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This was a nonrandomized, open-label, multicenter, Phase 2 study. The study was evaluated in 3 different histologic subtypes: DTC, MTC, and ATC. The enrollment of DTC subjects started only after the recruitment of the multicenter, randomized, double-blind, placebo-controlled, Phase 3 study for radioiodine (^{131}I) refractory DTC (E7080-G000-303) was completed.

The study consisted of 3 phases: a Pretreatment Phase, a Treatment Phase, and a Follow-up Phase.

The Pretreatment Phase included the processes of informed consent, screening, enrollment, and baseline assessments. Informed consent was obtained up to 28 days before the first dose. After screening, subjects were scheduled to receive lenvatinib within 7 days after the date of enrollment. The Baseline assessment was performed immediately before the study drug administration.

The Treatment Phase started from the study drug administration on Day 1 of Cycle 1 and continued until a subject met one or more of the “Discontinuation Criteria for Individual Subject.” The safety assessment and tumor assessment were performed periodically during the study period. For DTC and MTC subjects, tumor assessments were performed every 8 weeks from Day 1 of Cycle 1. For ATC subjects, tumor assessments were performed at 4, 8, 12, and 16 weeks from Day 1 of Cycle 1, and every 8 weeks subsequently. An off-treatment visit occurred within 7 days after the study discontinuation. The final observation visit occurred at 30 days after the final dose.

Survival was followed up during the Follow-up Phase. After treatment discontinuation, all subjects were followed up every 12 weeks (DTC and MTC) and every 4 weeks (ATC) unless subjects withdrew their consent or the sponsor decided to discontinue the follow-up.

This study is ongoing. This clinical study report presents the data through a data cutoff date of 15 Sep 2013.

Number of Subjects (Planned and Enrolled)

Planned: 16 or more subjects

Enrolled: 36 subjects (22 DTC subjects, 5 MTC subjects, and 9 ATC subjects through the data cutoff date)

Treated: 35 subjects (22 DTC subjects, 4 MTC subjects, and 9 ATC subjects through the data cutoff date)

Diagnosis and Main Criteria for Inclusion

Diagnosis: advanced thyroid cancer (DTC, MTC, or ATC)

Inclusion Criteria:

For DTC only

1. Histologically or cytologically confirmed diagnosis of DTC
2. Had evidence of disease progression according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 within 12 months before informed consent, using computerized tomography (CT) or magnetic resonance imaging (MRI)
3. Had measurable lesion meeting the following criteria:
 - a. At least one lesion of ≥ 1.0 cm in the long axis for a non-lymph node or ≥ 1.5 cm in the short axis diameter for a lymph node that was sequentially measurable according to RECIST 1.1 using CT or MRI
 - b. Lesions previously treated with external beam radiotherapy or locoregional therapy such as radiofrequency ablation had to show radiographic evidence of disease progression (according to RECIST 1.1) to be deemed a target lesion
4. Had been receiving thyroxine suppression therapy (thyroid stimulating hormone [TSH] was ≤ 5.50 mcu/mL)
5. Had been confirmed as ^{131}I -refractory or resistant defined by at least one of the following criteria:
 - a. One or more measurable lesions with no iodine uptake detected by radioiodine scanning
 - b. One or more measurable lesions that had progressed by RECIST 1.1 within 12 months of ^{131}I therapy, despite demonstration of ^{131}I uptake at the time of that treatment by pre- or post-treatment scanning
 - c. Cumulative activity of ^{131}I of >600 mCi or 22 gigabecquerel (GBq), with the last dose administered at

<p>least 6 months before study entry</p> <p><u>For MTC only</u></p> <p>6. Histologically or cytologically confirmed diagnosis of MTC</p> <p>7. Met at least one of the following criteria</p> <ol style="list-style-type: none"> Evidence of disease progression according to RECIST 1.1 within 12 months before informed consent, using CT or MRI Clinical progressive disease (with clinical symptom or elevated tumor marker) in the opinion of the investigator <p>8. Had evaluable target lesion or non-target lesion according to RECIST 1.1</p> <p><u>For ATC only</u></p> <p>9. Histologically or cytologically confirmed diagnosis of ATC</p> <p>10. Had evaluable target lesion according to RECIST 1.1</p> <p>11. Had agreed to hospitalization in Cycle 1 (4 weeks)</p> <p>12. Expected to survive for 8 weeks or longer after the first dose of study drug</p> <p><u>For all subtypes</u></p> <p>13. Radical surgery was not applicable</p> <p>14. Had adequate organ function meeting the following criteria:</p> <ol style="list-style-type: none"> Renal function: Estimated glomerular filtration rate (eGFR) ≥ 60 mL/min/1.73 m² eGFR was calculated using the following formula by gender Male: $194 \times (\text{serum creatinine})^{-1.094} \times (\text{age})^{-0.287}$ Female: Above value $\times 0.739$ Bone marrow function: <ol style="list-style-type: none"> Absolute neutrophil count $\geq 1.5 \times 10^3/\mu\text{L}$ Platelet count $\geq 10 \times 10^4/\mu\text{L}$ Hemoglobin ≥ 9.0 g/dL Liver function: <ol style="list-style-type: none"> Bilirubin $\leq 1.5 \times$ upper limit of normal (ULN: site reference), except for unconjugated hyperbilirubinemia or Gilbert's syndrome Alkaline phosphatase (ALP), alanine aminotransferase, and aspartate aminotransferase $\leq 3.0 \times \text{ULN}$ ($\leq 5.0 \times \text{ULN}$ in the presence of liver metastasis). If ALP was $> 3 \times \text{ULN}$ (in the absence of liver metastasis) or $> 5 \times \text{ULN}$ (in the presence of liver metastasis) AND the subject also was known to have bone metastasis, liver-specific ALP was separated from the total and used to assess the liver function instead of total ALP. Blood coagulation function: International normalized ratio (INR) ≤ 1.5 <p>15. Systolic pressure ≤ 140 mmHg and diastolic pressure ≤ 90 mmHg with or without antihypertensive medications and no change in antihypertensive medications within 1 week before study entry (additional antihypertensive therapy was allowable if using antihypertensive agents).</p> <p>16. Aged 20 years or older when informed consent was obtained</p> <p>17. Eastern Cooperative Oncology Group (ECOG) performance status was 0 to 2</p> <p>18. Females must not have been lactating or pregnant at Screening or Baseline (as documented by a negative beta-human chorionic gonadotropin [β-hCG] test with a minimum sensitivity of 25 IU/L or equivalent units of β-hCG). A separate baseline assessment was required if a negative screening pregnancy test was obtained more than 72 hours before the first dose of study drug.</p> <p>19. All females were considered to be of childbearing potential unless they were postmenopausal (amenorrheic for at least 12 consecutive months, regardless of age group or other cause) or sterilized surgically (ie, bilateral tubal ligation, total hysterectomy, or bilateral oophorectomy, all with surgery at least 1 month</p>
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before the first dose of study drug).

20. Females of childbearing potential must not have had unprotected sexual intercourse within 30 days before study entry and were required to agree to use a medically appropriate method of contraception throughout the entire study period and for 30 days after study drug discontinuation. If currently abstinent, the subject was required to agree to use a method as described above if she became sexually active during the study period and for 30 days after study drug discontinuation. Females of childbearing potential who were using hormonal contraceptives had to be on a stable dose of the same hormonal contraceptive product for at least 4 weeks before dosing and were required to continue to use the same contraceptive during the study and for 30 days after study drug discontinuation.
21. Male subjects were required to have a successful vasectomy (confirmed azoospermia) or they and their female partners were required to meet the criteria above (ie, not of childbearing potential or practicing medically appropriate contraception throughout the study period and for 30 days after study drug discontinuation).
22. Voluntarily agreed to provide written informed consent and the willingness and ability to comply with all aspects of the protocol

Exclusion Criteria (for all subtypes):

1. Had a complication or history of the following disease(s)
 - a. Concomitant brain metastasis (except for metastasis if previously treated and clinically stable for at least 1 month before screening)
 - b. Concomitant systemic infection requiring medical treatment
 - c. Medical history of clinically significant cardiovascular impairment: congestive heart failure greater than New York Heart Association (NYHA) Class II, unstable angina pectoris, myocardial infarction or stroke within 6 months before of the first dose of study drug, or cardiac arrhythmia requiring medical treatment
 - d. QT interval corrected for heart rate (QTc) greater than 480 ms (Fridericia's method)
 - e. Active hemoptysis (bright red of a half or more of teaspoon) within 3 weeks before enrollment
 - f. Bleeding or thrombotic disorders or use of anticoagulants such as warfarin or similar drugs requiring INR monitoring (low molecular weight heparin was allowed)
 - g. $\geq 2+$ proteinuria on urine dipstick testing underwent 24 h urine collection for quantitative assessment of proteinuria. Subjects with urine protein ≥ 1 g/24 h were ineligible
 - h. Gastrointestinal malabsorption or any other condition in the opinion of the investigator or subinvestigator that might affect the absorption of lenvatinib
 - i. Major surgery within 3 weeks before enrollment
 - j. Effusion requiring drainage
2. Previously treated with lenvatinib
3. Had received any anticancer treatment such as radiotherapy, chemotherapy, or immunotherapy (except for TSH suppression therapy) within 21 days or any other investigational agent within 30 days before the first dose of lenvatinib (but not applicable to ATC subjects)
4. Had not recovered from toxicities as a result of prior anticancer therapy to \leq Grade 1, according to Common Terminology Criteria for Adverse Events (CTCAE) v4.0 (except for alopecia and infertility)
5. Scheduled for surgery during the study
6. Any medical or other condition that, in the opinion of the investigator or subinvestigator, would preclude participation in a clinical study
7. Known intolerance to any of the study drug (or any of its excipients)
8. Currently participating in another clinical study
9. Active malignancy within 24 months of the start of study drug administration (except for thyroid cancer, definitively treated melanoma in situ, basal or squamous cell carcinoma of the skin, or carcinoma in situ of the cervix)

Test Treatment, Dose, Mode of Administration, and Batch Number(s)

Lenvatinib was supplied as 4 mg and 10 mg capsules. Subjects received 24 mg lenvatinib (two 10 mg capsules and one 4 mg capsule) orally once daily in the morning. A treatment cycle was defined as 4 weeks. The study drug was administered at approximately the same time every morning.

Dose adjustments were made according to the instructions below when a toxicity relating to study drug administration occurred. Once a dose was reduced, dose escalation was prohibited.

Dose Reduction and Interruption Instructions

Treatment-related toxicity ^a	Treatment management	Adjusted dose
Grade 1 or tolerable Grade 2^b		
	Continue study treatment	No change
Intolerable Grade 2^b or Grade 3		
First occurrence	Interrupt until resolved to Grade 0-1 or baseline ^c	20 mg QD
Second occurrence		14 mg QD
Third occurrence		10 mg QD
Fourth occurrence		Discuss with sponsor

Grade 4^d: Discontinue study treatment

Note: For grading see CTCAE v4.0. All CTCAE grades of adverse events (AEs) and increases in CTCAE grade were collected.

QD = once daily.

- a: Optimal medical management for nausea, vomiting, and/or diarrhea was initiated before any study treatment, dose interruption, or dose reduction.
- b: Tolerability of Grade 2 was determined by investigators (investigators or subinvestigators) or subjects.
- c: An interruption of study treatment for more than 28 days (due to treatment-related toxicities) required a discussion with the sponsor before treatment was resumed.
- d: Laboratory abnormalities judged to be non-life-threatening were excluded and these were managed as Grade 3.

The management of hypertension was required to follow the instructions below, not those above for dose reduction and dose interruption shown above.

1. One blood pressure assessment was defined as the mean value of 3 measurements at least 5 minutes apart.
2. For previously normotensive subjects, monotherapy with one of the classes of antihypertensive was started when blood pressure was confirmed to be ≥ 140 mmHg systolic and ≥ 90 mmHg diastolic on 2 measurements 1 hour apart. For those subjects already on antihypertensive medication, the dose of the current agent was increased, if appropriate, or one or more agents of a different class of antihypertensive were added.
3. If systolic blood pressure ≥ 160 mmHg and diastolic blood pressure ≥ 100 mmHg continued despite optimal hypertension management, the study drug was suspended and resumed at a dose of 20 mg QD when systolic blood pressure was ≤ 150 mmHg and diastolic blood pressure was ≤ 95 mmHg and the subject had been on a stable dose of antihypertensive medication for at least 48 hours. If systolic blood pressure ≥ 160 mmHg and diastolic blood pressure ≥ 100 mmHg recurred despite the optimal hypertension management, a one-dose level reduction (20 mg, 14 mg, and 10 mg per day) was attempted.
4. Additional dose reduction was discussed with the sponsor.
5. Study drug administration was discontinued when Grade 4 hypertension (life-threatening) was present.

Batch numbers: 4 mg capsule [REDACTED] 10 mg capsule [REDACTED]

<p>Reference Therapy, Dose, Mode of Administration, and Batch Number(s)</p> <p>Not applicable.</p>
<p>Duration of Treatment</p> <p>Study drug administration continued until a subject met one or more of the “Discontinuation Criteria by Individual Subject.”</p> <p>Discontinuation Criteria by Individual Subject</p> <ol style="list-style-type: none"> 1. Progression of disease based on RECIST 1.1 was present (including emergence of new lesions). (When PR or dSD [SD lasting ≥ 23 weeks for DTC and MTC, ≥ 11 weeks for ATC] was seen, the study drug administration was allowed at the discretion of the investigator or subinvestigator until clinical progression of disease was confirmed when clinical benefit of study treatment was maintained and no other effective treatments were available.) 2. Unable to continue the study participation due to intolerable toxicities in the opinion of the investigator or subinvestigator 3. Major violations from inclusion or exclusion criteria in the protocol were found after study enrollment 4. Subject’s pregnancy 5. Subject’s refusal of the continued participation or withdrawal of the consent 6. The investigator or subinvestigator deemed that the subject was unable to comply with the protocol and it was inappropriate to continue study participation for safety reasons 7. The investigator or subinvestigator deemed it appropriate for other reason(s)
<p>Assessments</p> <p>Efficacy</p> <p>Tumor assessment was performed by the investigator using RECIST 1.1.</p> <p><u>Primary efficacy endpoint:</u></p> <p>Not applicable.</p> <p><u>Secondary efficacy endpoint:</u></p> <p>PFS: Defined as the time from the date of first dose to the date of first documentation of disease progression or death from any cause (whichever occurred first).</p> <p>OS: Defined as the time from the date of first dose to the date of death from any cause. If death was not observed for a subject, the survival time was censored at the date the subject was last known alive or the data cutoff date (whichever occurred first).</p> <p>BOR: The best response observed between the time of first dose and the study completion, assessed by either of CR, PR, SD (≥ 7 weeks for DTC and MTC, ≥ 3 weeks for ATC), progressive disease (PD), or not evaluable (NE). The CR and PR were determined only when these responses met each criterion even after 28 days from the time observed.</p> <p>ORR: Proportion of subjects who had BOR of CR or PR</p> <p>DCR: Proportion of subjects who had BOR of CR, PR, or SD</p> <p>CBR: Proportion of subjects who had BOR of CR, PR, or dSD (SD lasting ≥ 23 weeks for DTC and MTC, ≥ 11 weeks for ATC)</p> <p>Pharmacokinetics</p> <p>PK profile of lenvatinib was assessed in all subjects enrolled in this study according to the following schedule of blood samplings.</p> <ol style="list-style-type: none"> 1. Cycle 1 <ul style="list-style-type: none"> Day 1: 0.5 to 4 hours postdose, 6 to 10 hours postdose

Day 15: predose, 2 to 12 hours postdose

2. Cycle 2

Day 1: predose, 0.5 to 4 hours postdose, 6 to 10 hours postdose

Pharmacodynamics

Not applicable.

Pharmacokinetics/Pharmacodynamics

Not applicable.

Pharmacogenomics

Blood samples were collected to identify and investigate the effect of gene mutation on ADME profiles of lenvatinib.

Safety

Safety assessments included all AEs including CTCAE v4.0-based grading (did not apply to Japan Clinical Oncology Group [JCOG] practices), serious adverse events (SAEs) and records, periodic hematology/blood chemistry/urinalysis values, vital signs, 12-lead electrocardiograms (ECGs), and physical examination findings.

Bioanalytical Methods

Plasma concentration of lenvatinib was quantified using the validated liquid chromatography/mass spectrometry/mass spectrometry (LC/MS/MS) methodology.

Statistical Methods

Analysis sets:

Safety Analysis Set included all subjects who received at least one dose of the study drug and had at least one postbaseline safety evaluation.

Full Analysis Set included all subjects who received at least one dose of the study drug.

PK Analysis Set included all subjects who received at least one dose of the study drug and had at least one drug concentration data.

Efficacy analysis:

All efficacy analyses conducted were based on the Full Analysis Set. PFS and OS were summarized by the Kaplan-Meier method using median time with 95% confidence interval (CI), minimum, and maximum by histologic stratum and overall. ORR, DCR, and CBR based on the investigator assessment were provided with corresponding exact 95% CI by histologic stratum and overall. BOR was summarized by histologic stratum and overall. Graphical displays of percent shrinkage of summed diameters in target lesions over time were provided for each subject. In addition, percent shrinkage of tumor summed diameter from baseline to the nadir was graphically presented (waterfall plot). Graphical displays of the tumor marker (calcitonin) over time were also provided for each subject.

Pharmacokinetic analysis:

The PK Analysis Set was used for the summaries of lenvatinib concentration data. Observed (actual) and dose normalized plasma concentrations were tabulated by nominal sample collection time for each PK sample collection visit by histologic stratum and overall. Sparse samples for lenvatinib from this study will be pooled and subjected to population PK analysis. Details of population PK analysis will be described in a separate plan and presented in a separate report.

Pharmacogenomic analysis:

Details of analyses to be performed to identify and validate DNA-sequence variants in genetic mutations influencing lenvatinib PK will be described in a separate analysis plan and presented in a separate report.

Safety analysis:

All safety analyses were performed on the Safety Analysis Set. The safety analysis was performed primarily in all subjects including all subtypes. Secondary assessments were performed for each subtype of DTC, MTC, or ATC.

The number and percentage of subjects with treatment-emergent AEs (TEAEs) and SAEs were calculated. All AEs were summarized by system organ class (SOC), preferred term (PT), CTCAE v4.0 grade, and causal relationship to the study treatment. Clinical laboratory values and vital signs were summarized using descriptive statistics. The number and percentage of subjects with treatment-emergent markedly abnormal laboratory values (TEMAVs) were summarized by scheduled visit and overall. A laboratory value was considered markedly abnormal if the result worsened to Grade 2 or higher from baseline. Shift tables presented changes from baseline in ECG interpretation (categorized as normal; abnormal, not clinically significant; and abnormal, clinically significant) for each scheduled visit. QT and QT interval corrected for heart rate using Fridericia's formula (QTcF) values, and changes from baseline were summarized at each scheduled visit. QT and QTcF values and changes from baseline were also summarized categorically.

Results**Subject Disposition/Analysis Sets**

A total of 36 subjects entered into the study (22 with DTC, 5 with MTC, and 9 with ATC). Because 1 subject with MTC started the study drug administration after the date of data cutoff (15 Sep 2013), 35 subjects who received at least one dose of study drug are included in this report. Of the 35 subjects, 25 were still receiving study drug, 9 had discontinued study drug due to disease progression, and 1 had discontinued study drug due to subject choice. All of the 35 subjects were included in the Full Analysis Set, Safety Analysis Set, and PK Analysis Set.

Efficacy

- At the time of data cutoff, the efficacy could be assessed in 21 subjects with DTC, in 4 subjects with MTC, and in 9 subjects with ATC, and the majority of subjects were ongoing.
- All evaluable subjects experienced tumor shrinkage after the initiation of lenvatinib treatment.
- The ORR (CR+PR) based on the investigator assessment was 47.6% in DTC subjects, 25.0% in MTC subjects, and 33.3% in ATC subjects.
- In DTC subjects, 10 subjects (47.6%) had a BOR of PR and 11 subjects (52.4%) had a BOR of SD. In MTC subjects, 1 subject (25.0%) had a BOR of PR and 3 subjects (75.0%) had a BOR of SD. In ATC subjects, 3 subjects (33.3%) had a BOR of PR, 5 subjects (55.6%) had a BOR of SD, and 1 subject (11.1%) had a BOR of PD. One subject with ATC had a BOR of PD based on non-target lesions.
- The DCR (CR+PR+SD) was 100.0% in both DTC and MTC subjects and 88.9% in ATC subjects.
- Clinical benefit was evaluated in 14 subjects with DTC, in 3 subjects with MTC, and in 8 subjects with ATC. The CBR (CR+PR+dSD) was 78.6% in DTC subjects, 100.0% in MTC subjects, and 75.0% in ATC subjects.
- The median PFS in DTC subjects had not been reached yet. The median PFS was 6.5 months (95% CI: 5.6, 7.3) in MTC subjects and 5.5 months (95% CI: 1.4, -) in ATC subjects. In all histologic subtypes,

the median OS had not been reached yet.

Safety

- In the Safety Analysis Set, all of 35 subjects (100.0%) experienced at least one TEAE, and each of these 35 subjects (100.0%) had at least one TEAE reported as treatment-related by the investigator.
- The most frequently reported TEAE was hypertension (85.7%, 30/35 subjects), followed by palmar-plantar erythrodysesthesia syndrome (74.3%, 26/35 subjects), fatigue (71.4%, 25/35 subjects), decreased appetite (68.6%, 24/35 subjects), proteinuria and stomatitis (51.4%, 18/35 subjects each), diarrhoea (42.9%, 15/35 subjects), and nausea (40.0%, 14/35 subjects). The most frequently reported treatment-related TEAE was hypertension (85.7%, 30/35 subjects), followed by palmar-plantar erythrodysesthesia syndrome (71.4%, 25/35 subjects), fatigue (68.6%, 24/35 subjects), decreased appetite (62.9%, 22/35 subjects), proteinuria and stomatitis (51.4%, 18/35 subjects each), and diarrhoea (42.9%, 15/35 subjects).
- Twenty-six of 35 subjects (74.3%) had at least one CTCAE Grade 3 or 4 TEAE. Grade 3 or 4 TEAEs occurred in 16 subjects (72.7%) with DTC, in 4 subjects (100.0%) with MTC, and in 6 subjects (66.7%) with ATC. The most frequently reported Grade 3 or 4 TEAE was hypertension (42.9%, 15 subjects), followed by diarrhoea (11.4%, 4 subjects). Three subjects experienced at least one Grade 4 TEAE (hypocalcaemia, hyponatraemia, and thrombocytopenia). Grade 4 TEAEs were resolved with treatment or study drug dose reduction except for hypocalcaemia which was reported as ongoing at the time of data cutoff (15 Sep 2013).
- Death, during the study treatment or within 30 days of the last dose of study drug, occurred in 1 subject, who died of disease progression.
- Fourteen subjects (40.0%) experienced 21 SAEs. SAEs that occurred in more than one subject were decreased appetite (4 subjects) and nausea (2 subjects). SAEs of decreased appetite (4 events), nausea (2 events), cholecystitis, diarrhoea, fatigue, gastric ulcer, gastroenteritis, lung infection, malignant pleural effusion, pneumonia, respiratory tract infection, and sepsis (1 event each) were reported as treatment-related by the investigator.
- No subjects required study drug withdrawal due to TEAEs. Thirty-four subjects (97.1%) reported TEAEs leading to study drug dose reduction. The most frequently reported TEAE leading to study drug dose reduction was fatigue (37.1%, 13 subjects), followed by decreased appetite, hypertension, and palmar-plantar erythrodysesthesia syndrome (22.9%, 8 subjects each).
- Fifteen subjects (42.9%) reported TEAEs leading to study drug interruption. The most frequently reported TEAE leading to study drug interruption was palmar-plantar erythrodysesthesia syndrome (11.4%, 4 subjects), followed by decreased appetite and fatigue (8.6%, 3 subjects each).
- The most frequently observed TEMAV was urine protein (markedly high; 45.7%, 16 subjects), followed by triglycerides (markedly high; 31.4%, 11 subjects), and cholesterol (markedly high; 28.6%, 10 subjects).
- An increase in mean systolic and diastolic blood pressure was observed compared with baseline. Most of the increases in blood pressure occurred during Cycle 1 or Cycle 2. Thirty subjects (85.7%) experienced hypertension as a TEAE. All events of hypertension were Grade 2 or Grade 3 and assessed as nonserious. Most events of hypertension were managed with antihypertensive medications. Hypertension led to study drug dose reduction in 8 subjects. No subjects required study drug withdrawal due to hypertension.
- TEAEs related to ECG abnormalities occurred in 2 subjects (sinus tachycardia, electrocardiogram QT prolonged). No subject reported a QTcF prolongation of >480 ms or an increase from baseline of >60 ms.

Four subjects (1 with MTC and 3 with ATC) had a QTcF prolongation of 450 to 480 ms. Four subjects (1 each with DTC and MTC, and 2 with ATC) had an increase from baseline in QTcF of 30 to 60 ms.

- No clinically important changes were observed in ECOG performance status.

Conclusions

- The oral administration of lenvatinib at a dose of 24 mg QD achieved an acceptable and manageable safety profile by following prespecified dose reduction or interruption instructions in subjects with advanced thyroid cancer including DTC, MTC, and ATC. There were no toxicities leading to deaths or withdrawal from the study.
- Efficacy results confirmed the antitumor activity of lenvatinib in all histologic subtypes of advanced thyroid cancer.

Date of Report

30 May 2014