

A Phase III Trial of Lenvatinib (E7080) in 131I-Refractory Differentiated Thyroid Cancer
This study is currently recruiting participants.
 Verified January 2012 by Eisai Inc.

First Received on March 10, 2011. Last Updated on January 31, 2012 [History of Changes](#)

Sponsor:	Eisai Inc.
Information provided by (Responsible Party):	Eisai Inc.
ClinicalTrials.gov Identifier:	NCT01321554

▶ Purpose

This is a multicenter, randomized, double-blind, Placebo-controlled Phase 3 study to compare the PFS of subjects with 131I-refractory DTC and radiographic evidence of disease progression within the prior 12 months, treated with **E7080** 24 mg by continuous once daily (QD) oral dosing versus Placebo.

Condition	Intervention	Phase
Thyroid Cancer	Drug: E7080 24 mg administered orally, once a day Drug: Placebo 24mg administered orally, once a day	Phase III

Study Type: Interventional

Study Design: Allocation: Randomized
 Endpoint Classification: Safety/Efficacy Study
 Intervention Model: Parallel Assignment
 Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
 Primary Purpose: Treatment

Official Title: A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial of **E7080** in 131I-Refractory Differentiated Thyroid Cancer

Resource links provided by NLM:

[MedlinePlus](#) related topics: [Cancer](#) [Thyroid Cancer](#) [Thyroid Diseases](#)

[Drug Information](#) available for: [Thyroid](#)

[U.S. FDA Resources](#)

Further study details as provided by Eisai Inc.:

Primary Outcome Measures:

- To compare the Progression-free Survival (PFS) of subjects with 131IRefractory differentiated thyroid cancer (DTC) with radiographic evidence of disease progression within the prior 12 months treated with **E7080** versus Placebo. [Time Frame: Date of randomization to the date of disease progression (measured every 8 weeks) or death (whichever occurs first) as determined by blinded independent imaging review] [Designated as safety issue: No]

Secondary Outcome Measures:

- To compare Overall Response Rate (ORR) (Complete and Partial Responses, CR and PR) of subjects treated with **E7080** versus Placebo. [Time Frame: Date of randomization to the date of disease progression (measured every 8 weeks) or death] [Designated as safety issue: No]

Estimated Enrollment: 360

Study Start Date: March 2011

Estimated Primary Completion Date: July 2013 (Final data collection date for primary outcome measure)

<u>Arms</u>	<u>Assigned Interventions</u>
Experimental: E7080	Drug: E7080 24 mg administered orally, once a day Subjects with confirmation of disease progression by independent imaging review, while receiving blinded study drug may request to receive open label E7080 and enter the Optional Open Label E7080 Treatment Period of the Extension Phase. Subjects who request to receive open label E7080 (at the time of confirmed progression) will be informed whether they received placebo or E7080 during the period of blinded study drug administration.. Subjects who received E7080 will not be eligible for the open-label phase.
Experimental: Placebo	Drug: Placebo 24mg administered orally, once a day Subjects with confirmation of disease progression by independent imaging review, while receiving blinded study drug may request to receive open label E7080 and enter the Optional Open Label E7080 Treatment Period of the Extension Phase. Subjects who request to receive open label E7080 (at the time of confirmed progression) will be informed whether they received placebo or E7080 during the period of blinded study drug administration.

Eligibility

Ages Eligible for Study: 18 Years and older

Genders Eligible for Study: Both

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria

Subjects must meet all of the following criteria to be included in this study:

1. Subjects must have histologically or cytologically confirmed diagnosis of one of the following DTC subtypes:
 - Papillary thyroid cancer (PTC)
 - Follicular variant
 - Variants (including but not limited to tall cell, columnar cell, cribriform-morular, solid, oxyphil, Warthin's-like, trabecular, tumor with nodular fasciitis-like stroma, Hürthle cell variant of papillary carcinoma, poorly differentiated)
 - Follicular thyroid cancer (FTC)
 - Hürthle cell
 - Clear cell
 - Insular
2. Measurable disease meeting the following criteria and confirmed by central radiographic review:
 - At least 1 lesion of ≥ 1.0 cm in the longest diameter for a non-lymph node or ≥ 1.5 cm in the short-axis diameter for a lymph node which is serially measurable according to RECIST 1.1 using computerized tomography/magnetic resonance imaging (CT/MRI). If there is only one target lesion and it is a non-lymph node, it should have a longest diameter of ≥ 1.5 cm
 - Lesions that have had external beam radiotherapy (EBRT) or loco-regional therapies such as radiofrequency (RF) ablation must show evidence of progressive disease based on RECIST 1.1 to be deemed a target lesion
3. Subjects must show evidence of disease progression within 12 months (an additional month will be allowed to accommodate actual dates of performance of scans, i.e., within ≤ 13 months) prior to signing informed consent, according to RECIST 1.1 assessed and confirmed by central radiographic review of CT and / or MRI scans
4. Subjects must be 131I-refractory / resistant as defined by at least one of the following:
 - One or more measurable lesions that do not demonstrate 131I uptake on any radioiodine scan
 - One or more measurable lesions that has progressed by RECIST 1.1 within 12 months of 131I therapy, despite demonstration of radioiodine avidity at the time of that treatment by pre- or post-treatment scanning

- Cumulative activity of ^{131}I of > 600 mCi or 22 gigabecquerels (GBq), with the last dose administered at least 6 months prior to study entry
- 5. Subjects may have received 0 or 1 prior VEGF / VEGFR-targeted therapy (for example sorafenib, sunitinib, pazopanib, etc.)
- 6. Patients with known brain metastases who have completed whole brain radiotherapy, stereotactic radiosurgery or complete surgical resection, will be eligible if they have remained clinically stable, asymptomatic and off of steroids for one month
- 7. Subjects must be receiving thyroxine suppression therapy and thyroid stimulating hormone (TSH) should not be elevated (TSH should be ≤ 5.50 mCu/mL). When tolerated by the subject, thyroxine dose should be changed to achieve TSH suppression (TSH < 0.50 mCu/mL) and this dose can be changed concurrently upon starting E7080
- 8. All chemotherapy or radiation-related toxicities must have resolved to $<$ Grade 2 severity, except alopecia and infertility
- 9. Subjects must have an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 – 2
- 10. Adequately controlled blood pressure with or without antihypertensive medications, defined as BP $< 150/90$ mmHg at screening and no change in antihypertensive medications within 1 week prior to the Screening Visit
- 11. Adequate renal function defined as calculated creatinine clearance ≥ 30 mL/min per the Cockcroft and Gault formula (Appendix 4)
- 12. Adequate bone marrow function:
 - Absolute neutrophil count (ANC) $\geq 1500/\text{mm}^3$ ($\geq 1.5 \times 10^3/\mu\text{L}$)
 - Platelets $\geq 100,000/\text{mm}^3$ ($\geq 100 \times 10^9/\text{L}$)
 - Hemoglobin ≥ 9.0 g/dL
- 13. Adequate blood coagulation function as evidenced by an International Normalized Ratio (INR) ≤ 1.5
- 14. Adequate liver function:
 - Bilirubin $\leq 1.5 \times$ the upper limit of normal (ULN) except for unconjugated hyperbilirubinemia or Gilbert's syndrome
 - Alkaline phosphatase, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) $\leq 3 \times$ the ULN ($\leq 5 \times$ ULN if subject has liver metastases)
- 15. Males or females age ≥ 18 years at the time of informed consent
- 16. All females must have a negative serum or urine pregnancy test. Females of childbearing potential and male subjects who are partners of women of childbearing potential must use or their partners must use a highly effective method of contraception
- 17. Voluntary provision of written informed consent and the willingness and ability to comply with all aspects of the protocol

Voluntary provision of written informed consent and the willingness and ability to comply with all aspects of the protocol

Exclusion Criteria

Subjects who meet any of the following criteria will be excluded from this study:

1. Anaplastic or Medullary carcinoma of the thyroid
2. Two or more prior VEGF / VEGFR-targeted therapies or any ongoing treatment for 131I-refractory DTC other than TSH-suppressive thyroid hormone therapy
3. Prior treatment with E7080
4. Subjects who have received any anti-cancer treatment within 21 days or any investigational agent within 30 days prior to the first dose of study drug and should have recovered from any toxicity related to previous anti-cancer treatment. This does not apply to the use of TSH-suppressive thyroid hormone therapy
5. Major surgery within 3 weeks prior to the first dose of study drug
6. Subjects having > 1+ proteinuria on urine dipstick testing will undergo 24h urine collection for quantitative assessment of proteinuria. Subjects with urine protein \geq 1 g/24h will be ineligible
7. Gastrointestinal malabsorption, or any other condition in the opinion of the investigator that might affect the absorption of E7080
8. Significant cardiovascular impairment: history of congestive heart failure greater than New York Heart Association (NYHA) Class II, unstable angina; myocardial infarction or stroke within 6 months of the first dose of study drug, or cardiac arrhythmia requiring medical treatment
9. Prolongation of QTcF interval to > 480 msec
10. Bleeding or thrombotic disorders or use of anticoagulants, such as warfarin, or similar agents requiring therapeutic international normalized ration (INR) monitoring. (Treatment with low molecular weight heparin (LMWH) is allowed)
11. Active hemoptysis (bright red blood of at least 0.5 teaspoon) within 3 weeks prior to the first dose of study drug
12. Active infection (any infection requiring treatment)
13. Active malignancy (except for differentiated thyroid carcinoma, or definitively treated melanoma in-situ, basal or squamous cell carcinoma of the skin, or carcinoma in-situ of the cervix) within the past 24 months
14. Known intolerance to any of the study drugs (or any of the excipients)
15. Any medical or other condition which, in the opinion of the investigator, would preclude participation in a clinical trial
16. Females who are pregnant or breastfeeding

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01321554

Contacts

Contact: Eisai Medical Services 1-888-422-4743

Contact: Eisai Medical Services +44 20 7538 7075 EUMedInfo@eisai.net

 [Show 143 Study Locations](#)

Sponsors and Collaborators

Eisai Inc.

Investigators

Study Director: Eisai Inc.

 **More Information**

No publications provided

Responsible Party: Eisai Inc.

ClinicalTrials.gov Identifier: [NCT01321554](#) [History of Changes](#)

Other Study ID Numbers: **E7080**-G000-303

Study First Received: March 10, 2011

Last Updated: January 31, 2012

Health Authority: United States: Food and Drug Administration