Clinical trial results:
An open-label, randomized, controlled, multicenter, phase II study evaluating safety and efficacy of intratumorally administered Intuvax pre-nephrectomy followed by Sunitinib post-nephrectomy, compared to Sunitinib post-nephrectomy in metastatic renal cell carcinoma patients

Summary

EudraCT number	2014-004510-28
Trial protocol	SE CZ HU LV GB ES
Global end of trial date	17 July 2019

Results information

Result version number	v1
This version publication date	24 May 2020
First version publication date	24 May 2020

Trial information

Trial identification

Sponsor protocol code	IM-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02432846
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Immunicum AB
Sponsor organisation address	Östermalmstorg 5, Stockholm, Sweden,
Public contact	Chief Medical Officer , Immunicum AB, +46 (0)8 732 84 00, info@immunicum.com
Scientific contact	Chief Medical Officer , Immunicum AB, +46 (0)8 732 84 00, info@immunicum.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	17 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 July 2019
Global end of trial reached?	Yes
Global end of trial date	17 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives are:
- To evaluate median overall survival (OS) from randomization in metastatic renal cell carcinoma (mRCC) patients overall and by subgroup, i.e. in high-risk and in intermediate-risk patients separately, receiving two (2) vaccine doses of Intuvax pre-nephrectomy, followed by sunitinib initiated five (5) to eight (8) weeks post-nephrectomy and in non-vaccinated mRCC patients receiving sunitinib initiated five (5) to eight (8) weeks post-nephrectomy
- To evaluate 18-month survival rate from randomization in mRCC patients overall and by subgroup, i.e. in high-risk and in intermediaterisk patients separately, receiving two (2) vaccine doses of Intuvax prenephrectomy followed by sunitinib post-nephrectomy and in nonvaccinated patients receiving sunitinib post-nephrectomy

Protection of trial subjects:

The final study protocol, including substantial amendments, and the final version of the subject information and consent form, were reviewed and approved by Independent Ethics Committee and Institutional Review board prior to inclusion of subjects. The study was conducted in compliance with the protocol, regulatory requirements, good clinical practice and the ethical principles of the latest revision of the Declaration of Helsinki as adopted by the World Medical Association.

All subjects received written and verbal information regarding the study at a prior interview. The given information emphasized that participation in the study was voluntary and that the subject could withdraw from the study at any time and for any reason. All subjects were given the opportunity to ask questions about the study and were given sufficient time to decide whether to participate in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 April 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Sweden: 31
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Czech Republic: 6

Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Latvia: 6
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	88
EEA total number of subjects	86

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)	53
From 65 to 84 years	34
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The first patient's first visit was 28 April 2015 and last patient's last visit was 17 June 2019. Patients were recruited from Sweden, France, United States, Czech Republic, Latvia, Poland, Spain, Hungary, United Kingdom.

Pre-assignment

Screening details:

117 patients with newly diagnosed metastatic renal cell cancer were screened according to the inclusion and exclusion criteria. The 88 eligible patients were randomized to either of two treatments: intuvax + sunitinib or sunitinib-only. Patients were stratified according to Heng criteria, as either high-risk or intermediate-risk.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Intuvax + sunitinib, high-risk

Arm description:

Intuvax + sunitinib, high-risk stratum

Arm type	Experimental
Investigational medicinal product name	Ilixadencel (formerly known as Intuvax)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intratumoral use

Dosage and administration details:

Two (2) doses of ilixadencel (formerly known as Intuvax) cell suspension (10x10^6 DCs) administered intratumorally into the primary tumor 14 ±3 days apart followed by nephrectomy.

Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment was initiated five (5) to eight (8) weeks after nephrectomy. Administered in accordance with SmPC / USPI.

Arm title	Sunitinib-only, high-risk

Arm description:

Sunitinib-only, high-risk stratum

Arm type	Active comparator
Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment was initiated five (5) to eight (8) weeks after nephrectomy. Administered in accordance with SmPC / USPI.

Arm title	Intuvax + sunitinib, intermediate-risk

Arm description:

Intuvax + sunitinib, intermediate-risk stratum

Arm type	Experimental
Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment was initiated five (5) to eight (8) weeks after nephrectomy. Administered in accordance with SmPC / USPI.

Investigational medicinal product name	Ilixadencel (formerly known as Intuvax)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intratumoral use

Dosage and administration details:

Two (2) doses of ilixadencel (formerly known as Intuvax) cell suspension (10x10^6 DCs) administered intratumorally into the primary tumor 14 ±3 days apart followed by nephrectomy.

Arm title	Sunitinib-only, intermediate-risk

Arm description:

Sunitinib-only, intermediate-risk stratum

Arm type	Active comparator
Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment was initiated five (5) to eight (8) weeks after nephrectomy. Administered in accordance with SmPC / USPI.

Arm title	Intuvax + sunitinib, total (both strata)

Arm description:

Intuvax + sunitinib, high and intermediate risk strata combined

Arm type	Experimental
Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment was initiated five (5) to eight (8) weeks after nephrectomy. Administered in accordance with SmPC / USPI.

Investigational medicinal product name	Ilixadencel (formerly known as Intuvax)
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Suspension for injection
Routes of administration	Intratumoral use

Dosage and administration details:

Two (2) doses of ilixadencel (formerly known as Intuvax) cell suspension (10x10^6 DCs) administered intratumorally into the primary tumor 14 ±3 days apart followed by nephrectomy.

Arm title	Sunitinib-only, total (both strata)

Arm description:

Sunitinib-only, high and intermediate risk strata combined

Arm type	Active comparator
Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment was initiated five (5) to eight (8) weeks after nephrectomy. Administered in accordance with SmPC / USPI.

Number of subjects in period 1	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk
Started	17	8	41
Completed	2	0	17
Not completed	15	8	24
Adverse event, serious fatal	3	2	4
Consent withdrawn by subject	2	-	1
Disease progression	8	5	15
Adverse event, non-fatal	-	1	1
Investigator's request	2	-	-
Other	-	-	2
Lost to follow-up	-	-	1

Number of subjects in period 1	Sunitinib-only, intermediate-risk	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)
Started	22	58	30
Completed	8	19	8
Not completed	14	39	22
Adverse event, serious fatal	3	7	5
Consent withdrawn by subject	1	3	1
Disease progression	9	23	14
Adverse event, non-fatal	-	1	1
Investigator's request	-	2	-
Other	1	2	1
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Intuvax + sunitinib, high-risk
Reporting group description: Intuvax + sunitinib, high-risk stratum	
Reporting group title	Sunitinib-only, high-risk
Reporting group description: Sunitinib-only, high-risk stratum	
Reporting group title	Intuvax + sunitinib, intermediate-risk
Reporting group description: Intuvax + sunitinib, intermediate-risk stratum	
Reporting group title	Sunitinib-only, intermediate-risk
Reporting group description: Sunitinib-only, intermediate-risk stratum	
Reporting group title	Intuvax + sunitinib, total (both strata)
Reporting group description: Intuvax + sunitinib, high and intermediate risk strata combined	
Reporting group title	Sunitinib-only, total (both strata)
Reporting group description: Sunitinib-only, high and intermediate risk strata combined	

Reporting group values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk
Number of subjects	17	8	41
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Age at Screening Visit			
Units: years arithmetic mean standard deviation	 62.0 ± 9.6	 60.5 ± 7.7	 61.0 ± 8.4
Gender categorical Units: Subjects			
Female Male	2 15	2 6	11 30
Race Units: Subjects			
Unknown	1	2	0

White	16	6	41
Karnofsky Performance Status			
Karnofsky Performance Status (KPS) at baseline			
Units: Subjects			
100%	2	1	17
90%	10	2	19
80%	5	3	5
70%	0	2	0
<70%	0	0	0
Primary Tumor Stage			
Tumor stage defined by AJCC classification system. As given by the inclusion criterion 3, the primary tumor was for all patients at least 4 cm in the greatest dimension (T1b, or higher).			
Units: Subjects			
T1b	0	0	9
T2	0	0	1
T2a	4	0	5
T2b	1	0	4
T3	3	2	2
T3a	5	4	11
T3b	1	1	1
T4	3	1	8
Regional Lymph Node Tumor Stage			
Tumor stage defined by AJCC classification system.			
Units: Subjects			
NX	3	1	7
N0	7	4	20
N1	7	3	14
Distant Metastasis Tumor Stage			
Tumor stage defined by AJCC classification system.			
Units: Subjects			
M0	0	0	0
M1	17	8	41
Height			
Height at baseline			
Units: cm			
arithmetic mean	173.0	177.1	174.4
standard deviation	± 12.8	± 10.9	± 9.4
Weight			
Weight at baseline			
Units: kilogram(s)			
arithmetic mean	77.8	78.6	86.4
standard deviation	± 13.8	± 8.8	± 20.3
mRCC duration			
Range from mRCC diagnosis to Screening Visit.			
Units: days			
median	20	20.0	18.0
full range (min-max)	3 to 52	4 to 36	4 to 83

Reporting group values	Sunitinib-only, intermediate-risk	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)
Number of subjects	22	58	30

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Age at Screening Visit			
Units: years			
arithmetic mean	65.5	61.3	64.2
standard deviation	± 10.3	± 8.7	± 9.8
Gender categorical Units: Subjects			
Female	7	13	9
Male	15	45	21
Race Units: Subjects			
Unknown	0	1	2
White	22	57	28
Karnofsky Performance Status			
Karnofsky Performance Status (KPS) at baseline			
Units: Subjects			
100%	9	19	10
90%	8	29	10
80%	5	10	8
70%	0	0	2
<70%	0	0	0
Primary Tumor Stage			
Tumor stage defined by AJCC classification system. As given by the inclusion criterion 3, the primary tumor was for all patients at least 4 cm in the greatest dimension (T1b, or higher).			
Units: Subjects			
T1b	2	9	2
T2	0	1	0
T2a	3	9	3
T2b	0	5	0
T3	1	5	3
T3a	10	16	14
T3b	2	2	3
T4	4	11	5
Regional Lymph Node Tumor Stage			
Tumor stage defined by AJCC classification system.			
Units: Subjects			
NX	4	10	5
N0	7	27	11
N1	11	21	14

Distant Metastasis Tumor Stage			
Tumor stage defined by AJCC classification system.			
Units: Subjects			
M0	0	0	0
M1	22	58	30
Height			
Height at baseline			
Units: cm			
arithmetic mean	170.3	173.9	172.1
standard deviation	± 10.8	± 10.4	± 11.1
Weight			
Weight at baseline			
Units: kilogram(s)			
arithmetic mean	84.4	83.8	82.9
standard deviation	± 20.1	± 18.9	± 17.8
mRCC duration			
Range from mRCC diagnosis to Screening Visit.			
Units: days			
median	26.5	18.5	25.0
full range (min-max)	5 to 104	3 to 83	4 to 104

Reporting group values	Total		
Number of subjects	88		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Age at Screening Visit			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	22		
Male	66		
Race			
Units: Subjects			
Unknown	3		
White	85		
Karnofsky Performance Status			
Karnofsky Performance Status (KPS) at baseline			
Units: Subjects			

100%	29		
90%	39		
80%	18		
70%	2		
<70%	0		
Primary Tumor Stage			
Tumor stage defined by AJCC classification system. As given by the inclusion criterion 3, the primary tumor was for all patients at least 4 cm in the greatest dimension (T1b, or higher).			
Units: Subjects			
T1b	11		
T2	1		
T2a	12		
T2b	5		
T3	8		
T3a	30		
T3b	5		
T4	16		
Regional Lymph Node Tumor Stage			
Tumor stage defined by AJCC classification system.			
Units: Subjects			
NX	15		
N0	38		
N1	35		
Distant Metastasis Tumor Stage			
Tumor stage defined by AJCC classification system.			
Units: Subjects			
M0	0		
M1	88		
Height			
Height at baseline			
Units: cm arithmetic mean standard deviation	 -		
Weight			
Weight at baseline			
Units: kilogram(s) arithmetic mean standard deviation	 -		
mRCC duration			
Range from mRCC diagnosis to Screening Visit.			
Units: days median full range (min-max)	 -		

Subject analysis sets	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description: All patients randomized being evaluable for any high or intermediate stratum related efficacy endpoint.	
Subject analysis set title	PPS
Subject analysis set type	Per protocol

Subject analysis set description:

All patients randomized to Intuvax who had both doses of Intuvax administered or subject randomized to sunitinib alone, both having the nephrectomy and who continued the trial without any major protocol violations that could interfere with the objectives of this study.

Analyses of primary endpoints related to each stratum were repeated using the PPS.

Subject analysis set title	SAF
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized patients who had at least 1 assessment made at Screening. Safety summaries were performed on the safety set.

Reporting group values	FAS	PPS	SAF
Number of subjects	86	73	88
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Age at Screening Visit			
Units: years arithmetic mean standard deviation	±	±	62.3 ± 9.1
Gender categorical Units: Subjects			
Female Male			22 66
Race Units: Subjects			
Unknown White			3 85
Karnofsky Performance Status			
Karnofsky Performance Status (KPS) at baseline			
Units: Subjects			
100% 90% 80% 70% <70%			29 39 18 2 0
Primary Tumor Stage			
Tumor stage defined by AJCC classification system. As given by the inclusion criterion 3, the primary tumor was for all patients at least 4 cm in the greatest dimension (T1b, or higher).			
Units: Subjects			

T1b			11
T2			1
T2a			12
T2b			5
T3			8
T3a			30
T3b			5
T4			16
Regional Lymph Node Tumor Stage			
Tumor stage defined by AJCC classification system.			
Units: Subjects			
NX			15
N0			38
N1			35
Distant Metastasis Tumor Stage			
Tumor stage defined by AJCC classification system.			
Units: Subjects			
M0			0
M1			88
Height			
Height at baseline			
Units: cm			
arithmetic mean			173.3
standard deviation	±	±	± 10.6
Weight			
Weight at baseline			
Units: kilogram(s)			
arithmetic mean			83.5
standard deviation	±	±	± 18.4
mRCC duration			
Range from mRCC diagnosis to Screening Visit.			
Units: days			
median			20.5
full range (min-max)			3 to 104

End points

End points reporting groups

Reporting group title	Intuvax + sunitinib, high-risk
Reporting group description: Intuvax + sunitinib, high-risk stratum	
Reporting group title	Sunitinib-only, high-risk
Reporting group description: Sunitinib-only, high-risk stratum	
Reporting group title	Intuvax + sunitinib, intermediate-risk
Reporting group description: Intuvax + sunitinib, intermediate-risk stratum	
Reporting group title	Sunitinib-only, intermediate-risk
Reporting group description: Sunitinib-only, intermediate-risk stratum	
Reporting group title	Intuvax + sunitinib, total (both strata)
Reporting group description: Intuvax + sunitinib, high and intermediate risk strata combined	
Reporting group title	Sunitinib-only, total (both strata)
Reporting group description: Sunitinib-only, high and intermediate risk strata combined	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description: All patients randomized being evaluable for any high or intermediate stratum related efficacy endpoint.	
Subject analysis set title	PPS
Subject analysis set type	Per protocol

Subject analysis set description:

All patients randomized to Intuvax who had both doses of Intuvax administered or subject randomized to sunitinib alone, both having the nephrectomy and who continued the trial without any major protocol violations that could interfere with the objectives of this study.

Analyses of primary endpoints related to each stratum were repeated using the PPS.

Subject analysis set title	SAF
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized patients who had at least 1 assessment made at Screening. Safety summaries were performed on the safety set.

Primary: Overall Survival - days (FAS)

End point title	Overall Survival - days (FAS)[1]

End point description:

Due to the large amount of censored data, estimates of median and/or a 95% CI could not be reliably determined in all reporting groups (marked by 'NA' below). The median (CI) were:
Intuvax high-risk: 323 (152, 682)
Sunitinib-only high-risk: 282 (39, NA)
Intuvax intermediate-risk: NA (NA, NA)
Sunitinib-only intermediate risk: 1024 (617, 1241)
Intuvax total (both strata): 1127 (482, NA)
Sunitinib-only total (both strata): 716 (234, 1241)

End point type	Primary

End point timeframe:

The follow-up time of OS was between 24-1198 days in the high-risk Intuvax group, 39-825 days in the high-risk sunitinib-only group, 37-1529 days in the intermediate-risk Intuvax group and 56-1323 days in the intermediate-risk sunitinib-only group.

Notes:

[1] - 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: Due to the large amount of censored data, estimates of median and/or a 95% CI could not be reliably determined in all reporting groups. Those groups have been omitted from the reporting form. However, all estimated values for median and CI are presented in the "Description" of the endpoint, where values that could not be estimated are marked by "NA".

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Sunitinib-only, intermediate-risk	Intuvax + sunitinib, total (both strata)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	8	22	56
Units: day				
number (not applicable)	323	282	1024	1127

End point values	Sunitinib-only, total (both strata)			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: day				
number (not applicable)	716			

Statistical analyses

Statistical analysis title	Overall Survival
Comparison groups	Intuvax + sunitinib, high-risk v Sunitinib-only, high-risk v Sunitinib-only, intermediate-risk
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.05
Method	Logrank

Notes:

[2] - Exploratory superiority (non-powered)

Primary: Overall survival - days (PPS)

End point title	Overall survival - days (PPS)[3]

End point description:

Due to the large amount of censored data, estimates of median and/or a 95% CI could not be reliably determined in all reporting groups (marked by 'NA' below). The median (CI) were:
Intuvax high-risk: 352 (240, NA)
Sunitinib-only high-risk: 282 (39, NA)
Intuvax intermediate-risk: NA (NA, NA)
Sunitinib-only intermediate risk: 1173 (678, NA)
Intuvax total (both strata): NA (NA, NA)

Sunitinib-only total (both strata): 1024 (342, 1241)

End point type	Primary

End point timeframe:

The follow-up time of OS was between 152-1198 days in the high-risk Intuvax group, 39-825 days in the high-risk sunitinib-only group, 37-1529 days in the intermediate-risk Intuvax group and 166-1323 days in the intermediate-risk sunitinib-only group.

Notes:

[3] - 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: Due to the large amount of censored data, estimates of median and/or a 95% CI could not be reliably determined in all reporting groups. Those groups have been omitted from the reporting form. However, all estimated values for median and CI are presented in the "Description" of the endpoint, where values that could not be estimated are marked by "NA".

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Sunitinib-only, intermediate-risk	Sunitinib-only, total (both strata)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	8	19	27
Units: day				
number (not applicable)	352	282	1173	1024

Statistical analyses

Statistical analysis title	Overall Survival
Comparison groups	Intuvax + sunitinib, high-risk v Sunitinib-only, high-risk v Sunitinib-only, intermediate-risk
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.05
Method	Logrank

Notes:

[4] - Exploratory superiority (non-powered)

Primary: 18-Months' Overall Survival - Rate (FAS)

End point title	18-Months' Overall Survival - Rate (FAS)

End point description:

End point type	Primary

End point timeframe:

At 18 months (544 days).

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	8	40	22
Units: Percent				
number (not applicable)	30	38	77	76

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	30		
Units: Percent				
number (not applicable)	63	66		

Statistical analyses

Statistical analysis title	Overall survival at 18 months
Comparison groups	Intuvax + sunitinib, high-risk v Sunitinib-only, high-risk v Intuvax + sunitinib, intermediate-risk v Sunitinib-only, intermediate-risk
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.05
Method	Logrank

Notes:

[5] - Exploratory superiority (non-powered)

Primary: 18-Months' Overall Survival Rate (PPS)

End point title	18-Months' Overall Survival Rate (PPS)

End point description:

End point type	Primary

End point timeframe:

At 18 months (544 days)

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	8	34	19
Units: percent				

number (not applicable)	31	38	82	84

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	27		
Units: percent				
number (not applicable)	68	70		

Statistical analyses

Statistical analysis title	Overall survival at 18 months
Comparison groups	Intuvax + sunitinib, high-risk v Sunitinib-only, high-risk v Intuvax + sunitinib, intermediate-risk v Sunitinib-only, intermediate-risk
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.05
Method	Logrank

Notes:

[6] - Exploratory superiority (non-powered)

Secondary: Progression-Free Survival

End point title	Progression-Free Survival[7]

End point description:

Due to the large amount of censored data, estimates of median and/or a 95% CI could not be reliably determined in all reporting groups (marked by 'NA' below). The median (CI) were:
Intuvax high-risk: 254 (43, NA)
Sunitinib-only high-risk: NA (NA, NA)
Intuvax intermediate-risk: 478 (249, NA)
Sunitinib-only intermediate risk: 417 (149, NA)
Intuvax total (both strata): 360 (249, NA)
Sunitinib-only total (both strata): 337 (149, NA)

End point type	Secondary

End point timeframe:

From Sun-Start to PD or death following sunitinib initiation from any cause, whichever occurred first.

Notes:

[7] - 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: Due to the large amount of censored data, estimates of median and/or a 95% CI could not be reliably determined in all reporting groups. Those groups have been omitted from the reporting form. However, all estimated values for median and CI are presented in the "Description" of the endpoint, where values that could not be estimated are marked by "NA".

End point values	Intuvax + sunitinib, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk	Intuvax + sunitinib, total (both strata)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	19	46
Units: day				
number (not applicable)	254	478	417	360

End point values	Sunitinib-only, total (both strata)			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: day				
number (not applicable)	337			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate

End point title	Objective Response Rate

End point description:

End point type	Secondary

End point timeframe:

From start of sunitinib treatment.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	32	19
Units: percent				
number (not applicable)	38.5	66.7	46.9	42.1

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	25		
Units: percent				

number (not applicable)	44.4	48.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response

End point title	Best Overall Response

End point description:

End point type	Secondary

End point timeframe:

From start of sunitinib treatment.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	32	19
Units: percent				
number (not applicable)				
Complete Response (CR)	7.7	0	12.5	5.3
Partial Response (PR)	30.8	66.7	34.4	36.8
Progressive Disease (PD)	30.8	0	9.4	10.5
Stable Disease (SD)	15.4	33.3	40.6	36.8
Non-CR/Non-PD	15.4	0	0	5.3
No Disease (ND)	0	0	3.1	5.3

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	45	25	70	
Units: percent				
number (not applicable)				
Complete Response (CR)	11.1	4.0	8.6	
Partial Response (PR)	33.3	44.0	37.1	
Progressive Disease (PD)	15.6	8.0	12.9	
Stable Disease (SD)	33.3	36.0	34.3	
Non-CR/Non-PD	4.4	4.0	4.3	
No Disease (ND)	2.2	4.0	2.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate

End point title	Disease Control Rate

End point description:

End point type	Secondary

End point timeframe:

From start of sunitinib treatment.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	32	19
Units: percent				
number (not applicable)	53.8	100.0	87.5	78.9

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	25		
Units: percent				
number (not applicable)	77.8	84.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

End point type	Secondary

End point timeframe:

From date at which CR or PR was first observed until first occurrence of PD or death.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	15	8
Units: day				
median (full range (min-max))	175.0 (101 to 219)	81.5 (42 to 126)	316.0 (1 to 512)	108.0 (1 to 409)

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	20	12	32	
Units: day				
median (full range (min-max))	215.0 (1 to 512)	87.0 (1 to 409)	169.5 (1 to 512)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Clinical Benefit

End point title	Duration of Clinical Benefit

End point description:

End point type	Secondary

End point timeframe:

From start of DCR until first occurrence of PD or death for patients.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	28	15
Units: day				
median (full range (min-max))	212.0 (1 to 434)	60.0 (1 to 206)	323.5 (29 to 512)	295.0 (1 to 451)

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	35	21	56	
Units: day				
median (full range (min-max))	219.0 (1 to 512)	133.0 (1 to 451)	211.0 (1 to 512)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Stable Disease

End point title	Duration of Stable Disease

End point description:

End point type	Secondary

End point timeframe:

From first date of SD until first occurrence of PD or death.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	13	7
Units: day				
median (full range (min-max))	63.5 (1 to 126)	10.5 (1 to 20)	169.0 (29 to 427)	210.0 (50 to 449)

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15	9	86	
Units: day				
median (full range (min-max))	126.0 (1 to 427)	133.0 (1 to 449)	129.5 (1 to 449)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression

End point title	Time to Progression

End point description:

Due to the large amount of censored data, estimates of median and/or a 95% CI could not be reliably determined in all reporting groups (marked by 'NA' below). The median (CI) were:
Intuvax high-risk: 169 (43, NA)
Sunitinib-only high-risk: 143 (48, 248)
Intuvax intermediate-risk: 388 (213, NA)
Sunitinib-only intermediate risk: 417 (93, NA)
Intuvax total (both strata): 254 (169, 478)
Sunitinib-only total (both strata): 251 (93, 434)

End point type	Secondary

End point timeframe:

Time from Sun-Start to date of either PD according to RECIST 1.1 or clinical progression as evaluated by the Investigator.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	33	19
Units: day				
number (not applicable)	169	143	388	417

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	25		
Units: day				
number (not applicable)	254	251		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Infiltrating CD8+ T-Cells

End point title	Number of Infiltrating CD8+ T-Cells

End point description:

Relative number of tumor-infiltrating CD8+ T-cells in the resected primary tumor compared to number of infiltrating CD8+ T-cells in available diagnostic pre-biopsy (sample from either primary tumor or metastasis), was not to be evaluated as described in the protocol due to missing pre-biopsy samples). Instead an automated and validated quantification of percentage of CD8+ tissue in deliniated tumor

area was made.

End point type	Secondary

End point timeframe:

At resection of primary tumor.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	7	38	20
Units: percent				
median (full range (min-max))	1.0 (0 to 8)	1.1 (0 to 4)	1.2 (0 to 13)	0.8 (0 to 8)

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	52	27	79	
Units: percent				
median (full range (min-max))	1.1 (0 to 13)	0.8 (0 to 8)	1.1 (0 to 13)	

Statistical analyses

No statistical analyses for this end point

Secondary: Physical Examination

End point title	Physical Examination

End point description:

Results presented for Screening and End of Study visits. All subjects were not evaluated at each visit.

End point type	Secondary

End point timeframe:

Assessed at each study visit: Screening, Sun-Start, Vaccination 1-2 (Intuvax group, only) SFU 6W, SFU 12W, SFU 24W, SFU 36W, SFU 48W, SFU 60W and End of Study.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	41	22
Units: percent				
number (not applicable)				

Abdomen - Baseline Normal	100.0	62.5	95.1	72.7
Abdomen - Baseline Abnormal NCS	0.0	12.5	0.0	4.5
Abdomen - Baseline Abnormal CS	0.0	25.0	4.9	22.7
Abdomen - EoS Normal	88.9	100.0	93.5	93.8
Abdomen - EoS Abnormal NCS	11.1	0.0	6.5	6.3
Abdomen - EoS Abnormal CS	0.0	0.0	0.0	0.0
Cardiovascular - Baseline Normal	100.0	100.0	95.1	86.4
Cardiovascular - Baseline Abnormal NCS	0.0	0.0	0.0	13.6
Cardiovascular - Baseline Abnormal CS	0.0	0.0	4.9	0.0
Cardiovascular - EoS Normal	100.0	75.0	93.5	100.0
Cardiovascular - EoS Abnormal NCS	0.0	0.0	6.5	0.0
Cardiovascular - EoS Abnormal CS	0.0	25.0	0.0	0.0
Ear - Baseline Normal	93.8	100.0	100.0	100.0
Ear - Baseline Abnormal NCS	6.3	0.0	0.0	0.0
Ear - Baseline Abnormal CS	0.0	0.0	0.0	0.0
Ear - EoS Normal	88.9	100.0	96.7	100.0
Ear - EoS Abnormal NCS	0.0	0.0	3.3	0.0
Ear - EoS Abnormal CS	11.1	0.0	0.0	0.0
Eye - Baseline Normal	94.1	100.0	97.6	95.5
Eye - Baseline Abnormal NCS	5.9	0.0	2.4	0.0
Eye - Baseline Abnormal CS	0.0	0.0	0.0	4.5
Eye - EoS Normal	88.9	100.0	96.7	100.0
Eye - EoS Abnormal NCS	0.0	0.0	0.0	0.0
Eye - EoS Abnormal CS	11.1	0.0	3.3	0.0
Lymphatic - Baseline Normal	100.0	100.0	100.0	95.5
Lymphatic - Baseline Abnormal NCS	0.0	0.0	0.0	0.0
Lymphatic - Baseline Abnormal CS	0.0	0.0	0.0	4.5
Lymphatic - EoS Normal	100.0	100.0	100.0	100.0
Lymphatic - EoS Abnormal NCS	0.0	0.0	0.0	0.0
Lymphatic - EoS Abnormal CS	0.0	0.0	0.0	0.0
Neurol./Musculoskeletal - Baseline Normal	100.0	85.7	97.5	94.4
Neurol./Musculoskeletal - Baseline Abnormal NCS	0.0	14.3	0.0	5.6
Neurol./Musculoskeletal - Baseline Abnormal CS	0.0	0.0	2.5	0.0
Neurol./Musculoskeletal - EoS Normal	100.0	100.0	90.0	92.3
Neurol./Musculoskeletal - EoS Abnormal NCS	0.0	0.0	0.0	0.0
Neurol./Musculoskeletal - EoS Abnormal CS	0.0	0.0	10.0	7.7
Nose and Throat - Baseline Normal	94.1	100.0	97.6	100.0
Nose and Throat - Baseline Abnormal NCS	5.9	0.0	2.4	0.0
Nose and Throat - Baseline Abnormal CS	0.0	0.0	0.0	0.0
Nose and Throat - EoS Normal	88.9	100.0	93.3	93.8
Nose and Throat - EoS Abnormal NCS	0.0	0.0	3.3	6.3
Nose and Throat - EoS Abnormal CS	11.1	0.0	3.3	0.0
Other - Baseline Normal	92.3	83.3	100.0	84.6
Other - Baseline Abnormal NCS	7.7	16.7	0.0	15.4
Other - Baseline Abnormal CS	0.0	0.0	0.0	0.0
Other - EoS Normal	85.7	66.7	100.0	91.7
Other - EoS Abnormal NCS	0.0	33.3	0.0	8.3
Other - EoS Abnormal CS	14.3	0.0	0.0	0.0

Respiratory - Baseline Normal	100.0	100.0	92.7	95.5
Respiratory - Baseline Abnormal NCS	0.0	0.0	7.3	0.0
Respiratory - Baseline Abnormal CS	0.0	0.0	0.0	4.5
Respiratory - EoS Normal	100.0	100.0	93.5	93.8
Respiratory - EoS Abnormal NCS	0.0	0.0	6.5	0.0
Respiratory - EoS Abnormal CS	0.0	0.0	0.0	6.3
Skin - Baseline Normal	87.5	87.5	85.4	90.5
Skin - Baseline Abnormal NCS	12.5	12.5	12.2	9.5
Skin - Baseline Abnormal CS	0.0	0.0	2.4	0.0
Skin - EoS Normal	88.9	100.0	86.7	81.3
Skin - EoS Abnormal NCS	11.1	0.0	13.3	12.5
Skin - EoS Abnormal CS	0.0	0.0	0.0	6.3

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	SAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	58	30	88	
Units: percent				
number (not applicable)				
Abdomen - Baseline Normal	96.6	70.0	87.5	
Abdomen - Baseline Abnormal NCS	0.0	6.7	2.3	
Abdomen - Baseline Abnormal CS	3.4	23.3	10.2	
Abdomen - EoS Normal	92.5	95.0	93.3	
Abdomen - EoS Abnormal NCS	7.5	5.0	6.7	
Abdomen - EoS Abnormal CS	0.0	0.0	0.0	
Cardiovascular - Baseline Normal	96.6	90.0	94.3	
Cardiovascular - Baseline Abnormal NCS	0.0	10.0	3.4	
Cardiovascular - Baseline Abnormal CS	3.4	0.0	2.3	
Cardiovascular - EoS Normal	95.0	95.0	95.0	
Cardiovascular - EoS Abnormal NCS	5.0	0.0	3.3	
Cardiovascular - EoS Abnormal CS	0.0	5.0	1.7	
Ear - Baseline Normal	98.2	100.0	98.8	
Ear - Baseline Abnormal NCS	1.8	0.0	1.2	
Ear - Baseline Abnormal CS	0.0	0.0	0.0	
Ear - EoS Normal	97.9	100.0	96.6	
Ear - EoS Abnormal NCS	2.6	0.0	1.7	
Ear - EoS Abnormal CS	2.6	0.0	1.7	
Eye - Baseline Normal	96.6	96.7	96.6	
Eye - Baseline Abnormal NCS	3.4	0.0	2.3	
Eye - Baseline Abnormal CS	0.0	3.3	1.1	
Eye - EoS Normal	94.9	100.0	96.6	
Eye - EoS Abnormal NCS	0.0	0.0	0.0	
Eye - EoS Abnormal CS	5.1	0.0	3.4	
Lymphatic - Baseline Normal	100.0	96.7	98.9	
Lymphatic - Baseline Abnormal NCS	0.0	0.0	0.0	
Lymphatic - Baseline Abnormal CS	0.0	3.3	1.1	
Lymphatic - EoS Normal	100.0	100.0	100.0	
Lymphatic - EoS Abnormal NCS	0.0	0.0	0.0	
Lymphatic - EoS Abnormal CS	0.0	0.0	0.0	

Neurol./Musculoskeletal - Baseline Normal	98.2	92.0	96.3	
Neurol./Musculoskeletal - Baseline Abnormal NCS	0.0	8.0	2.4	
Neurol./Musculoskeletal - Baseline Abnormal CS	1.8	0.0	1.2	
Neurol./Musculoskeletal - EoS Normal	92.3	94.1	92.9	
Neurol./Musculoskeletal - EoS Abnormal NCS	0.0	0.0	0.0	
Neurol./Musculoskeletal - EoS Abnormal CS	7.7	5.9	7.1	
Nose and Throat - Baseline Normal	96.6	100.0	97.7	
Nose and Throat - Baseline Abnormal NCS	3.4	0.0	2.3	
Nose and Throat - Baseline Abnormal CS	0.0	0.0	0.0	
Nose and Throat - EoS Normal	92.3	95.0	93.2	
Nose and Throat - EoS Abnormal NCS	2.6	5.0	3.4	
Nose and Throat - EoS Abnormal CS	5.1	0.0	3.4	
Other - Baseline Normal	97.6	84.2	93.3	
Other - Baseline Abnormal NCS	2.4	15.8	6.7	
Other - Baseline Abnormal CS	0.0	0.0	0.0	
Other - EoS Normal	95.8	86.7	92.3	
Other - EoS Abnormal NCS	0.0	13.3	5.1	
Other - EoS Abnormal CS	4.2	0.0	2.6	
Respiratory - Baseline Normal	94.8	96.7	95.5	
Respiratory - Baseline Abnormal NCS	5.2	0.0	3.4	
Respiratory - Baseline Abnormal CS	0.0	3.3	1.1	
Respiratory - EoS Normal	95.0	95.0	95.0	
Respiratory - EoS Abnormal NCS	5.0	0.0	5.0	
Respiratory - EoS Abnormal CS	0.0	5.0	0.0	
Skin - Baseline Normal	86.0	89.7	87.2	
Skin - Baseline Abnormal NCS	12.3	10.3	11.6	
Skin - Baseline Abnormal CS	1.8	0.0	1.2	
Skin - EoS Normal	87.2	85.0	86.4	
Skin - EoS Abnormal NCS	12.8	10.0	11.9	
Skin - EoS Abnormal CS	0.0	5.0	1.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Vital Signs - Weight

End point title	Vital Signs - Weight

End point description:

Results presented for Screening and End of Study visits. All subjects were not evaluated at each visit.

End point type	Secondary

End point timeframe:

Assessed at each study visit: Screening, Sun-Start, Vaccination 1-2 (Intuvax group, only) SFU 6W, SFU 12W, SFU 24W, SFU 36W, SFU 48W, SFU 60W and End of Study.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	41	22
Units: kilogram(s)				
arithmetic mean (standard deviation)				
Screening	77.8 (± 13.8)	78.6 (± 8.8)	86.4 (± 20.3)	84.4 (± 20.1)
End of Study	76.7 (± 19.1)	80.8 (± 16.4)	88.3 (± 25.5)	87.9 (± 23.0)

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	SAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	58	30	88	
Units: kilogram(s)				
arithmetic mean (standard deviation)				
Screening	83.8 (± 18.9)	82.9 (± 17.8)	83.5 (± 18.4)	
End of Study	85.4 (± 24.4)	85.9 (± 21.3)	85.6 (± 23.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Vital Signs - Blood Pressure

End point title	Vital Signs - Blood Pressure

End point description:

Results presented for Screening and End of Study visits. All subjects were not evaluated at each visit.

End point type	Secondary

End point timeframe:

Assessed at each study visit: Screening, Sun-Start, Vaccination 1-2 (Intuvax group, only) SFU 6W, SFU 12W, SFU 24W, SFU 36W, SFU 48W, SFU 60W and End of Study.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	41	22
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic Blood Pressure - Baseline	131.0 (± 13.8)	132.1 (± 17.3)	139.2 (± 18.0)	141.7 (± 20.7)

Systolic Blood Pressure - End of Study	140.4 (± 22.7)	126.8 (± 13.8)	133.0 (± 15.6)	140.4 (± 12.8)
Diastolic Blood Pressure - Baseline	74.2 (± 9.8)	74.3 (± 10.7)	81.0 (± 8.7)	77.2 (± 10.3)
Diastolic Blood Pressure - End of Study	79.9 (± 9.4)	77.5 (± 13.6)	81.0 (± 11.6)	79.8 (± 12.4)

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	SAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	58	30	88	
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic Blood Pressure - Baseline	136.7 (± 17.1)	139.1 (± 20.1)	137.5 (± 18.1)	
Systolic Blood Pressure - End of Study	134.8 (± 17.5)	136.8 (± 14.1)	135.5 (± 16.3)	
Diastolic Blood Pressure - Baseline	78.9 (± 9.5)	76.4 (± 10.3)	78.0 (± 9.8)	
Diastolic Blood Pressure - End of Study	80.8 (± 11.0)	79.2 (± 12.4)	80.2 (± 11.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Vital Signs - Heart Rate

End point title	Vital Signs - Heart Rate

End point description:

Results presented for Screening and End of Study visits. All subjects were not evaluated at each visit.

End point type	Secondary

End point timeframe:

Assessed at each study visit: Screening, Sun-Start, Vaccination 1-2 (Intuvax group, only) SFU 6W, SFU 12W, SFU 24W, SFU 36W, SFU 48W, SFU 60W and End of Study.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	41	22
Units: beats/min				
arithmetic mean (standard deviation)				
Screening	77.8 (± 11.9)	82.5 (± 13.7)	81.2 (± 12.5)	89.0 (± 12.9)
End of Study	78.3 (± 14.0)	72.3 (± 13.0)	85.9 (± 10.2)	78.2 (± 20.0)

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	SAF	

Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	58	30	88	
Units: beats/min				
arithmetic mean (standard deviation)				
Screening	76.3 (± 11.4)	80.1 (± 13.5)	79.4 (± 12.7)	
End of Study	76.2 (± 14.3)	69.9 (± 8.9)	76.1 (± 13.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Vital Signs - Temperature

End point title	Vital Signs - Temperature

End point description:

Results presented for Screening and End of Study visits. All subjects were not evaluated at each visit.

End point type	Secondary

End point timeframe:

Assessed at each study visit: Screening, Sun-Start, Vaccination 1-2 (Intuvax group, only) SFU 6W, SFU 12W, SFU 24W, SFU 36W, SFU 48W, SFU 60W and End of Study.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	41	22
Units: degrees Celcius				
arithmetic mean (standard deviation)				
Screening	36.6 (± 0.7)	36.9 (± 0.4)	36.6 (± 0.5)	36.5 (± 0.5)
End of Study	36.6 (± 0.4)	36.7 (± 0.8)	36.4 (± 0.6)	36.4 (± 0.4)

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	SAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	58	30	88	
Units: degrees Celcius				
arithmetic mean (standard deviation)				
Screening	36.6 (± 0.6)	36.6 (± 0.5)	36.6 (± 0.6)	
End of Study	36.5 (± 0.6)	36.5 (± 0.5)	36.5 (± 0.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Laboratory Evaluation - Hematology

End point title	Laboratory Evaluation - Hematology

End point description:

Results presented for Screening and End of Study visits. All subjects were not evaluated at each visit.

End point type	Secondary

End point timeframe:

Assessed at each study visit: Screening, Sun-Start, Vaccination 1-2 (Intuvax group, only) SFU 6W, SFU 12W, SFU 24W, SFU 36W, SFU 48W, SFU 60W and End of Study.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	41	22
Units: percent				
number (not applicable)				
Basophils - Baseline Low	0.0	0.0	0.0	0.0
Basophils - Baseline Normal	100.0	100.0	100.0	100.0
Basophils - Baseline High	0.0	0.0	0.0	0.0
Basophils - EoS Low	0.0	0.0	0.0	0.0
Basophils - EoS Normal	100.0	100.0	100.0	100.0
Basophils - EoS High	0.0	0.0	0.0	0.0
Eosinophils - Baseline Low	0.0	0.0	0.0	0.0
Eosinophils - Baseline Normal	93.8	100.0	92.5	100.0
Eosinophils - Baseline High	6.3	0.0	7.5	0.0
Eosinophils - EoS Low	0.0	0.0	0.0	0.0
Eosinophils - EoS Normal	100.0	100.0	100.0	100.0
Eosinophils - EoS High	0.0	0.0	0.0	0.0
Hemoglobin - Baseline Low	100.0	85.7	35.0	50.0
Hemoglobin - Baseline Normal	0.0	14.3	57.5	50.0
Hemoglobin - Baseline High	0.0	0.0	7.5	0.0
Hemoglobin - EoS Low	60.0	50.0	39.3	50.0
Hemoglobin - EoS Normal	40.0	50.0	60.7	50.0
Hemoglobin - EoS High	0.0	0.0	0.0	0.0
Lymphocytes - Baseline Low	12.5	0.0	12.5	18.2
Lymphocytes - Baseline Normal	87.5	100.0	82.5	81.8
Lymphocytes - Baseline High	0.0	0.0	5.0	0.0
Lymphocytes - EoS Low	40.0	33.3	21.4	6.3
Lymphocytes - EoS Normal	50.0	50.0	78.6	93.8
Lymphocytes - EoS High	10.0	16.7	0.0	0.0
Monocytes - Baseline Low	0.0	0.0	2.5	4.5
Monocytes - Baseline Normal	50.0	85.7	90.0	86.4
Monocytes - Baseline High	50.0	14.3	7.5	9.1
Monocytes - EoS Low	0.0	16.7	17.9	0.0
Monocytes - EoS Normal	90.0	66.7	75.0	93.8
Monocytes - EoS High	10.0	16.7	7.1	6.3

Platelets - Baseline Low	0.0	0.0	0.0	0.0
Platelets - Baseline Normal	37.5	28.6	100.0	100.0
Platelets - Baseline High	62.5	71.4	0.0	0.0
Platelets - EoS Low	0.0	0.0	10.7	0.0
Platelets - EoS Normal	100.0	83.3	82.1	100.0
Platelets - EoS High	0.0	16.7	7.1	0.0
Neutrophils - Baseline Low	0.0	0.0	0.0	0.0
Neutrophils - Baseline Normal	68.8	57.1	95.0	90.9
Neutrophils - Baseline High	31.3	42.9	5.0	9.1
Neutrophils - EoS Low	0.0	16.7	32.1	12.5
Neutrophils - EoS Normal	100.0	66.7	64.3	87.5
Neutrophils - EoS High	0.0	16.7	3.6	0.0
Erythrocytes - Baseline Low	37.5	42.9	2.5	13.6
Erythrocytes - Baseline Normal	62.5	57.1	90.0	86.4
Erythrocytes - Baseline High	0.0	0.0	7.5	0.0
Erythrocytes - EoS Low	70.0	50.0	60.7	56.3
Erythrocytes - EoS Normal	30.0	50.0	39.3	43.8
Erythrocytes - EoS High	0.0	0.0	0.0	0.0
Leukocytes - Baseline Low	0.0	0.0	0.0	0.0
Leukocytes - Baseline Normal	68.8	57.1	100.0	95.5
Leukocytes - Baseline High	31.3	42.9	0.0	4.5
Leukocytes - EoS Low	0.0	16.7	35.7	12.5
Leukocytes - EoS Normal	100.0	83.3	60.7	87.5
Leukocytes - EoS High	0.0	0.0	3.6	0.0

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	SAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	58	30	88	
Units: percent				
number (not applicable)				
Basophils - Baseline Low	0.0	0.0	0.0	
Basophils - Baseline Normal	100.0	100.0	100.0	
Basophils - Baseline High	0.0	0.0	0.0	
Basophils - EoS Low	0.0	0.0	0.0	
Basophils - EoS Normal	100.0	100.0	100.0	
Basophils - EoS High	0.0	0.0	0.0	
Eosinophils - Baseline Low	0.0	0.0	0.0	
Eosinophils - Baseline Normal	92.9	100.0	95.3	
Eosinophils - Baseline High	7.1	0.0	4.7	
Eosinophils - EoS Low	0.0	0.0	0.0	
Eosinophils - EoS Normal	100.0	100.0	100.0	
Eosinophils - EoS High	0.0	0.0	0.0	
Hemoglobin - Baseline Low	53.6	58.6	55.3	
Hemoglobin - Baseline Normal	41.1	41.4	41.2	
Hemoglobin - Baseline High	5.4	0.0	3.5	
Hemoglobin - EoS Low	44.7	50.0	46.7	
Hemoglobin - EoS Normal	55.3	50.0	53.3	
Hemoglobin - EoS High	0.0	0.0	0.0	

Lymphocytes - Baseline Low	12.5	13.8	12.9	
Lymphocytes - Baseline Normal	83.9	86.2	84.7	
Lymphocytes - Baseline High	3.6	0.0	2.4	
Lymphocytes - EoS Low	26.3	13.6	21.7	
Lymphocytes - EoS Normal	71.1	81.8	75.0	
Lymphocytes - EoS High	2.6	4.5	3.3	
Monocytes - Baseline Low	1.8	3.4	2.4	
Monocytes - Baseline Normal	78.6	86.2	81.2	
Monocytes - Baseline High	19.6	10.3	16.5	
Monocytes - EoS Low	13.2	4.5	10.0	
Monocytes - EoS Normal	78.9	86.4	81.7	
Monocytes - EoS High	7.9	9.1	8.3	
Platelets - Baseline Low	0.0	0.0	0.0	
Platelets - Baseline Normal	82.1	82.8	82.4	
Platelets - Baseline High	17.9	17.2	17.6	
Platelets - EoS Low	7.9	0.0	5.0	
Platelets - EoS Normal	86.8	95.5	90.0	
Platelets - EoS High	5.3	4.5	5.0	
Neutrophils - Baseline Low	0.0	0.0	0.0	
Neutrophils - Baseline Normal	87.5	82.8	85.9	
Neutrophils - Baseline High	12.5	17.2	14.1	
Neutrophils - EoS Low	23.7	13.6	20.0	
Neutrophils - EoS Normal	73.7	81.8	76.7	
Neutrophils - EoS High	2.6	4.5	3.3	
Erythrocytes - Baseline Low	12.5	20.7	15.3	
Erythrocytes - Baseline Normal	82.1	79.3	81.2	
Erythrocytes - Baseline High	5.4	0.0	3.5	
Erythrocytes - EoS Low	63.2	54.5	60.0	
Erythrocytes - EoS Normal	36.8	45.5	40.0	
Erythrocytes - EoS High	0.0	0.0	0.0	
Leukocytes - Baseline Low	0.0	0.0	0.0	
Leukocytes - Baseline Normal	91.1	86.2	89.4	
Leukocytes - Baseline High	8.9	13.8	10.6	
Leukocytes - EoS Low	26.3	13.6	21.7	
Leukocytes - EoS Normal	71.1	86.4	76.7	
Leukocytes - EoS High	2.6	0.0	1.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Laboratory Evaluation - Clinical Chemistry

End point title	Laboratory Evaluation - Clinical Chemistry

End point description:

Samples were evaluated for albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, bilirubin, calcium, creatinine, c-reactive protein, glomerular filtration rate, gamma glutamyl transferase, glucose, potassium, lactate dehydrogenase, sodium, thyroxine free, thyrotropin. Out of these, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin are presented as these parameters are known AEs for sunitinib treatment, and calcium and creatinine are presented as they are related to the diagnosis.

End point type	Secondary

End point timeframe:

Assessed at each study visit: Screening, Sun-Start, Vaccination 1-2 (Intuvax group, only) SFU 6W, SFU 12W, SFU 24W, SFU 36W, SFU 48W, SFU 60W and End of Study.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	41	22
Units: percent				
number (not applicable)				
ALT - Baseline Low	0.0	0.0	0.0	0.0
ALT - Baseline Normal	88.2	87.5	97.6	90.5
ALT - Baseline High	11.8	12.5	2.4	9.5
ALT - EoS Low	0.0	0.0	0.0	0.0
ALT - EoS Normal	90.0	83.3	96.4	86.7
ALT - EoS High	10.0	16.7	3.6	13.3
AST - Baseline Low	0.0	0.0	0.0	0.0
AST - Baseline Normal	94.1	100.0	97.6	95.5
AST - Baseline High	5.9	0.0	2.4	4.5
AST - EoS Low	0.0	0.0	0.0	0.0
AST - EoS Normal	70.0	100.0	100.0	86.7
AST - EoS High	30.0	0.0	0.0	13.3
Bilirubin - Baseline Low	0.0	0.0	0.0	0.0
Bilirubin - Baseline Normal	100.0	100.0	100.0	100.0
Bilirubin - Baseline High	0.0	0.0	0.0	0.0
Bilirubin - EoS Low	0.0	0.0	0.0	0.0
Bilirubin - EoS Normal	90.0	100.0	100.0	100.0
Bilirubin - EoS High	10.0	0.0	0.0	0.0
Calcium - Baseline Low	0.0	0.0	0.0	0.0
Calcium - Baseline Normal	52.9	50.0	92.7	100.0
Calcium - Baseline High	47.1	50.0	7.3	0.0
Calcium - EoS Low	0.0	0.0	11.1	6.3
Calcium - EoS Normal	90.0	100.0	85.2	93.8
Calcium - EoS High	10.0	0.0	3.7	0.0
Creatinine - Baseline Low	0.0	12.5	2.4	9.1
Creatinine - Baseline Normal	82.4	87.5	85.4	72.7
Creatinine - Baseline High	17.6	0.0	12.2	18.2
Creatinine - EoS Low	10.0	0.0	3.6	0.0
Creatinine - EoS Normal	40.0	33.3	35.7	37.5
Creatinine - EoS High	50.0	66.7	60.7	62.5

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	SAF	

Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	58	30	88	
Units: percent				
number (not applicable)				
ALT - Baseline Low	0.0	0.0	0.0	
ALT - Baseline Normal	94.8	89.7	93.1	
ALT - Baseline High	5.2	10.3	6.9	
ALT - EoS Low	0.0	0.0	0.0	
ALT - EoS Normal	94.7	85.7	91.5	
ALT - EoS High	5.3	14.3	8.5	
AST - Baseline Low	0.0	0.0	0.0	
AST - Baseline Normal	96.6	96.7	96.6	
AST - Baseline High	3.4	3.3	3.4	
AST - EoS Low	0.0	0.0	0.0	
AST - EoS Normal	92.1	90.5	91.5	
AST - EoS High	7.9	9.5	8.5	
Bilirubin - Baseline Low	0.0	0.0	0.0	
Bilirubin - Baseline Normal	100.0	100.0	100.0	
Bilirubin - Baseline High	0.0	0.0	0.0	
Bilirubin - EoS Low	0.0	0.0	0.0	
Bilirubin - EoS Normal	97.4	100.0	98.3	
Bilirubin - EoS High	2.6	0.0	1.7	
Calcium - Baseline Low	0.0	0.0	0.0	
Calcium - Baseline Normal	81.0	86.7	83.0	
Calcium - Baseline High	19.0	13.3	17.0	
Calcium - EoS Low	8.1	4.5	6.8	
Calcium - EoS Normal	86.5	95.5	89.8	
Calcium - EoS High	5.4	0.0	3.4	
Creatinine - Baseline Low	1.7	10.0	4.5	
Creatinine - Baseline Normal	84.5	76.7	81.8	
Creatinine - Baseline High	13.8	13.3	13.6	
Creatinine - EoS Low	5.3	0.0	3.3	
Creatinine - EoS Normal	36.8	36.4	36.7	
Creatinine - EoS High	57.9	63.6	60.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Laboratory Evaluation - Coagulation

End point title	Laboratory Evaluation - Coagulation

End point description:

Results presented for Screening and End of Study (Final Visit). All subjects were not evaluated at each visit.

End point type	Secondary

End point timeframe:

Assessed at Screening, Vaccination 1-2 (Intuvax group, only), Surgery-Nephrectomy and End of Study (Final Visit).

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	41	22
Units: percent				
number (not applicable)				
APTT - Baseline Low	0.0	20.0	2.8	10.0
APTT - Baseline Normal	75.0	60.0	77.8	75.0
APTT - Baseline High	25.0	20.0	19.4	15.0
APTT - EoS Low	0.0	20.0	8.3	10.0
APTT - EoS Normal	68.8	60.0	77.8	75.0
APTT - EoS High	31.3	20.0	13.9	15.0
PT-INR - Baseline Low	0.0	0.0	0.0	4.8
PT-INR - Baseline Normal	83.3	80.0	92.9	76.2
PT-INR - Baseline High	16.7	20.0	7.1	19.0
PT-INR - EoS Low	0.0	0.0	3.2	0.0
PT-INR - EoS Normal	58.3	100.0	87.1	90.5
PT-INR - EoS High	41.7	0.0	9.7	9.5

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	SAF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	58	30	88	
Units: percent				
number (not applicable)				
APTT - Baseline Low	1.9	12.0	5.2	
APTT - Baseline Normal	76.9	72.0	75.3	
APTT - Baseline High	21.2	16.0	19.5	
APTT - EoS Low	5.8	12.0	7.8	
APTT - EoS Normal	75.0	72.0	74.0	
APTT - EoS High	19.2	16.0	18.2	
PT-INR - Baseline Low	0.0	3.8	1.5	
PT-INR - Baseline Normal	90.0	76.9	84.8	
PT-INR - Baseline High	10.0	19.2	13.6	
PT-INR - EoS Low	2.3	0.0	1.4	
PT-INR - EoS Normal	79.1	92.3	84.1	
PT-INR - EoS High	18.6	7.7	14.5	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: ECOG Performance Status

End point title	ECOG Performance Status

End point description:

The proportion of patients with improvement since the Screening is presented for each visit. All subjects were not evaluated at each visit.

End point type	Other pre-specified

End point timeframe:

Assessed at each study visit: Screening, Sun-Start, SFU 6W, SFU 12W, SFU 24W, SFU 36W, SFU 48W, SFU 60W and End of Study.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	8	40	22
Units: percent				
number (not applicable)				
Sun-Start	30.8	16.7	19.4	27.8
SFU 6 Weeks	27.3	0.0	25.0	29.4
SFU 12 Weeks	30.0	0.0	18.5	28.6
SFU 24 Weeks	12.5	0.0	13.0	30.8
SFU 36 Weeks	40.0	0.0	10.5	27.3
SFU 48 Weeks	0.0	0.0	15.8	27.3
SFU 60 Weeks	0.0	0.0	12.5	37.5
End of Study	50.0	33.3	35.5	41.2

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	56	30	86	
Units: percent				
number (not applicable)				
Sun-Start	22.7	25.0	23.5	
SFU 6 Weeks	25.6	23.8	25.0	
SFU 12 Weeks	21.6	22.2	21.8	
SFU 24 Weeks	12.9	28.6	17.8	
SFU 36 Weeks	16.7	27.3	20.0	
SFU 48 Weeks	14.3	27.3	18.8	
SFU 60 Weeks	11.1	37.5	19.2	
End of Study	39.5	39.1	39.4	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Quality of Life - EORTC QLQ-C30

End point title	Quality of Life - EORTC QLQ-C30

End point description:

The proportion of patients with improvementat at End of Study compared to Screening is presented. All subjects were not evaluated at each visit.

End point type	Other pre-specified

End point timeframe:

Assessed at each study visit: Screening, Sun-Start, SFU 6W, SFU 12W, SFU 24W, SFU 36W, SFU 48W, SFU 60W and End of Study.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	8	40	22
Units: percent				
number (not applicable)				
Cognitive functioning	8.3	40.0	11.1	35.3
Emotional functioning	33.3	60.0	59.3	52.9
Global Health Status	41.7	20.0	22.2	58.8
Physical functioning	0.0	0.0	18.5	23.5
Role functioning	18.2	20.0	7.4	35.3
Social functioning	25.0	20.0	7.4	29.4

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	39	22	86	
Units: percent				
number (not applicable)				
Cognitive functioning	10.3	36.4	19.7	
Emotional functioning	51.3	54.5	52.5	
Global Health Status	28.2	50.0	36.1	
Physical functioning	12.8	18.2	14.8	
Role functioning	10.5	31.8	18.3	
Social functioning	12.8	27.3	18.0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Correlation between MHC mismatch and infiltrating CD8+ T cells

End point title	Correlation between MHC mismatch and infiltrating CD8+ T cells[8]

End point description:

End point type	Other pre-specified

End point timeframe:

HLA type collected at Screening and number of infiltrating CD8+ T cells evaluated at nephrectomy.

Notes:

[8] - 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 is only applicable to patients in the Intuvax group.

End point values	Intuvax + sunitinib, high-risk	Intuvax + sunitinib, intermediate-risk	Intuvax + sunitinib, total (both strata)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	40	56	
Units: unitless				
number (not applicable)				
Spearman correlation	0.0829	0.0083	0.0647	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Auto- and allo-immunization

End point title	Auto- and allo-immunization[9]

End point description:

Proportion of patients positive for antibodies at start of sunitinib treatment. For alloimmunization (HLA class I/II), only patients who developed antibodies de novo are presented.

End point type	Other pre-specified

End point timeframe:

From Vaccination visit 1 to start of sunitinib treatment

Notes:

[9] - 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 is only applicable to patients in the Intuvax group.

End point values	Intuvax + sunitinib, high-risk	Intuvax + sunitinib, intermediate-risk	Intuvax + sunitinib, total (both strata)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	40	56	
Units: percent				
number (not applicable)				
<1:160 antinuclear antibodies	100.0	100.0	100.0	
Antimitochondrial antibodies	8.3	0.0	2.5	
HLA class I/II	66.7	57.1	60.0	

Liver kidney microsomal type 1	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to Treatment Failure

End point title	Time to Treatment Failure[10]

End point description:

Due to the large amount of censored data, estimates of median and/or a 95% CI could not be reliably determined in all reporting groups (marked by 'NA' below). The median (CI) were:
Intuvax high-risk: 403 (201, NA)
Sunitinib-only high-risk: 302 (271, 333)
Intuvax intermediate-risk: NA (NA, NA)
Sunitinib-only intermediate risk: NA (NA, NA)
Intuvax total (both strata): NA (NA, NA)
Sunitinib-only total (both strata): NA (NA, NA)

End point type	Other pre-specified

End point timeframe:

Following PD or clinical progression.

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: Due to the large amount of censored data, estimates of median and/or a 95% CI could not be reliably determined in all reporting groups. Those groups have been omitted from the reporting form. However, all estimated values for median and CI are presented in the "Description" of the endpoint, where values that could not be estimated are marked by "NA".

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	8		
Units: day				
number (not applicable)	403	302		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Tumor Response from Screening to Sun-Start

End point title	Tumor Response from Screening to Sun-Start

End point description:

End point type	Other pre-specified

End point timeframe:

From Screening to start of sunitinib treatment.

End point values	Intuvax + sunitinib, high-risk	Sunitinib-only, high-risk	Intuvax + sunitinib, intermediate-risk	Sunitinib-only, intermediate-risk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	5	29	16
Units: percent				
number (not applicable)				
Complete Response (CR)	0.0	0.0	0.0	6.3
Partial Response (PR)	0.0	0.0	3.4	0.0
Progressive Disease (PD)	66.7	100.0	62.1	43.8
Stable Disease (SD)	25.0	0.0	20.7	43.8
Non-CR/Non-PD	8.3	0.0	0.0	6.3
No Disease (ND)	0.0	0.0	13.8	0.0

End point values	Intuvax + sunitinib, total (both strata)	Sunitinib-only, total (both strata)	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	41	21	86	
Units: percent				
number (not applicable)				
Complete Response (CR)	0.0	4.8	1.6	
Partial Response (PR)	2.4	0.0	1.6	
Progressive Disease (PD)	63.4	57.1	61.3	
Stable Disease (SD)	22.0	33.3	25.8	
Non-CR/Non-PD	2.4	4.8	3.2	
No Disease (ND)	9.8	0.0	6.5	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Exploratory Cox Model Analyses

End point title	Exploratory Cox Model Analyses

End point description:

Comparison between treatment groups: Intuvax group compared to sunitinib-only group.

End point type	Other pre-specified

End point timeframe:

Number of tumor-infiltrating CD8+ T-cells evaluated at nephrectomy. TNM staging assessed at baseline. Sunitinib dose density assessed during treatment period. Survival (overall survival [OS], progression-free survival [PFS]) evaluated throughout study.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: unitless p-value				
number (not applicable)				
CD8+ vs. OS (by treatment group)	0.6194			
CD8+ vs. OS (reduced model)	0.2559			
CD8+ vs. PFS (by treatment group)	0.8095			
CD8+ vs. PFS (reduced model)	0.2325			
N1 vs. OS (by treatment group)	0.4178			
N1 vs. OS (reduced model)	0.3017			
N1 vs. PFS (by treatment group)	0.6060			
N1 vs. PFS (reduced model)	0.4733			
T3a vs. OS (by treatment group)	0.4707			
T3a vs. OS (reduced model)	0.3636			
T3a vs. PFS (by treatment group)	0.9023			
T3a vs. PFS (reduced model)	0.8381			
Dose density vs. OS (by treatment group)	0.2519			
Dose density vs. OS (reduced model)	0.0013			
Dose density vs. PFS (by treatment group)	0.0445			
Dose density vs. PFS (reduced model)	0.6034			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first dose to last follow-up.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Intuvax+sunitinib group (Intuvax)
Reporting group description: Intuvax, high and intermediate risk strata combined. "Occurrences causally related to treatment" and "deaths causally related to treatment" is reporting AEs related to Intuvax.	
Reporting group title	Sunitinib-only group
Reporting group description: Sunitinib-only, high and intermediate risk strata combined.	
Reporting group title	Intuvax+sunitinib group (sunitinib)
Reporting group description: Intuvax, high and intermediate risk strata combined. "Occurrences causally related to treatment" and "deaths causally related to treatment" is reporting AEs related to sunitinib.	

Serious adverse events	Intuvax+sunitinib group (Intuvax)	Sunitinib-only group	Intuvax+sunitinib group (sunitinib)
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 58 (46.55%)	17 / 30 (56.67%)	27 / 58 (46.55%)
number of deaths (all causes)	7	6	7
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Metastatic bone disease prophylaxis	Additional description: Recorded as "Metastatic pain"		
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			

subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 58 (1.72%)	2 / 30 (6.67%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Death			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
General physical health deterioration			
subjects affected / exposed	3 / 58 (5.17%)	1 / 30 (3.33%)	3 / 58 (5.17%)
occurrences causally related to treatment / all	0 / 3	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Multi-organ disorder	Additional description: Listed as "multi-organ failure"		
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Pyrexia			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Pleural effusion			
subjects affected / exposed	1 / 58 (1.72%)	1 / 30 (3.33%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical condition abnormal			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Injury, poisoning and procedural complications			
Humerus fracture			

subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	2 / 58 (3.45%)	0 / 30 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Procedural pain			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Wound evisceration			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Cardiac disorders			
Left ventricular dysfunction			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	0 / 58 (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
Paresis			
subjects affected / exposed	1 / 58 (1.72%)	1 / 30 (3.33%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Spinal cord compression			
subjects affected / exposed	1 / 58 (1.72%)	1 / 30 (3.33%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 58 (1.72%)	1 / 30 (3.33%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	0 / 58 (0.00%)	2 / 30 (6.67%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 58 (3.45%)	0 / 30 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (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
Pathological fracture			
subjects affected / exposed	0 / 58 (0.00%)	2 / 30 (6.67%)	0 / 58 (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
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	0 / 58 (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
Lymphangitis			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 58 (0.00%)	2 / 30 (6.67%)	0 / 58 (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

Post procedural infection			
subjects affected / exposed	2 / 58 (3.45%)	0 / 30 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 58 (0.00%)	1 / 30 (3.33%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 58 (3.45%)	0 / 30 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal viral infection			
subjects affected / exposed	1 / 58 (1.72%)	0 / 30 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 58 (3.45%)	0 / 30 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 58 (1.72%)	2 / 30 (6.67%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
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	Intuvax+sunitinib group (Intuvax)	Sunitinib-only group	Intuvax+sunitinib group (sunitinib)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 58 (93.10%)	27 / 30 (90.00%)	54 / 58 (93.10%)
Vascular disorders			
Hypertension			

subjects affected / exposed	12 / 58 (20.69%)	6 / 30 (20.00%)	12 / 58 (20.69%)
occurrences (all)	18	6	18
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	11 / 58 (18.97%)	5 / 30 (16.67%)	11 / 58 (18.97%)
occurrences (all)	19	5	19
Fatigue			
subjects affected / exposed	14 / 58 (24.14%)	8 / 30 (26.67%)	14 / 58 (24.14%)
occurrences (all)	14	11	14
General physical health deterioration			
subjects affected / exposed	3 / 58 (5.17%)	1 / 30 (3.33%)	3 / 58 (5.17%)
occurrences (all)	3	1	3
Mucosal inflammation			
subjects affected / exposed	6 / 58 (10.34%)	1 / 30 (3.33%)	6 / 58 (10.34%)
occurrences (all)	10	1	10
Pain			
subjects affected / exposed	3 / 58 (5.17%)	0 / 30 (0.00%)	3 / 58 (5.17%)
occurrences (all)	3	0	3
Pyrexia			
subjects affected / exposed	11 / 58 (18.97%)	4 / 30 (13.33%)	11 / 58 (18.97%)
occurrences (all)	18	6	18
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 58 (6.90%)	1 / 30 (3.33%)	4 / 58 (6.90%)
occurrences (all)	4	1	4
Dyspnoea			
subjects affected / exposed	4 / 58 (6.90%)	2 / 30 (6.67%)	4 / 58 (6.90%)
occurrences (all)	4	2	4
Epistaxis			
subjects affected / exposed	5 / 58 (8.62%)	2 / 30 (6.67%)	5 / 58 (8.62%)
occurrences (all)	8	2	8
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 58 (8.62%)	0 / 30 (0.00%)	5 / 58 (8.62%)
occurrences (all)	6	0	6
Investigations			

Blood creatinine increased			
subjects affected / exposed	6 / 58 (10.34%)	4 / 30 (13.33%)	6 / 58 (10.34%)
occurrences (all)	9	5	9
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 58 (5.17%)	0 / 30 (0.00%)	3 / 58 (5.17%)
occurrences (all)	3	0	3
Glomerular filtration rate decreased			
subjects affected / exposed	3 / 58 (5.17%)	1 / 30 (3.33%)	3 / 58 (5.17%)
occurrences (all)	3	1	3
Neutrophil count decreased			
subjects affected / exposed	4 / 58 (6.90%)	4 / 30 (13.33%)	4 / 58 (6.90%)
occurrences (all)	5	4	5
Platelet count decreased			
subjects affected / exposed	2 / 58 (3.45%)	3 / 30 (10.00%)	2 / 58 (3.45%)
occurrences (all)	3	4	3
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	3 / 58 (5.17%)	3 / 30 (10.00%)	3 / 58 (5.17%)
occurrences (all)	3	3	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 58 (5.17%)	3 / 30 (10.00%)	3 / 58 (5.17%)
occurrences (all)	3	4	3
Dysgeusia			
subjects affected / exposed	9 / 58 (15.52%)	5 / 30 (16.67%)	9 / 58 (15.52%)
occurrences (all)	14	7	14
Headache			
subjects affected / exposed	7 / 58 (12.07%)	1 / 30 (3.33%)	7 / 58 (12.07%)
occurrences (all)	8	1	8
Paresis			
subjects affected / exposed	1 / 58 (1.72%)	2 / 30 (6.67%)	1 / 58 (1.72%)
occurrences (all)	1	2	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 58 (24.14%)	4 / 30 (13.33%)	14 / 58 (24.14%)
occurrences (all)	19	4	19

Neutropenia			
subjects affected / exposed	4 / 58 (6.90%)	1 / 30 (3.33%)	4 / 58 (6.90%)
occurrences (all)	5	1	5
Thrombocytopenia			
subjects affected / exposed	5 / 58 (8.62%)	0 / 30 (0.00%)	5 / 58 (8.62%)
occurrences (all)	7	0	7
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 58 (5.17%)	2 / 30 (6.67%)	3 / 58 (5.17%)
occurrences (all)	3	2	3
Abdominal pain upper			
subjects affected / exposed	4 / 58 (6.90%)	3 / 30 (10.00%)	4 / 58 (6.90%)
occurrences (all)	4	3	4
Constipation			
subjects affected / exposed	7 / 58 (12.07%)	2 / 30 (6.67%)	7 / 58 (12.07%)
occurrences (all)	7	2	7
Diarrhoea			
subjects affected / exposed	14 / 58 (24.14%)	7 / 30 (23.33%)	14 / 58 (24.14%)
occurrences (all)	23	13	23
Gastritis			
subjects affected / exposed	3 / 58 (5.17%)	0 / 30 (0.00%)	3 / 58 (5.17%)
occurrences (all)	3	0	3
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 58 (5.17%)	1 / 30 (3.33%)	3 / 58 (5.17%)
occurrences (all)	8	1	8
Nausea			
subjects affected / exposed	14 / 58 (24.14%)	7 / 30 (23.33%)	14 / 58 (24.14%)
occurrences (all)	21	8	21
Oral pain			
subjects affected / exposed	3 / 58 (5.17%)	3 / 30 (10.00%)	3 / 58 (5.17%)
occurrences (all)	3	3	3
Stomatitis			
subjects affected / exposed	6 / 58 (10.34%)	6 / 30 (20.00%)	6 / 58 (10.34%)
occurrences (all)	8	10	8
Vomiting			

subjects affected / exposed	14 / 58 (24.14%)	0 / 30 (0.00%)	14 / 58 (24.14%)
occurrences (all)	21	0	21
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 58 (0.00%)	2 / 30 (6.67%)	0 / 58 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	4 / 58 (6.90%)	2 / 30 (6.67%)	4 / 58 (6.90%)
occurrences (all)	4	2	4
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 58 (5.17%)	0 / 30 (0.00%)	3 / 58 (5.17%)
occurrences (all)	3	0	3
Renal failure	Additional description: Registered as "Renal failure acute" (in Intuvax group, 1 subject [1 unique event], in sunitinib-only group, 2 subjects [2 unique events]) and "Renal failure chronic" (in each group, 2 subjects are affected by 2 unique events		
subjects affected / exposed	3 / 58 (5.17%)	4 / 30 (13.33%)	3 / 58 (5.17%)
occurrences (all)	3	4	3
Renal impairment			
subjects affected / exposed	2 / 58 (3.45%)	2 / 30 (6.67%)	2 / 58 (3.45%)
occurrences (all)	3	2	3
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	8 / 58 (13.79%)	3 / 30 (10.00%)	8 / 58 (13.79%)
occurrences (all)	9	3	9
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 58 (8.62%)	3 / 30 (10.00%)	5 / 58 (8.62%)
occurrences (all)	5	3	5
Back pain			
subjects affected / exposed	10 / 58 (17.24%)	3 / 30 (10.00%)	10 / 58 (17.24%)
occurrences (all)	13	3	13
Musculoskeletal pain			
subjects affected / exposed	4 / 58 (6.90%)	0 / 30 (0.00%)	4 / 58 (6.90%)
occurrences (all)	4	0	4
Neck pain			

subjects affected / exposed	0 / 58 (0.00%)	2 / 30 (6.67%)	0 / 58 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	5 / 58 (8.62%)	2 / 30 (6.67%)	5 / 58 (8.62%)
occurrences (all)	7	2	7
Pathological fracture			
subjects affected / exposed	0 / 58 (0.00%)	3 / 30 (10.00%)	0 / 58 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 58 (1.72%)	2 / 30 (6.67%)	1 / 58 (1.72%)
occurrences (all)	1	2	1
Urinary tract infection			
subjects affected / exposed	6 / 58 (10.34%)	2 / 30 (6.67%)	6 / 58 (10.34%)
occurrences (all)	6	2	6
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	7 / 58 (12.07%)	3 / 30 (10.00%)	7 / 58 (12.07%)
occurrences (all)	8	3	8
Pruritus			
subjects affected / exposed	3 / 58 (5.17%)	0 / 30 (0.00%)	3 / 58 (5.17%)
occurrences (all)	4	0	4
Rash			
subjects affected / exposed	3 / 58 (5.17%)	1 / 30 (3.33%)	3 / 58 (5.17%)
occurrences (all)	4	1	4
Hyperkalaemia			
subjects affected / exposed	3 / 58 (5.17%)	0 / 30 (0.00%)	3 / 58 (5.17%)
occurrences (all)	3	0	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 58 (17.24%)	5 / 30 (16.67%)	10 / 58 (17.24%)
occurrences (all)	12	5	12
Hypercalcaemia			
subjects affected / exposed	4 / 58 (6.90%)	2 / 30 (6.67%)	4 / 58 (6.90%)
occurrences (all)	6	3	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2015	The primary objective/endpoint was updated. The previous secondary objective on 18 months' survival rate in intermediate-risk patients was included as a primary objective to include intermediate-risk patients in the primary objective of the study. Clarification of exclusion criteria regarding hypertension, cardiomyopathy, and diabetes mellitus (No. 4 and 9 in CSP ver 2.0). Patients with uncontrolled diabetes mellitus are excluded from the study. Cardiomyopathy was moved to list of exclusion criteria. Clarification of exploratory objectives/endpoints. Routine histology was removed as an exploratory endpoint. CD163 will be analyzed and not CD133. Section on withdrawals was updated to include more details. Patients who discontinued treatment with Intuvax and/or patients whose condition deteriorated much more quickly than expected after enrolment so that the planned nephrectomy could not be performed was not considered withdrawn from study unless there were other reasons for withdrawal. Discontinuation of Intuvax/Sunitinib for safety reasons did not result in withdrawal from study unless there are other reasons for withdrawal. Progressive disease after initiation of Sunitinib, need for change of systemic anti-cancer treatment, and histological findings that does not confirm RCC diagnosis were added to the withdrawal from study criteria. Collection of survival data after EoS visit was added. An optional confirmatory biopsy assessment of the RCC diagnosis for patients randomized to vaccination was included. Information on the IMP to reflect the updated IMPD was included. Study period and contact information were updated. Language and typographic errors were corrected. Minor adjustments and clarifications were performed.
04 December 2015	Initiation of sunitinib for the intermediate-risk population was updated to between five (5) and eight (8) weeks post-nephrectomy (as for the high-risk population), thus not demanding tumor progression after nephrectomy before starting sunitinib treatment. This change in study design was performed in order to adapt the study treatment to current treatment recommendations in the majority of participating countries. Also, during the initial stage of the IND process FDA has come back to Immunicum AB with strong recommendations to perform this update on intermediate risk patients as US is one of the countries where this start-point after nephrectomy (not demanding tumor progression after nephrectomy before starting sunitinib treatment) forms part of the current standard of care. This approach is in line with current ESMO and NCCN guidelines. As a result, the secondary objectives/endpoints for the intermediate-risk patient population with baseline previously defined at Screening or sunitinib start visit, i.e. when PD has been confirmed, were removed. Inclusion criterion 1 was updated to specify a minimum size of metastases and to clarify that histological/cytological verification of diagnosis is optional. Update of inclusion criterion and concomitant therapy relating to Hemoglobin. The lower limit of hemoglobin (Hb) at Screening and acceptance of blood transfusion or epoetin alpha treatment were changed. Liver function assessments were changed. Child-Pugh assessment has been replaced with assessments of Serum-Bilirubin, Aspartate Aminotransferase (ASAT), and Alanine Aminotransferase (ALAT). PT-INR analysis is no longer needed post nephrectomy. Clarification regarding pregnancy precautions to accommodate potential withdrawals and comply with restrictions in SmPC. Participating patients have to agree to use contraception from Screening until 90 days after last dose of Intuvax and/or until completed sunitinib treatment whichever occurs later. [more info available]

11 July 2016	Substantial amendment 3 was submitted to FDA (US) only but was never implemented. All changes made in substantial amendment 3 are described in substantial amendment 4.
26 October 2016	The primary, secondary and exploratory objectives and endpoints were updated: Previous evaluation of OS from randomization in vaccinated vs. non-vaccinated high-risk mRCC patients has been extended to also include evaluation of OS in intermediate-risk patients and in total. Previous evaluation of 18-month survival rate from randomization in vaccinated vs. non-vaccinated intermediate-risk mRCC patients has been extended to also include evaluation of 18-month survival rate in high-risk patients and in total. Previous secondary objective / endpoint evaluation of "response" has been updated to also include duration of response and duration of SD. Evaluation of TTP has been added as a new secondary objective/endpoint. To confirm mode of action of Intuvax, previous secondary objective/endpoint on evaluation of CD8+ T-cells has been updated to include analysis of CD8+ T-cells from diagnostic pre-biopsies when available and to compare the results with the tumor biopsies collected at nephrectomy. An additional exploratory endpoint has been included in order to further evaluate correlation and degree of MHC mismatch between vaccine donor cells and the treated patient. TTF in patients scheduled for second line systemic therapy has been added to the list of exploratory objectives/endpoints. The countries, number of sites and study period were updated. Inclusion and exclusion criteria were changed: Clarification of inclusion criterion 1 that US patients must have clear-cell renal tumor histology. As non clear cell carcinomas were not excluded in Europe, Immunicum AB will monitor the clear cell to non clear cell distribution and whether the response to Intuvax treatment is dependent on the histopathology. In addition, inclusion criterion 1 was updated to stress that an eligible patient should have at least one assessable metastasis in place after surgery. Change of exclusion criterion 3 to allow up to 10 mg/day per oral systemic corticosteroids. [more info available]
17 October 2017	Inclusion of additional immunohistology analysis for CD8+ cells at the GLP-compliant laboratory Histalim, to increase the quality of data. Collection of local laboratory results for creatinine at Nephrectomy visit. It was discovered that patients included in the study before 28 August 2017 had no central analysis of creatinine performed at Vaccination visit 1, Vaccination visit 2, and Nephrectomy visit, as specified in the protocol. A corrective action plan (CAPA) was written that described the situation and all actions to be made to resolve the issue, of which updating the protocol with collection of local creatinine results, if available, was one. Submissions of this serious breach were made to involved competent authorities and IECs in all countries as applicable. Merging of French-specific protocol criterion with the global (i.e. other country) protocol by addition of a country-specific exclusion criterion. The following non-substantial changes were made: removal of pre-defined stratification ratio, updated number of sites, updated study-administrative structure and extension of Intuvax shelf life.
25 June 2018	Added definition of the safety evaluation, that SAEs will be collected, and a description on how it is done in practice. Non-substantial changes were made to update the definition of EoS, updated procedure for collection and statistical analyses of post-study survival data as well as a study-administrative change.

12 February 2019	A new exploratory objective and endpoint relating to tumor response rate between screening and the first post-nephrectomy assessment has been added. The definition of baseline has been clarified for secondary endpoints based on RECIST for intermediate-risk patients included in the trial according to protocol versions before version Final 4.0 Non-substantial changes were made to clarify local and central imaging assessments, information about persons involved in conduct and reporting of the study, it was clarified that CR and PR do not need to be confirmed by repeat tumor measurements, the assessment of mismatch between patient and donor HLA types was clarified as well as the process of data collection in eCRF regarding AE follow-up.
29 May 2019	A non-substantial amendment was made to allow collection of post-study survival information more frequently; up to twice per year, instead of once per year.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27444986

http://www.ncbi.nlm.nih.gov/pubmed/31427204

http://www.ncbi.nlm.nih.gov/pubmed/30779531

http://www.ncbi.nlm.nih.gov/pubmed/30779529

http://www.ncbi.nlm.nih.gov/pubmed/29860937