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Trial record **1 of 1** for: CRAD001C2239

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Safety/Efficacy of Everolimus in Adults With Advanced Pancreatic Neuroendocrine Cancer Not Responsive to Chemotherapy

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00363051

First received: August 2, 2006
Last updated: May 6, 2013
Last verified: May 2013
History of Changes

Full Text View | Tabular View | **Study Results** | Disclaimer | How to Read a Study Record

Results First Received: December 2, 2011

Study Type:	Interventional
Study Design:	Endpoint Classification: Safety/Efficacy Study; Intervention Model: Single Group Assignment; Masking: Open Label; Primary Purpose: Treatment
Conditions:	Islet Cell Carcinoma Neuroendocrine Carcinoma Neuroendocrine Tumor Pancreatic Neoplasms
	Drug: Everolimus 10 mg

Interventions:	Drug: Octreotide Depot

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Participant Flow: Overall Study

	Stratum 1: Everolimus 10 mg	**Stratum 2: Everolimus 10 mg + Octreotide Depot**

STARTED	**115**	**45**
COMPLETED	**77** [1]	**23**
NOT COMPLETED	**38**	**22**
Adminstrative problems	**1**	**1**
Adverse Event	**21**	**12**
New Cancer Therapy	**2**	**1**
Withdrawal by Subject	**11**	**3**
Lost to Follow-up	**0**	**1**
Protocol Violation	**0**	**2**
Death	**3**	**2**

[1] Patients with documented disease progression per RECIST criteria

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot.
Total	Total of all reporting groups

Baseline Measures

	Stratum 1: Everolimus 10 mg	Stratum 2: Everolimus 10 mg + Octreotide Depot	Total
Number of Participants [units: participants]	**115**	**45**	**160**
Age [units: years] Mean (Standard Deviation)	**55.1 (11.8)**	**53.64 (12.478)**	**54.33 (11.98)**
Gender [units: participants]			
Female	**49**	**21**	**70**
Male	**66**	**24**	**90**

Outcome Measures

Hide All Outcome Measures

1. Primary: Objective Response Rate: Percentage of Participants With Best Over All Response of Complete Response or Partial Response by Central Radiology Review (Stratum 1) Based on Response Evaluation Criteria in Solid Tumors (RECIST) [Time Frame: from date of randomization/start of treatment until first documented response confirmed 4 weeks later(at least 3 months)]

Measure Type	Primary
Measure Title	Objective Response Rate: Percentage of Participants With Best Over All Response of Complete Response or Partial Response by Central Radiology Review (Stratum 1) Based on Response Evaluation Criteria in Solid Tumors (RECIST)
Measure Description	Objective response rate was defined by RECIST criteria: Partial response (PR) must have ≥ 30% decrease in the sum

	of longest diameter of all target lesions, from the baseline sum. Complete response (CR) must have disappearance of all target and non-target lesions. For CR or PR, tumor measurements must be confirmed by 2nd assessments within 4 weeks. Progression = 20% increase in the sum of longest diameter of all target lesions, from smallest sum of longest diameter of all target lesions recorded at or after baseline; or a new lesion; or progression of non-target lesions.
Time Frame	from date of randomization/start of treatment until first documented response confirmed 4 weeks later(at least 3 months)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The full analysis set (FAS) consisted of all patients who received at least one dose of everolimus.

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Measured Values

	Stratum 1: Everolimus 10 mg
Number of Participants Analyzed [units: participants]	**115**
Objective Response Rate: Percentage of Participants With Best Over All Response of Complete Response or Partial Response by Central Radiology Review (Stratum 1) Based on Response Evaluation Criteria in Solid Tumors (RECIST) [units: percentage of participants] Number (95% Confidence Interval)	**9.6 (4.9 to 16.5)**

No statistical analysis provided for Objective Response Rate: Percentage of Participants With Best Over All Response of Complete Response or Partial Response by Central Radiology Review (Stratum 1) Based on Response Evaluation Criteria in Solid Tumors (RECIST)

2. Secondary: Duration of Overall Response (Stratum 1) Based on Response Evaluation Criteria in Solid Tumors (RECIST)- Central Radiology Review [Time Frame: from date of first documented confirmed response to time to progression, at least 3 months]

Measure Type	Secondary
Measure Title	Duration of Overall Response (Stratum 1) Based on Response Evaluation Criteria in Solid Tumors (RECIST)- Central Radiology Review
Measure Description	Duration of overall response applies only to patients whose best overall response was complete response (CR) or partial response (PR): • Complete Response (CR) = at least two determinations of CR at least 4 weeks apart before progression. • Partial response (PR) = at least two determinations of PR or better at least 4 weeks apart before progression. Progression = 20% increase in the sum of the longest diameter of all target lesions, from the smallest sum of longest diameter of all target lesions recorded at or after baseline; or a new lesion; or progression of non-target lesions
Time Frame	from date of first documented confirmed response to time to progression, at least 3 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full Analysis Set (FAS) consisted of all patients who received at least one dose of everolimus. Only those patients whose best overall response was complete response (CR) or partial response (PR) were included in this analysis.

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive

	everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Measured Values

	Stratum 1: Everolimus 10 mg
Number of Participants Analyzed [units: participants]	**11**
Duration of Overall Response (Stratum 1) Based on Response Evaluation Criteria in Solid Tumors (RECIST)- Central Radiology Review [units: Months] Median (95% Confidence Interval)	**10.64** [1]

[1] The upper limit was not estimable in the study as it is longer than duration of study.

No statistical analysis provided for Duration of Overall Response (Stratum 1) Based on Response Evaluation Criteria in Solid Tumors (RECIST)- Central Radiology Review

3. Secondary: Duration of Overall Response (Stratum 2) Based on Response Evaluation Criteria in Solid Tumors (RECIST)- Central Radiology Review [Time Frame: from date of first documented confirmed response to time to progression, at least 3 months]

Measure Type	Secondary
Measure Title	Duration of Overall Response (Stratum 2) Based on Response Evaluation Criteria in Solid Tumors (RECIST)- Central Radiology Review
Measure Description	Duration of overall response applies only to patients whose best overall response was complete response (CR) or partial response (PR): • Complete Response (CR) = at least two determinations of CR at least 4 weeks apart before progression. • Partial response (PR) = at least two determinations of PR or better at least 4 weeks apart before progression. Progression = 20% increase in the sum of the longest diameter of all target lesions, from the smallest sum of longest

	diameter of all target lesions recorded at or after baseline; or a new lesion; or progression of non-target lesions
Time Frame	from date of first documented confirmed response to time to progression, at least 3 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Very low number of patients demonstrated a partial response, the median duration of response as per central review has not been calculated.

Reporting Groups

	Description
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Measured Values

	Stratum 2: Everolimus 10 mg + Octreotide Depot
Number of Participants Analyzed [units: participants]	**0**
Duration of Overall Response (Stratum 2) Based on Response Evaluation Criteria in Solid Tumors (RECIST)- Central Radiology Review	

No statistical analysis provided for Duration of Overall Response (Stratum 2) Based on Response Evaluation Criteria in Solid Tumors (RECIST)- Central Radiology Review

4. Secondary: Objective Response Rate: Percentage of Participants With Best Over All Response of Complete Response or Partial Response by Central Radiology Review (Stratum 2) Based on Response Evaluation Criteria in Solid Tumors (RECIST) [Time Frame: from date of randomization/start of treatment until first documented response confirmed 4 weeks later (at least 3 months)]

Measure Type	Secondary
Measure Title	Objective Response Rate: Percentage of Participants With Best Over All Response of Complete Response or Partial Response by Central Radiology Review (Stratum 2) Based on Response Evaluation Criteria in Solid Tumors (RECIST)
Measure Description	Objective response rate was defined by RECIST criteria: Partial response (PR) must have ≥ 30% decrease in the sum of longest diameter of all target lesions, from the baseline sum. Complete response (CR) must have disappearance of all target and non-target lesions. For CR or PR, tumor measurements must be confirmed by 2nd assessments within 4 weeks. Progression = 20% increase in the sum of longest diameter of all target lesions, from smallest sum of longest diameter of all target lesions recorded at or after baseline; or a new lesion; or progression of non-target lesions.
Time Frame	from date of randomization/start of treatment until first documented response confirmed 4 weeks later (at least 3 months)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full Analysis Set (FAS) was consisted of all patients who received at least one dose of everolimus.

Reporting Groups

	Description
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the

	same time every day.

Measured Values

	Stratum 2: Everolimus 10 mg + Octreotide Depot
Number of Participants Analyzed [units: participants]	**45**
Objective Response Rate: Percentage of Participants With Best Over All Response of Complete Response or Partial Response by Central Radiology Review (Stratum 2) Based on Response Evaluation Criteria in Solid Tumors (RECIST) [units: percentage of participants] Number (95% Confidence Interval)	**4.4 (0.5 to 15.1)**

No statistical analysis provided for Objective Response Rate: Percentage of Participants With Best Over All Response of Complete Response or Partial Response by Central Radiology Review (Stratum 2) Based on Response Evaluation Criteria in Solid Tumors (RECIST)

5. Secondary: Number of Participants With Adverse Events (AEs), Death, Serious Adverse Events (SAEs)[Stratum 1] [Time Frame: on or after the day of the first intake of study treatment to starting no later than 28 days after study treatment discontinuation, at least every month]

Measure Type	Secondary
Measure Title	Number of Participants With Adverse Events (AEs), Death, Serious Adverse Events (SAEs)[Stratum 1]
Measure Description	Adverse events are defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. Serious adverse events are any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalization, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgment of investigators represent significant hazards.
Time Frame	on or after the day of the first intake of study treatment to starting no later than 28 days after study treatment

	discontinuation, at least every month
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The safety population consists of all patients who received at least one dose of everolimus and had at least one post-baseline safety assessment.

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Measured Values

	Stratum 1: Everolimus 10 mg
Number of Participants Analyzed [units: participants]	**115**
Number of Participants With Adverse Events (AEs), Death, Serious Adverse Events (SAEs)[Stratum 1] [units: Participants]	
Adverse Events	**115**
Death	**10**
Serious Adverse Events	**63**

No statistical analysis provided for Number of Participants With Adverse Events (AEs), Death, Serious Adverse Events (SAEs)[Stratum 1]

6. Secondary: Number of Participants With Adverse Events (AEs), Death, Serious Adverse Events (SAEs) [Stratum 2] [Time Frame: on or after the day of the first intake of study treatment to starting no later than 28 days after study treatment discontinuation, at least every month]

Measure Type	Secondary
Measure Title	Number of Participants With Adverse Events (AEs), Death, Serious Adverse Events (SAEs) [Stratum 2]
Measure Description	Adverse events are defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. Serious adverse events are any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalization, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgment of investigators represent significant hazards.
Time Frame	on or after the day of the first intake of study treatment to starting no later than 28 days after study treatment discontinuation, at least every month
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The safety population consists of all patients who received at least one dose of everolimus and had at least one post-baseline safety assessment.

Reporting Groups

	Description
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot.

Measured Values

	Stratum 2: Everolimus 10 mg + Octreotide Depot
Number of Participants Analyzed [units: participants]	**45**
Number of Participants With Adverse Events (AEs), Death, Serious Adverse Events (SAEs) [Stratum 2] [units: Participants]	
Adverse Events	**45**
Death	**2**
Serious Adverse Events	**27**

No statistical analysis provided for Number of Participants With Adverse Events (AEs), Death, Serious Adverse Events (SAEs) [Stratum 2]

7. Secondary: Time to Progression Free Survival (PFS) Per Central Radiology Review (Stratum 1) [Time Frame: from randomisation to dates of disease progression, death from any cause or last tumor assessment, reported between day of first patient randomised, 26 June 2006, until cut-off date 13 September 2010]

Measure Type	Secondary
Measure Title	Time to Progression Free Survival (PFS) Per Central Radiology Review (Stratum 1)
Measure Description	Progression free survival (PFS) is defined as the time from randomization to the date of first documented disease progression or death from any cause. The Kaplan-Meier estimate of the PFS survival function was constructed. Median PFS was obtained and displayed along with 95% confidence intervals.
Time Frame	from randomisation to dates of disease progression, death from any cause or last tumor assessment, reported between day of first patient randomised, 26 June 2006, until cut-off date 13 September 2010
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The full analysis set (FAS) consisted of all patients who received at least one dose of everolimus.

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Measured Values

	Stratum 1: Everolimus 10 mg
Number of Participants Analyzed [units: participants]	**115**
Time to Progression Free Survival (PFS) Per Central Radiology Review (Stratum 1) [units: Months] Median (95% Confidence Interval)	**9.69 (8.25 to 13.31)**

No statistical analysis provided for Time to Progression Free Survival (PFS) Per Central Radiology Review (Stratum 1)

8. Secondary: Time to Progression Free Survival (PFS) Per Central Radiology Review (Stratum 2) [Time Frame: from randomisation to dates of disease progression, death from any cause or last tumor assessment, reported between day of first patient randomised, 26 June 2006, until cut-off date 13 September 2010]

Measure Type	Secondary
Measure Title	Time to Progression Free Survival (PFS) Per Central Radiology Review (Stratum 2)
Measure Description	Progression free survival (PFS) is defined as the time from randomization to the date of first documented disease progression or death from any cause. The Kaplan-Meier estimate of the PFS survival function was constructed.

	Median PFS was obtained and displayed along with 95% confidence intervals.
Time Frame	from randomisation to dates of disease progression, death from any cause or last tumor assessment, reported between day of first patient randomised, 26 June 2006, until cut-off date 13 September 2010
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The full analysis set (FAS) consisted of all patients who received at least one dose of everolimus.

Reporting Groups

	Description
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot.

Measured Values

	Stratum 2: Everolimus 10 mg + Octreotide Depot
Number of Participants Analyzed [units: participants]	**45**
Time to Progression Free Survival (PFS) Per Central Radiology Review (Stratum 2) [units: Months] Median (95% Confidence Interval)	**16.69** [1]

[1] The upper limit was not estimable in the study as it is longer than duration of study.

No statistical analysis provided for Time to Progression Free Survival (PFS) Per Central Radiology Review (Stratum 2)

9. Secondary: Time to Overall Survival (OS)(Stratum 1) [Time Frame: from randomisation to dates of disease progression, death from any cause, reported between day of first patient randomised, 26 June 2006, until cut-off date 13 April 2012]

Measure Type	Secondary
Measure Title	Time to Overall Survival (OS)(Stratum 1)
Measure Description	Overall survival measures the time of survival , with any response or disease progression, until death. The OS is defined as the time from date of start of treatment to date of death due to any cause. If a patient is not known to have died, survival was censored at the date of last contact. In each treatment stratum, the Kaplan-Meier estimate of the overall survival function was constructed.
Time Frame	from randomisation to dates of disease progression, death from any cause, reported between day of first patient randomised, 26 June 2006, until cut-off date 13 April 2012
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The full analysis set consisted of all patients who received at least one dose of everolimus.

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Measured Values

	Stratum 1: Everolimus 10 mg
Number of Participants Analyzed [units: participants]	**115**

Time to Overall Survival (OS)(Stratum 1) [units: months] Median (95% Confidence Interval)	**28.78 (20.24 to 36.37)**

No statistical analysis provided for Time to Overall Survival (OS)(Stratum 1)

10. Secondary: Time to Overall Survival (OS) (Stratum 2) [Time Frame: from randomisation to dates of disease progression, death from any cause, reported between day of first patient randomised, 26 June 2006, until cut-off date 13 April 2012]

Measure Type	Secondary
Measure Title	Time to Overall Survival (OS) (Stratum 2)
Measure Description	Overall survival measures the time of survival , with any response or disease progression, until death. The OS is defined as the time from date of start of treatment to date of death due to any cause. If a patient is not known to have died, survival was censored at the date of last contact. In each treatment stratum, the Kaplan-Meier estimate of the overall survival function was constructed.
Time Frame	from randomisation to dates of disease progression, death from any cause, reported between day of first patient randomised, 26 June 2006, until cut-off date 13 April 2012
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The full analysis set consisted of all patients who received at least one dose of everolimus.

Reporting Groups

	Description
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide

	Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Measured Values

	Stratum 2: Everolimus 10 mg + Octreotide Depot
Number of Participants Analyzed [units: participants]	**45**
Time to Overall Survival (OS) (Stratum 2) [units: months] Median (95% Confidence Interval)	**38.77** [1]

[1] The upper limit was not estimable in the study as it is longer than duration of study.

No statistical analysis provided for Time to Overall Survival (OS) (Stratum 2)

11. Secondary: Everolimus Trough Level Determination by Pharmacokinetics Parameter in Both Strata (Stratum 1 and 2) [Time Frame: Cycle 1 Day 15]

Measure Type	Secondary
Measure Title	Everolimus Trough Level Determination by Pharmacokinetics Parameter in Both Strata (Stratum 1 and 2)
Measure Description	For all patients in both strata, a blood sample for everolimus trough level determination will be collected immediately prior to the everolimus administration on Cycle 1 Day 15, Cycle 2 Day 1, and every month thereafter. A treatment cycle was defined as 28 days of consecutive daily treatment with everolimus and treatment continued until tumor progression. It is critical that patients not take their daily everolimus dose before the sample is drawn.
Time Frame	Cycle 1 Day 15
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full Analysis Set (FAS) is consisted of all patients who received at least one dose of everolimus. Patients with everolimus pharmacokinteic samples, with nonzero concentration, at Cycle 1 Day 15 were included

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Measured Values

	Stratum 1: Everolimus 10 mg	**Stratum 2: Everolimus 10 mg + Octreotide Depot**
Number of Participants Analyzed [units: participants]	**92**	**30**
Everolimus Trough Level Determination by Pharmacokinetics Parameter in Both Strata (Stratum 1 and 2) [units: ng/ml] Mean (Standard Deviation)	**15.7 (15.82)**	**17.3 (18.08)**

No statistical analysis provided for Everolimus Trough Level Determination by Pharmacokinetics Parameter in Both Strata (Stratum 1 and 2)

12. Secondary: Effect of Octreotide Depot on the Trough Concentrations of Everolimus [Time Frame: Cycle 1 Day 1, Cycle 2 Day 1]

Measure Type	Secondary
Measure Title	Effect of Octreotide Depot on the Trough Concentrations of Everolimus
Measure Description	The effect of Octreotide Depot on the trough concentrations of everolimus was assessed at Cycle 1 Day 15.
Time Frame	Cycle 1 Day 1, Cycle 2 Day 1
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full Analysis Set (FAS) is consisted of all patients who received at least one dose of everolimus. Patients with Octreotide Depot pharmacokinetic samples, with nonzero concentration, at Cycle 1 Day 1 or Cycle 2 Day 1 were included.

Reporting Groups

	Description
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.

Measured Values

	Stratum 2: Everolimus 10 mg + Octreotide Depot
Number of Participants Analyzed	

[units: participants]	**38**
Effect of Octreotide Depot on the Trough Concentrations of Everolimus [units: ng/ml] Mean (Standard Deviation)	
Cycle 1 Day 1 (pre-treatment baseline) (n=37)	**3.2 (2.81)**
Cycle 2 Day 1 (n= 38)	**3.7 (3.47)**

No statistical analysis provided for Effect of Octreotide Depot on the Trough Concentrations of Everolimus

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10 mg/day in addition to continuing their entry dose of Octreotide Depot.

Serious Adverse Events

	Stratum 1: Everolimus 10 mg	**Stratum 2: Everolimus 10 mg + Octreotide Depot**

Total, serious adverse events		
# participants affected / at risk	**63/115 (54.78%)**	**27/45 (60.00%)**
Blood and lymphatic system disorders		
Anaemia † [1]		
# participants affected / at risk	**3/115 (2.61%)**	**0/45 (0.00%)**
Lymphopenia † [1]		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Neutropenia † [1]		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Thrombocytopenia † [1]		
# participants affected / at risk	**0/115 (0.00%)**	**3/45 (6.67%)**
Cardiac disorders		
Acute myocardial infarction † [1]		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Cardiac failure † [1]		
# participants affected / at risk	**1/115 (0.87%)**	**3/45 (6.67%)**
Cardiac failure congestive † [1]		
# participants affected / at risk	**0/115 (0.00%)**	**2/45 (4.44%)**
Cardio-respiratory arrest † [1]		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Myocardial infarction † [1]		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Tachycardia † [1]		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Congenital, familial and genetic disorders		

Gastrointestinal angiodysplasia † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Eye disorders		
Optic ischaemic neuropathy † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Gastrointestinal disorders		
Abdominal distension † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Abdominal pain † 1		
# participants affected / at risk	**10/115 (8.70%)**	**4/45 (8.89%)**
Abdominal pain upper † 1		
# participants affected / at risk	**2/115 (1.74%)**	**0/45 (0.00%)**
Ascites † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Colitis † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Diarrhoea † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Gastritis † 1		
# participants affected / at risk	**1/115 (0.87%)**	**1/45 (2.22%)**
Gastrointestinal haemorrhage † 1		
# participants affected / at risk	**2/115 (1.74%)**	**0/45 (0.00%)**
Inguinal hernia † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Intestinal ischaemia † 1		

# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Intestinal obstruction † 1		
# participants affected / at risk	0/115 (0.00%)	1/45 (2.22%)
Nausea † 1		
# participants affected / at risk	3/115 (2.61%)	2/45 (4.44%)
Small intestinal obstruction † 1		
# participants affected / at risk	2/115 (1.74%)	0/45 (0.00%)
Subileus † 1		
# participants affected / at risk	2/115 (1.74%)	0/45 (0.00%)
Swollen tongue † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Upper gastrointestinal haemorrhage † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Vomiting † 1		
# participants affected / at risk	4/115 (3.48%)	3/45 (6.67%)
General disorders		
Asthenia † 1		
# participants affected / at risk	6/115 (5.22%)	0/45 (0.00%)
Device dislocation † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Device occlusion † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Fatigue † 1		
# participants affected / at risk	4/115 (3.48%)	0/45 (0.00%)
General physical health deterioration † 1		
# participants affected / at risk	2/115 (1.74%)	0/45 (0.00%)

Hyperthermia † 1		
# participants affected / at risk	**1/115 (0.87%)**	**1/45 (2.22%)**
Hypothermia † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Local swelling † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Multi-organ failure † 1		
# participants affected / at risk	**1/115 (0.87%)**	**1/45 (2.22%)**
Non-cardiac chest pain † 1		
# participants affected / at risk	**1/115 (0.87%)**	**1/45 (2.22%)**
Oedema peripheral † 1		
# participants affected / at risk	**0/115 (0.00%)**	**2/45 (4.44%)**
Performance status decreased † 1		
# participants affected / at risk	**2/115 (1.74%)**	**0/45 (0.00%)**
Pyrexia † 1		
# participants affected / at risk	**6/115 (5.22%)**	**2/45 (4.44%)**
Systemic inflammatory response syndrome † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Hepatobiliary disorders		
Bile duct obstruction † 1		
# participants affected / at risk	**1/115 (0.87%)**	**1/45 (2.22%)**
Cholangitis † 1		
# participants affected / at risk	**4/115 (3.48%)**	**0/45 (0.00%)**
Cholelithiasis † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**

Hepatic failure † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Jaundice † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Jaundice cholestatic † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Portal vein thrombosis † 1		
# participants affected / at risk	**2/115 (1.74%)**	**0/45 (0.00%)**
Immune system disorders		
Anaphylactic reaction † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Infections and infestations		
Abscess soft tissue † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Bacteraemia † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Bacterial infection † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Biliary tract infection † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Bronchitis † 1		
# participants affected / at risk	**1/115 (0.87%)**	**1/45 (2.22%)**
Cellulitis † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Device related infection † 1		

# participants affected / at risk	1/115 (0.87%)	1/45 (2.22%)
Diverticulitis † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Escherichia infection † 1		
# participants affected / at risk	0/115 (0.00%)	1/45 (2.22%)
Folliculitis † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Gastroenteritis † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Gastroenteritis viral † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Infection † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Influenza † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Liver abscess † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Lobar pneumonia † 1		
# participants affected / at risk	2/115 (1.74%)	0/45 (0.00%)
Lung infection † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Peritonitis bacterial † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Pharyngitis streptococcal † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)

Pneumocystis jiroveci pneumonia † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Pneumonia † 1		
# participants affected / at risk	**5/115 (4.35%)**	**1/45 (2.22%)**
Post procedural infection † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Pyelonephritis † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Sepsis † 1		
# participants affected / at risk	**3/115 (2.61%)**	**1/45 (2.22%)**
Sepsis syndrome † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Serratia infection † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Sinusitis † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Soft tissue infection † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Staphylococcal infection † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Subcutaneous abscess † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Injury, poisoning and procedural complications		
Accidental overdose † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**

Lumbar vertebral fracture † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Radiation oesophagitis † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Investigations		
Ammonia increased † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Blood creatinine increased † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Haematocrit decreased † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Metabolism and nutrition disorders		
Cachexia † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Decreased appetite † 1		
# participants affected / at risk	**4/115 (3.48%)**	**0/45 (0.00%)**
Dehydration † 1		
# participants affected / at risk	**3/115 (2.61%)**	**2/45 (4.44%)**
Diabetes mellitus † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Hypercalcaemia † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Hypoglycaemia † 1		
# participants affected / at risk	**1/115 (0.87%)**	**1/45 (2.22%)**
Hyponatraemia † 1		

# participants affected / at risk	1/115 (0.87%)	1/45 (2.22%)
Malnutrition † 1		
# participants affected / at risk	3/115 (2.61%)	0/45 (0.00%)
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Back pain † 1		
# participants affected / at risk	0/115 (0.00%)	1/45 (2.22%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Bladder transitional cell carcinoma † 1		
# participants affected / at risk	0/115 (0.00%)	1/45 (2.22%)
Breast cancer † 1		
# participants affected / at risk	0/115 (0.00%)	1/45 (2.22%)
Colon adenoma † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Colon cancer † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Metastases to liver † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Metastases to small intestine † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Metastases to spine † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Tumour necrosis † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)

Nervous system disorders		
Altered state of consciousness † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Cerebral haemorrhage † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Cerebrovascular accident † 1		
# participants affected / at risk	**2/115 (1.74%)**	**0/45 (0.00%)**
Coma hepatic † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Hepatic encephalopathy † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Hyperaesthesia † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Loss of consciousness † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Metabolic encephalopathy † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Unresponsive to stimuli † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Visual field defect † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Psychiatric disorders		
Confusional state † 1		
# participants affected / at risk	**2/115 (1.74%)**	**1/45 (2.22%)**
Depression † 1		

# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Insomnia † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Mental status changes † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Renal and urinary disorders		
Dysuria † 1		
# participants affected / at risk	0/115 (0.00%)	1/45 (2.22%)
Pollakiuria † 1		
# participants affected / at risk	0/115 (0.00%)	1/45 (2.22%)
Renal failure † 1		
# participants affected / at risk	2/115 (1.74%)	3/45 (6.67%)
Renal failure acute † 1		
# participants affected / at risk	0/115 (0.00%)	1/45 (2.22%)
Respiratory, thoracic and mediastinal disorders		
Acute respiratory distress syndrome † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Aspiration † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Cough † 1		
# participants affected / at risk	1/115 (0.87%)	0/45 (0.00%)
Dyspnoea † 1		
# participants affected / at risk	4/115 (3.48%)	3/45 (6.67%)
Dyspnoea exertional † 1		
# participants affected / at risk	1/115 (0.87%)	1/45 (2.22%)

Hydropneumothorax † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Interstitial lung disease † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Lung consolidation † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Lung disorder † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Pleural effusion † 1		
# participants affected / at risk	**0/115 (0.00%)**	**2/45 (4.44%)**
Pleuritic pain † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**
Pneumonitis † 1		
# participants affected / at risk	**2/115 (1.74%)**	**0/45 (0.00%)**
Pulmonary embolism † 1		
# participants affected / at risk	**1/115 (0.87%)**	**2/45 (4.44%)**
Pulmonary hypertension † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Pulmonary infarction † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Pulmonary oedema † 1		
# participants affected / at risk	**1/115 (0.87%)**	**1/45 (2.22%)**
Skin and subcutaneous tissue disorders		
Rash † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**

Swelling face † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Vascular disorders		
Deep vein thrombosis † 1		
# participants affected / at risk	**0/115 (0.00%)**	**1/45 (2.22%)**
Hypotension † 1		
# participants affected / at risk	**1/115 (0.87%)**	**0/45 (0.00%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Stratum 1: Everolimus 10 mg	Stratum 1 patients who were not receiving regular Octreotide Depot therapy. These patients were to receive everolimus monotherapy at 10 mg/day. Patients were instructed to take two 5 mg tablets of everolimus orally with a glass of water, once daily (preferably in the morning). Dosing was strongly recommended to occur at the same time every day.
Stratum 2: Everolimus 10 mg + Octreotide Depot	Stratum 2 participants who had received at least three consecutive months of Octreotide Long Acting Depot therapy prior to enrollment. These patients also received Everolimus 10

	mg/day in addition to continuing their entry dose of Octreotide Depot.

Other Adverse Events

	Stratum 1: Everolimus 10 mg	Stratum 2: Everolimus 10 mg + Octreotide Depot
Total, other (not including serious) adverse events		
# participants affected / at risk	**115/115 (100.00%)**	**44/45 (97.78%)**
Blood and lymphatic system disorders		
Anaemia † [1]		
# participants affected / at risk	**22/115 (19.13%)**	**11/45 (24.44%)**
Leukopenia † [1]		
# participants affected / at risk	**10/115 (8.70%)**	**2/45 (4.44%)**
Lymphopenia † [1]		
# participants affected / at risk	**10/115 (8.70%)**	**0/45 (0.00%)**
Neutropenia † [1]		
# participants affected / at risk	**10/115 (8.70%)**	**5/45 (11.11%)**
Thrombocytopenia † [1]		
# participants affected / at risk	**11/115 (9.57%)**	**6/45 (13.33%)**
Eye disorders		
Conjunctivitis † [1]		
# participants affected / at risk	**4/115 (3.48%)**	**4/45 (8.89%)**
Vision blurred † [1]		
# participants affected / at risk	**0/115 (0.00%)**	**4/45 (8.89%)**
Gastrointestinal disorders		
Abdominal distension † [1]		
# participants affected / at risk	**9/115 (7.83%)**	**5/45 (11.11%)**

Abdominal pain † 1		
# participants affected / at risk	**38/115 (33.04%)**	**9/45 (20.00%)**
Abdominal pain upper † 1		
# participants affected / at risk	**25/115 (21.74%)**	**7/45 (15.56%)**
Aphthous stomatitis † 1		
# participants affected / at risk	**24/115 (20.87%)**	**6/45 (13.33%)**
Ascites † 1		
# participants affected / at risk	**9/115 (7.83%)**	**0/45 (0.00%)**
Constipation † 1		
# participants affected / at risk	**30/115 (26.09%)**	**8/45 (17.78%)**
Diarrhoea † 1		
# participants affected / at risk	**63/115 (54.78%)**	**25/45 (55.56%)**
Dry mouth † 1		
# participants affected / at risk	**7/115 (6.09%)**	**2/45 (4.44%)**
Dyspepsia † 1		
# participants affected / at risk	**6/115 (5.22%)**	**1/45 (2.22%)**
Flatulence † 1		
# participants affected / at risk	**6/115 (5.22%)**	**4/45 (8.89%)**
Haemorrhoids † 1		
# participants affected / at risk	**2/115 (1.74%)**	**3/45 (6.67%)**
Mouth ulceration † 1		
# participants affected / at risk	**7/115 (6.09%)**	**2/45 (4.44%)**
Nausea † 1		
# participants affected / at risk	**54/115 (46.96%)**	**22/45 (48.89%)**
Steatorrhoea † 1		
# participants affected / at risk	**1/115 (0.87%)**	**3/45 (6.67%)**

Stomatitis † 1		
# participants affected / at risk	**57/115 (49.57%)**	**24/45 (53.33%)**
Toothache † 1		
# participants affected / at risk	**7/115 (6.09%)**	**2/45 (4.44%)**
Vomiting † 1		
# participants affected / at risk	**40/115 (34.78%)**	**12/45 (26.67%)**
General disorders		
Asthenia † 1		
# participants affected / at risk	**38/115 (33.04%)**	**9/45 (20.00%)**
Chills † 1		
# participants affected / at risk	**10/115 (8.70%)**	**4/45 (8.89%)**
Fatigue † 1		
# participants affected / at risk	**53/115 (46.09%)**	**20/45 (44.44%)**
Non-cardiac chest pain † 1		
# participants affected / at risk	**6/115 (5.22%)**	**1/45 (2.22%)**
Oedema peripheral † 1		
# participants affected / at risk	**34/115 (29.57%)**	**14/45 (31.11%)**
Pain † 1		
# participants affected / at risk	**7/115 (6.09%)**	**3/45 (6.67%)**
Pyrexia † 1		
# participants affected / at risk	**41/115 (35.65%)**	**14/45 (31.11%)**
Infections and infestations		
Bronchitis † 1		
# participants affected / at risk	**4/115 (3.48%)**	**4/45 (8.89%)**
Influenza † 1		

# participants affected / at risk	7/115 (6.09%)	4/45 (8.89%)
Nasopharyngitis † [1]		
# participants affected / at risk	18/115 (15.65%)	5/45 (11.11%)
Pneumonia † [1]		
# participants affected / at risk	4/115 (3.48%)	3/45 (6.67%)
Rhinitis † [1]		
# participants affected / at risk	7/115 (6.09%)	2/45 (4.44%)
Sinusitis † [1]		
# participants affected / at risk	12/115 (10.43%)	4/45 (8.89%)
Upper respiratory tract infection † [1]		
# participants affected / at risk	11/115 (9.57%)	4/45 (8.89%)
Urinary tract infection † [1]		
# participants affected / at risk	11/115 (9.57%)	5/45 (11.11%)
Injury, poisoning and procedural complications		
Fall † [1]		
# participants affected / at risk	0/115 (0.00%)	4/45 (8.89%)
Investigations		
Alanine aminotransferase increased † [1]		
# participants affected / at risk	7/115 (6.09%)	1/45 (2.22%)
Aspartate aminotransferase increased † [1]		
# participants affected / at risk	7/115 (6.09%)	0/45 (0.00%)
Blood alkaline phosphatase increased † [1]		
# participants affected / at risk	9/115 (7.83%)	1/45 (2.22%)
Blood creatinine increased † [1]		
# participants affected / at risk	1/115 (0.87%)	6/45 (13.33%)

Haemoglobin decreased † 1		
# participants affected / at risk	**4/115 (3.48%)**	**3/45 (6.67%)**
International normalised ratio increased † 1		
# participants affected / at risk	**1/115 (0.87%)**	**3/45 (6.67%)**
Weight decreased † 1		
# participants affected / at risk	**32/115 (27.83%)**	**12/45 (26.67%)**
Metabolism and nutrition disorders		
Decreased appetite † 1		
# participants affected / at risk	**27/115 (23.48%)**	**10/45 (22.22%)**
Dehydration † 1		
# participants affected / at risk	**5/115 (4.35%)**	**6/45 (13.33%)**
Diabetes mellitus † 1		
# participants affected / at risk	**11/115 (9.57%)**	**1/45 (2.22%)**
Hypercholesterolaemia † 1		
# participants affected / at risk	**14/115 (12.17%)**	**2/45 (4.44%)**
Hyperglycaemia † 1		
# participants affected / at risk	**21/115 (18.26%)**	**9/45 (20.00%)**
Hypoglycaemia † 1		
# participants affected / at risk	**9/115 (7.83%)**	**3/45 (6.67%)**
Hypokalaemia † 1		
# participants affected / at risk	**15/115 (13.04%)**	**5/45 (11.11%)**
Hyponatraemia † 1		
# participants affected / at risk	**7/115 (6.09%)**	**1/45 (2.22%)**
Hypophosphataemia † 1		
# participants affected / at risk	**11/115 (9.57%)**	**4/45 (8.89%)**
Musculoskeletal and connective tissue disorders		

Arthralgia † 1		
# participants affected / at risk	**15/115 (13.04%)**	**12/45 (26.67%)**
Back pain † 1		
# participants affected / at risk	**28/115 (24.35%)**	**9/45 (20.00%)**
Muscle spasms † 1		
# participants affected / at risk	**6/115 (5.22%)**	**2/45 (4.44%)**
Musculoskeletal pain † 1		
# participants affected / at risk	**8/115 (6.96%)**	**2/45 (4.44%)**
Myalgia † 1		
# participants affected / at risk	**12/115 (10.43%)**	**4/45 (8.89%)**
Neck pain † 1		
# participants affected / at risk	**8/115 (6.96%)**	**3/45 (6.67%)**
Pain in extremity † 1		
# participants affected / at risk	**5/115 (4.35%)**	**6/45 (13.33%)**
Nervous system disorders		
Dizziness † 1		
# participants affected / at risk	**5/115 (4.35%)**	**7/45 (15.56%)**
Dysgeusia † 1		
# participants affected / at risk	**14/115 (12.17%)**	**7/45 (15.56%)**
Headache † 1		
# participants affected / at risk	**40/115 (34.78%)**	**9/45 (20.00%)**
Psychiatric disorders		
Anxiety † 1		
# participants affected / at risk	**8/115 (6.96%)**	**3/45 (6.67%)**
Confusional state † 1		

# participants affected / at risk	6/115 (5.22%)	2/45 (4.44%)
Depression † [1]		
# participants affected / at risk	10/115 (8.70%)	2/45 (4.44%)
Insomnia † [1]		
# participants affected / at risk	15/115 (13.04%)	5/45 (11.11%)
Renal and urinary disorders		
Nocturia † [1]		
# participants affected / at risk	2/115 (1.74%)	4/45 (8.89%)
Respiratory, thoracic and mediastinal disorders		
Cough † [1]		
# participants affected / at risk	31/115 (26.96%)	8/45 (17.78%)
Dyspnoea † [1]		
# participants affected / at risk	18/115 (15.65%)	11/45 (24.44%)
Epistaxis † [1]		
# participants affected / at risk	17/115 (14.78%)	5/45 (11.11%)
Lung disorder † [1]		
# participants affected / at risk	4/115 (3.48%)	3/45 (6.67%)
Oropharyngeal pain † [1]		
# participants affected / at risk	8/115 (6.96%)	9/45 (20.00%)
Pleural effusion † [1]		
# participants affected / at risk	4/115 (3.48%)	3/45 (6.67%)
Pneumonitis † [1]		
# participants affected / at risk	5/115 (4.35%)	4/45 (8.89%)
Skin and subcutaneous tissue disorders		
Acne † [1]		

# participants affected / at risk	7/115 (6.09%)	2/45 (4.44%)
Dermatitis acneiform † 1		
# participants affected / at risk	2/115 (1.74%)	5/45 (11.11%)
Dry skin † 1		
# participants affected / at risk	15/115 (13.04%)	7/45 (15.56%)
Erythema † 1		
# participants affected / at risk	5/115 (4.35%)	5/45 (11.11%)
Hyperhidrosis † 1		
# participants affected / at risk	6/115 (5.22%)	1/45 (2.22%)
Nail disorder † 1		
# participants affected / at risk	9/115 (7.83%)	2/45 (4.44%)
Pruritus † 1		
# participants affected / at risk	18/115 (15.65%)	7/45 (15.56%)
Rash † 1		
# participants affected / at risk	54/115 (46.96%)	21/45 (46.67%)
Vascular disorders		
Hypertension † 1		
# participants affected / at risk	13/115 (11.30%)	4/45 (8.89%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** The terms and conditions of Novartis's agreements with it's investigators vary. However, Novartis does not prohibit any investigator from publishing. Any publication from a single-center site is postponed until the publication of the pooled data (i.e. data from all sites) in the clinical trial.

Results Point of Contact:

Name/Title: Novartis Study Director
Organization: Novartis Pharmaceuticals
phone: (862 778-8300

No publications provided

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00363051 History of Changes
Other Study ID Numbers:	**CRAD001C2239**
Study First Received:	August 2, 2006
Results First Received:	December 2, 2011
Last Updated:	May 6, 2013
Health Authority:	United States: Food and Drug Administration