 16.43)			
Week 96, n=136	-6.9 (± 18.48)			
Week 108, n=122	-8.2 (± 19.33)			
Final visit, n=200	-3.6 (± 22.54)			

Notes:

[19] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Disease Effects Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)

End point title	Mean Change From Baseline in Disease Effects Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)
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End point description:

EORTC QLQ-CLL16 is comprised of 16 questions that address 5 domains of health-related quality of life important in CLL. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the disease effects scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[20]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-10.7 (± 19.58)			
Week 8, n=189	-10.0 (± 21.80)			
Week 12, n=190	-12.4 (± 23.48)			
Week 24, n=181	-13.7 (± 23.63)			
Week 36, n=168	-13.9 (± 23.34)			
Week 48, n=158	-13.4 (± 23.68)			
Week 60, n=154	-13.1 (± 23.18)			

Week 72, n=145	-13.8 (± 23.22)			
Week 84, n=141	-13.6 (± 22.69)			
Week 96, n=136	-13.2 (± 22.59)			
Week 108, n=122	-15.6 (± 24.93)			
Final visit, n=200	-10.2 (± 25.97)			

Notes:

[20] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Infection Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)

End point title	Mean Change From Baseline in Infection Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)
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End point description:

EORTC QLQ-CLL16 is comprised of 16 questions that address 5 domains of health-related quality of life important in CLL. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the infection scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	200 ^[21]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=196	-3.5 (± 21.66)			
Week 8, n=189	-6.0 (± 29.00)			
Week 12, n=190	-4.6 (± 28.67)			
Week 24, n=181	-6.1 (± 26.50)			
Week 36, n=168	-8.9 (± 26.04)			
Week 48, n=158	-9.0 (± 25.54)			
Week 60, n=154	-7.9 (± 25.13)			
Week 72, n=145	-8.5 (± 28.97)			
Week 84, n=141	-9.9 (± 24.18)			
Week 96, n=136	-8.5 (± 25.34)			
Week 108, n=122	-10.3 (± 25.41)			
Final visit, n=200	-5.5 (± 29.97)			

Notes:

[21] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Social Problems Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)

End point title	Mean Change From Baseline in Social Problems Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)
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End point description:

EORTC QLQ-CLL16 is comprised of 16 questions that address 5 domains of health-related quality of life important in CLL. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the social problems scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	198 ^[22]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=194	-4.0 (± 37.50)			
Week 8, n=187	-7.5 (± 39.15)			
Week 12, n=188	-8.5 (± 41.06)			
Week 24, n=179	-10.6 (± 41.72)			
Week 36, n=166	-13.7 (± 38.15)			
Week 48, n=156	-15.6 (± 40.85)			
Week 60, n=152	-15.6 (± 37.18)			
Week 72, n=143	-17.5 (± 42.76)			
Week 84, n=139	-15.3 (± 42.14)			
Week 96, n=134	-14.7 (± 41.79)			
Week 108, n=120	-16.1 (± 43.85)			
Final visit, n=198	-4.0 (± 48.50)			

Notes:

[22] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Future Health Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)

End point title	Mean Change From Baseline in Future Health Subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Lymphocytic Leukemia Module (EORTC QLQ-CLL16)
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End point description:

EORTC QLQ-CLL16 is comprised of 16 questions that address 5 domains of health-related quality of life important in CLL. Participants rate items and a score ranging from 0 to 100 is calculated. A higher score on the future health scale indicates a lower level of functioning, and negative changes from baseline indicate improvement. A change of 5 – 10 points is considered a small change, and a change of 10 – 20 points is considered a moderate change.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	198 ^[23]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=194	-17.2 (± 37.82)			
Week 8, n=187	-21.6 (± 42.94)			
Week 12, n=188	-25.5 (± 41.77)			
Week 24, n=180	-23.0 (± 38.96)			
Week 36, n=167	-24.4 (± 43.97)			
Week 48, n=156	-24.1 (± 41.75)			
Week 60, n=153	-25.1 (± 46.09)			
Week 72, n=144	-27.8 (± 40.59)			
Week 84, n=140	-20.7 (± 39.68)			
Week 96, n=135	-24.9 (± 44.18)			

Week 108, n=121	-23.7 (± 46.63)			
Final visit, n=198	-16.7 (± 49.90)			

Notes:

[23] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in EuroQol 5 Dimension 5 Level (EQ-5D-5L) Visual Analog Scale Score

End point title	Mean Change From Baseline in EuroQol 5 Dimension 5 Level (EQ-5D-5L) Visual Analog Scale Score
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End point description:

The EQ-5D 5L measures quality of life in five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each of which are rated on five levels of severity (1: no problems, 2: slight problems, 3: moderate problems, 4: severe problems, 5: extreme problems), and a separate visual analog scale (VAS). Participants rated their health on a vertical visual analogue scale, where the endpoints were labelled 100, "The best health you can imagine" and 0, "The worst health you can imagine". Positive values indicate improvement from baseline.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	199 ^[24]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=195	3.67 (± 12.683)			
Week 8, n=188	6.00 (± 15.982)			
Week 12, n=189	7.75 (± 14.498)			
Week 24, n=181	7.78 (± 16.158)			
Week 36, n=167	9.08 (± 16.342)			
Week 48, n=157	10.34 (± 16.808)			
Week 60, n=153	10.84 (± 17.180)			
Week 72, n=144	11.19 (± 17.890)			
Week 84, n=140	10.22 (± 15.431)			
Week 96, n=134	9.98 (± 16.310)			
Week 108, n=120	10.77 (± 17.500)			

Final visit, n=199	6.22 (\pm 19.262)			
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Notes:

[24] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in EuroQol 5 Dimension 5 Level (EQ-5D-5L) Health Index Score

End point title	Mean Change From Baseline in EuroQol 5 Dimension 5 Level (EQ-5D-5L) Health Index Score
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End point description:

The EQ-5D 5L measures quality of life in five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each of which are rated on five levels of severity (1: no problems, 2: slight problems, 3: moderate problems, 4: severe problems, 5: extreme problems), and a separate visual analog scale (VAS). The scores for the 5 dimensions are used to compute a single utility index score ranging from zero (0.0) to 1 (1.0) representing the general health status of the individual, with '0' defined as a health state equivalent to being dead and '1' is full health. The higher the score the better the health status. Positive values indicate improvement from baseline.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108, Final visit

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	201 ^[25]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 4, n=197	0.02 (\pm 0.135)			
Week 8, n=190	0.02 (\pm 0.130)			
Week 12, n=191	0.03 (\pm 0.122)			
Week 24, n=183	0.03 (\pm 0.112)			
Week 36, n=168	0.04 (\pm 0.121)			
Week 48, n=159	0.04 (\pm 0.124)			
Week 60, n=155	0.04 (\pm 0.129)			
Week 72, n=146	0.03 (\pm 0.132)			
Week 84, n=142	0.03 (\pm 0.111)			
Week 96, n=136	0.01 (\pm 0.134)			
Week 108, n=122	0.02 (\pm 0.124)			
Final visit, n=201	-0.01 (\pm 0.172)			

Notes:

[25] - All enrolled subjects who received at least one dose of venetoclax with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Remission Rate (Complete Remission [CR] + Complete Remission With Incomplete Marrow Recovery [CRi])

End point title	Complete Remission Rate (Complete Remission [CR] + Complete Remission With Incomplete Marrow Recovery [CRi])
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End point description:

Complete remission rate (CR + CRi) is defined as the percentage of participants achieving a CR or CRi as their best response (per the investigator assessment) based on 2008 Modified International Workshop on Chronic Lymphocytic Leukemia (IWCLL) National Cancer Institute-Working Group (NCI-WG) Guidelines criteria.

End point type	Secondary
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End point timeframe:

Screening, Week 24, Week 36 and Week 48; median time on follow-up was 184 weeks

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	210 ^[26]			
Units: percentage of participants				
number (confidence interval 95%)	18.6 (13.6 to 24.5)			

Notes:

[26] - All enrolled participants who received at least one dose of venetoclax

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)
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End point description:

ORR is defined as the percentage of participants who achieved complete remission (CR), complete remission with incomplete marrow recovery (CRi), nodular partial remission (nPR), or confirmed partial remission (PR) based on the 2008 Modified International Workshop on Chronic Lymphocytic Leukemia (IWCLL) National Cancer Institute-Working Group (NCI-WG) Guidelines criteria as assessed by investigator using the best response at any time during the study.

End point type	Secondary
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End point timeframe:

Screening, Week 24, Week 36 and Week 48; median time on follow-up was 184 weeks

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	210 ^[27]			
Units: percentage of participants				
number (confidence interval 95%)	76.7 (70.4 to 82.2)			

Notes:

[27] - Subjects who rcvd ≥ 1 dose of venetoclax; those who didn't respond were considered non-responders

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Overall Response (DOR)

End point title	Duration of Overall Response (DOR)
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End point description:

DoR is defined as the number of days from the date of first response (complete remission (CR), complete remission with incomplete marrow recovery (CRi), nodular partial remission (nPR), or confirmed partial remission (PR) based on the 2008 Modified International Workshop on Chronic Lymphocytic Leukemia (IWCLL) National Cancer Institute Working Group (NCI-WG) Guidelines criteria to the earliest date of progressive disease (PD) or death. DOR was analyzed by Kaplan-Meier (K-M) methodology.

End point type	Secondary
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End point timeframe:

Screening, Week 24, Week 36 and Week 48; median time on follow-up was 184 weeks

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	161 ^[28]			
Units: months				
median (confidence interval 95%)	36.0 (30.0 to 38.9)			

Notes:

[28] - Subjects rcvd ≥ 1 dose venetoclax, active disease at baseline, achieved response of PR or better

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP)

End point title	Time to Progression (TTP)
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End point description:

TTP is defined as the number of days from the date of first dose of venetoclax to the date of earliest disease progression (PD). TTP was analyzed by Kaplan-Meier (K-M) methodology.

End point type	Secondary
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End point timeframe:

Screening, Week 24, Week 36 and Week 48; median time on follow-up was 184 weeks

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	210 ^[29]			
Units: months				
median (confidence interval 95%)	43.0 (33.4 to 47.2)			

Notes:

[29] - All enrolled participants who received at least one dose of venetoclax

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)
End point description:	
PFS is defined as the number of days from the date of first dose of venetoclax to the date of earliest disease progression (PD) or death. PFS was analyzed by Kaplan-Meier methodology.	
End point type	Secondary
End point timeframe:	
Screening, Week 24, Week 36 and Week 48; median time on follow-up was 184 weeks	

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	210 ^[30]			
Units: months				
median (confidence interval 95%)	35.5 (32.9 to 42.9)			

Notes:

[30] - All enrolled participants who received at least one dose of venetoclax

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS is defined as the number of days from the date of first dose of venetoclax to the date of death. For participants who did not die, their data was censored at the date of last study visit or the last known date to be alive, whichever was later. OS was estimated using Kaplan-Meier methodology. In the table below, -999 and 99999 mean not calculable/estimable due to low number of participants with events.	
End point type	Secondary
End point timeframe:	
Screening, Week 24, Week 36 and Week 48; median time on follow-up was 184 weeks	

End point values	Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	210 ^[31]			
Units: months				
median (confidence interval 95%)	53.1 (-999 to 99999)			

Notes:

[31] - All enrolled participants who received at least one dose of venetoclax

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality is reported from enrollment to 30 d after last dose of study drug; median time on follow up = 184 wks. TEAEs and SAEs were collected from first dose of study drug until 30 d after last dose of study drug; mean on study drug = 123 wks

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	Venetoclax
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Reporting group description:

Venetoclax was administered orally once daily (QD) for a planned duration of up to 2 years or until disease progression; median time on treatment was 127 days. The starting dose was 20 mg daily, increasing over a period of 5 weeks up to the daily dose of 400 mg.

Serious adverse events	Venetoclax		
Total subjects affected by serious adverse events			
subjects affected / exposed	106 / 210 (50.48%)		
number of deaths (all causes)	65		
number of deaths resulting from adverse events	16		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CHRONIC LYMPHOCYTIC LEUKAEMIA			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MALIGNANT MELANOMA			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LUNG ADENOCARCINOMA			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEPATIC NEOPLASM			

subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DIFFUSE LARGE B-CELL LYMPHOMA				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
METASTATIC MALIGNANT MELANOMA				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SQUAMOUS CELL CARCINOMA				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
SKIN SQUAMOUS CELL CARCINOMA METASTATIC				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PROSTATE CANCER				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OVARIAN CANCER METASTATIC				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OESOPHAGEAL SQUAMOUS CELL CARCINOMA				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
METASTATIC SQUAMOUS CELL				

CARCINOMA				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
SQUAMOUS CELL CARCINOMA OF HEAD AND NECK				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SQUAMOUS CELL CARCINOMA OF SKIN				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
AORTIC ANEURYSM				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CIRCULATORY COLLAPSE				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
HYPOTENSION				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
PERIPHERAL ARTERY ANEURYSM				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PERIPHERAL ISCHAEMIA				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Surgical and medical procedures			
STEM CELL TRANSPLANT			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DEATH			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
PYREXIA			
subjects affected / exposed	10 / 210 (4.76%)		
occurrences causally related to treatment / all	7 / 15		
deaths causally related to treatment / all	0 / 0		
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
FATIGUE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
SUDDEN DEATH			

subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
CYTOKINE RELEASE SYNDROME			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PLEURAL EFFUSION			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONITIS			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMOTHORAX			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RESPIRATORY FAILURE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CLOSTRIDIUM TEST POSITIVE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
FEMORAL NECK FRACTURE			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HIP FRACTURE			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
INJURY			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PELVIC FRACTURE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TRANSFUSION REACTION			

subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SUBDURAL HAEMATOMA			
subjects affected / exposed	1 / 210 (0.48%)		
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 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ARRHYTHMIA			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIAC ARREST			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ATRIOVENTRICULAR BLOCK			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIAC FAILURE ACUTE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PERICARDIAL EFFUSION			

subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
ISCHAEMIC STROKE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEADACHE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
BRAIN OEDEMA			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
PRESYNCOPE			

subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
SEIZURE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
AUTOIMMUNE HAEMOLYTIC ANAEMIA			
subjects affected / exposed	4 / 210 (1.90%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
EVANS SYNDROME			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
ANAEMIA			
subjects affected / exposed	5 / 210 (2.38%)		
occurrences causally related to treatment / all	4 / 5		
deaths causally related to treatment / all	0 / 0		
PANCYTOPENIA			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
THROMBOCYTOPENIA			
subjects affected / exposed	6 / 210 (2.86%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 0		
NEUTROPENIA			

subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
FEBRILE NEUTROPENIA			
subjects affected / exposed	7 / 210 (3.33%)		
occurrences causally related to treatment / all	6 / 7		
deaths causally related to treatment / all	0 / 0		
IMMUNE THROMBOCYTOPENIA			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
CATARACT CORTICAL			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CATARACT NUCLEAR			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PANCREATITIS			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PROCTALGIA			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VOMITING			

subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTRITIS			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
DIARRHOEA			
subjects affected / exposed	3 / 210 (1.43%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
MELAENA			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
RASH ERYTHEMATOUS			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RASH PRURITIC			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
RENAL COLIC			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

CHRONIC KIDNEY DISEASE			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
ACUTE KIDNEY INJURY			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
RENAL IMPAIRMENT			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
NECK PAIN			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HAEMARTHROSIS			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BACK PAIN			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
ARTHRALGIA			
subjects affected / exposed	3 / 210 (1.43%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
OSTEOARTHRITIS			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations COVID-19 PNEUMONIA subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	3 / 210 (1.43%) 0 / 5 0 / 2		
CELLULITIS STAPHYLOCOCCAL subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 210 (0.48%) 0 / 1 0 / 0		
CELLULITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 210 (0.95%) 0 / 2 0 / 0		
BRONCHITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 210 (0.48%) 0 / 1 0 / 0		
ACUTE SINUSITIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 210 (0.48%) 0 / 1 0 / 0		
ESCHERICHIA URINARY TRACT INFECTION subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 210 (0.48%) 0 / 1 0 / 0		
FUNGAL SEPSIS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 210 (0.48%) 0 / 2 0 / 1		
INFLUENZA subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	4 / 210 (1.90%) 2 / 4 0 / 0		

INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INFECTION				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HERPES ZOSTER				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HERPES VIRUS INFECTION				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HAEMOPHILUS INFECTION				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
KLEBSIELLA SEPSIS				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA KLEBSIELLA				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	21 / 210 (10.00%)			
occurrences causally related to treatment / all	10 / 26			
deaths causally related to treatment / all	0 / 0			
PHARYNGITIS				

subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NEUTROPENIC SEPSIS				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
MENINGITIS ASEPTIC				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LOWER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
LIVER ABSCESS				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SEPSIS				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
SALMONELLOSIS				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PSEUDOMONAL SEPSIS				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA VIRAL				

subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA RESPIRATORY SYNCYTIAL VIRAL			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA PSEUDOMONAL			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
SEPTIC SHOCK			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
PNEUMONIA PARAINFLUENZAE VIRAL			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SERRATIA SEPSIS			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
STREPTOCOCCAL INFECTION			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 210 (1.43%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

DEHYDRATION				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERCALCAEMIA				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERKALAEMIA				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
HYPONATRAEMIA				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERVOLAEMIA				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERPHOSPHATAEMIA				
subjects affected / exposed	5 / 210 (2.38%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
OBESITY				
subjects affected / exposed	1 / 210 (0.48%)			
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	Venetoclax		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	179 / 210 (85.24%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	11 / 210 (5.24%)		
occurrences (all)	16		
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	19 / 210 (9.05%)		
occurrences (all)	21		
Nervous system disorders			
HEADACHE			
subjects affected / exposed	18 / 210 (8.57%)		
occurrences (all)	23		
Blood and lymphatic system disorders			
THROMBOCYTOPENIA			
subjects affected / exposed	39 / 210 (18.57%)		
occurrences (all)	60		
NEUTROPENIA			
subjects affected / exposed	90 / 210 (42.86%)		
occurrences (all)	189		
ANAEMIA			
subjects affected / exposed	26 / 210 (12.38%)		
occurrences (all)	33		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	19 / 210 (9.05%)		
occurrences (all)	24		
OEDEMA PERIPHERAL			
subjects affected / exposed	11 / 210 (5.24%)		
occurrences (all)	11		
FATIGUE			
subjects affected / exposed	15 / 210 (7.14%)		
occurrences (all)	18		
Gastrointestinal disorders			

DIARRHOEA			
subjects affected / exposed	66 / 210 (31.43%)		
occurrences (all)	105		
CONSTIPATION			
subjects affected / exposed	18 / 210 (8.57%)		
occurrences (all)	19		
GASTROESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	12 / 210 (5.71%)		
occurrences (all)	13		
NAUSEA			
subjects affected / exposed	35 / 210 (16.67%)		
occurrences (all)	42		
VOMITING			
subjects affected / exposed	15 / 210 (7.14%)		
occurrences (all)	20		
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	21 / 210 (10.00%)		
occurrences (all)	24		
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	16 / 210 (7.62%)		
occurrences (all)	18		
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	13 / 210 (6.19%)		
occurrences (all)	13		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	21 / 210 (10.00%)		
occurrences (all)	22		
BACK PAIN			
subjects affected / exposed	15 / 210 (7.14%)		
occurrences (all)	16		
Infections and infestations			

BRONCHITIS			
subjects affected / exposed	18 / 210 (8.57%)		
occurrences (all)	24		
PNEUMONIA			
subjects affected / exposed	11 / 210 (5.24%)		
occurrences (all)	12		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	58 / 210 (27.62%)		
occurrences (all)	113		
Metabolism and nutrition disorders			
HYPOKALAEMIA			
subjects affected / exposed	13 / 210 (6.19%)		
occurrences (all)	13		
HYPOCALCAEMIA			
subjects affected / exposed	12 / 210 (5.71%)		
occurrences (all)	12		
HYPOMAGNESAEMIA			
subjects affected / exposed	11 / 210 (5.24%)		
occurrences (all)	11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2016	<p>Amendment 1</p> <ul style="list-style-type: none">• Modified text as it related to patients previously treated with a B-cell receptor inhibitor• Clarified Exclusion Criteria, Criterion 11 regarding a subject's known history of HIV status• Allowed urine pregnancy testing at the Investigator's discretion• Removed requirement of subject diaries throughout the protocol
30 January 2018	<p>Amendment 2</p> <ul style="list-style-type: none">• Updated number of planned study sites• Clarified that relapsed/refractory subjects with or without the 17p deletion or TP53 mutation, including subjects with an unknown status, can be enrolled in the study, as well as subjects previously treated with B-cell receptor inhibitor therapy• Clarified all screening procedures must be done in the screening period of 28 days, except a CT scan, which can be performed within 35 days of study drug administration• Clarified that study visits occur within 72 hours of dosing and on the first and second day of Week 1 and 2 of the dose titration phase, for all subjects. Additionally, clarification was added beginning on Week 3 through Week 5, study visits will be conducted within 72 hours of dosing and on Day 1 of each week. Additional study visits on Day 2 of each week should be performed for subjects who continue to be at risk of TLS, based on investigator assessment.• Implemented a Data Monitoring Committee (DMC) to review safety data• Clarified that MRI will be accepted in the case when CT scan with contrast is medically contraindicated• Included a 30-day safety follow up visit after the last dose of venetoclax to allow for continued AE collection• Clarified that plasma values may be used in place of serum values for estimated creatinine clearance calculations depending on local laboratory standard testing requirements• Clarified the treatment period for all subjects is 2 years• Updated text to align with the current approach to TLS prophylaxis and management• Clarified that the maximum dose of venetoclax administered for this protocol is 400 mg• Clarified that overall survival is an efficacy endpoint• Clarified timing of pre-and post-dose hematology/chemistry requirements and which labs are drawn and when for managing TLS• Specified that immunizations with live virus vaccines should not be administered prior to, during, or after treatment with venetoclax until B-cell recovery occurs

09 October 2018	<p>Amendment 3</p> <ul style="list-style-type: none"> • Updated Venetoclax Clinical Data section to align with the most recent version of the Investigator's Brochure. • Added a \pm 2 day visit window as of Week 8 • Clarified that Bone Marrow samples will be collected for subjects with Complete Response to confirm response • Added that in countries where venetoclax is commercially available extension of therapy may not be allowed • Removed requirement to evaluate lymph nodes at physical examinations at visits other than Screening and Weeks 24, 36 and 48 • Clarified that if the CT is negative a bone marrow biopsy will be obtained to confirm clinical response. If a CT scan is performed and does not confirm a clinical response, a bone marrow biopsy should not be obtained • Added that for subjects with only Partial Remission at Week 48, an additional CT and a bone marrow examination can be done between Week 48 and Week 108 to confirm Complete Response if there is a possibility that a subject is in Complete Remission based on laboratory tests and a disease assessment physical examination • Clarified that subjects will be followed for survival information every 6 months even if subjects had an event of progression, they require alternate therapy, etc. • Added a window (\pm 7 days) to the post-treatment calls • Added that Adverse Event/Concomitant medication assessment is to be done also at the following visits: within 72 hours of W2 D1, W3 D1, W4 D1 and W5 D1
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported