Clinical trial results:
A Phase 2, Open-label Study to Evaluate the Safety and Efficacy of Switching to Tenofovir Alafenamide (TAF) from Tenofovir Disoproxil Fumarate (TDF) and/or Other Oral Antiviral Treatment (OAV) in Virologically Suppressed Chronic Hepatitis B Subjects with Renal and/or Hepatic Impairment

Summary

EudraCT number	2016-004625-16
Trial protocol	GB FR IT
Global end of trial date	04 September 2020

Results information

Result version number	v1 (current)
This version publication date	15 September 2021
First version publication date	15 September 2021

Trial information

Trial identification

Sponsor protocol code	GS-US-320-4035

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03180619
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	04 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 March 2019
Global end of trial reached?	Yes
Global end of trial date	04 September 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 evaluate the safety and tolerability and virologic response of tenofovir alafenamide (TAF) in virologically suppressed chronic hepatitis B participants with renal and/or hepatic impairment.

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	29 June 2017
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 Kingdom: 2
Country: Number of subjects enrolled	Taiwan: 33
Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	Korea, Republic of: 20
Country: Number of subjects enrolled	Hong Kong: 17
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	New Zealand: 2
Worldwide total number of subjects	124
EEA total number of subjects	15

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)	71
From 65 to 84 years	52
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Asia Pacific, North America, and Europe. The first participant was screened on 29 June 2017. The last study visit occurred on 04 September 2020.

Pre-assignment

Screening details:

147 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A (Renal Impairment): Moderate or Severe Renal Impairment

Arm description:

Participants with chronic hepatitis B (CHB) and moderate or severe renal impairment who were virologically suppressed and took tenofovir disoproxil fumarate (TDF), a TDF-containing anti-hepatitis B virus (HBV) regimen, or other oral antivirals (OAVs), switched to tenofovir alafenamide (TAF) and received TAF 25 mg tablet once daily orally for 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	Vemlidy®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg administered once daily

Arm title	Part A (Renal Impairment): End Stage Renal Disease

Arm description:

Participants with CHB and end stage renal disease who were virologically suppressed and took TDF, a TDF-containing anti-HBV regimen, or OAVs, switched to TAF and received TAF 25 mg tablet once daily orally for 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	Vemlidy®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg administered once daily

Arm title	Part B: Hepatic Impairment

Arm description:

Participants with CHB and moderate or severe hepatic impairment who were virologically suppressed and took TDF, a TDF-containing anti-HBV regimen, or OAVs, switched to TAF and received TAF 25 mg tablet once daily orally for 96 weeks.

Arm type	Experimental

Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	Vemlidy®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg administered once daily

Number of subjects in period 1	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment
Started	78	15	31
Completed	67	14	25
Not completed	11	1	6
Death	2	1	2
Adverse event	2	-	1
Withdrew consent	5	-	2
Investigator's discretion	2	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Part A (Renal Impairment): Moderate or Severe Renal Impairment

Reporting group description:

Participants with chronic hepatitis B (CHB) and moderate or severe renal impairment who were virologically suppressed and took tenofovir disoproxil fumarate (TDF), a TDF-containing anti-hepatitis B virus (HBV) regimen, or other oral antivirals (OAVs), switched to tenofovir alafenamide (TAF) and received TAF 25 mg tablet once daily orally for 96 weeks.

Reporting group title	Part A (Renal Impairment): End Stage Renal Disease

Reporting group description:

Participants with CHB and end stage renal disease who were virologically suppressed and took TDF, a TDF-containing anti-HBV regimen, or OAVs, switched to TAF and received TAF 25 mg tablet once daily orally for 96 weeks.

Reporting group title	Part B: Hepatic Impairment

Reporting group description:

Participants with CHB and moderate or severe hepatic impairment who were virologically suppressed and took TDF, a TDF-containing anti-HBV regimen, or OAVs, switched to TAF and received TAF 25 mg tablet once daily orally for 96 weeks.

Reporting group values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment
Number of subjects	78	15	31
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	66	54	55
standard deviation	± 10.1	± 12.8	± 10.8
Gender categorical Units: Subjects			
Female	21	3	10
Male	57	12	21
Race Units: Subjects			
Asian	59	13	25
Black or African American	3	0	1
Native Hawaiian or Pacific Islander	0	2	0
White	15	0	4
Other	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	78	15	30
ALT Level Based on Central Lab Normal Range			
Central laboratory upper limit of normal (ULN) for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years.			

Units: Subjects			
<= ULN	75	15	27
> ULN - 5xULN	3	0	4
> 5xULN	0	0	0
ALT Level Based on 2018 American Association for the Study of Liver Diseases (AASLD) Normal Range			
The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males.			
Units: Subjects			
<= ULN	73	15	21
> ULN - 5xULN	5	0	10
> 5xULN	0	0	0
Hepatitis B Virus (HBV) Deoxyribonucleic Acid (DNA) Categories Units: Subjects			
< 20 IU/mL	77	14	31
>= 20 IU/mL - < 69 IU/mL	0	1	0
>= 69 IU/mL	1	0	0
Hepatitis B e Antigen/Antibody (HBeAg/HBeAb) Status Units: Subjects			
Positive/Negative	13	3	3
Positive/Positive	0	0	0
Negative/Negative	15	1	10
Negative/Positive	50	11	18
Alanine Aminotransferase (ALT)			
Units: U/L			
arithmetic mean	20	14	28
standard deviation	± 9.6	± 5.2	± 12.4
Estimated Glomerular Filtration Rate by the Cockcroft-Gault Formula (eGFRcg)			
GFR is a measure of the rate at which blood is filtered by the kidney. Cockcroft-Gault is an equation (calculation) used to estimate GFR based on serum creatinine, weight, and gender. eGFRcg = (140 – age in years) * (body weight in kg) * (0.85 if female) divided by 72 * serum creatinine in mg/dL.			
Units: mL/min			
arithmetic mean	45.5	7.8	98.8
standard deviation	± 10.89	± 2.63	± 33.94
Hepatitis s-Antigen (HBsAg)			
Units: log10 IU/mL			
arithmetic mean	2.51	2.72	1.90
standard deviation	± 0.782	± 1.405	± 1.169
FibroTest® Score			
The FibroTest® score is used to assess liver fibrosis. Scores range from 0.00 to 1.00, with higher scores indicating a greater degree of fibrosis.			
Units: units on a scale			
arithmetic mean	0.53	0.37	0.75
standard deviation	± 0.199	± 0.199	± 0.206

Reporting group values	Total		
Number of subjects	124		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	34		
Male	90		
Race Units: Subjects			
Asian	97		
Black or African American	4		
Native Hawaiian or Pacific Islander	2		
White	19		
Other	2		
Ethnicity Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	123		
ALT Level Based on Central Lab Normal Range			
Central laboratory upper limit of normal (ULN) for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years.			
Units: Subjects			
<= ULN	117		
> ULN - 5xULN	7		
> 5xULN	0		
ALT Level Based on 2018 American Association for the Study of Liver Diseases (AASLD) Normal Range			
The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males.			
Units: Subjects			
<= ULN	109		
> ULN - 5xULN	15		
> 5xULN	0		
Hepatitis B Virus (HBV) Deoxyribonucleic Acid (DNA) Categories Units: Subjects			
< 20 IU/mL	122		
>= 20 IU/mL - < 69 IU/mL	1		
>= 69 IU/mL	1		
Hepatitis B e Antigen/Antibody (HBeAg/HBeAb) Status Units: Subjects			
Positive/Negative	19		
Positive/Positive	0		
Negative/Negative	26		
Negative/Positive	79		
Alanine Aminotransferase (ALT) Units: U/L arithmetic mean standard deviation	- -		

Estimated Glomerular Filtration Rate by the Cockcroft-Gault Formula (eGFRcg)			
GFR is a measure of the rate at which blood is filtered by the kidney. Cockcroft-Gault is an equation (calculation) used to estimate GFR based on serum creatinine, weight, and gender. eGFRcg = (140 – age in years) * (body weight in kg) * (0.85 if female) divided by 72 * serum creatinine in mg/dL.			
Units: mL/min arithmetic mean standard deviation	- 		
Hepatitis s-Antigen (HBsAg) Units: log10 IU/mL arithmetic mean standard deviation	- 		
FibroTest® Score			
The FibroTest® score is used to assess liver fibrosis. Scores range from 0.00 to 1.00, with higher scores indicating a greater degree of fibrosis.			
Units: units on a scale arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Part A (Renal Impairment): Moderate or Severe Renal Impairment

Reporting group description:

Participants with chronic hepatitis B (CHB) and moderate or severe renal impairment who were virologically suppressed and took tenofovir disoproxil fumarate (TDF), a TDF-containing anti-hepatitis B virus (HBV) regimen, or other oral antivirals (OAVs), switched to tenofovir alafenamide (TAF) and received TAF 25 mg tablet once daily orally for 96 weeks.

Reporting group title	Part A (Renal Impairment): End Stage Renal Disease

Reporting group description:

Participants with CHB and end stage renal disease who were virologically suppressed and took TDF, a TDF-containing anti-HBV regimen, or OAVs, switched to TAF and received TAF 25 mg tablet once daily orally for 96 weeks.

Reporting group title	Part B: Hepatic Impairment

Reporting group description:

Participants with CHB and moderate or severe hepatic impairment who were virologically suppressed and took TDF, a TDF-containing anti-HBV regimen, or OAVs, switched to TAF and received TAF 25 mg tablet once daily orally for 96 weeks.

Primary: Percentage of Participants Achieving Virologic Response (Plasma Hepatitis B Virus [HBV] Deoxyribonucleic Acid [DNA] < 20 IU/mL) at Week 24

End point title	Percentage of Participants Achieving Virologic Response (Plasma Hepatitis B Virus [HBV] Deoxyribonucleic Acid [DNA] < 20 IU/mL) at Week 24[1]

End point description:

The percentage of participants with HBV DNA < 20 IU/mL at Week 24 was determined by the Missing = Failure (M = F) approach. The Full Analysis Set included all participants who were enrolled and received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed since this is a single treatment design.

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)	97.4	100.0	100.0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Experienced Graded Treatment-Emergent Adverse Events (AEs) at Week 24

End point title	Percentage of Participants Who Experienced Graded Treatment-Emergent Adverse Events (AEs) at Week 24[2]

End point description:

Treatment-emergent AEs were defined as:
- Any AEs with an onset date on or after the study drug start date and no later than the study drug stop date + 3 days after permanent discontinuation of study drug;
- Any AEs with onset date on or after the study drug start date for those who have not permanently discontinued study drug;
- Any AEs leading to premature discontinuation of study drug.

The most severe graded AE from all tests was counted for each participant.
The Safety Analysis Set included all participants who were enrolled and received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Week 24

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)				
Any treatment-emergent AEs	53.8	73.3	54.8	
Grade 3 and above treatment-emergent AEs	6.4	13.3	6.5	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Experienced Graded Treatment-Emergent Laboratory Abnormalities at Week 24

End point title	Percentage of Participants Who Experienced Graded Treatment-Emergent Laboratory Abnormalities at Week 24[3]

End point description:

Graded treatment-emergent laboratory abnormalities were defined as values that increased at least 1 toxicity grade from baseline at any postbaseline visit, up to and including the date of last dose of study drug + 3 days for participants who permanently discontinued study drug or the last available date in the database snapshot for participants who were on treatment at the time of the analysis.
The most severe graded abnormality from all tests was counted for each participant.
Participants in the Safety Analysis Set were analyzed.

End point type	Primary

End point timeframe:

Week 24

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)				
Any Graded Laboratory Abnormality	96.2	100.0	90.3	
Grade 3 and Above Laboratory Abnormality	11.5	46.7	48.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experienced Graded Treatment-Emergent AEs at Week 48

End point title	Percentage of Participants Who Experienced Graded Treatment-Emergent AEs at Week 48

End point description:

Treatment-emergent AEs were defined as: Any AEs with an onset date on or after the study drug start date and no later than the study drug stop date + 3 days after permanent discontinuation of study drug; Any AEs with onset date on or after the study drug start date for those who have not permanently discontinued study drug; Any AEs leading to premature discontinuation of study drug. The most severe graded AE from all tests was counted for each participant. Participants in the Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)				
Any Treatment-emergent AE	71.8	86.7	71.0	
Grade 3 and Above Treatment-emergent AEs	15.4	20.0	12.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experienced Graded Treatment-Emergent AEs at Week 96

End point title	Percentage of Participants Who Experienced Graded Treatment-Emergent AEs at Week 96

End point description:

Treatment-emergent AEs were defined as: Any AEs with an onset date on or after the study drug start date and no later than the study drug stop date + 3 days after permanent discontinuation of study drug; Any AEs with onset date on or after the study drug start date for those who have not permanently discontinued study drug; Any AEs leading to premature discontinuation of study drug. The most severe graded AE from all tests was counted for each participant. Participants in the Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)				
Any Treatment-emergent AEs	74.4	100.0	77.4	
Grade 3 and Above Treatment-emergent AEs	17.9	26.7	25.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experienced Graded Treatment-Emergent Laboratory Abnormalities at Week 48

End point title	Percentage of Participants Who Experienced Graded Treatment-Emergent Laboratory Abnormalities at Week 48

End point description:

Graded treatment-emergent laboratory abnormalities were defined as values that increased at least 1 toxicity grade from baseline at any postbaseline visit, up to and including the date of last dose of study drug + 3 days for participants who permanently discontinued study drug or the last available date in the

database snapshot for participants who were on treatment at the time of the analysis. The most severe graded abnormality from all tests was counted for each participant. Participants in the Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)				
Any Graded Laboratory Abnormality	96.2	100.0	90.3	
Grade 3	12.8	40.0	41.9	
Grade 4	0	26.7	9.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experienced Graded Treatment-Emergent Laboratory Abnormalities at Week 96

End point title	Percentage of Participants Who Experienced Graded Treatment-Emergent Laboratory Abnormalities at Week 96

End point description:

Graded treatment-emergent laboratory abnormalities were defined as values that increased at least 1 toxicity grade from baseline at any post-baseline visit, up to and including the date of last dose of study drug + 3 days for participants who permanently discontinued study drug or the last available date in the database snapshot for participants who were on treatment at the time of the analysis. The most severe graded abnormality from all tests was counted for each participant. Participants in the Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				

number (not applicable)				
Any Graded Laboratory Abnormality	96.2	100.0	100.0	
Grade 3	15.4	46.7	41.9	
Grade 4	1.3	26.7	12.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate by the Cockcroft-Gault Formula (eGFRcg) in Participants With Moderate or Severe Renal Impairment and Hepatically Impaired Participants at Week 24

End point title	Change From Baseline in Estimated Glomerular Filtration Rate by the Cockcroft-Gault Formula (eGFRcg) in Participants With Moderate or Severe Renal Impairment and Hepatically Impaired Participants at Week 24[4]

End point description:

GFR is a measure of the rate at which blood is filtered by the kidney. Cockcroft-Gault is an equation (calculation) used to estimate GFR based on serum creatinine, weight, and gender. eGFRcg = (140 – age in years) x (body weight in kg) x (0.85 if female) divided by 72 x serum creatinine in mg/dL. Moderate renal impairment= 30 mL/min ≤ eGFRCG ≤ 59 mL/min Severe renal impairment= 15 mL/min ≤ eGFRCG < 30 mL/min Change from baseline was calculated as the value at Week 24 minus the value at Baseline.
Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 24

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for participants with moderate or severe renal impairment and hepatic impairment. Only descriptive analysis was planned.

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part B: Hepatic Impairment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	31		
Units: mL/min				
median (inter-quartile range (Q1-Q3))	-0.4 (-3.9 to 4.5)	1.9 (-5.6 to 12.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in eGFRcg in Participants With Moderate or Severe Renal Impairment and Hepatically Impaired Participants at Week 48

End point title	Change From Baseline in eGFRcg in Participants With Moderate or Severe Renal Impairment and Hepatically Impaired

	Participants at Week 48[5]

End point description:

GFR is a measure of the rate at which blood is filtered by the kidney. Cockcroft-Gault is an equation (calculation) used to estimate GFR based on serum creatinine, weight, and gender. eGFRcg = (140 – age in years) x (body weight in kg) x (0.85 if female) divided by 72 x serum creatinine in mg/dL. Moderate renal impairment= 30 mL/min ≤ eGFRCG ≤ 59 mL/min Severe renal impairment= 15 mL/min ≤ eGFRCG < 30 mL/min Change from baseline was calculated as the value at Week 48 minus the value at Baseline.
Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 48

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for participants with moderate or severe renal impairment and hepatic impairment. Only descriptive analysis was planned.

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part B: Hepatic Impairment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	31		
Units: mL/min				
median (inter-quartile range (Q1-Q3))	-0.5 (-4.1 to 3.0)	1.2 (-13.5 to 6.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in eGFRcg in Participants With Moderate or Severe Renal Impairment and Hepatically Impaired Participants at Week 96

End point title	Change From Baseline in eGFRcg in Participants With Moderate or Severe Renal Impairment and Hepatically Impaired Participants at Week 96[6]

End point description:

GFR is a measure of the rate at which blood is filtered by the kidney. Cockcroft-Gault is an equation (calculation) used to estimate GFR based on serum creatinine, weight, and gender. eGFRcg = (140 – age in years) x (body weight in kg) x (0.85 if female) divided by 72 x serum creatinine in mg/dL. Moderate renal impairment= 30 mL/min ≤ eGFRCG ≤ 59 mL/min Severe renal impairment= 15 mL/min ≤ eGFRCG < 30 mL/min Change from baseline was calculated as the value at Week 96 minus the value at Baseline.
Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 96

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for participants with moderate or severe renal impairment and hepatic impairment. Only descriptive analysis was planned.

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part B: Hepatic Impairment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	25		
Units: mL/min				
median (inter-quartile range (Q1-Q3))	1.0 (-2.8 to 4.5)	-2.4 (-11.4 to 10.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Hip Bone Mineral Density (BMD) at Week 24

End point title	Percent Change From Baseline in Hip Bone Mineral Density (BMD) at Week 24

End point description:

Percent change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in the Hip Dual-Energy X-Ray Absorptiometry (DXA) Analysis Set (all participants who were enrolled and received at least 1 dose of study drug and had non-missing baseline hip BMD values) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74	15	31	
Units: percent change				
arithmetic mean (standard deviation)	0.135 (± 1.8348)	0.322 (± 2.1835)	0.322 (± 2.5105)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Hip BMD at Week 48

End point title	Percent Change From Baseline in Hip BMD at Week 48

End point description:

Percent change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in Hip DXA Analysis Set with available data were analyzed.

End point type	Secondary
End point timeframe: Baseline, Week 48	

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	14	31	
Units: percent change				
arithmetic mean (standard deviation)	0.565 (± 2.6160)	-1.075 (± 3.6355)	-0.221 (± 3.0158)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Hip BMD at Week 96

End point title	Percent Change From Baseline in Hip BMD at Week 96
End point description: Percent change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in Hip DXA Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline, Week 96	

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	13	24	
Units: percent change				
arithmetic mean (standard deviation)	0.425 (± 2.8381)	-0.834 (± 4.7171)	0.277 (± 3.2549)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Spine BMD at Week 24

End point title	Percent Change From Baseline in Spine BMD at Week 24

End point description:

Percent change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in the Spine DXA Analysis Set (all participants who were enrolled and received at least 1 dose of study drug and had non-missing baseline spine BMD values) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	15	31	
Units: percent change				
arithmetic mean (standard deviation)	1.229 (± 3.4252)	0.683 (± 3.1307)	1.258 (± 2.3416)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Spine BMD at Week 48

End point title	Percent Change From Baseline in Spine BMD at Week 48

End point description:

Percent change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in the Spine DXA Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	14	31	
Units: percent change				
arithmetic mean (standard deviation)	1.516 (± 3.7486)	0.016 (± 4.1636)	0.535 (± 3.4386)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Spine BMD at Week 96

End point title	Percent Change From Baseline in Spine BMD at Week 96

End point description:

Percent change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in the Spine DXA Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	13	23	
Units: percent change				
arithmetic mean (standard deviation)	1.293 (± 4.4136)	-0.283 (± 4.5327)	-0.249 (± 3.9127)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Virologic Response (Plasma HBV DNA < 20 IU/mL) at Week 48

End point title	Percentage of Participants Achieving Virologic Response (Plasma HBV DNA < 20 IU/mL) at Week 48

End point description:

The percentage of participants with HBV DNA < 20 IU/mL at Week 48 was determined by the Missing = Failure (M = F) approach. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Weeks 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				

number (not applicable)	92.3	93.3	100.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Virologic Response (Plasma HBV DNA < 20 IU/mL) at Week 96

End point title	Percentage of Participants Achieving Virologic Response (Plasma HBV DNA < 20 IU/mL) at Week 96

End point description:

The percentage of participants with HBV DNA < 20 IU/mL at Week 48 was determined by the Missing = Failure (M = F) approach. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Weeks 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)	83.3	86.7	77.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Detected (≥ Lower Limit of Detection [LLOD]) at Week 24

End point title	Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Detected (≥ Lower Limit of Detection [LLOD]) at Week 24

End point description:

The percentage of participants with HBV DNA < 20 IU/mL and target detected (≥ LLOD; i.e. 10 IU/mL) at Week 24 was determined by the M = F approach. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)	21.8	40.0	22.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Detected (≥ LLOD) at Week 48

End point title	Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Detected (≥ LLOD) at Week 48

End point description:

The percentage of participants with HBV DNA < 20 IU/mL and target detected (≥ LLOD; i.e. 10 IU/mL) at Week 48 was determined by the M = F approach. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)	26.9	26.7	25.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Detected (≥ LLOD) at Week 96

End point title	Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Detected (≥ LLOD) at Week 96

End point description:

The percentage of participants with HBV DNA < 20 IU/mL and target detected (≥ LLOD; i.e. 10 IU/mL) at Week 96 was determined by the M = F approach. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)	14.1	20.0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Not Detected (< LLOD) at Week 24

End point title	Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Not Detected (< LLOD) at Week 24

End point description:

The percentage of participants with HBV DNA < 20 IU/mL and target not detected (< LLOD; i.e. 10 IU/mL) at Week 24 was determined by the M = F approach. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)	75.6	60.0	77.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Not Detected (< LLOD) at Week 48

End point title	Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Not Detected (< LLOD) at Week 48

End point description:

The percentage of participants with HBV DNA < 20 IU/mL and target not detected (< LLOD; i.e. 10 IU/mL) at Week 48 was determined by the M = F approach. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Weeks 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)	65.4	66.7	74.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Not Detected (< LLOD) at Week 96

End point title	Percentage of Participants With Plasma HBV DNA < 20 IU/mL and Target Not Detected (< LLOD) at Week 96

End point description:

The percentage of participants with HBV DNA < 20 IU/mL and target not detected (< LLOD; i.e. 10 IU/mL) at Week 96 was determined by the M = F approach. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Weeks 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	

Units: percentage of participants				
number (not applicable)	69.2	66.7	77.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Loss of Hepatitis B s-Antigen (HBsAg) at Week 24

End point title	Percentage of Participants With Serological Response: Loss of Hepatitis B s-Antigen (HBsAg) at Week 24

End point description:

HBsAg loss was defined as HBsAg changing from positive at baseline to negative at a postbaseline. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBsAg Loss/Seroconversion (all participants who were enrolled and received at least 1 dose of study drug, and with HBsAg positive and HBsAb negative or missing at baseline) with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Loss of HBsAg at Week 48

End point title	Percentage of Participants With Serological Response: Loss of HBsAg at Week 48

End point description:

HBsAg loss was defined as HBsAg changing from positive at baseline to negative at a postbaseline. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBsAg Loss/Seroconversion with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	30	
Units: percentage of participants				
number (not applicable)	0	6.7	3.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Loss of HBsAg at Week 96

End point title	Percentage of Participants With Serological Response: Loss of HBsAg at Week 96

End point description:

HBsAg loss was defined as HBsAg changing from positive at baseline to negative at a postbaseline. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBsAg Loss/Seroconversion with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	30	
Units: percentage of participants				
number (not applicable)	0	0	6.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Seroconversion to Anti-HBs at Week 24

End point title	Percentage of Participants With Serological Response: Seroconversion to Anti-HBs at Week 24

End point description:

HBsAg seroconversion was defined as HBsAg loss and HBsAb test changing from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBsAg Loss/Seroconversion were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	30	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Seroconversion to Anti-HBs at Week 48

End point title	Percentage of Participants With Serological Response: Seroconversion to Anti-HBs at Week 48

End point description:

HBsAg seroconversion was defined as HBsAg loss and HBsAb test changing from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBsAg Loss/Seroconversion were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	30	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Seroconversion to Anti-HBs at Week 96

End point title	Percentage of Participants With Serological Response: Seroconversion to Anti-HBs at Week 96

End point description:

HBsAg seroconversion was defined as HBsAg loss and HBsAb test changing from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBsAg Loss/Seroconversion were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	30	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Loss of HBeAg in HBeAg-Positive Participants at Week 24

End point title	Percentage of Participants With Serological Response: Loss of HBeAg in HBeAg-Positive Participants at Week 24

End point description:

HBeAg loss was defined as HBeAg changing from positive at baseline to negative at a postbaseline. The M = F approach was used for this analysis. The Serologically Evaluable Full Analysis Set for HBeAg Loss/Seroconversion included all participants who were enrolled and received at least 1 dose of study drug, and with HBeAg positive and HBeAb negative or missing at baseline.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	3	3	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Loss of HBeAg in HBeAg-Positive Participants at Week 48

End point title	Percentage of Participants With Serological Response: Loss of HBeAg in HBeAg-Positive Participants at Week 48

End point description:

HBeAg loss was defined as HBeAg changing from positive at baseline to negative at a postbaseline. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	3	3	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Loss of HBeAg in HBeAg-Positive Participants at Week 96

End point title	Percentage of Participants With Serological Response: Loss of HBeAg in HBeAg-Positive Participants at Week 96

End point description:

HBeAg loss was defined as HBeAg changing from positive at baseline to negative at a postbaseline. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	3	3	
Units: percentage of participants				
number (not applicable)	0	33.3	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Seroconversion to Anti-HBe in HBeAg-Positive Participants at Week 24

End point title	Percentage of Participants With Serological Response: Seroconversion to Anti-HBe in HBeAg-Positive Participants at Week 24

End point description:

HBeAg seroconversion was defined as HBeAg loss and HBeAb test changing from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBeAg Loss/Seroconversion were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	3	3	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Seroconversion to Anti-HBe in HBeAg-Positive Participants at Week 48

End point title	Percentage of Participants With Serological Response: Seroconversion to Anti-HBe in HBeAg-Positive Participants at Week 48

End point description:

HBeAg seroconversion was defined as HBeAg loss and HBeAb test changing from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBeAg Loss/Seroconversion were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	3	3	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serological Response: Seroconversion to Anti-HBe in HBeAg-Positive Participants at Week 96

End point title	Percentage of Participants With Serological Response: Seroconversion to Anti-HBe in HBeAg-Positive Participants at Week 96

End point description:

HBeAg seroconversion was defined as HBeAg loss and HBeAb test changing from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBeAg Loss/Seroconversion were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	3	3	
Units: percentage of participants				

number (not applicable)	0	33.3	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Normal Alanine Aminotransferase (ALT) at Week 24 by Central Laboratory and the American Association for the Study of Liver Diseases (AASLD) Criteria

End point title	Percentage of Participants With Normal Alanine Aminotransferase (ALT) at Week 24 by Central Laboratory and the American Association for the Study of Liver Diseases (AASLD) Criteria

End point description:

Central laboratory ULN for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. The M = F approach was used for this analysis. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)				
ALT by central laboratory	92.3	93.3	83.9	
ALT by AASLD criteria	87.2	93.3	80.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Normal ALT at Week 48 by Central Laboratory and the AASLD Criteria

End point title	Percentage of Participants With Normal ALT at Week 48 by Central Laboratory and the AASLD Criteria

End point description:

Central laboratory ULN for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged

≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. The M = F approach was used for this analysis. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)				
ALT by central laboratory	89.7	86.7	90.3	
ALT by AASLD criteria	87.2	80.0	80.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Normal ALT at Week 96 by Central Laboratory and the AASLD Criteria

End point title	Percentage of Participants With Normal ALT at Week 96 by Central Laboratory and the AASLD Criteria

End point description:

Central laboratory ULN for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. The M = F approach was used for this analysis. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	15	31	
Units: percentage of participants				
number (not applicable)				
ALT by central laboratory	82.1	86.7	71.0	
ALT by AASLD criteria	74.4	86.7	58.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Normalized ALT at Week 24 by Central Laboratory and the AASLD Criteria

End point title	Percentage of Participants With Normalized ALT at Week 24 by Central Laboratory and the AASLD Criteria

End point description:

ALT normalization was defined as an ALT value that changed from above the normal range at baseline to within the normal range at the given postbaseline visit. Central laboratory ULN for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. The M = F approach was used for this analysis. Participants in the Full Analysis Set with Baseline ALT > ULN were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	0[7]	10	
Units: percentage of participants				
number (not applicable)				
Normalized ALT by Central Laboratory (n=3, 0, 4))	66.7		50.0	
Normalized ALT by AASLD Criteria (n=5, 0, 10)	40.0		60.0	

Notes:

[7] - Number of participants analyzed were 0.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Normalized ALT at Week 48 by Central Laboratory and the AASLD Criteria

End point title	Percentage of Participants With Normalized ALT at Week 48 by Central Laboratory and the AASLD Criteria

End point description:

ALT normalization was defined as an ALT value that changed from above the normal range at baseline to within the normal range at the given postbaseline visit. Central laboratory ULN for ALT were as follows:

≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. The M = F approach was used for this analysis. Participants in the Full Analysis Set with Baseline ALT > ULN were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	0[8]	10	
Units: percentage of participants				
number (not applicable)				
Normalized ALT by Central Laboratory (n=3, 0, 4)	33.3		75	
Normalized ALT by AASLD Criteria (n=5, 0, 10)	60		60	

Notes:

[8] - Number of participants analyzed were 0 at a given time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Normalized ALT at Week 96 by Central Laboratory and the AASLD Criteria

End point title	Percentage of Participants With Normalized ALT at Week 96 by Central Laboratory and the AASLD Criteria

End point description:

ALT normalization was defined as an ALT value that changed from above the normal range at baseline to within the normal range at the given postbaseline visit. Central laboratory ULN for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. The M = F approach was used for this analysis. Participants in the Full Analysis Set with Baseline ALT > ULN were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	0[9]	10	
Units: percentage of participants				

number (not applicable)				
Normalized ALT by Central Laboratory (n=3, 0, 4)	33.3		50	
Normalized ALT by AASLD Criteria (n=5, 0, 10)	20		50	

Notes:

[9] - Number of participants analyzed were 0 at given time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FibroTest® Score at Week 24

End point title	Change From Baseline in FibroTest® Score at Week 24

End point description:

The FibroTest® score is used to assess liver fibrosis. Scores range from 0.00 to 1.00, with higher scores indicating a greater degree of fibrosis. Change from baseline was calculated as the value at Week 24 minus the value at Baseline. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74	15	31	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.01 (± 0.099)	-0.01 (± 0.064)	-0.05 (± 0.106)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FibroTest® Score at Week 48

End point title	Change From Baseline in FibroTest® Score at Week 48

End point description:

The FibroTest® score is used to assess liver fibrosis. Scores range from 0.00 to 1.00, with higher scores indicating a greater degree of fibrosis. Change from baseline was calculated as the value at Week 48 minus the value at Baseline. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	14	31	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.03 (± 0.102)	-0.01 (± 0.071)	-0.03 (± 0.102)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FibroTest® Score at Week 96

End point title	Change From Baseline in FibroTest® Score at Week 96

End point description:

The FibroTest® score is used to assess liver fibrosis. Scores range from 0.00 to 1.00, with higher scores indicating a greater degree of fibrosis. Change from baseline was calculated as the value at Week 96 minus the value at Baseline. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 96

End point values	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	13	26	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.01 (± 0.114)	0.03 (± 0.107)	-0.02 (± 0.118)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Child-Pugh-Turcotte (CPT) Score in Hepatically Impaired Participants at Week 24

End point title	Change From Baseline in Child-Pugh-Turcotte (CPT) Score in Hepatically Impaired Participants at Week 24[10]

End point description:

CPT scores grade the severity of cirrhosis and are used to determine the need for liver transplantation. Scores can range from 5 to 15, with higher scores indicating a greater severity of disease. Participants in the Full Analysis Set only from Part B (Hepatic Impairment) were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 24

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for participants with hepatic impairment. Only descriptive analysis was planned.

End point values	Part B: Hepatic Impairment			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)	0 (± 1.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CPT Score in Hepatically Impaired Participants at Week 48

End point title	Change From Baseline in CPT Score in Hepatically Impaired Participants at Week 48[11]

End point description:

CPT scores grade the severity of cirrhosis and are used to determine the need for liver transplantation. Scores can range from 5 to 15, with higher scores indicating a greater severity of disease. Participants in the Full Analysis Set only from Part B (Hepatic Impairment) were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 48

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for participants with hepatic impairment. Only descriptive analysis was planned.

End point values	Part B: Hepatic Impairment			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)	0 (± 1.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CPT Score in Hepatically Impaired Participants at Week 96

End point title	Change From Baseline in CPT Score in Hepatically Impaired Participants at Week 96[12]

End point description:

CPT scores grade the severity of cirrhosis and are used to determine the need for liver transplantation. Scores can range from 5 to 15, with higher scores indicating a greater severity of disease. Participants in the Full Analysis Set only from Part B (Hepatic Impairment) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 96

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for participants with hepatic impairment. Only descriptive analysis was planned.

End point values	Part B: Hepatic Impairment			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: units on a scale				
arithmetic mean (standard deviation)	0 (± 1.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Model for End-Stage Liver Disease (MELD) Score in Hepatically Impaired Participants at Week 24

End point title	Change From Baseline in Model for End-Stage Liver Disease (MELD) Score in Hepatically Impaired Participants at Week 24[13]

End point description:

MELD scores are used to assess prognosis and suitability for liver transplantation. Scores can range from 6 to 40, with higher scores indicating greater disease severity. Participants in the Full Analysis Set only from Part B (Hepatic Impairment) were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 24

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for participants with hepatic impairment. Only descriptive analysis was planned.

End point values	Part B: Hepatic Impairment			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.6 (± 1.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MELD Score in Hepatically Impaired Participants at Week 48

End point title	Change From Baseline in MELD Score in Hepatically Impaired Participants at Week 48[14]

End point description:

MELD scores are used to assess prognosis and suitability for liver transplantation. Scores can range from 6 to 40, with higher scores indicating greater disease severity. Participants in the Full Analysis Set only from Part B (Hepatic Impairment) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 48

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for participants with hepatic impairment. Only descriptive analysis was planned.

End point values	Part B: Hepatic Impairment			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: units on a scale				
arithmetic mean (standard deviation)	0.1 (± 2.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MELD Score in Hepatically Impaired Participants at Week 96

End point title	Change From Baseline in MELD Score in Hepatically Impaired Participants at Week 96[15]

End point description:

MELD scores are used to assess prognosis and suitability for liver transplantation. Scores can range from 6 to 40, with higher scores indicating greater disease severity. Participants in the Full Analysis Set only from Part B (Hepatic Impairment) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 96

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed only for participants with hepatic impairment. Only descriptive analysis was planned.

End point values	Part B: Hepatic Impairment			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: units on a scale				
arithmetic mean (standard deviation)	-1.0 (± 1.61)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: From the first dose date up to last dose date (maximum: 108 .1 weeks) plus 3 days; All-Cause Mortality: Enrollment up to last dose date (maximum: 166.2 weeks) plus 3 days

Adverse event reporting additional description:

Adverse Events: The Safety Analysis Set included all participants who were enrolled and received at least 1 dose of study drug.

All-Cause Mortality: The Full Analysis Set included all participants who were enrolled and received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Part A (Renal Impairment): Moderate or Severe Renal Impairment

Reporting group description:

Participants with chronic hepatitis B (CHB) and moderate or severe renal impairment who were virologically suppressed and took tenofovir disoproxil fumarate (TDF), a TDF-containing anti-hepatitis B virus (HBV) regimen, or other oral antivirals (OAVs), switched to tenofovir alafenamide (TAF) and received TAF 25 mg tablet once daily orally for 96 weeks.

Reporting group title	Part A (Renal Impairment): End Stage Renal Disease

Reporting group description:

Participants with CHB and end stage renal disease who were virologically suppressed and took TDF, a TDF containing anti-HBV regimen, or OAVs, switched to TAF and received TAF 25 mg tablet once daily orally for 96 weeks.

Reporting group title	Part B: Hepatic Impairment

Reporting group description:

Participants with CHB and moderate or severe hepatic impairment who were virologically suppressed and took TDF, a TDF-containing anti-HBV regimen, or OAVs, switched to TAF and received TAF 25 mg tablet once daily orally for 96 weeks.

Serious adverse events	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 78 (15.38%)	8 / 15 (53.33%)	10 / 31 (32.26%)
number of deaths (all causes)	2	1	2
number of deaths resulting from adverse events	0	1	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bladder cancer			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Catheter site discharge			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 78 (0.00%)	2 / 15 (13.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchospasm			

subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Carcinoembryonic antigen increased			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Model for end stage liver disease score ~ increased			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula thrombosis			

subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drain site complication			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt occlusion			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	2 / 78 (2.56%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			

subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	2 / 31 (6.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 20	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	2 / 78 (2.56%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingival bleeding			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			

subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatorenal syndrome			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Endocrine disorders			
Adrenal mass			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal myositis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 78 (2.56%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fungal cystitis			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part A (Renal Impairment): Moderate or Severe Renal Impairment	Part A (Renal Impairment): End Stage Renal Disease	Part B: Hepatic Impairment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 78 (43.59%)	15 / 15 (100.00%)	23 / 31 (74.19%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Hepatocellular carcinoma			
subjects affected / exposed	1 / 78 (1.28%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Ovarian cancer stage I			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 78 (2.56%)	4 / 15 (26.67%)	1 / 31 (3.23%)
occurrences (all)	2	4	1
Hypotension			
subjects affected / exposed	0 / 78 (0.00%)	2 / 15 (13.33%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Thrombosis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Venous occlusion			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 78 (0.00%)	3 / 15 (20.00%)	5 / 31 (16.13%)
occurrences (all)	0	4	6
Oedema peripheral			
subjects affected / exposed	1 / 78 (1.28%)	1 / 15 (6.67%)	2 / 31 (6.45%)
occurrences (all)	1	1	2
Fatigue			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Chest discomfort			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	4 / 78 (5.13%)	0 / 15 (0.00%)	6 / 31 (19.35%)
occurrences (all)	4	0	6
Pleural effusion			
subjects affected / exposed	0 / 78 (0.00%)	3 / 15 (20.00%)	2 / 31 (6.45%)
occurrences (all)	0	4	2
Oropharyngeal pain			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	3
Dyspnoea			
subjects affected / exposed	1 / 78 (1.28%)	2 / 15 (13.33%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Productive cough			
subjects affected / exposed	0 / 78 (0.00%)	2 / 15 (13.33%)	1 / 31 (3.23%)
occurrences (all)	0	4	1
Rhinorrhoea			
subjects affected / exposed	1 / 78 (1.28%)	2 / 15 (13.33%)	0 / 31 (0.00%)
occurrences (all)	1	4	0
Haemoptysis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Nasal congestion			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Nasal obstruction			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Pulmonary oedema			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 78 (5.13%)	1 / 15 (6.67%)	2 / 31 (6.45%)
occurrences (all)	4	1	2
Investigations			

Bone density decreased			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	5 / 31 (16.13%)
occurrences (all)	1	0	5
Blood creatinine increased			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Blood bilirubin increased			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 78 (1.28%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Arteriovenous fistula site complication			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Incision site pain			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Shunt occlusion			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 78 (3.85%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	3	1	0
Headache			

subjects affected / exposed	2 / 78 (2.56%)	0 / 15 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	2
Cognitive disorder			
subjects affected / exposed	1 / 78 (1.28%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Amnesia			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Carotid arteriosclerosis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Cerebral atrophy			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Cerebrovascular accident			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Dementia			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Dyskinesia			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Hydrocephalus			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Vascular encephalopathy			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 78 (2.56%)	3 / 15 (20.00%)	1 / 31 (3.23%)
occurrences (all)	2	3	1
Thrombocytopenia			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences (all)	0	1	1

Blood loss anaemia			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Coagulopathy			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 78 (1.28%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Deafness neurosensory			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Ear haemorrhage			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 78 (1.28%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences (all)	1	1	1
Conjunctival haemorrhage			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Cataract nuclear			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Iridocyclitis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	3 / 78 (3.85%)	3 / 15 (20.00%)	6 / 31 (19.35%)
occurrences (all)	3	4	7
Constipation			
subjects affected / exposed	2 / 78 (2.56%)	4 / 15 (26.67%)	3 / 31 (9.68%)
occurrences (all)	2	4	4
Ascites			
subjects affected / exposed	0 / 78 (0.00%)	2 / 15 (13.33%)	4 / 31 (12.90%)
occurrences (all)	0	2	5
Abdominal pain			
subjects affected / exposed	2 / 78 (2.56%)	1 / 15 (6.67%)	2 / 31 (6.45%)
occurrences (all)	2	1	2
Toothache			
subjects affected / exposed	3 / 78 (3.85%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	3	2	0
Dental caries			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Haemorrhoids			
subjects affected / exposed	2 / 78 (2.56%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	2	1	0
Nausea			
subjects affected / exposed	1 / 78 (1.28%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences (all)	1	1	1
Vomiting			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Abdominal pain lower			
subjects affected / exposed	1 / 78 (1.28%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Flatulence			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Portal hypertensive gastropathy			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2

Mouth ulceration			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Peptic ulcer			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 78 (3.85%)	2 / 15 (13.33%)	1 / 31 (3.23%)
occurrences (all)	3	3	1
Dermatitis			
subjects affected / exposed	1 / 78 (1.28%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Skin lesion			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 78 (3.85%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences (all)	3	1	1
Chronic kidney disease			
subjects affected / exposed	0 / 78 (0.00%)	0 / 15 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Renal mass			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	0 / 78 (0.00%)	2 / 15 (13.33%)	3 / 31 (9.68%)
occurrences (all)	0	3	3
Musculoskeletal pain			
subjects affected / exposed	1 / 78 (1.28%)	3 / 15 (20.00%)	1 / 31 (3.23%)
occurrences (all)	1	6	1
Back pain			
subjects affected / exposed	2 / 78 (2.56%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	2	1	0
Bone loss			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	11 / 78 (14.10%)	3 / 15 (20.00%)	6 / 31 (19.35%)
occurrences (all)	25	8	22
Nasopharyngitis			
subjects affected / exposed	6 / 78 (7.69%)	0 / 15 (0.00%)	0 / 31 (0.00%)
occurrences (all)	14	0	0
Pneumonia			
subjects affected / exposed	2 / 78 (2.56%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences (all)	2	1	1
Urinary tract infection			
subjects affected / exposed	3 / 78 (3.85%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	3	1	0
Conjunctivitis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Cellulitis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Endophthalmitis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0

Hordeolum			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 78 (1.28%)	2 / 15 (13.33%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Hyperlipidaemia			
subjects affected / exposed	1 / 78 (1.28%)	0 / 15 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Hypokalaemia			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Metabolic acidosis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 78 (0.00%)	1 / 15 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2017	1. Clarified that imaging for HCC must have been performed within 6 months of screening. 2. Total bilirubin > 2.5 × ULN was included as a biochemical abnormality. 3. Clarified that for subjects who had sequence analysis for HBV resistance mutations, phenotypic analysis would also be performed. 4. Clarified that for subjects receiving hemodialysis, study drug would not be administered until after any postdialysis samples had been collected. 5. Clarified in-clinic dosing requirements at Weeks 4, 8, and 12.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported