Clinical trial results:
Phase 3 Study of Sacituzumab Govitecan (IMMU-132) Versus Treatment of Physician's Choice (TPC) in Subjects With Hormonal Receptor-Positive (HR+) Human Epidermal Growth Factor Receptor 2 (HER2) Negative Metastatic Breast Cancer (MBC) Who Have Failed at Least Two Prior Chemotherapy Regimens

Summary

EudraCT number	2018-004201-33
Trial protocol	GB FR DE NL ES BE IT
Global end of trial date	20 October 2023

Results information

Result version number	v1 (current)
This version publication date	11 October 2024
First version publication date	11 October 2024

Trial information

Trial identification

Sponsor protocol code	IMMU-132-09

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03901339
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	20 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 October 2023
Global end of trial reached?	Yes
Global end of trial date	20 October 2023
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 assess and compare the efficacy and safety of sacituzumab govitecan-hzi versus treatment of physician's choice (TPC) in participants with hormonal receptor-positive (HR+) human epidermal growth factor receptor 2 (HER2-) negative metastatic breast cancer (MBC).

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 May 2019
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	Belgium: 25
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	France: 137
Country: Number of subjects enrolled	Germany: 46
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Spain: 69
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	United States: 228
Worldwide total number of subjects	543
EEA total number of subjects	300

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)	403
From 65 to 84 years	139
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Belgium, Canada, France, Germany, Italy, the Netherlands, Spain, the United Kingdom, and the United States.

Pre-assignment

Screening details:

776 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sacituzumab Govitecan

Arm description:

Participants received sacituzumab govitecan 10 mg/kg of body weight, administered as a slow intravenous (IV) infusion on Days 1 and 8 of a 21-day treatment cycle until progression of disease, occurrence of unacceptable adverse events (AEs), or another treatment discontinuation criterion was met (up to 40.1 months).

Arm type	Experimental
Investigational medicinal product name	Sacituzumab govitecan
Investigational medicinal product code	
Other name	IMMU-132, Trodelvy®
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg of body weight, administered as a slow intravenous (IV) infusion either by gravity or with an infusion pump.

Arm title	Treatment of Physician's Choice (TPC)

Arm description:

Participants received TPC (eribulin, capecitabine, gemcitabine, or vinorelbine) as single-agent treatment determined by investigator before participant randomization until progression of disease, occurrence of unacceptable AEs, or another treatment discontinuation criterion was met. Dosing per National Comprehensive Cancer Network guidelines (with dose modifications for if toxic)

- Eribulin was administered IV at dose 1.4 mg/m^2 at North American sites; 1.2 mg/m^2 at European sites on Days 1 and 8 of a 21-day cycle (up to 22.5 months).
- Capecitabine 1000 to 1250 mg/m^2 was administered in a 21-day cycle, with capecitabine administered orally twice daily for 2 weeks followed by 1-week rest period (up to 12.9 months).
- Gemcitabine 800 to 1200 mg/m^2 was administered IV on Days 1, 8, and 15 of a 28-day cycle (up to 22.3 months).
- Vinorelbine 25 mg/m^2 was administered as weekly IV injection (up to 8.1 months) and was not allowed as TPC for any participant with Grade 2 neuropathy

Arm type	Active comparator
Investigational medicinal product name	Eribulin
Investigational medicinal product code	
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Eribulin was administered IV at a dose 1.4 mg/m^2 at North American sites and 1.23 mg/m^2 at

European sites.

Investigational medicinal product name	Vinorelbine
Investigational medicinal product code	
Other name	Navelbine
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vinorelbine 25 mg/m^2 was administered as a weekly IV injection.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	Gemzar
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine 800 to 1200 mg/m^2 was administered IV.

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	Xeloda
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Capecitabine 1000 to 1250 mg/m^2 was administered orally twice daily for 2 weeks followed by 1-week rest period.

Number of subjects in period 1	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)
Started	272	271
Completed	0	0
Not completed	272	271
Death	220	192
Sponsor request	30	23
Reason not specified	5	7
Lost to follow-up	4	7
Informed consent withdrawn	13	40
Covid19	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Sacituzumab Govitecan
Reporting group description:	
Participants received sacituzumab govitecan 10 mg/kg of body weight, administered as a slow intravenous (IV) infusion on Days 1 and 8 of a 21-day treatment cycle until progression of disease, occurrence of unacceptable adverse events (AEs), or another treatment discontinuation criterion was met (up to 40.1 months).	
Reporting group title	Treatment of Physician's Choice (TPC)
Reporting group description:	
Participants received TPC (eribulin, capecitabine, gemcitabine, or vinorelbine) as single-agent treatment determined by investigator before participant randomization until progression of disease, occurrence of unacceptable AEs, or another treatment discontinuation criterion was met. Dosing per National Comprehensive Cancer Network guidelines (with dose modifications for if toxic) • Eribulin was administered IV at dose 1.4 mg/m^2 at North American sites; 1.2 mg/m^2 at European sites on Days 1 and 8 of a 21-day cycle (up to 22.5 months). • Capecitabine 1000 to 1250 mg/m^2 was administered in a 21-day cycle, with capecitabine administered orally twice daily for 2 weeks followed by 1-week rest period (up to 12.9 months). • Gemcitabine 800 to 1200 mg/m^2 was administered IV on Days 1, 8, and 15 of a 28-day cycle (up to 22.3 months). • Vinorelbine 25 mg/m^2 was administered as weekly IV injection (up to 8.1 months) and was not allowed as TPC for any participant with Grade 2 neuropathy	

Reporting group values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)	Total
Number of subjects	272	271	543
Age categorical Units: Subjects			
Adults (18-64 years)	199	204	403
From 65-84 years	72	67	139
85 years and over	1	0	1
Gender categorical Units: Subjects			
Female	270	268	538
Male	2	3	5
Race Units: Subjects			
White	184	178	362
Unknown or Not Reported	69	70	139
Black or African American	8	13	21
Asian	11	5	16
Other or More Than One Race	0	4	4
Native Hawaiian or Other Pacific Islander	0	1	1
Ethnicity			
PLACEHOLDER0			
Units: Subjects			
Hispanic or Latino	6	12	18
Not Hispanic or Latino	222	204	426
Unknown or Not Reported	44	55	99

End points

End points reporting groups

Reporting group title	Sacituzumab Govitecan

Reporting group description:

Participants received sacituzumab govitecan 10 mg/kg of body weight, administered as a slow intravenous (IV) infusion on Days 1 and 8 of a 21-day treatment cycle until progression of disease, occurrence of unacceptable adverse events (AEs), or another treatment discontinuation criterion was met (up to 40.1 months).

Reporting group title	Treatment of Physician's Choice (TPC)

Reporting group description:

Participants received TPC (eribulin, capecitabine, gemcitabine, or vinorelbine) as single-agent treatment determined by investigator before participant randomization until progression of disease, occurrence of unacceptable AEs, or another treatment discontinuation criterion was met. Dosing per National Comprehensive Cancer Network guidelines (with dose modifications for if toxic)

- Eribulin was administered IV at dose 1.4 mg/m^2 at North American sites; 1.2 mg/m^2 at European sites on Days 1 and 8 of a 21-day cycle (up to 22.5 months).
- Capecitabine 1000 to 1250 mg/m^2 was administered in a 21-day cycle, with capecitabine administered orally twice daily for 2 weeks followed by 1-week rest period (up to 12.9 months).
- Gemcitabine 800 to 1200 mg/m^2 was administered IV on Days 1, 8, and 15 of a 28-day cycle (up to 22.3 months).
- Vinorelbine 25 mg/m^2 was administered as weekly IV injection (up to 8.1 months) and was not allowed as TPC for any participant with Grade 2 neuropathy

Primary: Progression-Free Survival (PFS) by Blinded Independent Central Review (BICR) Assessment

End point title	Progression-Free Survival (PFS) by Blinded Independent Central Review (BICR) Assessment

End point description:

PFS was defined as the time from the date of randomization to the date of the first documentation of disease progression or death (whichever occurred first) according to BICR using Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1). Disease progression was defined as an increase of greater than 20% in the sum of the longest diameter (LD) of target lesions and a 5 mm absolute increase, taking as a reference the smallest sum LD recorded since the baseline assessment or the appearance of new non-target lesions. PFS was estimated using Kaplan-Meier estimate. The ITT Population included all participants who were randomized, regardless of whether they received study treatment or not.

End point type	Primary

End point timeframe:

Up to 42.8 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	271		
Units: months				
median (confidence interval 95%)	5.5 (4.2 to 6.9)	4.0 (3.0 to 4.4)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC

Statistical analysis description:

Sacituzumab Govitecan vs Treatment of Physician's Choice (TPC)

Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.653
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.526
upper limit	0.812

Notes:

[1] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: prior chemotherapy regimens for metastatic disease, presence of visceral metastasis and endocrine therapy in the metastatic setting for at least 6 months.

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from the date of randomization to the date of death from any cause. OS was estimated using Kaplan-Meier estimate. Participants without documentation of death were censored on the date they were last known to be alive. Participants in the ITT Population were analyzed.

End point type	Secondary

End point timeframe:

Up to 42.8 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	271		
Units: months				
median (confidence interval 95%)	14.5 (13.0 to 16.0)	11.2 (10.2 to 12.6)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC

Statistical analysis description:

Sacituzumab govitecan v Treatment of Physician’s Choice (TPC)

Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)

Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0133 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.788
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.652
upper limit	0.952

Notes:

[2] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: prior chemotherapy regimens for metastatic disease, presence of visceral metastasis, and endocrine therapy in the metastatic setting for at least 6 months.

Secondary: Objective Response Rate (ORR) by BICR and Local Investigator Review (LIR) Assessment

End point title	Objective Response Rate (ORR) by BICR and Local Investigator Review (LIR) Assessment

End point description:

ORR was defined as the percentage of participants who had the best overall response of either complete response (CR) or partial response (PR) that was confirmed at 4 weeks or later after initial response by BICR and LIR using RECIST 1.1. CR: Disappearance of all target and non-target lesions; and normalization of tumor marker levels initially above upper limits of normal; PR: ≥30% decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD. Participants in the ITT Population with available data were analyzed.

End point type	Secondary

End point timeframe:

Up to 42.8 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	271		
Units: percentage of participants				
number (confidence interval 95%)				
ORR by BICR Assessment	21.3 (16.6 to 26.7)	14.0 (10.1 to 18.7)		
ORR by LIR Assessment	16.5 (12.3 to 21.5)	9.2 (6.1 to 13.3)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC

Statistical analysis description:

ORR by BICR Assessment

Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)

Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0268
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.662
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.058
upper limit	2.609

Statistical analysis title	Sacituzumab Govitecan vs TPC
Statistical analysis description:	
ORR by LIR Assessment	
Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0098
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.989
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.174
upper limit	3.369

Secondary: Clinical Benefit Rate (CBR) by BICR and LIR Assessment

End point title	Clinical Benefit Rate (CBR) by BICR and LIR Assessment

End point description:

CBR was defined as the percentage of participants with the best overall response of CR, PR, or durable stable disease (duration of SD ≥ 6 months after randomization). CBR was analyzed based on both BICR and LIR assessments. CR: Disappearance of all target and non-target lesions; and normalization of tumor marker levels initially above upper limits of normal; PR: ≥30% decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD. SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum LD since the treatment started. PD: Disease progression was defined as an increase of greater than 20% in the sum of the LD of target lesions and a 5 mm absolute increase, taking as a reference the smallest sum LD recorded since the baseline assessment or the appearance of new non-target lesions. Participants in the ITT Population with available data were analyzed.

End point type	Secondary

End point timeframe:

Up to 42.8 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	271		
Units: percentage of participants				
number (confidence interval 95%)				
CBR by BICR Assessment	33.8 (28.2 to 39.8)	22.1 (17.3 to 27.6)		
CBR by LIR Assessment	32.4 (26.8 to 38.3)	21.0 (16.3 to 26.4)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Statistical analysis description: CBR by BICR Assessment	
Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0025
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.796
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.227
upper limit	2.628

Statistical analysis title	Sacituzumab Govitecan vs TPC
Statistical analysis description: CBR by LIR Assessment	
Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0024
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.834

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.237
upper limit	2.717

Secondary: Duration of Response (DOR) by BICR and LIR Assessment

End point title	Duration of Response (DOR) by BICR and LIR Assessment

End point description:

DOR was defined as the time from the date a response of CR or PR was first documented until the date of the first documentation of disease progression or date of death (whichever occurred first). DOR was analyzed based on both BICR and LIR assessments. CR: Disappearance of all target and non-target lesions; and normalization of tumor marker levels initially above upper limits of normal; PR: ≥30% decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD. Disease progression was defined as an increase of greater than 20% in the sum of the LD of target lesions and a 5 mm absolute increase, taking as a reference the smallest sum LD recorded since the baseline assessment or the appearance of new non-target lesions. DOR was estimated using Kaplan-Meier estimate. Participants in the ITT Population with confirmed objective response were analyzed.

End point type	Secondary

End point timeframe:

Up to 42.8 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	38		
Units: months				
median (confidence interval 95%)				
DOR by BICR Assessment	8.1 (6.7 to 8.9)	5.6 (3.8 to 7.9)		
DOR by LIR Assessment N=45,25	7.0 (5.6 to 8.9)	4.3 (4.2 to 6.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS by LIR Assessment

End point title	PFS by LIR Assessment

End point description:

PFS was defined as the time from the date of randomization to the date of the first documentation of disease progression or death (whichever occurred first) according to LIR using RECIST 1.1. Disease progression was defined as an increase of greater than 20% in the sum of the LD of target lesions and a 5 mm absolute increase, taking as a reference the smallest sum LD recorded since the baseline assessment or the appearance of new non-target lesions. PFS was estimated using Kaplan-Meier estimate. Participants in the ITT Population were analyzed.

End point type	Secondary

End point timeframe:

Up to 42.8 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	271		
Units: months				
median (confidence interval 95%)	4.3 (3.8 to 5.4)	3.1 (2.7 to 4.0)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Statistical analysis description: PFS by LIR Assessment	
Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.728
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.602
upper limit	0.881

Notes:

[3] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: prior chemotherapy regimens for metastatic disease, presence of visceral metastasis, and endocrine therapy in the metastatic setting for at least 6 months.

Secondary: Time to Deterioration (TTD) of Global Health Status/Quality of Life (QoL) Scale as Measured by European Organization for Research and Treatment of Cancer Quality of Life for Cancer Patients, Core Questionnaire Version 3.0 (EORTC QLQ-C30)

End point title	Time to Deterioration (TTD) of Global Health Status/Quality of Life (QoL) Scale as Measured by European Organization for Research and Treatment of Cancer Quality of Life for Cancer Patients, Core Questionnaire Version 3.0 (EORTC QLQ-C30)

End point description:

TTD was defined as the time from randomization to the first date a subject achieves 10-point deterioration from baseline in the global health status/QoL scale.The EORTC QLQ-C30 is a 30-item questionnaire to assess QoL of cancer patients.Responses to global health status,'How would you rate your overall health during the past week?' (Item 29)and the QoL 'How would you rate your overall quality of life during the past week?'(Item 30)questions were scored on 7-point scale (1=very poor; 7=excellent). All scales and single-item measures range in score from 0 to 100. Summed raw scores were standardized by linear transformation so that scores ranged from 0 to 100. Higher scores for GHS show a better level of functioning. The HRQOL-Evaluable Population included all participants who had an evaluable assessment at baseline and at least 1 evaluable assessment at postbaseline visits. Participants with a baseline global health status/QOL score ≥ 10 were analyzed.

End point type	Secondary
End point timeframe:	
Up to 37.8 months	

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	207		
Units: months				
median (confidence interval 95%)	4.3 (3.1 to 5.7)	3.0 (2.2 to 3.9)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Statistical analysis description:	
Sacituzumab Govitecan vs Treatment of Physician's Choice (TPC))	
Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	441
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0059 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.751
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.612
upper limit	0.922

Notes:

[4] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: prior chemotherapy regimens for metastatic disease, presence of visceral metastasis, and endocrine therapy in the metastatic setting for at least 6 months.

Secondary: Percentage of Participants Who Experienced Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Percentage of Participants Who Experienced Treatment Emergent Serious Adverse Events (TESAEs)

End point description:

Treatment-emergent adverse events (TEAEs) were defined as any adverse events (AEs) that begin or worsen on or after the start of study drug through 30 days after the last dose of study drug. The severity was graded based on the National Cancer Institute's Common Terminology Criteria for Adverse Events Version 5.0. An AE that met one or more of the following outcomes was classified as serious:
- Fatal
- Life-threatening
- Disabling/incapacitating
- Results in hospitalization or prolongs a hospital stay
- A congenital abnormality
- Other important medical events may also be considered serious AEs if they may require medical or

surgical intervention to prevent one of the outcomes listed above Participants in the Safety Population were analyzed.

End point type	Secondary

End point timeframe:

Up to 43.4 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	249		
Units: percentage of participants				
number (not applicable)	27.6	19.3		

Statistical analyses

No statistical analyses for this end point

Secondary: TTD of Fatigue Score as Measured by EORTC QLQ-C30

End point title	TTD of Fatigue Score as Measured by EORTC QLQ-C30

End point description:

TTD was defined as the time from randomization to the first date a subject achieves 10-point deterioration from baseline in the fatigue score.The EORTC QLQ-C30 is a questionnaire to assess quality of life, it is composed of 30 questions(items) resulting in functional scales,1 global health status scale,symptom scales,and single items.All of the scales and single-item measures range in score from 0 to 100.Participant responses to 3 questions about fatigue 'Did you need to rest', 'Have you felt weak' and 'Were you tired' were scored on a 4-point scale (1=not at all;4=very much).Summed raw scores were standardized by linear transformation so that scores ranged from 0 to 100. Higher scores on the symptom scales indicate a higher level of symptoms (i.e. a worse state of the participant). Participants in the HRQOL-Evaluable Population with baseline fatigue score ≤ 90 were analyzed.

End point type	Secondary

End point timeframe:

Up to 37.8 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	205		
Units: months				
median (confidence interval 95%)	2.2 (1.6 to 2.8)	1.4 (1.1 to 1.9)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC

Statistical analysis description:

Sacituzumab govitecan v Treatment of Physician’s Choice (TPC)

Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	439
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0021 [5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.732
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.598
upper limit	0.894

Notes:

[5] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: prior chemotherapy regimens for metastatic disease, presence of visceral metastasis, and endocrine therapy in the metastatic setting for at least 6 months.

Secondary: Percentage of Participants Who Experienced Treatment Emergent Adverse Events (TEAEs)

End point title	Percentage of Participants Who Experienced Treatment Emergent Adverse Events (TEAEs)

End point description:

An AE was defined as any untoward medical occurrence in a subject administered a medicinal product that does not necessarily have a causal relationship with this treatment. TEAEs were defined as any AEs that begin or worsen on or after the start of study drug through 30 days after the last dose of the study drug. The severity was graded based on the National Cancer Institute's Common Terminology Criteria for Adverse Events Version 5.0. The Safety Population included all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Up to 43.4 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	249		
Units: percentage of participants				
number (not applicable)	100.0	96.0		

Statistical analyses

No statistical analyses for this end point

Secondary: TTD of Pain Score as Measured by EORTC QLQ-C30

End point title	TTD of Pain Score as Measured by EORTC QLQ-C30

End point description:

TTD was defined as the time from randomization to the first date a subject achieves 10-point deterioration from baseline in the pain score.The EORTC QLQ-C30 is a questionnaire to assess quality of life, it is composed of 30 questions(items) resulting in functional scales,global health status scale,3 symptom scales,and 6 single items.All of the scales and single-item measures range in score from 0 to 100. Participant responses to 2 questions about pain, 'Have you had pain' and 'Did pain interfere with your daily activities' were scored on 4-point scale (1=not at all;4=very much). Summed raw scores were standardized by linear transformation so that scores ranges from 0 to 100. Higher scores on the symptom scales indicate a higher level of symptoms (i.e. a worse state of the participant). Participants in the HRQOL-Evaluable Population with baseline pain score ≤ 90 were analyzed.

End point type	Secondary

End point timeframe:

Up to 37.8 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	202		
Units: months				
median (confidence interval 95%)	3.8 (2.8 to 5.0)	3.5 (2.8 to 5.0)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC

Statistical analysis description:

Sacituzumab govitecan v Treatment of Physician’s Choice (TPC)

Comparison groups	Sacituzumab Govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4151 [6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.918
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.748
upper limit	1.126

Notes:

[6] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: prior chemotherapy regimens for metastatic disease, presence of visceral metastasis, and endocrine therapy in the metastatic setting for at least 6 months.

Secondary: Percentage of Participants Who Experienced the Worst Laboratory Abnormalities Grade 3 or 4 Post-Baseline

End point title	Percentage of Participants Who Experienced the Worst Laboratory Abnormalities Grade 3 or 4 Post-Baseline

End point description:

Blood samples were collected for hematology, serum chemistry, and the laboratory abnormalities were assessed. A treatment-emergent laboratory abnormality was defined as an increase of at least 1 toxicity grade from baseline at any time postbaseline up to and including the date of last study drug dose plus 30 days.The most severe graded abnormality observed post-baseline for each graded test was counted for each participant. Safety as assessed by grading of laboratory values and AEs according to the National Cancer Institutes' Common Terminology Criteria for Adverse Events (NCI CTCAE) covering grades 0-5 (0=Normal, 1=Mild, 2=Moderate, 3=Severe, 4=Life-threatening, 5=Death). The percentage of participants with worst postbaseline grades 3 or 4 are reported. Participants in the Safety Population with post-baseline values were analyzed.'Number Analyzed' indicates participants with post-baseline values with available data were analyzed.

End point type	Secondary

End point timeframe:

Up to 43.4 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	242		
Units: percentage of participants				
number (not applicable)				
Alanine Aminotransferase Increased N=264,237	1.1	2.1		
Hypoalbuminemia N=262,236	0	0.4		
Alkaline Phosphatase Increased N=263,237	0	0.8		
Aspartate Aminotransferase Increased N=264,237	1.5	1.3		
Bilirubin Increased N=264,237	2.3	0.8		
Creatinine Increased N=263,237	0.4	1.7		
Creatinine Clearance Decreased N=263,237	2.3	1.3		
Hypoglycemia N=262,237	1.1	0.8		
Hypermagnesemia N=260,233	0.4	0		
Hypomagnesemia N=260,233	0.8	0		
Hyperkalemia N=263,237	1.9	0		
Hypokalemia N=263,237	4.2	0.4		
Hyponatremia N=263,237	0.8	0.4		
Anemia N=265,241	7.5	5.0		
Hemoglobin Increased N=265,241	1.1	0		
Leukocytes Decreased N=265,241	38.9	25.7		
Leukocytosis N=265,241	0.4	0.4		
Lymphocytes Decreased N=265,241	21.5	13.7		
Lymphocytes Increased N=265,241	1.9	2.1		
Neutrophils Decreased N=265,241	53.2	40.2		
Platelets Decreased N=265,241	1.9	3.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) - Shift from Baseline Value to Best Value During Treatment

End point title	Percentage of Participants With Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) - Shift from Baseline Value to Best Value During Treatment

End point description:

ECOG performance status (PS) measured on-therapy assessed participant's performance status on 5 point scale: 0=Fully active/able to carry on all pre-disease performance without restriction;1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature;2=Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours;3=Capable of only limited self-care;confined to bed or chair more than 50% of waking hours;4=Completely disabled; cannot carry on any self-care; totally confined to bed or chair;5=Dead. Lower score indicated good performance status. Percentage of participants with Baseline ECOG PS score and corresponding changes to the best values post-baseline have been reported. Participants in the Safety Population were analyzed.

End point type	Secondary

End point timeframe:

Up to 43.4 months

End point values	Sacituzumab Govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	249		
Units: percentage of participants				
number (not applicable)				
Baseline ECOG 0, During Treatment ECOG 0	34.9	38.7		
Baseline ECOG 0, During Treatment ECOG 1	7.8	8.9		
Baseline ECOG 0, During Treatment ECOG 2	0	0.4		
Baseline ECOG 1, During Treatment ECOG 0	19.4	11.5		
Baseline ECOG 1, During Treatment ECOG 1	36.4	38.3		
Baseline ECOG 1, During Treatment ECOG 2	1.6	2.1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events and All-Cause Mortality: Up to 43.4 months

Adverse event reporting additional description:

Adverse Events: The Safety Population included all participants who received at least 1 dose of study drug; All-Cause Mortality: The ITT Population included all participants who were randomized, regardless of whether they received study treatment or not.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Treatment of Physician's Choice (TPC)

Reporting group description:

Participants received TPC (eribulin, capecitabine, gemcitabine, or vinorelbine) as single-agent treatment determined by investigator before participant randomization until progression of disease, occurrence of unacceptable AEs, or another treatment discontinuation criterion was met. Dosing per National Comprehensive Cancer Network guidelines (with dose modifications for if toxic) • Eribulin was administered IV at dose 1.4 mg/m^2 at North American sites; 1.2 mg/m^2 at European sites on Days 1 and 8 of a 21-day cycle (up to 22.5 months). • Capecitabine 1000 to 1250 mg/m^2 was administered in a 21-day cycle,
with capecitabine administered orally twice daily for 2 weeks followed by 1-week rest period (up to 12.9 months). • Gemcitabine 800 to 1200 mg/m^2 was administered IV on Days 1, 8, and 15 of a 28-day cycle (up to 22.3 months). • Vinorelbine 25 mg/m^2 was administered as weekly IV injection (up to 8.1 months)
and was not allowed as TPC for any participant with Grade 2 neuropathy.

Reporting group title	Sacituzumab Govitecan

Reporting group description:

Participants received sacituzumab govitecan 10 mg/kg of body weight, administered as a slow intravenous (IV) infusion on Days 1 and 8 of a 21-day treatment cycle until progression of disease, occurrence of unacceptable adverse events (AEs), or another treatment discontinuation criterion was met (up to 40.1 months).

Serious adverse events	Treatment of Physician's Choice (TPC)	Sacituzumab Govitecan	
Total subjects affected by serious adverse events			
subjects affected / exposed	48 / 249 (19.28%)	74 / 268 (27.61%)	
number of deaths (all causes)	238	234	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Haematoma			
subjects affected / exposed	1 / 249 (0.40%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 249 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 249 (0.40%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 249 (0.80%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	2 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Asthenia			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health ~ deterioration			
subjects affected / exposed	1 / 249 (0.40%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 249 (0.40%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 249 (1.61%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumothorax			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 249 (0.40%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 249 (0.80%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cough			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	2 / 249 (0.80%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device leakage			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Liver function test increased			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose decreased			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Compression fracture			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			

subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pneumothorax			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial infarction			
subjects affected / exposed	1 / 249 (0.40%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Nervous system disorder			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epilepsy			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	2 / 249 (0.80%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			

subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	10 / 249 (4.02%)	11 / 268 (4.10%)	
occurrences causally related to treatment / all	10 / 10	11 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 249 (0.80%)	8 / 268 (2.99%)	
occurrences causally related to treatment / all	2 / 2	8 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 249 (0.40%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 249 (0.40%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytosis			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Blepharospasm			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 249 (0.00%)	6 / 268 (2.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 249 (0.80%)	5 / 268 (1.87%)	
occurrences causally related to treatment / all	2 / 2	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	5 / 249 (2.01%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	5 / 5	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 249 (0.40%)	13 / 268 (4.85%)	
occurrences causally related to treatment / all	1 / 1	12 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 249 (0.40%)	4 / 268 (1.49%)	
occurrences causally related to treatment / all	0 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			

subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 249 (0.40%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	0 / 249 (0.00%)	5 / 268 (1.87%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Urinary tract obstruction			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	1 / 249 (0.40%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Secondary adrenocortical ~ insufficiency			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 249 (1.20%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 249 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			

subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lower respiratory tract infection ~ viral			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 249 (2.01%)	4 / 268 (1.49%)	
occurrences causally related to treatment / all	1 / 5	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection			
subjects affected / exposed	2 / 249 (0.80%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 3	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 249 (0.40%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19 pneumonia			
subjects affected / exposed	1 / 249 (0.40%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis			
subjects affected / exposed	1 / 249 (0.40%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	0 / 249 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Anal abscess			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster disseminated			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			

subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastitis			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii infection			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	1 / 249 (0.40%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 249 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 249 (0.40%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 249 (0.80%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Treatment of Physician's Choice (TPC)	Sacituzumab Govitecan	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	234 / 249 (93.98%)	264 / 268 (98.51%)	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	44 / 249 (17.67%)	34 / 268 (12.69%)	
occurrences (all)	66	54	
Alanine aminotransferase increased			
subjects affected / exposed	37 / 249 (14.86%)	30 / 268 (11.19%)	
occurrences (all)	52	46	
Blood alkaline phosphatase increased			
subjects affected / exposed	27 / 249 (10.84%)	25 / 268 (9.33%)	
occurrences (all)	30	36	
Weight decreased			

subjects affected / exposed	14 / 249 (5.62%)	15 / 268 (5.60%)	
occurrences (all)	14	15	
Blood lactate dehydrogenase increased			
subjects affected / exposed	13 / 249 (5.22%)	9 / 268 (3.36%)	
occurrences (all)	15	9	
Blood bilirubin increased			
subjects affected / exposed	14 / 249 (5.62%)	8 / 268 (2.99%)	
occurrences (all)	16	9	
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 249 (4.42%)	16 / 268 (5.97%)	
occurrences (all)	12	19	
Nervous system disorders			
Headache			
subjects affected / exposed	36 / 249 (14.46%)	44 / 268 (16.42%)	
occurrences (all)	44	54	
Dizziness			
subjects affected / exposed	10 / 249 (4.02%)	23 / 268 (8.58%)	
occurrences (all)	11	30	
Neuropathy peripheral			
subjects affected / exposed	20 / 249 (8.03%)	11 / 268 (4.10%)	
occurrences (all)	24	12	
Peripheral sensory neuropathy			
subjects affected / exposed	16 / 249 (6.43%)	10 / 268 (3.73%)	
occurrences (all)	18	10	
Paraesthesia			
subjects affected / exposed	14 / 249 (5.62%)	8 / 268 (2.99%)	
occurrences (all)	14	8	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	41 / 249 (16.47%)	17 / 268 (6.34%)	
occurrences (all)	61	23	
Lymphopenia			
subjects affected / exposed	29 / 249 (11.65%)	32 / 268 (11.94%)	
occurrences (all)	39	70	
Leukopenia			

subjects affected / exposed	25 / 249 (10.04%)	37 / 268 (13.81%)	
occurrences (all)	38	67	
Anaemia			
subjects affected / exposed	68 / 249 (27.31%)	97 / 268 (36.19%)	
occurrences (all)	82	128	
Neutropenia			
subjects affected / exposed	134 / 249 (53.82%)	184 / 268 (68.66%)	
occurrences (all)	257	409	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	14 / 249 (5.62%)	17 / 268 (6.34%)	
occurrences (all)	14	19	
Pain			
subjects affected / exposed	11 / 249 (4.42%)	14 / 268 (5.22%)	
occurrences (all)	11	14	
Mucosal inflammation			
subjects affected / exposed	14 / 249 (5.62%)	23 / 268 (8.58%)	
occurrences (all)	16	36	
Pyrexia			
subjects affected / exposed	44 / 249 (17.67%)	38 / 268 (14.18%)	
occurrences (all)	65	46	
Asthenia			
subjects affected / exposed	49 / 249 (19.68%)	62 / 268 (23.13%)	
occurrences (all)	56	97	
Fatigue			
subjects affected / exposed	81 / 249 (32.53%)	106 / 268 (39.55%)	
occurrences (all)	90	114	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	86 / 249 (34.54%)	157 / 268 (58.58%)	
occurrences (all)	107	233	
Diarrhoea			
subjects affected / exposed	57 / 249 (22.89%)	163 / 268 (60.82%)	
occurrences (all)	76	311	
Abdominal pain			

subjects affected / exposed	34 / 249 (13.65%)	51 / 268 (19.03%)	
occurrences (all)	37	70	
Vomiting			
subjects affected / exposed	39 / 249 (15.66%)	63 / 268 (23.51%)	
occurrences (all)	70	95	
Constipation			
subjects affected / exposed	61 / 249 (24.50%)	93 / 268 (34.70%)	
occurrences (all)	71	125	
Dry mouth			
subjects affected / exposed	5 / 249 (2.01%)	16 / 268 (5.97%)	
occurrences (all)	5	16	
Gastrooesophageal reflux disease			
subjects affected / exposed	9 / 249 (3.61%)	14 / 268 (5.22%)	
occurrences (all)	9	15	
Abdominal distension			
subjects affected / exposed	8 / 249 (3.21%)	17 / 268 (6.34%)	
occurrences (all)	9	18	
Dyspepsia			
subjects affected / exposed	7 / 249 (2.81%)	19 / 268 (7.09%)	
occurrences (all)	7	21	
Stomatitis			
subjects affected / exposed	18 / 249 (7.23%)	23 / 268 (8.58%)	
occurrences (all)	20	34	
Abdominal pain upper			
subjects affected / exposed	15 / 249 (6.02%)	26 / 268 (9.70%)	
occurrences (all)	16	27	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	38 / 249 (15.26%)	48 / 268 (17.91%)	
occurrences (all)	43	59	
Cough			
subjects affected / exposed	18 / 249 (7.23%)	33 / 268 (12.31%)	
occurrences (all)	21	40	
Epistaxis			

subjects affected / exposed	6 / 249 (2.41%)	22 / 268 (8.21%)	
occurrences (all)	6	23	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	14 / 249 (5.62%)	24 / 268 (8.96%)	
occurrences (all)	14	27	
Alopecia			
subjects affected / exposed	46 / 249 (18.47%)	128 / 268 (47.76%)	
occurrences (all)	47	129	
Pruritus			
subjects affected / exposed	6 / 249 (2.41%)	32 / 268 (11.94%)	
occurrences (all)	6	37	
Dry skin			
subjects affected / exposed	8 / 249 (3.21%)	18 / 268 (6.72%)	
occurrences (all)	8	18	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	14 / 249 (5.62%)	6 / 268 (2.24%)	
occurrences (all)	16	6	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	19 / 249 (7.63%)	21 / 268 (7.84%)	
occurrences (all)	21	24	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	29 / 249 (11.65%)	40 / 268 (14.93%)	
occurrences (all)	30	46	
Back pain			
subjects affected / exposed	30 / 249 (12.05%)	35 / 268 (13.06%)	
occurrences (all)	32	40	
Bone pain			
subjects affected / exposed	16 / 249 (6.43%)	21 / 268 (7.84%)	
occurrences (all)	18	24	
Myalgia			
subjects affected / exposed	20 / 249 (8.03%)	17 / 268 (6.34%)	
occurrences (all)	22	26	
Muscle spasms			

subjects affected / exposed	11 / 249 (4.42%)	19 / 268 (7.09%)	
occurrences (all)	12	23	
Pain in extremity			
subjects affected / exposed	13 / 249 (5.22%)	17 / 268 (6.34%)	
occurrences (all)	15	22	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	24 / 249 (9.64%)	24 / 268 (8.96%)	
occurrences (all)	32	36	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	52 / 249 (20.88%)	57 / 268 (21.27%)	
occurrences (all)	54	74	
Hypokalaemia			
subjects affected / exposed	9 / 249 (3.61%)	30 / 268 (11.19%)	
occurrences (all)	9	32	
Hyperglycaemia			
subjects affected / exposed	17 / 249 (6.83%)	10 / 268 (3.73%)	
occurrences (all)	21	19	
Hypomagnesaemia			
subjects affected / exposed	9 / 249 (3.61%)	16 / 268 (5.97%)	
occurrences (all)	15	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2021	- Changes made to align with the Health Authority Requirements - With cancellation of interim analysis, ORR was no longer a primary endpoint - BICR assessment added in alignment of Health Authority requirement - Clarified alpha allocation - Text added to update Sponsor's position to not conduct interim analysis - Primary analysis of PFS was conducted on BICR assessment - All tumor-based endpoints were summarized based on both BICR and LIR
23 August 2021	- Change in Sponsor language throughout to reflect Immunomedics, Inc. is now part of the Gilead group of companies. - The Sponsor signature page was moved to Appendix 1 and other appendices have been re-numbered. - Abbreviations were added to the Schedule of Procedures table.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/37633306

http://www.ncbi.nlm.nih.gov/pubmed/36027558

http://www.ncbi.nlm.nih.gov/pubmed/32223649

http://www.ncbi.nlm.nih.gov/pubmed/38748596

http://www.ncbi.nlm.nih.gov/pubmed/38270051

http://www.ncbi.nlm.nih.gov/pubmed/39067902