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Trial record **1 of 1** for: CRAD001H2401

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RESCUE Study - Everolimus in Liver Transplantation Recipients With Renal Insufficiency

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by:
Novartis

ClinicalTrials.gov Identifier:
NCT00267189

First received: December 19, 2005
Last updated: April 11, 2011
Last verified: April 2011
History of Changes

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Results First Received: December 20, 2010

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Liver Transplantation
Interventions:	Drug: Everolimus Drug: Calcineurin inhibitors (CNI) Drug: Mycophenolate acid (MPA)/ Azathioprine (AZA) Drug: Steroids

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
Group 1 (Everolimus)	Reduced or discontinued CNI dose + everolimus (3-12 ng/mL) ± steroids
Group 2 (Control)	Standard CNI dose ± mycophenolate acid (MPA)/azathioprine (AZA) ± steroids

Participant Flow: Overall Study

	Group 1 (Everolimus)	Group 2 (Control)
STARTED	**72** [1]	**73**
Completed Study Medication	**54**	**72**

COMPLETED	**67** [2]	**72**
NOT COMPLETED	**5**	**1**
Patient withdrew consent	**1**	**1**
Death	**1**	**0**
Missing	**3**	**0**

[1] Intention to treat (ITT) population.
[2] "Completed" indicates completed study.

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
Group 1 (Everolimus)	Reduced or discontinued CNI dose + everolimus (3-12 ng/mL) ± steroids
Group 2 (Control)	Standard CNI dose ± mycophenolate acid (MPA)/azathioprine (AZA) ± steroids
Total	Total of all reporting groups

Baseline Measures

	Group 1 (Everolimus)	**Group 2 (Control)**	**Total**
Number of Participants [units: participants]	**72**	**73**	**145**
Age [units: Years] Mean (Standard Deviation)	**57.0 (8.45)**	**57.8 (6.93)**	**57.4 (7.70)**
Age, Customized [units: Paricipants]			
< 40 years	**1**	**2**	**3**
>= 40 - < 50 years	**12**	**7**	**19**
>= 50 - < 60 years	**29**	**33**	**62**
>= 60 years	**30**	**31**	**61**
Gender [units: participants]			
Female	**27**	**33**	**60**
Male	**45**	**40**	**85**

Outcome Measures

Hide All Outcome Measures

1. Primary: Mean Change From Baseline in Cockcroft-Gault Calculated Creatinine Clearance (CrCl) [Time Frame: From baseline to 6 months]

Measure Type	Primary
Measure Title	Mean Change From Baseline in Cockcroft-Gault Calculated Creatinine Clearance (CrCl)
Measure Description	The primary variable was renal function assessed by calculated creatinine clearance using the Cockcroft-Gault formula, and was assessed at all visits. CrCl[mL/min] = (140 – A) * W / (72 * C) * R. Where A is age at sample date [years], W is body weight at specific visit [kg], C is the serum concentration of creatinine [mg/dL], R = 1 if the patient is male and = 0.85 if female.
Time Frame	From baseline to 6 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.
Intention to treat (ITT) population includes all patients who were randomized to one of the treatment groups and received at least one dose of study medication. Patients with baseline and 6 month creatinine clearance were included in analysis. Missing values at 6 months were imputed using the last observation carried forward (LOCF) approach.

Reporting Groups

	Description
Group 1 (Everolimus)	Reduced or discontinued CNI dose + everolimus (3-12 ng/mL) ± steroids
Group 2 (Control)	Standard CNI dose ± mycophenolate acid (MPA)/azathioprine (AZA) ± steroids

Measured Values

	Group 1 (Everolimus)	**Group 2 (Control)**
Number of Participants Analyzed [units: participants]	**71**	**71**
Mean Change From Baseline in Cockcroft-Gault Calculated Creatinine Clearance (CrCl) [units: mL/min] Mean (Standard Deviation)	**0.99 (10.25)**	**2.26 (7.79)**

No statistical analysis provided for Mean Change From Baseline in Cockcroft-Gault Calculated Creatinine Clearance (CrCl)

2. Secondary: Percentage of Patients With Efficacy Failure (Biopsy Proven Acute Rejection [BPAR], Graft Loss or Death) [Time Frame: 6 months]

Measure Type	Secondary
Measure Title	Percentage of Patients With Efficacy Failure (Biopsy Proven Acute Rejection [BPAR], Graft Loss or Death)
Measure Description	The composite efficacy failure endpoint encompasses at least one of: biopsy proven acute rejection, graft loss, or death for the patient. BPAR was defined as a clinically suspected acute rejection confirmed by biopsy. Acute rejection episodes were recorded as Liver Allograft Rejection. The allograft was presumed to be lost if a patient had a liver retransplant or died.
Time Frame	6 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.
Intention to treat (ITT) population includes all patients who were randomized to one of the treatment groups and received at least one dose of study medication.

Reporting Groups

	Description
Group 1 (Everolimus)	Reduced or discontinued CNI dose + everolimus (3-12 ng/mL) ± steroids
Group 2 (Control)	Standard CNI dose ± mycophenolate acid (MPA)/azathioprine (AZA) ± steroids

Measured Values

	Group 1 (Everolimus)	Group 2 (Control)
Number of Participants Analyzed [units: participants]	**72**	**73**
Percentage of Patients With Efficacy Failure (Biopsy Proven Acute Rejection [BPAR], Graft Loss or Death) [units: Percentage of patients]		
Composite efficacy failure (total)	**2.8**	**1.4**
Biopsy proven acute rejection	**1.4**	**1.4**
Graft Loss	**0**	**0**
Death	**1.4**	**0**

No statistical analysis provided for Percentage of Patients With Efficacy Failure (Biopsy Proven Acute Rejection [BPAR], Graft Loss or Death)

3. Secondary: Number of Patients With Discontinuation of Study Medication [Time Frame: 6 months]

Measure Type	Secondary
Measure Title	Number of Patients With Discontinuation of Study Medication
Measure Description	No text entered.
Time Frame	6 months
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.
Intention to treat (ITT) population includes all patients who were randomized to one of the treatment groups and received at least one dose of study medication.

Reporting Groups

	Description
Group 1 (Everolimus)	Reduced or discontinued CNI dose + everolimus (3-12 ng/mL) ± steroids
Group 2 (Control)	Standard CNI dose ± mycophenolate acid (MPA)/azathioprine (AZA) ± steroids

Measured Values

	Group 1 (Everolimus)	Group 2 (Control)
Number of Participants Analyzed [units: participants]	**72**	**73**
Number of Patients With Discontinuation of Study Medication [units: Patients]		
Total # of discontinuation of study medication	**18**	**1**

Adverse Event	**14**	**0**
Patient withdrew consent	**2**	**1**
Abnormal laboratory value(s)	**1**	**0**
Administrative problems	**1**	**0**

No statistical analysis provided for Number of Patients With Discontinuation of Study Medication

Serious Adverse Events

Hide Serious Adverse Events

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

Reporting Groups

	Description
Group 1 (Everolimus)	Reduced calcineurin inhibitor dose + everolimus (1.5 mg twice daily) ± steroids
Group 2 (Control)	Standard calcineurin inhibitor dose ± mycophenolate acid/azathioprine ± steroids

Serious Adverse Events

	Group 1 (Everolimus)	**Group 2 (Control)**
Total, serious adverse events		
# participants affected / at risk	**18/72 (25.00%)**	**14/73 (19.18%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**1/72 (1.39%)**	**2/73 (2.74%)**
Coagulopathy † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Leukopenia † 1		
# participants affected / at risk	**1/72 (1.39%)**	**1/73 (1.37%)**
Pancytopenia † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Thrombocytopenia † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Thrombotic microangiopathy † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Cardiac disorders		
Arrhythmia † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Cardiac failure † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Myocardial infarction † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Eye disorders		

Diplopia † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Gastrointestinal disorders		
Diarrhoea † 1		
# participants affected / at risk	**1/72 (1.39%)**	**1/73 (1.37%)**
Mouth haemorrhage † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Subileus † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Umbilical hernia † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Vomiting † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
General disorders		
Hyperpyrexia † 1		
# participants affected / at risk	**2/72 (2.78%)**	**0/73 (0.00%)**
Inflammation † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Influenza like illness † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Pyrexia † 1		
# participants affected / at risk	**1/72 (1.39%)**	**2/73 (2.74%)**
Hepatobiliary disorders		
Cholangitis † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Cytolytic hepatitis † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Immune system disorders		
Liver transplant rejection † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Infections and infestations		
Cytomegalovirus infection † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Gastroenteritis † 1		
# participants affected / at risk	**1/72 (1.39%)**	**1/73 (1.37%)**
Septic shock † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Urinary tract infection † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Injury, poisoning and procedural complications		
Contusion † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Overdose † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**

Traumatic shock † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Metabolism and nutrition disorders		
Hyperglycaemia † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Hyperkalaemia † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Nervous system disorders		
Headache † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Ischaemic stroke † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Renal and urinary disorders		
Haematuria † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Renal failure acute † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Renal failure chronic † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Respiratory, thoracic and mediastinal disorders		
Dyspnoea † 1		
# participants affected / at risk	**2/72 (2.78%)**	**1/73 (1.37%)**
Interstitial lung disease † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Lung disorder † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Pulmonary fibrosis † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Skin and subcutaneous tissue disorders		
Skin erosion † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Toxic skin eruption † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**
Vascular disorders		
Arteritis † 1		
# participants affected / at risk	**0/72 (0.00%)**	**1/73 (1.37%)**
Phlebitis † 1		
# participants affected / at risk	**1/72 (1.39%)**	**0/73 (0.00%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 9.0

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
Group 1 (Everolimus)	Reduced calcineurin inhibitor dose + everolimus (1.5 mg twice daily) ± steroids
Group 2 (Control)	Standard calcineurin inhibitor dose ± mycophenolate acid/azathioprine ± steroids

Other Adverse Events

	Group 1 (Everolimus)	Group 2 (Control)
Total, other (not including serious) adverse events		
# participants affected / at risk	**58/72 (80.56%)**	**31/73 (42.47%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**6/72 (8.33%)**	**2/73 (2.74%)**
Leukopenia † 1		
# participants affected / at risk	**8/72 (11.11%)**	**3/73 (4.11%)**
Thrombocytopenia † 1		
# participants affected / at risk	**4/72 (5.56%)**	**0/73 (0.00%)**
Gastrointestinal disorders		
Aphthous stomatitis † 1		
# participants affected / at risk	**11/72 (15.28%)**	**0/73 (0.00%)**
Diarrhoea † 1		
# participants affected / at risk	**7/72 (9.72%)**	**2/73 (2.74%)**
Dyspepsia † 1		
# participants affected / at risk	**4/72 (5.56%)**	**2/73 (2.74%)**
Mouth ulceration † 1		
# participants affected / at risk	**8/72 (11.11%)**	**0/73 (0.00%)**
Nausea † 1		
# participants affected / at risk	**6/72 (8.33%)**	**5/73 (6.85%)**
General disorders		
Asthenia † 1		
# participants affected / at risk	**5/72 (6.94%)**	**1/73 (1.37%)**
Oedema peripheral † 1		
# participants affected / at risk	**4/72 (5.56%)**	**1/73 (1.37%)**
Pyrexia † 1		
# participants affected / at risk	**4/72 (5.56%)**	**3/73 (4.11%)**

Infections and infestations		
Bronchitis † 1		
# participants affected / at risk	**4/72 (5.56%)**	**5/73 (6.85%)**
Herpes simplex † 1		
# participants affected / at risk	**6/72 (8.33%)**	**3/73 (4.11%)**
Nasopharyngitis † 1		
# participants affected / at risk	**5/72 (6.94%)**	**5/73 (6.85%)**
Urinary tract infection † 1		
# participants affected / at risk	**0/72 (0.00%)**	**4/73 (5.48%)**
Investigations		
Blood creatine phosphokinase increased † 1		
# participants affected / at risk	**4/72 (5.56%)**	**0/73 (0.00%)**
Hepatitis C virus † 1		
# participants affected / at risk	**5/72 (6.94%)**	**0/73 (0.00%)**
Metabolism and nutrition disorders		
Hypercholesterolaemia † 1		
# participants affected / at risk	**10/72 (13.89%)**	**2/73 (2.74%)**
Hyperkalaemia † 1		
# participants affected / at risk	**6/72 (8.33%)**	**3/73 (4.11%)**
Hyperlipidaemia † 1		
# participants affected / at risk	**7/72 (9.72%)**	**2/73 (2.74%)**
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	**5/72 (6.94%)**	**1/73 (1.37%)**
Back pain † 1		
# participants affected / at risk	**2/72 (2.78%)**	**5/73 (6.85%)**
Nervous system disorders		
Headache † 1		
# participants affected / at risk	**6/72 (8.33%)**	**2/73 (2.74%)**
Renal and urinary disorders		
Renal failure † 1		
# participants affected / at risk	**0/72 (0.00%)**	**4/73 (5.48%)**
Respiratory, thoracic and mediastinal disorders		
Cough † 1		
# participants affected / at risk	**6/72 (8.33%)**	**2/73 (2.74%)**
Skin and subcutaneous tissue disorders		
Dry skin † 1		
# participants affected / at risk	**5/72 (6.94%)**	**0/73 (0.00%)**
Eczema † 1		
# participants affected / at risk	**5/72 (6.94%)**	**0/73 (0.00%)**
Erythema † 1		
# participants affected / at risk	**4/72 (5.56%)**	**1/73 (1.37%)**
Rash † 1		

# participants affected / at risk	**5/72 (6.94%)**	**0/73 (0.00%)**
Vascular disorders		
Hypertension † 1		
# participants affected / at risk	**3/72 (4.17%)**	**5/73 (6.85%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 9.0

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.

Results Point of Contact:

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

Publications of Results:

De Simone P, Metselaar HJ, Fischer L, Dumortier J, Boudjema K, Hardwigsen J, Rostaing L, De Carlis L, Saliba F, Nevens F. Conversion from a calcineurin inhibitor to everolimus therapy in maintenance liver transplant recipients: a prospective, randomized, multicenter trial. Liver Transpl. 2009 Oct;15(10):1262-9. doi: 10.1002/lt.21827.

Publications automatically indexed to this study:

Schrader J, Sterneck M, Klose H, Lohse AW, Nashan B, Fischer L. Everolimus-induced pneumonitis: report of the first case in a liver transplant recipient and review of treatment options. Transpl Int. 2010 Jan;23(1):110-3. doi: 10.1111/j.1432-2277.2009.00900.x. Epub 2009 May 29.

Responsible Party: External Affairs, Novartis Pharmaceuticals
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Results First Received:	December 20, 2010
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Health Authority:	France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)