



# RADIANT 4 - Everolimus Plus Best Supportive Care vs Placebo Plus Best Supportive Care in the Treatment of Patients With Advanced Neuroendocrine Tumors (GI or Lung Origin)

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## Main Information

### Primary registry identifying number

LBCTR2020011379

### Protocol number

CRAD001T2302

### MOH registration number

262/ص

### Study registered at the country of origin

Yes

### Study registered at the country of origin: Specify

### Type of registration

Retrospective

### Type of registration: Justify

This study was submitted prior to LBCTR initiation

### Date of registration in national regulatory agency

13/01/2015

### Primary sponsor

Novartis Pharmaceuticals

### Primary sponsor: Country of origin

Novartis Pharmaceuticals

### Date of registration in primary registry

07/01/2020

### Date of registration in national regulatory agency

13/01/2015

### Public title

RADIANT 4 - Everolimus Plus Best Supportive Care vs Placebo Plus Best Supportive Care in the Treatment of Patients With Advanced Neuroendocrine Tumors (GI or Lung Origin)

### Acronym

### Scientific title

A Randomized, Double-blind, Multicenter, Phase III Study of Everolimus (RAD001) Plus Best Supportive Care Versus Placebo Plus Best Supportive Care in the Treatment of Patients With Advanced NET of GI or Lung Origin

### Acronym

### Brief summary of the study: English

The purpose of this study is to compare the antitumor activity of everolimus plus best supportive care versus placebo plus best supportive care in patients with advanced nonfunctional neuroendocrine tumor of gastrointestinal or lung origin.

### Brief summary of the study: Arabic

بالإضافة إلى أفضل رعاية داعمة مقابل (RAD001) إيفيروليموس Everolimus دراسة عشوائية ومتعددة المراكز في المرحلة الثالثة لدواء العلاج الإرضائي وأفضل رعاية داعمة في علاج المرضى المصابين بحالة متقدمة من أورام الغدد الصمّ العصبية يكون مصدرها معدياً معويّاً أو 4مَشع-(RADIANT-4) - رثنوياً

### Health conditions/problem studied: Specify

Advanced Nonfunctional NeuroEndocrine Tumor

### Interventions: Specify

•Drug: Everolimus

After randomization, patients will receive everolimus once daily until disease progression, intolerable toxicity, or consent withdrawal

Other Name: RAD001





•Drug: Everolimus Placebo

After randomization, patients will receive everolimus placebo once daily until disease progression, intolerable toxicity, or consent withdrawal

**Key inclusion and exclusion criteria: Inclusion criteria**

- Pathologically confirmed, well differentiated (G1 or G2), advanced (unresectable or metastatic), neuroendocrine tumor of GI or lung origin
- No history of and no active symptoms related to carcinoid syndrome
- In addition to treatment-naïve patients, patients previously treated with SSA, Interferon (IFN), one prior line of chemotherapy, and/or PRRT are allowed into the study. Pretreated patients must have progressed on or after the last treatment
- Radiological documented disease progression within 6 months prior to randomization
- Measurable disease
- WHO performance status  $\leq 1$
- Adequate bone marrow, liver and renal function

**Key inclusion and exclusion criteria: Gender**

Both

**Key inclusion and exclusion criteria: Specify gender**

**Key inclusion and exclusion criteria: Age minimum**

18

**Key inclusion and exclusion criteria: Age maximum**

99

**Key inclusion and exclusion criteria: Exclusion criteria**

- Patients with poorly differentiated neuroendocrine carcinoma, high-grade neuroendocrine carcinoma, adenocarcinoid, pancreatic islet cell carcinoma, insulinoma, glucagonoma, gastrinoma, goblet cell carcinoid, large cell neuroendocrine carcinoma and small cell carcinoma
- Patients with pancreatic NET or NET of origins other than GI or Lung
- Patients with history of or active symptoms of carcinoid syndrome (e.g. flushing, diarrhea)
- Patients with more than one line of prior chemotherapy
- Prior targeted therapy
- Hepatic locoregional therapy within the last 6 months
- Prior therapy with mTOR inhibitors (e.g. sirolimus, temsirolimus, deforolimus)
- Known intolerance or hypersensitivity to everolimus or other rapamycin analogs (e.g. sirolimus, temsirolimus)
- Known impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of oral everolimus
- Uncontrolled diabetes mellitus as defined by HbA1c  $>8\%$  despite adequate therapy
- Patients who have any severe and/or uncontrolled medical conditions such as:
  - unstable angina pectoris, symptomatic congestive heart failure, myocardial infarction  $\leq 6$  months prior to randomization, serious uncontrolled cardiac arrhythmia
  - active or uncontrolled severe infection
  - liver disease such as cirrhosis, decompensated liver disease, and chronic hepatitis (i.e. quantifiable HBV-DNA and/or positive HbsAg, quantifiable HCV-RNA)
- Chronic treatment with corticosteroids or other immunosuppressive agents
- Known history of HIV seropositivity
- Pregnant or nursing (lactating) women

Other protocol-defined inclusion/exclusion criteria may apply.

**Type of study**

Interventional

**Type of intervention**

Pharmaceutical

**Type of intervention: Specify type**

N/A

**Trial scope**

Therapy

**Trial scope: Specify scope**

N/A

**Study design: Allocation**

Randomized controlled trial

**Study design: Masking**

Open (masking not used)

**Study design: Control**

Placebo

**Study phase**

3

**Study design: Purpose**

Treatment

**Study design: Specify purpose**

N/A

**Study design: Assignment**

**Study design: Specify assignment**

Parallel	N/A	
<b>IMP has market authorization</b>	<b>IMP has market authorization: Specify</b>	
Yes, Lebanon and Worldwide	Austria, Belgium, Canada, China, Colombia, Czechia, Germany, ...	
<b>Name of IMP</b>	<b>Year of authorization</b>	<b>Month of authorization</b>
everolimus (RAD001)	2010	5
<b>Type of IMP</b>		
Cell therapy		
<b>Pharmaceutical class</b>		
proliferation signal inhibitor in the mammalian target of rapamycin (mTOR)		
<b>Therapeutic indication</b>		
proliferation signal inhibitor in the mammalian target of rapamycin (mTOR)		
<b>Therapeutic benefit</b>		
Progression Free Survival (PFS)		
<b>Study model</b>	<b>Study model: Explain model</b>	
N/A	N/A	
<b>Study model: Specify model</b>		
N/A		
<b>Time perspective</b>	<b>Time perspective: Explain time perspective</b>	
N/A	N/A	
<b>Time perspective: Specify perspective</b>		
N/A		
<b>Target follow-up duration</b>	<b>Target follow-up duration: Unit</b>	
<b>Number of groups/cohorts</b>		
<b>Biospecimen retention</b>	<b>Biospecimen description</b>	
Samples without DNA	Samples are sent to central quintiles laboratories	
<b>Target sample size</b>	<b>Actual enrollment target size</b>	
5	5	
<b>Date of first enrollment: Type</b>	<b>Date of first enrollment: Date</b>	
Actual	25/09/2012	
<b>Date of study closure: Type</b>	<b>Date of study closure: Date</b>	



Actual

31/12/2021

**Recruitment status**

Complete

**Recruitment status: Specify**

**Date of completion**

17/07/2013

**IPD sharing statement plan**

No

**IPD sharing statement description**

Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data availability is according to the criteria and process described on [www.clinicalstudydatarequest.com](http://www.clinicalstudydatarequest.com)

**Additional data URL**

<https://clinicaltrials.gov/ct2/show/record/NCT01524783>

**Admin comments**

**Trial status**

Approved

## Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinical trials.gov	NCT01524783

## Sources of Monetary or Material Support

Name
Novartis Pharmaceuticals

## Secondary Sponsors

Name
NA



## Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Ali Shamseddin	Beirut	Lebanon	03344277	as04@aub.edu.lb	American University of Beirut Medical Center
Scientific	Hind Khairallah	Sin elfil	Lebanon	01512002#271	Hind.Khairallah@fattal.com.lb	Khalil Fattal et Fils s.a.l.
Public	Joseph Kattan	Beirut	Lebanon	011424942	jkattan62@hotmail.com	Hotel Dieu De France

## Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
American University of Beirut Medical Center	Ali Shamseddin	Hematology	Approved
Hotel Dieu De France	Joseph Kattan	Hematology	Approved

## Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	11/03/2013	Fuad Ziyadeh	fz05@aub.edu.lb	961 (0) 1 350 000 ext:5445
Hotel Dieu de France	07/05/2012	Nancy Alam	nancy.alam@usj.edu.lb	961 (0) 1 421000 ext 2335



## Countries of Recruitment

Name
Lebanon
Australia
Belgium
Canada
China
Colombia
Greece
Italy
Norway
Saudi Arabia
Turkey
United Arab Emirates
United States of America

## Health Conditions or Problems Studied

Condition	Code	Keyword
Neuroendocrine tumor	Endocrine gland, unspecified (C75.9)	Neuroendocrine tumor

## Interventions

Intervention	Description	Keyword
ICF, Lab tests , physical exam, radiology	ICF, Lab tests , physical exam, radiology	ICF, Lab tests , physical exam, radiology

## Primary Outcomes

Name	Time Points	Measure
Progression Free Survival (PFS) Based on Central Radiology Assessment Per Kaplan-Meier	18 months	18 months



## Key Secondary Outcomes

Name	Time Points	Measure
•Overall Survival (OS) Using Kaplan-Meier	18 Months	18 Months
•Overall Safety Evaluation of Everolimus Versus Placebo	5 years	5 years

## Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files