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Trial record **1 of 1** for: Axitinib AND NET

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Sandostatin LAR and Axitinib vs Pbo in Pnts With Advanced Well-differentiated Non-pancreatic Neuroendocrine Carcinomas

This study is currently recruiting participants.

See Contacts and Locations

Verified August 2017 by Grupo Espanol de Tumores Neuroendocrinos

Sponsor:
Grupo Espanol de Tumores Neuroendocrinos

ClinicalTrials.gov Identifier:
NCT01744249

First Posted: December 6, 2012
Last Update Posted: August 24, 2017

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

Collaborator:
Pfizer
Information provided by (Responsible Party):
Grupo Espanol de Tumores Neuroendocrinos

Full Text View | Tabular View | No Study Results Posted | Disclaimer

How to Read a Study Record

Purpose

Assess whether therapy with **axitinib**, a potent angiogenic inhibitor of the tyrosine kinase receptors of VEGF bioavailable by oral administration, is capable of improving PFS in patients with advanced G1-G2 **NETs** of nonpancreatic origin with progressive disease documented in the 12 months prior to entering the study.

Condition	Intervention	Phase
Neuroendocrine Tumors Advanced Cancer	Drug: **Axitinib** Drug: Sandostatin LAR Drug: Placebo	Phase 2 Phase 3

Study Type: Interventional

Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: A Phase II/III Randomized Double-blind Study of Sandostatin LAR in Combination With **Axitinib** Versus Sandostatin LAR With Placebo in Patients With Advanced G1-G2 Neuroendocrine Tumours (WHO 2010) of Non-pancreatic Origin

Resource links provided by NLM:

MedlinePlus related topics: Carcinoid Tumors

Drug Information available for: Octreotide acetate Octreotide Axitinib

Genetic and Rare Diseases Information Center resources: Carcinoid Tumor Neuroepithelioma

U.S. FDA Resources

Further study details as provided by Grupo Espanol de Tumores Neuroendocrinos:

Primary Outcome Measures:

- Effectiveness of **axitinib** in terms of PFS [Time Frame: until disease progression, end of treatment or minimum 6 months]

  calculated from the date of random assignment until the date of first progressive disease or tumor-related death

Secondary Outcome Measures:

- Objective response rate (ORR) and the duration of response. [Time Frame: Until disease progression, end of treatment or minimum 6 months]

  Measured according to RECIST 1.1 criteria; Sum of longest diameter of target lesions measured in mm

- Functional response rate using F-DOPA-PET (optional, depending on availability) [Time Frame: Until disease progression, end of treatment or minimum 6 months]

  measured in SUV (standardized uptake value)

- Biochemical response (5-OH-indoleacetic acid and chromogranin A) [Time Frame: Until death, last follow-up, or minimum 6 months]

  measurable in mL/ 24h and ng/ml respectively, through blood and urine test

- Safety and tolerability of **axitinib** (National Cancer Institute Common Terminology Criteria for Adverse Events [NCI-CTCAE], version 4.0) [Time Frame: Until disease progression, end of treatment or minimum 6 months]

  All adverse events and serious adverse events will be monitored with regular monitoring of hematology and blood chemistry parameters and regular physical examinations. Adverse events will be evaluated continuously throughout the study. Safety and tolerability will be assessed according to the National Institute of Health/National Cancer Institute (NIH/NCI) Common Terminology Criteria for Adverse Events version 4 (CTCAE v4)

- Explore potential biomarkers [Time Frame: Until disease progression or or minimum 6 months]

  The following parameters will be measured: circulating tumor cells, circulating endothelial cells, hypertension (mmHg), and other serum or tumoral biomarkers of angiogenesis).

  Peripheral blood samples (9ml) will be obtained before treatment, after 1 month since the start of treatment and after disease progression and or the end of study visit. The blood samples will be processed for mRNA extraction. Hypoxia dependant genes and marker genes which transcription depends on the activation of VEGF, will be analyzed using qPCR.

The dynamic profile of those genes will then be analyzed in relation to the response to axitinib, evaluating their predictive value of response.

Paraffin-embedded tumor tissue will also be collected from all patients to investigate the prognostic value and predictive potential of the different intracellular pathways related to VEGFR, PDGFR and other signaling pathways.

- Evaluate overall survival. [Time Frame: from the date of randomization to the date of death from any cause whichever came first, assessed up to 50 months.]

Estimated Enrollment:	253
Actual Study Start Date:	November 2011
Estimated Study Completion Date:	October 2020
Estimated Primary Completion Date:	November 2019 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: **Axitinib** + Sandostatin LAR **Axitinib** 5 mg BID + Sandostatin LAR 30mg/28 days	Drug: **Axitinib** Orally, 5mg, twice daily, until progression or until unacceptable toxicity, with or without food intake. Drug: Sandostatin LAR Intramuscular, 30mg, single injection every 28 days, until disease progression or unacceptable toxicity
Placebo Comparator: Placebo + Sandostatin LAR Placebo BID + Sandostatin LAR 30mg/28 days	Drug: Sandostatin LAR Intramuscular, 30mg, single injection every 28 days, until disease progression or unacceptable toxicity Drug: Placebo orally, twice daily, until disease progression or unacceptable toxicity, with or without food intake.

Detailed Description:

Phase II/III, prospective, multicenter, randomized (1:1), double-blind study to evaluate the efficacy and tolerability of axitinib in patients diagnosed with advanced G1-G2 neuroendocrine tumors (WHO 2010) of nonpancreatic origin that have presented documented disease progression in the 12 months prior to entering the study. In the first part of the study (Phase II), 105 patients were enrolled. The second part of the study is the expansion to Phase III, which is expected to include 148 additional patients. Patients will be randomized to receive Sandostatin LAR with axitinib or Sandostatin LAR with placebo until disease progression or unacceptable toxicity occurs. Randomization will be stratified by the time from diagnosis to

enrollment in the study (more vs less than or equal to 12 months), the origin of the primary tumor (gastrointestinal tract vs non-gastrointestinal tract [lung or other sites]) and ki-67 (< 5% vs > 5%).

Eligibility

Information from the National Library of Medicine NIH NLM

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. G1-G2 neuroendocrine tumor (WHO 2010) of histologically confirmed non-pancreatic origin, functioning and nonfunctioning
2. Metastatic or locally advanced disease not amenable to treatment with curative intent
3. Clinical and/or radiological disease progression documented in the 12 months prior to study entry.
4. Patients should have at least one measurable lesion as defined by RECIST 1.1 criteria. Patients should not have undergone local or regional ablative procedures (embolization, cryoablation, radiofrequency ablation, or others) in the 6 months prior to entering the study, unless there are other locations of measurable disease or clear radiological progression after carrying out these procedures (in these cases, local and regional ablation procedures shall be permitted if they have been performed at least 1 month prior to enrollment in the study).
5. Ki-67 < 20%
6. Prior treatment with somatostatin analogues is allowed
7. Prior treatment with interferon is allowed
8. Prior treatment is allowed with up to 2 antineoplastic systemic treatment lines different from SAs or IFN (systemic treatment is understood as conventional cytotoxic chemotherapy or new drugs for therapeutic targets as mTOR or other, as long as it is not

directed against VEGF/VEGFR). Treatment with SAs or IFN does not count as prior lines of antineoplastic treatment.

9. Prior treatment with targeted therapy against VEGF or VEGFR is not allowed.
10. Adequate organ function as defined by the following criteria:
    - Absolute neutrophil count ≥ 1500 cells/mm3,
    - Platelet count ≥ 75,000 cells/mm3,
    - Hemoglobin ≥ 9.0 g/dL,
    - AST y ALT ≤ 2.5 x upper limit of normal (ULN), except if liver metastases exist, in which case AST and ALT 5.0 ≤ x ULN is allowed,
    - Total bilirubin ≤ 1.5 x ULN,
    - Serum creatinine ≤ 1.5 x ULN or calculated creatinine clearance ≥ 60 mL/min,
    - Proteinuria < 2+ by reactive strip. If the reactive strip is ≥ 2+, a 24-hour urine sample should be collected and the patient may be eligible if urinary protein excretion is < 2 g every 24 hours.
11. Men or women aged ≥ 18 years.
12. ECOG performance status 0-2
13. Life expectancy ≥ 12 weeks
14. At least 4 weeks should pass from the end of the previous systemic treatment with resolution of all treatment-related toxicities to grade ≤ 1 according to NCI CTCAE Version 4.0 or to baseline, except for alopecia or properly treated hypothyroidism.
15. No prior evidence of uncontrolled hypertension should exist, as documented by 2 baseline blood pressure readings taken at least 1 hour apart. Baseline readings of systolic blood pressure should be ≤ 150 mm Hg and baseline readings of diastolic pressure should be ≤ 90 mm Hg. Patients whose hypertension is being controlled with antihypertensive therapy are eligible.
16. Women (or their partners) should be surgically sterilized or postmenopausal, or must agree to use an effective contraceptive method during and for at least 6 months after receiving study treatment. All women of childbearing age should have a negative pregnancy test (serum/urine) within 7 days prior to starting treatment. Men (or their partners) should be surgically sterilized or must agree to use an effective contraceptive method during and for at least 6 months after receiving study treatment. The definition of an effective contraceptive method must comply with local regulations and will be based on the criterion of the principal investigator or a designated associate. Lactating women may not participate in this study.
17. Signed and dated informed consent document stating that the patient has been informed of all the pertinent aspects of the trial prior to recruitment.

18. Willingness and ability to comply with scheduled visits, treatment plans (including willingness to take axitinib or placebo according to randomization), laboratory tests, and other study procedures.

Exclusion Criteria:

1. Subjects must be evaluated with regard to the following exclusion criteria:
    1. The following types of endocrine tumors will not be included: paraganglioma, adrenal endocrine tumor, thyroid, parathyroid, or pituitary.
    2. Major surgery within previous 4 weeks, or radiation therapy within 2 weeks prior to the start of treatment. Prior palliative radiotherapy for metastatic lesions is permitted if there is at least one measurable lesion that has not been irradiated (i.e., if there are other non-irradiated target lesions).
    3. Gastrointestinal abnormalities, including:
        - Inability to swallow oral medication;
        - Need for intravenous feeding;
        - Prior surgical procedures that affect absorption, including total gastric resection;
        - Treatment for active peptic ulcer in the last 6 months;
        - Uncontrolled active gastrointestinal bleeding unrelated to cancer, as evidenced by hematemesis, hematochezia or clinically significant melena in the last 3 months without evidence of resolution documented by endoscopy or colonoscopy;
        - Malabsorption syndromes;
    4. Current or anticipated need for treatment with drugs that are potent inhibitors of CYP3A4 (grapefruit juice, verapamil, ketoconazole, miconazole, itraconazole, erythromycin, telithromycin, clarithromycin, indinavir, saquinavir, ritonavir, nelfinavir, lopinavir, atazanavir, amprenavir, fosamprenavir, and delavirdine) unless they can be replaced by another medication with minimal potential for CYP3A4/5 inhibition. The use of low-dose oral steroids (< 5 mg/day prednisone or equivalent) is allowed. Co-administration of steroids may increase plasma concentrations of axitinib.
    5. Current use or anticipated need for treatment with drugs that are known potent CYP3A4/5 inducers (carbamazepine, dexamethasone, felbamate, phenobarbital, phenytoin, amobarbital, nevirapine, primidone, rifabutin, rifampicin, and St. John's wort) unless they can be replaced by another medication with minimal potential for CYP3A4 induction. Co-administration of CYP3A4/5 inducers may decrease plasma concentrations of axitinib.
    6. Need for anticoagulant therapy with oral vitamin K antagonists. Low doses of anticoagulants to maintain the patency of a central venous access device or to prevent deep vein thrombosis are permitted. Use with therapeutic doses of low molecular weight heparin is allowed.

7. Clinically relevant history of bleeding in the last 6 months, including severe hemoptysis or hematuria, unless it has been due to a treated cause (e.g., completely resected bleeding intestinal tumor).
8. Active epilepsy or evidence of brain metastases, spinal cord compression, or carcinomatous meningitis.
9. Serious uncontrolled illness or active infections that may interfere with the patient's ability to receive the study treatment.
10. Any of the following events in the 12 months prior to administration of the study drug: myocardial infarction, uncontrolled angina, implantation of a coronary or peripheral bypass, symptomatic congestive heart failure, stroke or transient ischemic attack. Deep vein thrombosis or pulmonary embolism in the prior 6 months.
11. Ongoing grade ≥ 2 cardiac arrhythmias according to NCI CTCAE: atrial fibrillation of any grade or QTc interval > 450 ms for men or > 470 ms for women.
12. Patients with human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome-related disease.
13. Prior history of cancer except those treated with curative intent for non-melanoma skin cancer in situ, breast or cervical cancer in situ, or those treated for any cancer with curative intent and no evidence of disease in the last 5 years prior to enrollment in the study.
14. Dementia or significantly altered mental status that could prevent compression, or submission of informed consent and compliance with the requirements of this protocol.
15. Any severe, acute or chronic medical or psychiatric condition, or laboratory abnormality that may increase the risk associated with participation in the study or with study drug administration, or that may interfere with the interpretation of results, and that could interfere with the patient's ability to take part in this study in the investigator's opinion.
16. The patient's participation or intention to participate (in the 4 weeks prior to starting drug administration) in a study in which the patient will receive an investigational medicinal product.
17. Subjects who are institutionalized by governmental or by judicial decision, or subjects who are dependent of the sponsor, the investigator or the trial site will be excluded from participation.

Contacts and Locations

Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number):
NCT01744249

Contacts

Contact: Rocio Garcia-Carbonero, MD 0034 93 253 11 68 rgcarbonero@gmail.com

Locations

Germany

Berlin Charité Universitätsmedizin — **Not yet recruiting**
Berlin, Germany
Principal Investigator: Frank-Ulrich Pape, Dr.

Marburg Universitätsklinikum Giessen und Marburg GmbH — **Recruiting**
Marburg, Germany, 35043
Principal Investigator: Anja Rinke, Dr.

Klinikum rechts der Isar — **Recruiting**
München, Germany, 81675
Principal Investigator: Alexander Von Werder, Dr.

Italy

Azienda Ospedaliera Universitaria di Perugia Santa — **Not yet recruiting**
Perugia, Italy, 06129
Principal Investigator: Vicenzo Minotti, Dr.

Sapienza, Universitá di Roma, Ospedale sant'Andrea — **Recruiting**
Rome, Italy, 00189
Principal Investigator: Gianfranco Delle Fave, Prof.

Spain

Hospital Central de Asturias — **Recruiting**
Oviedo, Asturias, Spain
Principal Investigator: Paula Jiménez Fonseca, MD

Institut Català d'Oncologia L'Hospitalet — **Recruiting**
L'Hospitalet de Llobregat, Barcelona, Spain
Principal Investigator: Alexandre Teulé, MD

Complejo Hospitalario Univ A Coruña — **Recruiting**
A Coruña, Spain
Principal Investigator: Luis antón Aparicio, MD

Sub-Investigator: María Quindós, MD

Hospital Universitari Vall d'Hebron — **Recruiting**
Barcelona, Spain
Principal Investigator: Jaume Capdevila, MD

Hospital Universitario de Burgos — **Suspended**
Burgos, Spain

Hospital Virgen de las Nieves — **Recruiting**
Granada, Spain
Principal Investigator: Encarnación González Flores, MD

Hospital universitario de Leon — **Suspended**
Leon, Spain

Hospital Clara Campal — **Suspended**
Madrid, Spain

Hospital Clínico San Carlos — **Recruiting**
Madrid, Spain
Principal Investigator: Javier Sastre

Hospital Gregorio Marañón — **Recruiting**
Madrid, Spain
Principal Investigator: Pilar García Alfonso, MD

Hospital Univ La Paz — **Recruiting**
Madrid, Spain
Principal Investigator: Ana Custodio, MD

Hospital Universitario 12 de Octubre — **Recruiting**
Madrid, Spain
Principal Investigator: Daniel Castellano, MD

Hospital Universitario Ramón y Cajal — **Recruiting**
Madrid, Spain
Principal Investigator: Enrique Grande Pulido, MD

Hospital Univ de Salamanca — **Recruiting**
Salamanca, Spain
Principal Investigator: Miguel Navarro, MD

Hospital de Donostia — **Recruiting**
San Sebastian, Spain
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Sub-Investigator: Sara Arévalo, MD

Hospital Marqués de Valdecilla — **Recruiting**

Santander, Spain
Principal Investigator: Carlos López, MD

Hospital Universitario Virgen del Rocío **Recruiting**
Sevilla, Spain
Principal Investigator: Marta Benavent, MD

Hospital La Fe **Recruiting**
Valencia, Spain
Contact: Ángel Segura, MD
Principal Investigator: Ángel Segura, MD

Hospital Universitario Miguel Servet **Recruiting**
Zaragoza, Spain
Contact: Vicente Alonso, M.D.
Principal Investigator: Vicente Alonso, M.D.

United Kingdom

Clatterbridge Cancer Centre **Not yet recruiting**
Bebington, Wirral, United Kingdom, CH63 4JY
Principal Investigator: Olusola Faluyi, Dr.

Queen Elisabeth Hospital Birmingham **Not yet recruiting**
Birmingham, United Kingdom, B15 2TH
Principal Investigator: Tahir Shah, Dr.

Royal Free Hospital **Not yet recruiting**
London, United Kingdom, NW3 2QG
Principal Investigator: Christine Thirlwell, Dr.

Sponsors and Collaborators

Grupo Espanol de Tumores Neuroendocrinos

Pfizer

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Principal Investigator:	Beatriz Nieto Mangudo, MD	Hospital Universitario de León
Principal Investigator:	Guillermo Crespo Herrero, MD	Hospital Universitario de Burgos
Principal Investigator:	Ángel Segura, MD	Hospital La Fe
Principal Investigator:	Marta Benavent	Hospitales Universitarios Virgen del

More Information

Responsible Party:	Grupo Espanol de Tumores Neuroendocrinos
ClinicalTrials.gov Identifier:	NCT01744249 History of Changes
Other Study ID Numbers:	AXI-IIG-02
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First Submitted:	September 25, 2012
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Advanced neuroendocrine tumours of non-pancreatic origin
axitinib

Additional relevant MeSH terms:

Axitinib	Carcinoma
Neuroendocrine Tumors	Neoplasms, Glandular and Epithelial
Carcinoid Tumor	Octreotide
Neuroectodermal Tumors	Protein Kinase Inhibitors

Neoplasms, Germ Cell and Embryonal
Neoplasms by Histologic Type
Neoplasms
Neoplasms, Nerve Tissue
Adenocarcinoma

Enzyme Inhibitors
Molecular Mechanisms of Pharmacological Action
Gastrointestinal Agents
Antineoplastic Agents, Hormonal
Antineoplastic Agents