

**Clinical trial results:****A Randomized Phase II Study of Afinitor (RAD001) vs. Sutent (Sunitinib) in Patients with Metastatic Non-Clear Cell Renal Cell Carcinoma (ASPEN)****Summary**

EudraCT number	2010-019966-95
Trial protocol	GB
Global end of trial date	14 July 2015

Results information

Result version number	v1 (current)
This version publication date	27 January 2022
First version publication date	27 January 2022
Summary attachment (see zip file)	Aspen Lancet Manuscript 2016 (ASPEN Lancet Publication 2016.pdf) Aspen Lancet Manuscript Supplement (ASPEN supplement Lancet 2016.pdf)

Trial information**Trial identification**

Sponsor protocol code	CRAD001L2402T
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01108445
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Duke University
Sponsor organisation address	2424 Erwin Road, Hock Plaza, Durham, United States, 27705
Public contact	Monika Anand, Dr. Andrew Armstrong, 9196818838 9196818838, monika.anand@duke.edu
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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	31 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint was a comparison of radiographic progression-free survival (rPFS) between the treatment arms following therapy initiation. Disease progression is defined by documentation of progressive disease according to RECIST 1.1 criteria, appearance of a new primary malignancy, or death (whichever occurs first), censored at the last tumor evaluation date.

Protection of trial subjects:

All patients provided written informed consent under a form issued by an institutional review board. Regulatory oversight and institutional review board or ethics board approval in the USA, Canada, and the UK was maintained for this trial

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 September 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 39
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	United States: 64
Worldwide total number of subjects	108
EEA total number of subjects	39

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)	61

From 65 to 84 years	44
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Between Sept 23, 2010, and Oct 28, 2013, 131 patients were assessed for eligibility and 109 patients were enrolled. 108 patients were evaluable. 51 patients were assigned sunitinib and 57 patients were assigned everolimus

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	131 ^[1]
Number of subjects completed	108

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen Failures: 23
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Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 131 patients consented to participate in the trial. These were considered to have started the pre-assignment period. 23 patients screen failed and were not assigned a study arm. 108 patients were enrolled to start treatment on trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sunitinib

Arm description:

Sunitinib malate was given orally at 50 mg once daily, for treatment cycles of 4 weeks on treatment and 2 weeks off treatment.

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

Dosage and administration details:

Sunitinib malate was given orally at 50 mg once daily, for treatment cycles of 4 weeks on treatment and 2 weeks off treatment.

Arm title	Everolimus
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Arm description:

Everolimus was given orally at 10 mg once daily.

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

Dosage and administration details:

10 mg tablet orally once daily

Number of subjects in period 1	Sunitinib	Everolimus
Started	51	57
Completed	41	44
Not completed	10	13
Consent withdrawn by subject	3	-
Adverse event, non-fatal	7	13

Baseline characteristics

Reporting groups

Reporting group title	Sunitinib
Reporting group description:	
Sunitinib malate was given orally at 50 mg once daily, for treatment cycles of 4 weeks on treatment and 2 weeks off treatment.	
Reporting group title	Everolimus
Reporting group description:	
Everolimus was given orally at 10 mg once daily.	

Reporting group values	Sunitinib	Everolimus	Total
Number of subjects	51	57	108
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	59	64	
full range (min-max)	24 to 100	29 to 90	-
Gender categorical			
Units: Subjects			
Female	14	13	27
Male	37	44	81
Ethnic Origin			
Units: Subjects			
White	42	52	94
Black	9	5	14
Unknown	0	0	0
MSKCC Risk Group			
Units: Subjects			
Low	15	14	29
Intermediate	32	32	64
High	4	11	15

End points

End points reporting groups

Reporting group title	Sunitinib
Reporting group description: Sunitinib malate was given orally at 50 mg once daily, for treatment cycles of 4 weeks on treatment and 2 weeks off treatment.	
Reporting group title	Everolimus
Reporting group description: Everolimus was given orally at 10 mg once daily.	

Primary: Radiographic Progression Free Survival

End point title	Radiographic Progression Free Survival
End point description:	
End point type	Primary
End point timeframe: Up to 24 months	

End point values	Sunitinib	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	57		
Units: Months				
median (full range (min-max))	8.3 (5.8 to 11.4)	5.6 (5.5 to 6.0)		

Statistical analyses

Statistical analysis title	Primary outcome
Statistical analysis description: The null hypothesis was that PFS in patients treated with sunitinib(S) would be comparable to that of everolimus(E); the alternative hypothesis was that E would cause a 60% improvement in median PFS from 6.0 months to 9.6 months in S and E groups respectively, compared with S (HR 0.625). Using a two-sided type I error rate of 0.20, 90 PFS events would allow us to detect this difference with 83% power. PFS was tested using stratified log rank test, adjusting for stratification factors.	
Comparison groups	Sunitinib v Everolimus
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Hazard ratio (HR)
Point estimate	1.41

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.03
upper limit	1.92

Secondary: Progression Free Survival at 12 Months

End point title	Progression Free Survival at 12 Months
End point description:	
End point type	Secondary
End point timeframe:	
Up to 12 months	

End point values	Sunitinib	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	57		
Units: Percentage				
number (not applicable)	37.7	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival at 24 Months

End point title	Progression Free Survival at 24 Months
End point description:	
End point type	Secondary
End point timeframe:	
Up to 24 months	

End point values	Sunitinib	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	57		
Units: Percentage				
number (not applicable)	22.8	9.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival at 6 Months

End point title	Progression Free Survival at 6 Months
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End point description:

End point type	Secondary
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End point timeframe:

Up to 6 months

End point values	Sunitinib	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	57		
Units: Percentage				
number (not applicable)	55	40.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival
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End point description:

End point type	Secondary
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End point timeframe:

Up to 36 months post randomization

End point values	Sunitinib	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	57		
Units: Months				
median (confidence interval 95%)	31.5 (14.8 to 45.43)	13.2 (9.7 to 37.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were assessed up to 28 days post last day of dose given to the last patient on treatment.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	NCI CTC
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Dictionary version	4
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Reporting groups

Reporting group title	Sunitinib
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Reporting group description:

Sunitinib malate was given orally at 50 mg once daily, for treatment cycles of 4 weeks on treatment and 2 weeks off treatment.

Reporting group title	Everolimus
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Reporting group description:

Everolimus was given orally at 10 mg once daily.

Serious adverse events	Sunitinib	Everolimus	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 51 (41.18%)	15 / 57 (26.32%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
HEMATOMA - SUBDURAL			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	2 / 51 (3.92%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DVT RT LWR LEG			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

MUCOSITIS			
subjects affected / exposed	0 / 51 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPEREMESIS			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 51 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
EPISTAXIS			
subjects affected / exposed	2 / 51 (3.92%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN - LEFT PLEURETIC CHEST PAIN			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

SHORTNESS OF BREATH			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	0 / 51 (0.00%)	5 / 57 (8.77%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOSIS / EMBOLISM			
subjects affected / exposed	0 / 51 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WORSENERD DYSYPNEA			
subjects affected / exposed	1 / 51 (1.96%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
CONFUSION			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ALTERED MENTAL STATUS			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
ACUTE RENAL FAILURE			
subjects affected / exposed	2 / 51 (3.92%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 51 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
LEFT LEG PAIN			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 51 (1.96%)	0 / 57 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
subjects affected / exposed	0 / 51 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION			
subjects affected / exposed	0 / 51 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEPHROTOXICITY			
subjects affected / exposed	0 / 51 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			

subjects affected / exposed	0 / 51 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Sunitinib	Everolimus	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 51 (100.00%)	57 / 57 (100.00%)	
Investigations			
Thrombocytopenia			
subjects affected / exposed	9 / 51 (17.65%)	4 / 57 (7.02%)	
occurrences (all)	15	5	
Vascular disorders			
Hypertension			
subjects affected / exposed	19 / 51 (37.25%)	2 / 57 (3.51%)	
occurrences (all)	30	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	14 / 51 (27.45%)	18 / 57 (31.58%)	
occurrences (all)	28	25	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 51 (3.92%)	13 / 57 (22.81%)	
occurrences (all)	2	22	
Gastrointestinal disorders			
Mucositis			
subjects affected / exposed	3 / 51 (5.88%)	8 / 57 (14.04%)	
occurrences (all)	3	8	
Nausea			
subjects affected / exposed	10 / 51 (19.61%)	10 / 57 (17.54%)	
occurrences (all)	13	11	
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	3 / 51 (5.88%)	8 / 57 (14.04%)	
occurrences (all)	4	8	

Infections and infestations Stomatitis subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 5	10 / 57 (17.54%) 15	
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all)	11 / 51 (21.57%) 14	4 / 57 (7.02%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported