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Trial record **1 of 1** for: CRAD001H2304E1

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Extension Study to Evaluate the Long-term Efficacy and Safety of Everolimus in Liver Transplant Recipients

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

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

ClinicalTrials.gov Identifier:
NCT01150097

First received: April 23, 2010
Last updated: March 12, 2015
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History of Changes

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Results First Received: May 1, 2014

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Liver Transplant Recipient
Interventions:	Drug: Tacrolimus (reduced tacrolimus) Drug: Everolimus (reduced tacrolimus) Drug: Tacrolimus (tacrolimus elimination) Drug: Everolimus (tacrolimus elimination) Drug: Tacrolimus (tacrolimus control) Drug: Corticosteroids

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
Two hundred eight four participants were eligible and enrolled into the extension. However, 2 participants withdrew from the extension prior to receiving treatment. Therefore, a total of 282 participants were accounted for in the extension.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Participants in the tacrolimus control group were studied for 12 months (from months 24 to 36 post transplant). Participants in the tacrolimus elimination and everolimus + reduced tacrolimus groups were studied for a minimum of 12 months up to 24 months (from months 24 to 48 months post transplant) depending on the participant's study start.

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Participants were maintained on whole blood trough levels of 3 - 8 ng/mL everolimus and 3 - 5 ng/mL tacrolimus.
Tacrolimus Elimination	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL everolimus.

Tacrolimus Control	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL tacrolimus.

Participant Flow for 2 periods

Period 1: Months 24 to 36 Post-transplantation

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control
STARTED	106	51	125
COMPLETED	96	49	117
NOT COMPLETED	10	2	8
Death	2	0	0
Administrative problems	5	2	2
Lost to Follow-up	0	0	3
Withdrawal by Subject	3	0	3

Period 2: Months 24 to 48 Post-transplantation

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control
STARTED	106	51	0
COMPLETED	95	47	0
NOT COMPLETED	11	4	0
Administrative problems	5	4	0
Withdrawal by Subject	4	0	0
Death	2	0	0

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
Everolimus + Reduced Tacrolimus	Participants were maintained on whole blood trough levels of 3 - 8 ng/mL everolimus and 3 - 5 ng/mL tacrolimus.
Tacrolimus Elimination	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL everolimus.
Tacrolimus Control	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL tacrolimus.
Total	Total of all reporting groups

Baseline Measures

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control	Total
Number of Participants [units: participants]	106	51	125	282
Age [units: Years] Mean (Standard Deviation)	53.5 (9.57)	54.9 (10.07)	55.2 (8.10)	54.5 (9.25)

Gender [units: Participants]				
Female	29	18	38	85
Male	77	33	87	197

Outcome Measures

Hide All Outcome Measures

1. Primary: Incidence Rate of Composite Efficacy Failure Defined as Treated Biopsy Proven Acute Rejection (tBPAR), Graft Loss or Death [Time Frame: from months 24 to 36]

Measure Type	Primary
Measure Title	Incidence Rate of Composite Efficacy Failure Defined as Treated Biopsy Proven Acute Rejection (tBPAR), Graft Loss or Death
Measure Description	The number of participants who experienced composite efficacy failure was analyzed. Composite efficacy failure was defined as treated biopsy proven acute rejection (tBPAR), graft loss, or death. A BPAR was defined as an acute rejection confirmed by biopsy with a Rejection Activity Index (RAI) score ≥ 3. tBPAR was defined as a BPAR which was treated with anti-rejection therapy. The RAI is used to score liver biopsies with acute rejection and is composed of 3 categories (portal inflammation, bile duct inflammation damage, and venous endothelial inflammation) each scored on a scale of 0 (absent) to 3 (severe) by a trained pathologist. The total RAI score = the sum of the scores of the 3 categories and ranges from 0 to 9, with a higher score indicating greater rejection. The graft was presumed to be lost on the day the patient was newly listed for a liver graft, received a graft re-transplant, or died.
Time Frame	from months 24 to 36
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.
All extension participants

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Participants were maintained on whole blood trough levels of 3 - 8 ng/mL everolimus and 3 - 5 ng/mL tacrolimus.
Tacrolimus Elimination	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL everolimus.
Tacrolimus Control	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL tacrolimus.

Measured Values

	Everolimus + Reduced Tacrolimus	**Tacrolimus Elimination**	**Tacrolimus Control**
Number of Participants Analyzed [units: participants]	**106**	**51**	**125**
Incidence Rate of Composite Efficacy Failure Defined as Treated Biopsy Proven Acute Rejection (tBPAR), Graft Loss or Death [units: Participants]	**2**	**1**	**3**

No statistical analysis provided for Incidence Rate of Composite Efficacy Failure Defined as Treated Biopsy Proven Acute Rejection (tBPAR), Graft Loss or Death

2. Primary: Incidence Rate of Composite Efficacy Failure Defined as Treated Biopsy Proven Acute Rejection (tBPAR), Graft Loss or Death [Time Frame: from months 36 to 48]

Measure Type	Primary
Measure Title	Incidence Rate of Composite Efficacy Failure Defined as Treated Biopsy Proven Acute Rejection (tBPAR), Graft Loss or Death
Measure Description	The number of participants who experienced composite efficacy failure was analyzed. Composite efficacy failure was defined as treated biopsy proven acute rejection (tBPAR), graft loss, or death. A BPAR was defined as an acute rejection confirmed by biopsy with a Rejection Activity Index (RAI) score ≥ 3. tBPAR was defined as a BPAR which was treated with anti-rejection therapy. The RAI is used to score liver biopsies with acute rejection and is composed of 3 categories (portal inflammation, bile duct inflammation damage, and venous endothelial inflammation) each scored on a scale of 0 (absent) to 3 (severe) by a trained pathologist. The total RAI score = the sum of the scores of the 3 categories and ranges from 0 to 9, with a higher score indicating greater rejection. The graft was presumed to be lost on the day the patient was newly listed for a liver graft, received a graft re-transplant, or died.
Time Frame	from months 36 to 48
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.
Participants from the everolimus + reduced tacrolimus group and the tacrolimus elimination group

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Participants were maintained on whole blood trough levels of 3 - 8 ng/mL everolimus and 3 - 5 ng/mL tacrolimus.
Tacrolimus Elimination	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL everolimus.

Measured Values

	Everolimus + Reduced Tacrolimus	**Tacrolimus Elimination**
Number of Participants Analyzed [units: participants]	**106**	**51**
Incidence Rate of Composite Efficacy Failure Defined as Treated Biopsy Proven Acute Rejection (tBPAR), Graft Loss or Death [units: Participants]	**1**	**0**

No statistical analysis provided for Incidence Rate of Composite Efficacy Failure Defined as Treated Biopsy Proven Acute Rejection (tBPAR), Graft Loss or Death

3. Primary: Incidence Rate of Composite Efficacy Failure Defined as Graft Loss or Death [Time Frame: from months 24 to 36]

Measure Type	Primary
Measure Title	Incidence Rate of Composite Efficacy Failure Defined as Graft Loss or Death
Measure Description	The number of participants who experienced graft loss or death was analyzed. The graft was presumed to be lost on the day the patient was newly listed for a liver graft, received a graft re-transplant, or died.
Time Frame	from months 24 to 36
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.
All extension participants

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Participants were maintained on whole blood trough levels of 3 - 8 ng/mL everolimus and 3 - 5 ng/mL tacrolimus.
Tacrolimus Elimination	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL everolimus.
Tacrolimus Control	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL tacrolimus.

Measured Values

	Everolimus + Reduced Tacrolimus	**Tacrolimus Elimination**	**Tacrolimus Control**
Number of Participants Analyzed [units: participants]	**106**	**51**	**125**
Incidence Rate of Composite Efficacy Failure Defined as Graft Loss or Death [units: Participants]	**2**	**0**	**1**

No statistical analysis provided for Incidence Rate of Composite Efficacy Failure Defined as Graft Loss or Death

4. Primary: Incidence Rate of Composite Efficacy Failure Defined as Graft Loss or Death [Time Frame: from months 36 - 48]

Measure Type	Primary
Measure Title	Incidence Rate of Composite Efficacy Failure Defined as Graft Loss or Death
Measure Description	The number of participants who experienced graft loss or death was analyzed. The graft was presumed to be lost on the day the patient was newly listed for a liver graft, received a graft re-transplant, or died.
Time Frame	from months 36 - 48
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.
Participants from the everolimus + reduced tacrolimus group and the tacrolimus elimination group

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Participants were maintained on whole blood trough levels of 3 - 8 ng/mL everolimus and 3 - 5 ng/mL tacrolimus.
Tacrolimus Elimination	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL everolimus.

Measured Values

	Everolimus + Reduced Tacrolimus	**Tacrolimus Elimination**
Number of Participants Analyzed [units: participants]	**106**	**51**
Incidence Rate of Composite Efficacy Failure Defined as Graft Loss or Death		

[units: Participants]	**0**	**0**

No statistical analysis provided for Incidence Rate of Composite Efficacy Failure Defined as Graft Loss or Death

5. Primary: Change in Renal Function [Time Frame: from months 24 to 36]

Measure Type	Primary
Measure Title	Change in Renal Function
Measure Description	Change in renal function was assessed by the estimated Glomerular Filtration Rate (eGFR) using the abbreviated (4 variables) Modification of Diet in Renal Disease (MDRD-4) formula which was developed by the MDRD Study Group and has been validated in patients with chronic kidney disease. The MDRD-4 formula used for the eGFR calculation is: eGFR (mL/min/1.73m^2) = 186.3*(C^-1.154)*(A^-0.203)*G*R, where C is the serum concentration of creatinine (mg/dL), A is age (years), G=0.742 when gender is female, otherwise G=1, R=1.21 when race is black, otherwise R=1.
Time Frame	from months 24 to 36
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 analysis population included extension participants who had both post-extension baseline and month 36 values only.

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Participants were maintained on whole blood trough levels of 3 - 8 ng/mL everolimus and 3 - 5 ng/mL tacrolimus.
Tacrolimus Elimination	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL everolimus.
Tacrolimus Control	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL tacrolimus.

Measured Values

	Everolimus + Reduced Tacrolimus	**Tacrolimus Elimination**	**Tacrolimus Control**
Number of Participants Analyzed [units: participants]	**100**	**50**	**115**
Change in Renal Function [units: mL/min/1.73m^2] Mean (Standard Deviation)	**-0.9 (16.13)**	**2.5 (12.40)**	**-3.3 (11.84)**

No statistical analysis provided for Change in Renal Function

6. Secondary: Incidence Rate of tBPAR [Time Frame: from months 24 - 36]

Measure Type	Secondary
Measure Title	Incidence Rate of tBPAR
Measure Description	The number of participants who had a tBPAR was analyzed. tBPAR was defined as a BPAR which was treated with anti-rejection therapy. The RAI is used to score liver biopsies with acute rejection and is composed of 3 categories (portal inflammation, bile duct inflammation damage, and venous endothelial inflammation) each scored on a scale of 0 (absent) to 3 (severe) by a trained pathologist. The total RAI score = the sum of the scores of the 3 categories and ranges from 0 to 9, with a higher score indicating greater rejection.

Time Frame	from months 24 - 36
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.
All extension participants

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Participants were maintained on whole blood trough levels of 3 - 8 ng/mL everolimus and 3 - 5 ng/mL tacrolimus.
Tacrolimus Elimination	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL everolimus.
Tacrolimus Control	Participants were maintained on a whole blood trough level of 6 - 10 ng/mL tacrolimus.

Measured Values

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control
Number of Participants Analyzed [units: participants]	**106**	**51**	**125**
Incidence Rate of tBPAR [units: Participants]	**0**	**1**	**2**

No statistical analysis provided for Incidence Rate of tBPAR

Serious Adverse Events

Hide Serious Adverse Events

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

Reporting Groups

	Description
Reduced TAC, Month 36	Reduced TAC, Month 36
TAC Elimination, Month 36	TAC Elimination, Month 36
TAC Control, Month 36	TAC Control, Month 36
Reduced RAD + TAC, Month 48	Reduced RAD + TAC, Month 48
TAC Elimination, Month 48	TAC Elimination, Month 48

Serious Adverse Events

	Reduced TAC, Month 36	TAC Elimination, Month 36	TAC Control, Month 36	Reduced RAD + TAC, Month 48	TAC Elimination, Month 48
Total, serious adverse events					
# participants affected / at risk	**32/106 (30.19%)**	**16/51 (31.37%)**	**28/125 (22.40%)**	**34/106 (32.08%)**	**24/51 (47.06%)**
Blood and lymphatic system disorders					

Anaemia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Haemolytic uraemic syndrome † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Lymphadenopathy † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Splenomegaly † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Cardiac disorders					
Acute myocardial infarction † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Cardiac failure † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Coronary artery stenosis † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Myocardial infarction † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Tachycardia † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Gastrointestinal disorders					
Abdominal adhesions † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Abdominal hernia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Abdominal pain † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**1/106 (0.94%)**	**1/51 (1.96%)**
Abdominal strangulated hernia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Constipation † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Crohn's disease † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Diarrhoea † 1					
# participants affected / at risk	**3/106 (2.83%)**	**0/51 (0.00%)**	**2/125 (1.60%)**	**4/106 (3.77%)**	**0/51 (0.00%)**
Gastrointestinal obstruction † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Hernial eventration † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**2/125 (1.60%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Intestinal obstruction † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Mouth ulceration † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Nausea † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**1/106 (0.94%)**	**1/51 (1.96%)**

Oesophageal ulcer † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Rectal haemorrhage † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Small intestinal obstruction † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Stomatitis † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Umbilical hernia, obstructive † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Vomiting † 1					
# participants affected / at risk	**2/106 (1.89%)**	**0/51 (0.00%)**	**2/125 (1.60%)**	**2/106 (1.89%)**	**1/51 (1.96%)**
General disorders					
Device occlusion † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
General physical health deterioration † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Generalised oedema † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Impaired healing † 1					
# participants affected / at risk	**2/106 (1.89%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**2/106 (1.89%)**	**2/51 (3.92%)**
Oedema peripheral † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Pyrexia † 1					
# participants affected / at risk	**3/106 (2.83%)**	**2/51 (3.92%)**	**2/125 (1.60%)**	**3/106 (2.83%)**	**4/51 (7.84%)**
Sudden death † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Hepatobiliary disorders					
Acute hepatic failure † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Autoimmune hepatitis † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Bile duct stenosis † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Biliary ischaemia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Cholangitis † 1					
# participants affected / at risk	**1/106 (0.94%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**1/51 (1.96%)**
Cholestasis † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Hepatic artery thrombosis † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Hepatic necrosis † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**

Hepatic steatosis † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Portal vein thrombosis † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Infections and infestations					
Abdominal sepsis † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Arthritis bacterial † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Bacteraemia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Bronchitis † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Cellulitis † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**2/106 (1.89%)**	**1/51 (1.96%)**
Epstein-Barr viraemia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Erysipelas † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Gastroenteritis † 1					
# participants affected / at risk	**2/106 (1.89%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**2/106 (1.89%)**	**0/51 (0.00%)**
Haematoma infection † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Hepatitis C † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Liver abscess † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Localised infection † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Oral herpes † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Orchitis † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Paronychia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Pneumonia † 1					
# participants affected / at risk	**2/106 (1.89%)**	**2/51 (3.92%)**	**3/125 (2.40%)**	**3/106 (2.83%)**	**3/51 (5.88%)**
Respiratory tract infection † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Sepsis † 1					
# participants affected / at risk	**2/106 (1.89%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**2/106 (1.89%)**	**1/51 (1.96%)**
Septic shock † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Sinusitis † 1					

# participants affected / at risk	1/106 (0.94%)	0/51 (0.00%)	0/125 (0.00%)	1/106 (0.94%)	0/51 (0.00%)
Streptococcal sepsis † 1					
# participants affected / at risk	1/106 (0.94%)	0/51 (0.00%)	0/125 (0.00%)	1/106 (0.94%)	0/51 (0.00%)
Urinary tract infection † 1					
# participants affected / at risk	1/106 (0.94%)	1/51 (1.96%)	2/125 (1.60%)	1/106 (0.94%)	1/51 (1.96%)
Viral infection † 1					
# participants affected / at risk	0/106 (0.00%)	0/51 (0.00%)	1/125 (0.80%)	0/106 (0.00%)	0/51 (0.00%)
Wound abscess † 1					
# participants affected / at risk	1/106 (0.94%)	0/51 (0.00%)	0/125 (0.00%)	1/106 (0.94%)	0/51 (0.00%)
Injury, poisoning and procedural complications					
Anastomotic stenosis † 1					
# participants affected / at risk	0/106 (0.00%)	0/51 (0.00%)	1/125 (0.80%)	0/106 (0.00%)	0/51 (0.00%)
Ankle fracture † 1					
# participants affected / at risk	1/106 (0.94%)	0/51 (0.00%)	0/125 (0.00%)	2/106 (1.89%)	0/51 (0.00%)
Clavicle fracture † 1					
# participants affected / at risk	1/106 (0.94%)	0/51 (0.00%)	0/125 (0.00%)	1/106 (0.94%)	0/51 (0.00%)
Graft loss † 1					
# participants affected / at risk	0/106 (0.00%)	0/51 (0.00%)	1/125 (0.80%)	0/106 (0.00%)	0/51 (0.00%)
Incisional hernia † 1					
# participants affected / at risk	1/106 (0.94%)	2/51 (3.92%)	1/125 (0.80%)	2/106 (1.89%)	4/51 (7.84%)
Incisional hernia, obstructive † 1					
# participants affected / at risk	0/106 (0.00%)	0/51 (0.00%)	0/125 (0.00%)	1/106 (0.94%)	1/51 (1.96%)
Joint dislocation † 1					
# participants affected / at risk	0/106 (0.00%)	1/51 (1.96%)	0/125 (0.00%)	0/106 (0.00%)	1/51 (1.96%)
Lower limb fracture † 1					
# participants affected / at risk	0/106 (0.00%)	1/51 (1.96%)	0/125 (0.00%)	0/106 (0.00%)	1/51 (1.96%)
Overdose † 1					
# participants affected / at risk	1/106 (0.94%)	0/51 (0.00%)	0/125 (0.00%)	1/106 (0.94%)	0/51 (0.00%)
Pelvic fracture † 1					
# participants affected / at risk	0/106 (0.00%)	0/51 (0.00%)	1/125 (0.80%)	0/106 (0.00%)	0/51 (0.00%)
Post procedural bile leak † 1					
# participants affected / at risk	0/106 (0.00%)	0/51 (0.00%)	0/125 (0.00%)	0/106 (0.00%)	1/51 (1.96%)
Postoperative hernia † 1					
# participants affected / at risk	0/106 (0.00%)	1/51 (1.96%)	0/125 (0.00%)	0/106 (0.00%)	1/51 (1.96%)
Radius fracture † 1					
# participants affected / at risk	1/106 (0.94%)	0/51 (0.00%)	0/125 (0.00%)	1/106 (0.94%)	0/51 (0.00%)
Tendon rupture † 1					
# participants affected / at risk	0/106 (0.00%)	0/51 (0.00%)	0/125 (0.00%)	1/106 (0.94%)	0/51 (0.00%)
Wound dehiscence † 1					
# participants affected / at risk	0/106 (0.00%)	1/51 (1.96%)	0/125 (0.00%)	0/106 (0.00%)	1/51 (1.96%)
Investigations					
Blood creatinine increased † 1					
# participants affected / at risk	0/106 (0.00%)	0/51 (0.00%)	1/125 (0.80%)	0/106 (0.00%)	0/51 (0.00%)

Blood glucose increased † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Haemoglobin decreased † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Weight decreased † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Metabolism and nutrition disorders					
Gout † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**1/51 (1.96%)**
Hyperglycaemia † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Hyperkalaemia † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Hypokalaemia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Hyponatraemia † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Musculoskeletal and connective tissue disorders					
Osteonecrosis † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Basal cell carcinoma † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**2/125 (1.60%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Diffuse large B-cell lymphoma † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Hepatocellular carcinoma † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Lung neoplasm malignant † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Oesophageal squamous cell carcinoma † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Prostate cancer † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Squamous cell carcinoma † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**2/125 (1.60%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Squamous cell carcinoma of lung † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Squamous cell carcinoma of skin † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**2/125 (1.60%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Nervous system disorders					
Cerebral ischaemia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**

Dysarthria † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Haemorrhage intracranial † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Headache † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Psychiatric disorders					
Depression † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Suicide attempt † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Renal and urinary disorders					
Acute prerenal failure † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Renal failure † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Renal failure acute † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Renal failure chronic † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**0/125 (0.00%)**	**0/106 (0.00%)**	**1/51 (1.96%)**
Renal impairment † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Renal injury † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Reproductive system and breast disorders					
Gynaecomastia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Ovarian cyst † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Respiratory, thoracic and mediastinal disorders					
Pleural effusion † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Pulmonary granuloma † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (0.00%)**
Skin and subcutaneous tissue disorders					
Night sweats † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Pruritus † 1					
# participants affected / at risk	**0/106 (0.00%)**	**0/51 (0.00%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**0/51 (0.00%)**
Vascular disorders					
Haematoma † 1					
# participants affected / at risk	**1/106 (0.94%)**	**0/51 (0.00%)**	**0/125 (0.00%)**	**1/106 (0.94%)**	**0/51 (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
Reduced TAC, Month 36	Reduced TAC, Month 36
TAC Elimination, Month 36	TAC Elimination, Month 36
TAC Control, Month 36	TAC Control, Month 36
Reduced RAD + TAC, Month 48	Reduced RAD + TAC, Month 48
TAC Elimination, Month 48	TAC Elimination, Month 48

Other Adverse Events

	Reduced TAC, Month 36	TAC Elimination, Month 36	TAC Control, Month 36	Reduced RAD + TAC, Month 48	TAC Elimination, Month 48
Total, other (not including serious) adverse events					
# participants affected / at risk	**38/106 (35.85%)**	**29/51 (56.86%)**	**43/125 (34.40%)**	**43/106 (40.57%)**	**36/51 (70.59%)**
Blood and lymphatic system disorders					
Anaemia † 1					
# participants affected / at risk	**4/106 (3.77%)**	**3/51 (5.88%)**	**3/125 (2.40%)**	**4/106 (3.77%)**	**3/51 (5.88%)**
Thrombocytopenia † 1					
# participants affected / at risk	**0/106 (0.00%)**	**1/51 (1.96%)**	**1/125 (0.80%)**	**0/106 (0.00%)**	**4/51 (7.84%)**
Gastrointestinal disorders					
Abdominal pain † 1					
# participants affected / at risk	**2/106 (1.89%)**	**2/51 (3.92%)**	**8/125 (6.40%)**	**3/106 (2.83%)**	**4/51 (7.84%)**
Diarrhoea † 1					
# participants affected / at risk	**10/106 (9.43%)**	**3/51 (5.88%)**	**4/125 (3.20%)**	**13/106 (12.26%)**	**4/51 (7.84%)**
Nausea † 1					
# participants affected / at risk	**3/106 (2.83%)**	**1/51 (1.96%)**	**9/125 (7.20%)**	**5/106 (4.72%)**	**2/51 (3.92%)**
General disorders					
Fatigue † 1					

# participants affected / at risk	1/106 (0.94%)	2/51 (3.92%)	10/125 (8.00%)	2/106 (1.89%)	6/51 (11.76%)
Oedema peripheral † 1					
# participants affected / at risk	4/106 (3.77%)	4/51 (7.84%)	2/125 (1.60%)	6/106 (5.66%)	5/51 (9.80%)
Infections and infestations					
Hepatitis C † 1					
# participants affected / at risk	1/106 (0.94%)	2/51 (3.92%)	3/125 (2.40%)	1/106 (0.94%)	3/51 (5.88%)
Influenza † 1					
# participants affected / at risk	2/106 (1.89%)	3/51 (5.88%)	0/125 (0.00%)	2/106 (1.89%)	3/51 (5.88%)
Nasopharyngitis † 1					
# participants affected / at risk	5/106 (4.72%)	5/51 (9.80%)	4/125 (3.20%)	6/106 (5.66%)	5/51 (9.80%)
Urinary tract infection † 1					
# participants affected / at risk	4/106 (3.77%)	2/51 (3.92%)	4/125 (3.20%)	4/106 (3.77%)	4/51 (7.84%)
Injury, poisoning and procedural complications					
Incisional hernia † 1					
# participants affected / at risk	2/106 (1.89%)	6/51 (11.76%)	2/125 (1.60%)	2/106 (1.89%)	7/51 (13.73%)
Metabolism and nutrition disorders					
Hypercholesterolaemia † 1					
# participants affected / at risk	6/106 (5.66%)	4/51 (7.84%)	3/125 (2.40%)	7/106 (6.60%)	5/51 (9.80%)
Musculoskeletal and connective tissue disorders					
Osteoporosis † 1					
# participants affected / at risk	0/106 (0.00%)	3/51 (5.88%)	1/125 (0.80%)	0/106 (0.00%)	3/51 (5.88%)
Pain in extremity † 1					
# participants affected / at risk	2/106 (1.89%)	3/51 (5.88%)	0/125 (0.00%)	2/106 (1.89%)	5/51 (9.80%)
Renal and urinary disorders					
Renal failure † 1					
# participants affected / at risk	1/106 (0.94%)	1/51 (1.96%)	10/125 (8.00%)	2/106 (1.89%)	1/51 (1.96%)
Vascular disorders					
Hypertension † 1					
# participants affected / at risk	8/106 (7.55%)	2/51 (3.92%)	5/125 (4.00%)	9/106 (8.49%)	2/51 (3.92%)

† 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' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial or disclosure of trial results in their entirety.

Results Point of Contact:

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

No publications provided

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT01150097 History of Changes
Other Study ID Numbers:	**CRAD001H2304E1** 2009-017311-15
Study First Received:	April 23, 2010
Results First Received:	May 1, 2014
Last Updated:	March 12, 2015
Health Authority:	United States: Food and Drug Administration