Clinical trial results:
A Phase 2 Randomized Single-Blind Study to Evaluate the Activity and Safety of Low Dose Oral Selinexor (KPT-330) in Patients with Severe COVID-19 Infection

Summary

EudraCT number	2020-001411-25
Trial protocol	DE FR AT GB ES IT
Global end of trial date	05 October 2020

Results information

Result version number	v1 (current)
This version publication date	23 October 2021
First version publication date	23 October 2021

Trial information

Trial identification

Sponsor protocol code	XPORT-COV-1001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04349098
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Karyopharm Therapeutics Inc.
Sponsor organisation address	85 Wells Avenue, Newton, MA, United States, 02459
Public contact	Clinical Trials Information, Karyopharm Therapeutics Inc., +1 617658 0600, clinicaltrials@karyopharm.com
Scientific contact	Clinical Trial Information, Karyopharm Therapeutics Inc., +1 617658 0600, clinicaltrials@karyopharm.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	05 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to determine if low-dose oral selinexor could expedite the clinical recovery, suppress the viral load, shorten the hospitalization, and reduce morbidity and mortality in subjects with severe COVID-19 compared with placebo.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles originating in the Declaration of Helsinki in place at the time of study conduct. The study was conducted in compliance with the International Council for Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP) (Committee for Proprietary Medicinal Products [CPMP] guideline CPMP/ICH/135/95), United States Code of Federal Code of Regulations, and all applicable local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 April 2020
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	United States: 175
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	France: 1
Worldwide total number of subjects	190
EEA total number of subjects	10

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)	130
From 65 to 84 years	49
85 years and over	11

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 20 sites in the United States of America, 3 sites in France, 3 sites in Israel, 2 sites in Spain, and 4 sites in the United Kingdom from 17 Apr 2020 to 05 Oct 2020.

Pre-assignment

Screening details:

A total of 190 subjects were enrolled and randomised, of which 188 subjects received study treatment in this study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Study design was changed as double-blinded (subjects and principal investigator) as per protocol version 4.1.

Arms

Are arms mutually exclusive?	Yes
Arm title	Selinexor 20 mg

Arm description:

Subjects received a single dose of Selinexor 20 milligrams (mg) tablets orally on Days 1, 3 and 5 of each week for up to 2 weeks. The subject tolerated therapy and showed clinical benefit, dosing continued for an additional 2 weeks (on Days 15, 17, 19, 22, 24, and 26) along with standard of care (SoC). As the treatment for COVID-19 is rapidly evolving, the SoC varied over time and across regions of the world.

Arm type	Experimental
Investigational medicinal product name	Selinexor
Investigational medicinal product code	KPT-330
Other name	XPOVIO®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single dose of Selinexor 20 mg tablets orally on Days 1, 3 and 5.

Arm title	Placebo

Arm description:

Subjects received a single dose of placebo matched to selinexor tablets orally on Days 1, 3 and 5 of each week for up to 2 weeks. The subject tolerated therapy and showed clinical benefit, dosing continued for an additional 2 weeks (on Days 15, 17, 19, 22, 24, and 26) along with SoC. As the treatment for COVID-19 is rapidly evolving, the SoC varied over time and across regions of the world.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single dose of placebo matched to selinexor tablets orally on Days 1, 3 and 5.

Number of subjects in period 1	Selinexor 20 mg	Placebo
Started	103	87
Completed	65	61
Not completed	38	26
Consent withdrawn by subject	8	5
Death	16	8
Unspecified	3	5
Lost to follow-up	11	8

Baseline characteristics

Reporting groups

Reporting group title	Selinexor 20 mg

Reporting group description:

Subjects received a single dose of Selinexor 20 milligrams (mg) tablets orally on Days 1, 3 and 5 of each week for up to 2 weeks. The subject tolerated therapy and showed clinical benefit, dosing continued for an additional 2 weeks (on Days 15, 17, 19, 22, 24, and 26) along with standard of care (SoC). As the treatment for COVID-19 is rapidly evolving, the SoC varied over time and across regions of the world.

Reporting group title	Placebo

Reporting group description:

Subjects received a single dose of placebo matched to selinexor tablets orally on Days 1, 3 and 5 of each week for up to 2 weeks. The subject tolerated therapy and showed clinical benefit, dosing continued for an additional 2 weeks (on Days 15, 17, 19, 22, 24, and 26) along with SoC. As the treatment for COVID-19 is rapidly evolving, the SoC varied over time and across regions of the world.

Reporting group values	Selinexor 20 mg	Placebo	Total
Number of subjects	103	87	190
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	56.5	56.5	
standard deviation	± 16.12	± 14.64	-
Gender categorical Units: Subjects			
Female	43	39	82
Male	60	48	108
Ethnicity Units: Subjects			
Hispanic or Latino	41	32	73
Not Hispanic or Latino	59	53	112
Unknown or Not Reported	3	2	5
Race Units: Subjects			
Asian	6	4	10
Native Hawaiian or Other Pacific Islander	2	0	2
Black or African American	23	24	47
White	44	34	78
More than one race	19	14	33
Unknown or Not Reported	9	11	20

End points

End points reporting groups

Reporting group title	Selinexor 20 mg

Reporting group description:

Subjects received a single dose of Selinexor 20 milligrams (mg) tablets orally on Days 1, 3 and 5 of each week for up to 2 weeks. The subject tolerated therapy and showed clinical benefit, dosing continued for an additional 2 weeks (on Days 15, 17, 19, 22, 24, and 26) along with standard of care (SoC). As the treatment for COVID-19 is rapidly evolving, the SoC varied over time and across regions of the world.

Reporting group title	Placebo

Reporting group description:

Subjects received a single dose of placebo matched to selinexor tablets orally on Days 1, 3 and 5 of each week for up to 2 weeks. The subject tolerated therapy and showed clinical benefit, dosing continued for an additional 2 weeks (on Days 15, 17, 19, 22, 24, and 26) along with SoC. As the treatment for COVID-19 is rapidly evolving, the SoC varied over time and across regions of the world.

Primary: Percentage of Subjects With At-least a 2-Point Improvement in Ordinal Scale

End point title	Percentage of Subjects With At-least a 2-Point Improvement in Ordinal Scale

End point description:

Ordinal Scale 2-Point improvement defined as percentage of subjects with at least 2 points improvement (increase from baseline) by Day 14. Baseline score defined as last score measured before first dosing. The 8-point ordinal scale ranges from 1 to 8: where, 1=death, 2=hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation; 3=hospitalized, on non-invasive ventilation or high flow oxygen devices; 4=hospitalized, requiring supplemental oxygen; 5=hospitalized, not requiring supplemental oxygen-requiring ongoing medical care (COVID-19) related or otherwise; 6=hospitalized, not requiring supplemental oxygen-no longer requires ongoing medical care; 7=not hospitalized, limitation on activities and/or requiring home oxygen; 8=not hospitalized, no limitations on activities. ITT population: all subjects who randomised with confirmed SARS-CoV2 infection under protocol V6.0 and above, regardless of receive study treatment.

End point type	Primary

End point timeframe:

Baseline up to Day 14

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	51		
Units: Percentage of subjects				
number (confidence interval 95%)	60.6 (47.8 to 72.4)	60.8 (46.1 to 74.2)		

Statistical analyses

Statistical analysis title	At least 2-point improvement in ordinal scale
Comparison groups	Selinexor 20 mg v Placebo

Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.675
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.79

Secondary: Percentage of Subjects With at Least a 2-Point Improvement in the Ordinal Scale up to Day 7

End point title	Percentage of Subjects With at Least a 2-Point Improvement in the Ordinal Scale up to Day 7

End point description:

Ordinal Scale 2-points improvement was defined as percentage of subjects with at least a 2 points improvement (increase from baseline) by Day 7. Baseline score was defined as the last score measured before first dosing. The 8-point ordinal scale ranges from 1 to 8: where, 1= death, 2= hospitalized, on invasive mechanical ventilation or ECMO; 3= hospitalized, on non-invasive ventilation or high flow oxygen devices; 4= hospitalized, requiring supplemental oxygen; 5= hospitalized, not requiring supplemental oxygen – requiring ongoing medical care (COVID-19 related or otherwise); 6= hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7= not hospitalized, limitation on activities and/or requiring home oxygen; 8= not hospitalized, no limitations on activities. PV 1-6 population included subjects randomised into the study under protocol versions 1-6.

End point type	Secondary

End point timeframe:

Baseline up to Day 7

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	87		
Units: Percentage of subjects				
number (confidence interval 95%)	30.1 (21.5 to 39.9)	32.2 (22.6 to 43.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least a 1-Point Improvement in the Ordinal Scale

End point title	Percentage of Subjects With at Least a 1-Point Improvement in the Ordinal Scale

End point description:

Ordinal Scale 1-point improvement was defined as percentage of subjects with at least 1 point improvement (increase from baseline) by Day 7 and 14. Baseline score was defined as the last score measured before first dosing. The 8-point ordinal scale ranges from 1 to 8: where 1= death, 2= hospitalized, on invasive mechanical ventilation or ECMO; 3= hospitalized, on non-invasive ventilation or high flow oxygen devices; 4= hospitalized, requiring supplemental oxygen; 5= hospitalized, not requiring supplemental oxygen – requiring ongoing medical care (COVID-19 related or otherwise); 6= hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7= not hospitalized, limitation on activities and/or requiring home oxygen; 8= not hospitalized, no limitations on activities. PV 1-6 population included subjects randomised into the study under protocol versions 1-6.

End point type	Secondary

End point timeframe:

Baseline up to Day 7 and 14

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	87		
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 7	51.5 (41.4 to 61.4)	50.6 (39.6 to 61.5)		
Day 14	72.8 (63.2 to 81.1)	72.4 (61.8 to 81.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Clinical Improvement of 2-Points Using Ordinal Scale (TTCI-2)

End point title	Time to Clinical Improvement of 2-Points Using Ordinal Scale (TTCI-2)

End point description:

TTCI-2 was defined as the time from randomisation to an improvement of 2 points using 8-points Ordinal Scale. The 8-point ordinal scale ranges from 1 to 8: where 1= death, 2= hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3= hospitalized, on non-invasive ventilation or high flow oxygen devices; 4= hospitalized, requiring supplemental oxygen; 5= hospitalized, not requiring supplemental oxygen – requiring ongoing medical care (coronavirus disease 2019 [COVID-19] related or otherwise); 6= hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7= not hospitalized, limitation on activities and/or requiring home oxygen; 8= not hospitalized, no limitations on activities. ITT Population included all subjects who were randomised in the study with confirmed SARS-CoV2 infection under protocol version 6.0 and above, regardless of whether or not they receive study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 28

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	51		
Units: Days				
median (confidence interval 95%)	10.0 (8.0 to 14.0)	10.0 (8.0 to 14.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Death Rate

End point title	Overall Death Rate

End point description:

Overall death rate was defined as the percentage of subjects who died on or before Day 28. ITT population included all subjects who were randomised in the study with confirmed SARS-CoV2 infection under protocol version 6.0 and above, regardless of whether or not they receive study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 28

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	51		
Units: Percentage of subjects				
number (confidence interval 95%)	15.2 (7.5 to 26.1)	3.9 (0.5 to 13.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Mechanical Ventilation (RMV)

End point title	Rate of Mechanical Ventilation (RMV)

End point description:

The rate of RMV was defined as the percentage of subjects who ever used invasive mechanical ventilation or ECMO during the hospital stay. ITT population included all subjects who were randomised in the study with confirmed SARS-CoV2 infection under protocol version 6.0 and above, regardless of whether or not they receive study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 28

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	51		
Units: Percentage of subjects				
number (confidence interval 95%)	13.6 (6.4 to 24.3)	11.8 (4.4 to 23.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Intensive Care Unit (ICU) Admission

End point title	Rate of Intensive Care Unit (ICU) Admission

End point description:

The rate of ICU admission was defined as the percentage of subjects with ICU admissions. ITT population included all subjects who were randomised in the study with confirmed SARS-CoV2 infection under protocol version 6.0 and above, regardless of whether or not they receive study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 28

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	51		
Units: Percentage of subjects				
number (confidence interval 95%)	48.5 (36.0 to 61.1)	41.2 (27.6 to 55.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of Hospitalization

End point title	Length of Hospitalization

End point description:

Length of hospitalization (days) was defined as (first hospital discharge date – date of randomisation + 1). ITT population included all subjects who were randomised in the study with confirmed SARS-CoV2 infection under protocol version 6.0 and above, regardless of whether or not they receive study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 67

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	51		
Units: Days				
median (full range (min-max))	9.0 (3 to 39)	9.0 (3 to 67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in C-reactive Protein (CRP) Levels

End point title	Change From Baseline in C-reactive Protein (CRP) Levels

End point description:

The anti-inflammatory and immune effects of selinexor were assessed by CRP levels. Baseline was defined as the most recent non-missing measurement prior to the first administration of study treatment. Change from Baseline at the indicated time points was calculated as the value at the indicated time points minus the value at Baseline. PV 1-6 population included subjects randomised into the study under protocol versions 1-6. Here "n= number of subjects" who were evaluable for this end point at a specified time points.

End point type	Secondary

End point timeframe:

Baseline, Day 3, 5, 8, 12, 15, 19, 22 and 26

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	87		
Units: milligram per liter (mg/L)				
arithmetic mean (standard deviation)				
Change at Day 3 (n= 88, 74)	-47.9660 (± 99.06082)	-42.9658 (± 89.09341)		
Change at Day 5 (n= 83, 69)	-74.4735 (± 114.52388)	-68.6191 (± 108.19671)		
Change at Day 8 (n= 57, 45)	-83.3460 (± 93.83500)	-74.4669 (± 117.66505)		
Change at Day 12 (n= 31, 27)	-86.9158 (± 123.54705)	-93.2744 (± 131.56709)		
Change at Day 15 (n= 10, 15)	-87.9800 (± 121.19999)	-98.7940 (± 87.65276)		
Change at Day 19 (n= 7, 9)	-66.2143 (± 86.55049)	-124.3233 (± 102.04161)		
Change at Day 22 (n= 10, 5)	-90.7100 (± 149.25579)	-47.5620 (± 171.49171)		

Change at Day 26 (n= 5, 5)	-37.2800 (± 141.41390)	-129.5020 (± 46.26178)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Ferritin Levels

End point title	Change From Baseline in Ferritin Levels

End point description:

The anti-inflammatory and immune effects of selinexor were assessed by ferritin levels. Baseline was defined as the most recent non-missing measurement prior to the first administration of study treatment. Change from Baseline at the indicated time points was calculated as the value at the indicated time points minus the value at Baseline. PV 1-6 population included subjects randomised into the study under protocol versions 1-6. Here "n= number of subjects" who were evaluable for this end point at a specified time points.

End point type	Secondary

End point timeframe:

Baseline, Day 3, 5, 8, 12, 15, 19, 22 and 26

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	87		
Units: microgram/liter (mcg/L)				
arithmetic mean (standard deviation)				
Change at Day 3 (n= 82, 70)	80.8415 (± 759.10075)	-61.9843 (± 542.09460)		
Change at Day 5 (n= 79, 63)	-25.7000 (± 856.16619)	-155.3111 (± 773.76777)		
Change at Day 8 (n= 53, 39)	226.6113 (± 1673.46162)	-292.2462 (± 738.07874)		
Change at Day 12 (n= 29, 25)	193.5793 (± 1203.33385)	-352.5280 (± 741.13673)		
Change at Day 15 (n= 10, 14)	204.3900 (± 557.29217)	-356.8429 (± 476.04151)		
Change at Day 19 (n= 6, 8)	-15.9333 (± 462.40358)	-231.2374 (± 599.98919)		
Change at Day 22 (n= 10, 4)	-103.9900 (± 636.89555)	-102.0000 (± 417.51247)		
Change at Day 26 (n= 6, 4)	-150.1167 (± 535.94141)	-25.7500 (± 231.43232)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Lactate Dehydrogenase (LDH) Levels

End point title	Change From Baseline in Lactate Dehydrogenase (LDH) Levels

End point description:

The anti-inflammatory and immune effects of selinexor were assessed by LDH levels. Baseline was defined as the most recent non-missing measurement prior to the first administration of study treatment. Change from Baseline at the indicated time points was calculated as the value at the indicated time points minus the value at Baseline. PV 1-6 population included subjects randomised into the study under protocol versions 1-6. Here "n= number of subjects" who were evaluable for this end point at a specified time points.

End point type	Secondary

End point timeframe:

Baseline, Day 3, 5, 8, 12, 15, 19, 22 and 26

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	87		
Units: units/liter (U/L)				
arithmetic mean (standard deviation)				
Change at Day 3 (n= 76, 63)	-13.86 (± 148.231)	-11.86 (± 151.630)		
Change at Day 5 (n= 74, 62)	-49.12 (± 175.722)	31.85 (± 326.281)		
Change at Day 8 (n= 52, 40)	-75.85 (± 264.840)	-10.93 (± 166.876)		
Change at Day 12 (n= 28, 25)	-107.39 (± 198.092)	-16.84 (± 232.605)		
Change at Day 15 (n= 11, 14)	-71.82 (± 193.543)	-51.50 (± 148.063)		
Change at Day 19 (n= 8, 7)	-96.38 (± 200.164)	-74.14 (± 114.271)		
Change at Day 22 (n= 10, 5)	-129.70 (± 177.454)	-75.40 (± 43.569)		
Change at Day 26 (n= 6, 4)	-169.50 (± 213.481)	4.50 (± 130.733)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes From Baseline in Blood Plasma Cytokines Levels-Interleukin-6 (IL-6)

End point title	Changes From Baseline in Blood Plasma Cytokines Levels-Interleukin-6 (IL-6)

End point description:

The anti-inflammatory and immune effects of selinexor were assessed by blood plasma cytokines like IL-6. Baseline was defined as the most recent non-missing measurement prior to the first administration of study treatment. Change from Baseline at the indicated time points was calculated as the value at the indicated time points minus the value at Baseline. PV 1-6 population included subjects randomised into the study under protocol versions 1-6. Here "n= number of subjects" who were evaluable for this end point at a specified time points. Here, '99999' indicates standard deviation was not estimated due to single subject and '9999' indicates no subject was estimated at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Day 3, 5, 8, 12, 15, 22 and 26

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	87		
Units: nanograms/milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Change at Day 3 (n= 38, 23)	-19.931 (± 51.2072)	2.046 (± 49.0258)		
Change at Day 5 (n= 38, 26)	-10.786 (± 102.9160)	-77.509 (± 408.0085)		
Change at Day 8 (n= 28, 15)	-13.909 (± 161.6803)	183.728 (± 662.7908)		
Change at Day 12 (n= 13, 9)	276.289 (± 1541.3692)	223.637 (± 715.5904)		
Change at Day 15 (n= 4, 4)	-34.850 (± 28.6357)	207.625 (± 408.5783)		
Change at Day 22 (n= 3, 0)	-8.600 (± 11.8072)	9999 (± 9999)		
Change at Day 26 (n= 1, 0)	-23.400 (± 99999)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs

End point description:

Adverse events are defined as any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. Serious adverse event (SAE) was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. TEAEs are defined as those AEs that develop or worsen after the first dose of study drug. TEAEs included both serious and non-serious TEAEs. All-treated population consisted of the subset of ITT subjects who took at least one dose of study drug.

End point type	Secondary

End point timeframe:

From start of study drug administration up to Day 58

End point values	Selinexor 20 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	86		
Units: Subjects				
Subjects with TEAEs	75	49		
Subjects with Serious TEAEs	23	14		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration up to Day 58

Adverse event reporting additional description:

All-treated population consisted of the subset of ITT subjects who took at least one dose of study treatment on this study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Selinexor 20 mg

Reporting group description:

Subjects received a single dose of Selinexor 20 mg tablets orally on Days 1, 3 and 5 of each week for up to 2 weeks. The subject tolerated therapy and showed clinical benefit, dosing continued for an additional 2 weeks (on Days 15, 17, 19, 22, 24, and 26).

Reporting group title	Placebo

Reporting group description:

Subjects received a single dose of placebo matched to selinexor tablets orally on Days 1, 3 and 5 of each week for up to 2 weeks. The subject tolerated therapy and showed clinical benefit, dosing continued for an additional 2 weeks (on Days 15, 17, 19, 22, 24, and 26).

Serious adverse events	Selinexor 20 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 102 (22.55%)	14 / 86 (16.28%)	
number of deaths (all causes)	16	8	
number of deaths resulting from adverse events	16	7	
Injury, poisoning and procedural complications			
Procedural pneumothorax			
subjects affected / exposed	1 / 102 (0.98%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 102 (0.98%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 16	0 / 8	
Cardiac arrest			

subjects affected / exposed	2 / 102 (1.96%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Cardiac failure			
subjects affected / exposed	1 / 102 (0.98%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Long QT syndrome			
subjects affected / exposed	1 / 102 (0.98%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Myocardial infarction			
subjects affected / exposed	0 / 102 (0.00%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 16	0 / 8	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 102 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 16	0 / 8	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 102 (0.00%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 16	0 / 8	
Systemic inflammatory response syndrome			

subjects affected / exposed	1 / 102 (0.98%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Gastrointestinal disorders			
Intestinal ischaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 16	0 / 8	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 102 (1.96%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 16	0 / 8	
Hypoxia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Pneumonia aspiration			
subjects affected / exposed	0 / 102 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 16	0 / 8	
Pneumothorax			
subjects affected / exposed	2 / 102 (1.96%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Pulmonary embolism			
subjects affected / exposed	4 / 102 (3.92%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 16	0 / 8	
Respiratory distress			
subjects affected / exposed	0 / 102 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 16	0 / 8	

Respiratory failure			
subjects affected / exposed	6 / 102 (5.88%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 16	0 / 8	
Psychiatric disorders			
Catatonia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 102 (1.96%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 16	0 / 8	
Renal failure			
subjects affected / exposed	1 / 102 (0.98%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 102 (0.00%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	13 / 16	5 / 7	
Pneumonia			
subjects affected / exposed	1 / 102 (0.98%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 16	0 / 8	
Sepsis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 16	0 / 8	
Viral myocarditis			

subjects affected / exposed	1 / 102 (0.98%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 16	0 / 8	
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 16	0 / 8	

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

Non-serious adverse events	Selinexor 20 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 102 (67.65%)	45 / 86 (52.33%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 102 (7.84%)	4 / 86 (4.65%)	
occurrences (all)	8	4	
Aspartate aminotransferase increased			
subjects affected / exposed	9 / 102 (8.82%)	7 / 86 (8.14%)	
occurrences (all)	9	7	
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 102 (2.94%)	5 / 86 (5.81%)	
occurrences (all)	3	5	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 102 (8.82%)	1 / 86 (1.16%)	
occurrences (all)	9	1	
Leukopenia			
subjects affected / exposed	5 / 102 (4.90%)	1 / 86 (1.16%)	
occurrences (all)	5	1	
Lymphopenia			
subjects affected / exposed	5 / 102 (4.90%)	2 / 86 (2.33%)	
occurrences (all)	5	2	
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	14 / 102 (13.73%)	9 / 86 (10.47%)	
occurrences (all)	14	9	
Diarrhoea			
subjects affected / exposed	10 / 102 (9.80%)	4 / 86 (4.65%)	
occurrences (all)	10	4	
Nausea			
subjects affected / exposed	13 / 102 (12.75%)	6 / 86 (6.98%)	
occurrences (all)	13	6	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	6 / 102 (5.88%)	2 / 86 (2.33%)	
occurrences (all)	6	2	
Infections and infestations			
COVID-19			
subjects affected / exposed	5 / 102 (4.90%)	0 / 86 (0.00%)	
occurrences (all)	5	0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	7 / 102 (6.86%)	3 / 86 (3.49%)	
occurrences (all)	7	3	
Hypoalbuminaemia			
subjects affected / exposed	4 / 102 (3.92%)	5 / 86 (5.81%)	
occurrences (all)	4	5	
Hypokalaemia			
subjects affected / exposed	5 / 102 (4.90%)	3 / 86 (3.49%)	
occurrences (all)	5	3	
Hyponatraemia			
subjects affected / exposed	24 / 102 (23.53%)	5 / 86 (5.81%)	
occurrences (all)	24	5	
Hypophosphataemia			
subjects affected / exposed	5 / 102 (4.90%)	0 / 86 (0.00%)	
occurrences (all)	5	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 April 2020	Protocol Version 4: • Amended the objectives and endpoints to add established World Health Organization (WHO) ordinal score and additional secondary endpoints to capture all relevant endpoints to facilitate interpretation and combination of results across studies and trials. • Added criteria to provide clarity for stopping criteria based on specific adverse events associated study drug or lack of activity and worsening clinical outcomes. • Specific criteria for early stopping rule was clarified to provide guidance based on increase mortality. • Clarified role and responsibilities of the Data Safety Monitoring Board.
08 May 2020	Protocol Version 6.0: • Primary endpoint changed to the proportion of subjects with at least a 2-point increase in Ordinal Scale from baseline to Day 14. • Added secondary endpoints: - Time to recovery defined as improvement from baseline score of 3 greater than or equal to (>=) 4 or from a baseline score of 4 to >=5 - Proportion of subjects with at least a 2 point improvement (increase) in the Ordinal Scale from baseline to Day 7 - Proportion of subjects with at least a 1-point improvement (increase) in the Ordinal Scale from baseline to Day 7 - Proportion of subjects with at least a 1-point improvement (increase) in the Ordinal Scale from baseline to Day 14 - Time to an improvement of 2 point using WHO Ordinal Scale Improvement TTCI-2 - Time to clinical improvement (TTCI-1): defined as the time from randomisation, to an improvement of 1-point on the Ordinal Scale • Deleted secondary endpoint of Time to mechanical ventilation. • Deleted the following additional secondary endpoints: - Time to ICU admission - Proportion of subjects discharged - Duration of oxygen supplementation - TTCI in subjects less than or equal to (<=) 70 years old - TTCI in subjects greater than (>) 70 years old - TTCI in subjects that are immune compromised, have hypertension, or have pulmonary disease (smoking history or moderate to severe chronic obstructive pulmonary disease [COPD)], cardiac disease - Time to an improvement of one point using WHO Ordinal Scale Improvement - Proportion of subjects experiencing WHO Ordinal Scale Improvement of >1 point

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported