

Lenvatinib in Patients With Advanced Grade 1/2 Pancreatic and Gastrointestinal Neuroendocrine Tumors: Results of the Phase II TALENT Trial (GETNE1509)

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PURPOSE Approved systemic therapies for advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs) have shown limited capacity to reduce tumor burden and no antitumor activity after progression to targeted agents (TAs). We investigated the efficacy and safety of lenvatinib in patients with previously treated advanced GEP-NETs.

PATIENTS AND METHODS This was a multicenter, single-arm, open-label, phase II trial with two parallel cohorts (ClinicalTrials.gov identifier: [NCT02678780](https://clinicaltrials.gov/ct2/show/study/NCT02678780)) involving 21 institutions in 4 European countries. Eligible patients had histologically confirmed advanced grade 1-2 pancreatic (panNET) or GI (GI-NET) NETs with documented tumor progression after treatment with a TA (panNET) or somatostatin analogs (GI-NET). Patients were treated with lenvatinib 24 mg once daily until disease progression or treatment intolerance. The primary end point was overall response rate by central radiology review. Secondary end points included progression-free survival, overall survival, duration of response, and safety.

RESULTS Between September 2015 and March 2017, a total of 111 patients were enrolled, with 55 (panNET) and 56 (GI-NET) patients in each cohort. The median follow-up was 23 months. The overall response rate was 29.9% (95% CI, 21.6 to 39.6): 44.2% (panNET) and 16.4% (GI-NET). The median (range) duration of response was 19.9 (8.4-30.8) and 33.9 (10.6-38.3) months in the panNET and GI-NET groups, respectively. The median progression-free survival was 15.7 months (95% CI, 14.1 to 19.5). The most common adverse events were fatigue, hypertension, and diarrhea; 93.7% of patients required dose reductions or interruptions.

CONCLUSION We report the highest centrally confirmed response reported to date with a multikinase inhibitor in advanced GEP-NETs, with a particularly strong response in the panNET cohort. This study provides novel evidence for the efficacy of lenvatinib in patients with disease progression following treatment with other TAs, suggesting the potential value of lenvatinib in the treatment of advanced GEP-NETs.

ASSOCIATED CONTENT

Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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INTRODUCTION

Despite the availability of systemic therapies to treat gastroenteropancreatic (GEP) neuroendocrine tumors (NETs), treatment resistance is a common challenge.¹ Poorly controlled hormone secretion and tumor progression can severely affect quality of life and survival, underscoring the need to achieve significant tumor shrinkage to improve outcomes.² The range of treatment strategies includes somatostatin analogs (SSAs), peptide receptor radionuclide therapy, chemotherapy, and molecular-targeted agents (TAs),

including mammalian target of rapamycin inhibitors and multikinase inhibitors (MKIs).¹ Although these TAs can extend progression-free survival (PFS), they have demonstrated only a limited capacity to reduce tumor size, as evidenced by the low overall response rates (ORR) reported in phase III trials.³⁻⁸

Neuroendocrine tumor cells overexpress a wide range of proangiogenic molecules and receptors, which explains the strong interest in antiangiogenic agents for the treatment of GEP-NETs. Lenvatinib is an inhibitor of vascular endothelial growth factor receptor 1-3

CONTEXT

Key Objective

To evaluate lenvatinib in a heavily pretreated population of patients with advanced neuroendocrine cancer.

Knowledge Generated

Lenvatinib achieved the highest objective response rate ever reported in this setting, reverting previous resistance to targeted agents and improving outcomes.

Relevance

These results show that a targeted agent can induce a strong tumor response and improve survival, even in an unselected population with disease progression to previous therapies. This finding suggests that lenvatinib could be used for neoadjuvant or salvage therapies to improve final outcomes.

(VEGFR1-3), fibroblast growth factor receptor 1-4 (FGFR1-4), platelet-derived growth factor receptor alpha, rearranged during transfection, c-KIT, and platelet-derived growth factor receptor-β. Lenvatinib has demonstrated a particularly high potency against FGFR-1—a key driver of resistance to antiangiogenic drugs—suggesting that it could potentially also reverse primary and acquired resistance to anti-VEGFR treatments or to other TAs.⁹⁻¹¹

Given this background, we conducted an international, parallel cohort phase II clinical trial (TALENT) to evaluate lenvatinib in patients with advanced grade 1/2 GEP-NETs.

PATIENTS AND METHODS

Study Design and Participants

The Trial to Assess the Efficacy of Lenvatinib in Metastatic Neuroendocrine Tumours (TALENT; ClinicalTrials.gov identifier: [NCT02678780](https://clinicaltrials.gov/ct2/show/study/NCT02678780)) was a prospective, international, open-label, parallel cohort, single-stage phase II trial. A total of 21 centers from Spain, Austria, Italy, and the United Kingdom participated. Eligible patients were required to have an advanced pancreatic or GI-NET with progressive disease after treatment with a TA (panNET group) or SSAs (GI-NET group). The main study inclusion criteria were: (1) age \geq 18 years; (2) histologically confirmed diagnosis of advanced G1/G2 (WHO criteria) panNET or GI-NET; (3) documented radiological disease progression (RECIST 1.1)¹² during the last 12 months; (4) Eastern Cooperative Oncology Group performance status: 0-1; (5) adequate hematologic, hepatic, and renal function; and (6) measurable disease. Previous treatment with chemotherapy was allowed in the panNET group. The main exclusion criteria were \geq 2 previous lines of TAs (panNET group), any previous line of targeted therapy (GI-NET group), or any ongoing antiproliferative treatment, except for SSAs.

This trial was performed in accordance with the principles of the Declaration of Helsinki and approved by the research ethics committee at all participating hospitals. All candidate patients were reviewed to determine protocol eligibility.

Patients who met all inclusion criteria, agreed to participate, and provided informed consent were consecutively enrolled in the study.

Procedures

Treatment consisted of once daily oral lenvatinib 24 mg administered until documented disease progression (RECIST v.1.1), intolerable toxicity despite dose reduction, withdrawal of consent, or death. Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events v. 4.03. Treatment interruptions and progressive dose reductions (20/14/10 mg) were permitted to manage adverse events.

Clinical assessments included complete physical examination, laboratory tests, tumor markers (chromogranin A, 5-HIAA, enolase), and tumor imaging, performed at baseline, weeks 6 and 12 after the first dose, and thereafter every 12 weeks until disease progression or initiation of an alternative treatment. The cutoff date for the main analysis was 12 weeks after the first dose of the study drug was administered to the last patient enrolled in the study.

Outcome Measures

The primary study end point was ORR by central radiology review, defined as the proportion of patients in each treatment group (GI-NETs and panNETs) with complete or partial response according to RECIST v.1.1. Patients were considered evaluable for response if at least one study drug was administered and at least one follow-up tumor evaluation imaging was performed. Secondary end points were overall survival (OS), PFS, safety, and duration of response (DoR). All end points were assessed for each individual treatment cohort and overall population.

PFS and OS were assessed by the individual investigator(s) at each participating hospital. OS was defined as the time elapsed from treatment initiation until death. PFS was defined as the time elapsed from treatment initiation to documented disease progression or death, whichever occurred first.

Statistical Considerations

The primary end point was ORR by central radiology review according to RECIST 1.1. On the basis of ORR data (9.3%) from the only MKI (sunitinib) currently approved for the treatment of NETs, our null hypothesis for lenvatinib was an ORR < 10% and the alternative hypothesis was that treatment with lenvatinib would yield an expected ORR \geq 25% in each independent treatment cohort. On the basis of these data, we determined that 55 patients per group would be needed to demonstrate this hypothesis, with a 90% power and α -error of 5%. Primary and secondary end points were assessed for the entire group of patients and independently for each cohort.

The ORR with 95% CIs was calculated. Two-sided *P* values of $\leq .05$ were considered to indicate statistical significance. PFS and median OS were estimated using the Kaplan-Meier method.

All analyses were performed with the R statistical software program v.2.14.2 (R Foundation for Statistical Computing, Vienna, Austria). This trial is registered at ClinicalTrials.gov (identifier: [NCT02678780](https://clinicaltrials.gov/ct2/show/study/NCT02678780)).

RESULTS

Between September 2015 and March 2017, a total of 111 patients were enrolled in the study. [Table 1](#) presents the patients' characteristics at baseline. In the GI-NET group, the most common primary tumor site was the small intestine (*n* = 44; 81.5%), followed by the rectum (*n* = 6, 11.1%), colon (*n* = 3; 5.6%), and stomach (*n* = 1; 1.9%).

Patient Characteristics

Efficacy outcomes. Overall response rate. As shown in [Table 2](#), the ORR by central radiology assessment for the full cohort was 29.9% (95% CI, 21.6 to 39.6): 44.2% (95% CI, 30.7 to 58.6) in the panNET and 16.4% (95% CI, 8.2 to 29.3) in the GI-NET cohort. [Figure 1](#) depicts the ORR results graphically for the individual patients in the two cohorts. These results, obtained by central radiology review, were similar to those reported by the investigators, who collectively reported an ORR of 33.6% (42.3% and 25.4% for the panNET and GI-NET cohorts, respectively).

Duration of response. Overall, the median DoR was 21.5 (8.4-38.3) months. [Figure 2](#) shows the DoR in the patients

TABLE 1. Patient Characteristics at Baseline

Clinical or Sociodemographic Variable	panNET (n = 55)	GI-NET (n = 56)
Median age, years (range)	58 (31-73)	61 (31-73)
Female gender, No. (%)	31 (56.4)	23 (41.1)
ECOG PS: 0, No. (%)	40 (72.7)	34 (60.7)
Ki67 index, median (range)	8 (0.8-25)	4 (1-20)
Ki67 index stratified, No. (%)		
0%-5%	16 (30.2)	28 (58.2)
5%-10%	12 (22.6)	13 (24.1)
10%-20%	26 (48.2)	13 (24.1)
Missing	1	2
Median years from initial diagnosis (range)	4.4 (0.98-13.2)	3.3 (0.4-19.3)
Tumor grade, No. (%) ^a		
G1	12 (21.8)	21 (37.5)
G2	42 (76.4)	34 (60.7)
Unknown	1 (1.8)	1 (1.8)
Previous treatments, No. (%)		
Resection of primary tumor	26 (47.3)	36 (64.3)
Resection of metastases	9 (16.4)	16 (28.6)
Somatostatin analogs	47 (85.5)	56 (100) ^b
Chemotherapy	18 (32.7)	0
Everolimus	38 (69.0)	0
Sunitinib	16 (29.1)	0
Other targeted agent	1 (1.8)	0

Abbreviations: ECOG, Eastern Cooperative Oncology Group; GI-NET, GI neuroendocrine tumor; panNET, pancreatic neuroendocrine tumor; PS, performance status.

^aWHO criteria.

^bOne patient also received interferon.

TABLE 2. Treatment Efficacy

Efficacy Parameter	panNETs (n = 55)	GI-NETs (n = 56)	Total (N = 111)
Patients with tumor assessment, No. (%)	52 (94.6) ^a	55 (98.2) ^a	107 (96.4) ^a
Best overall response, No. (%)			
Complete response	0	0	0
Partial response	23 (44.2)	9 (16.4)	32 (29.9)
Stable disease	27 (51.9)	42 (76.4)	69 (64.5)
Progressive disease	2 (3.9)	1 (1.8)	3 (2.8)
Not evaluable	0	3 (5.5) ^b	3 (2.8) ^b
Overall response rate (95% CI)	44.2% (30.7 to 58.6)	16.4% (8.2 to 29.3)	29.9% (21.6 to 39.6)
Disease control rate	96.2% (85.7 to 99.3)	92.7% (81.6 to 97.6)	94.4% (87.7 to 97.7)
Median duration of response, months (range)	19.9 (8.4-30.8)	33.9 (10.6-38.3)	21.5 (8.4-38.3)

Abbreviations: GI-NET, GI neuroendocrine tumor; panNET, pancreatic neuroendocrine tumor.

^aFour patients (three panNETs and one GI-NET) withdrew informed consent before the first postbaseline tumor assessment.

^bTarget lesions considered not evaluable on central radiology review.

with confirmed radiological response. By primary tumor site, the median (range) DoR was 19.9 (8.4-30.8) months (panNETs; Fig 2A) and 33.9 (10.6-38.3) months (GI-NETs; Fig 2B).

PFS. Figure 3 shows the PFS outcomes by primary tumor site. At a median follow-up of 23 months, the median PFS for the full cohort was 15.7 months (95% CI, 14.1 to 19.5). In the panNET and GI-NET groups, the median PFS was 15.6 (95% CI, 11.4 to not reached) and 15.7 (95% CI, 12.1 to 19.5) months, respectively.

OS. A total of 37 deaths (33.3%) were observed during the follow-up. The median OS was 32 months (95% CI, 26.47 to not reached) in the panNET group and not reached in the GI-NET group.

Safety profile. Most patients required at least one dose reduction (81.1%) or temporary treatment interruption (92.8%). The median duration of treatment with the study drug was 11.3 and 11.4 months in the panNET and GI-NET cohorts, respectively. The median dose of lenvatinib was 20 mg/d. Sixteen patients (14.4%) required definitive treatment discontinuation of the study drug because of severe treatment-related toxicity: panNETs (n = 6, 10.9%) and GI-NETs (n = 10, 17.8%).

Table 3 shows the most common adverse events (AEs) by toxicity grade. The most common grade 1/2 AEs were asthenia, hypertension, diarrhea, dysphonia, and hypothyroidism. The most prevalent grade 3/4 AEs were hypertension (22.7%), asthenia (13.6%), and diarrhea (10.9%).

DISCUSSION

Treatment with lenvatinib 24 mg daily was active and safe in patients with advanced GEP-NETs pretreated with TAs and SSAs. To the best of our knowledge, the ORR reported in

the present trial is the highest centrally confirmed response rate achieved to date with a TA in advanced NETs.

In patients with GI-NETs, radiological response with currently available systemic therapies is minimal, except in highly selected patients—that is, those with tumors expressing high levels of somatostatin receptors treated with peptide receptor radionuclide therapy,⁵ in which the ORR is only 18%. By contrast, we report an ORR of 16.4% in our unselected cohort of patients with GI-NETs, indicating a substantial reduction in tumor burden. The 44.2% centrally confirmed ORR in the panNET group compares favorably with other TAs (< 10%)⁶⁻⁸ and is slightly higher than the ORR provided by current chemotherapy regimens (28%-33%).¹³ Additionally, some initial phase II trials with combination therapies^{14,15} have shown promising activity in panNETs, with ORRs ranging from 31% to 41%, suggesting that these treatments may merit future development in this setting. Surufatinib has showed a slightly better ORR in panNETs (19%) and extrapancreatic NETs (10%); however, those trials were carried out in China and the treatment population in those studies differed significantly from the typical profile of this patient population in western countries, which tend to be more uniform and heavily pretreated compared with the Chinese patients included in the SANET trials.^{16,17} Finally, promising results from an international phase II/III clinical trial comparing axitinib plus octreotide versus octreotide alone in patients with advanced G1-2 extrapancreatic NETs were recently reported at the 2021 ASCO GI meeting, with an ORR of 17.5% and a trend toward better PFS (17.2 v 12.3 months) in the axitinib-treated group.¹⁸

The consistency of response observed in our panNET cohort in terms of the partial response rate and tumor shrinkage suggests that lenvatinib is an effective cytoreductive therapy, a finding that is especially relevant given the absence of a standard treatment in these patients.¹⁹ Although the proportion of patients with a confirmed

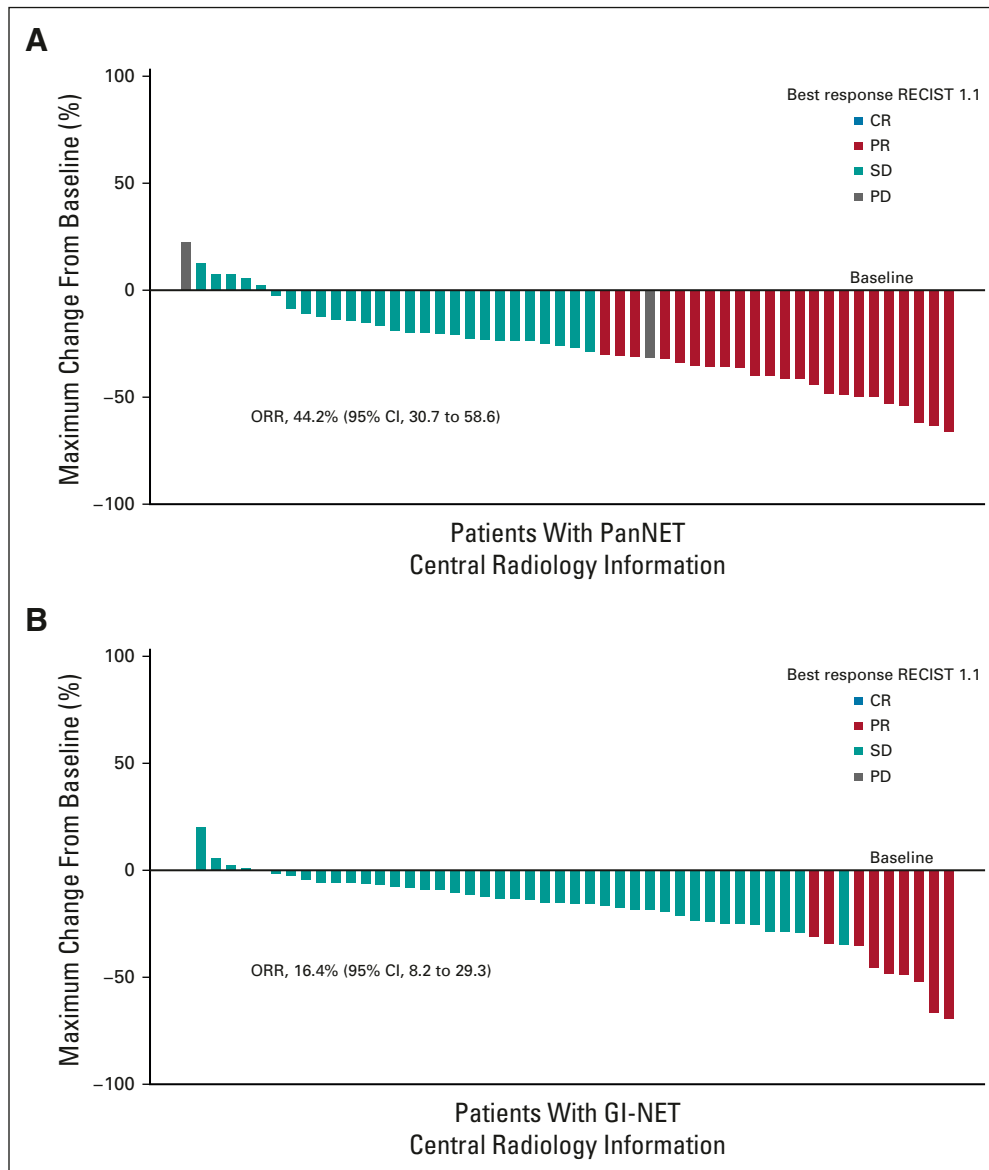


FIG 1. ORRs by primary tumor site: (A) panNETs, and (B) GI-NETs. CR, complete response; GI-NET, GI neuroendocrine tumor; ORR, overall response rate; panNET, pancreatic neuroendocrine tumor; PD, progressive disease; PR, partial response; SD, stable disease.

radiological response in our study was high (29.9% overall), the DoR—19.9 and 33.9 months in the panNETs and GI-NETs groups, respectively—together with the good PFS outcomes (28 and 37 months, respectively)—underscores the importance of tumor reduction in patients with advanced NETs. This finding suggests that DoR, a measure that has not been previously evaluated as a primary treatment aim in this clinical setting, should be reconsidered as a highly relevant treatment end point.

Treatment-related resistance is common in patients treated with VEGF inhibitors, with hyperactivation of FGFR signaling considered a hallmark of NETs that have become resistant to anti-VEGF therapies.²⁰ Given the demonstrated capacity of lenvatinib to inhibit VEGFR1-3 and FGFR1-4,²¹

the available data suggest that this drug may increase the efficacy of other MKIs and could even revert primary and acquired resistance.⁹ The results in the panNETs cohort in the present trial appear to support this hypothesis. In addition to the strong ORR (44%), we also observed highly promising outcomes in both PFS and OS (15.7 and 31 months, respectively) in this heavily pretreated population. To the best of our knowledge, lenvatinib is the first drug to demonstrate activity in patients with advanced GEP-NETs with documented disease progression after administration of other TAs, including MKIs.

In our full cohort, the median PFS was 15.7 months (95% CI, 14.1 to 19.5), with both diagnostic groups presenting similar PFS outcomes (Fig 3). These results compare

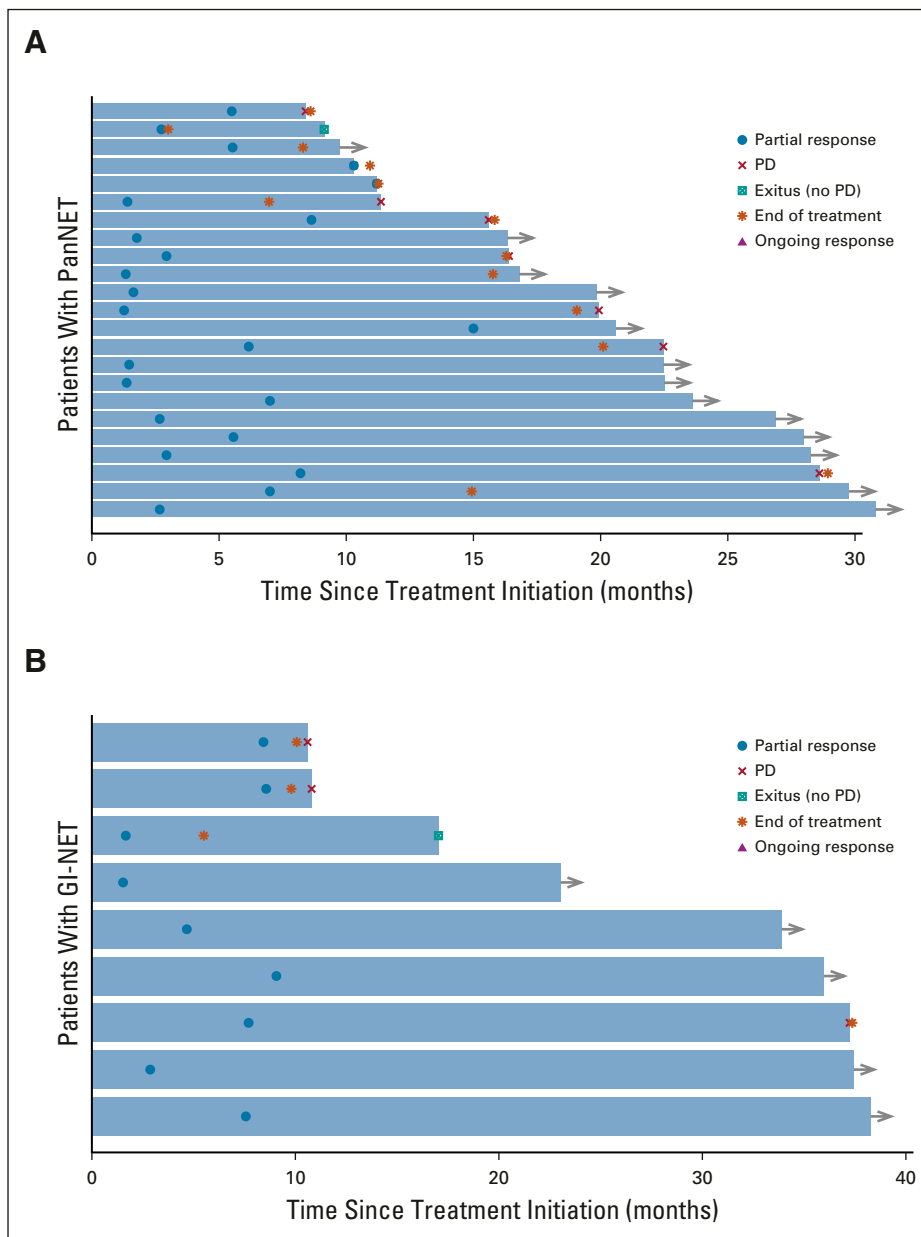


FIG 2. Duration of response in patients with confirmed radiological response by primary tumor site: (A) patients with pancreatic NETs ($n = 23$) and (B) patients with GI-NETs ($n = 9$). GI-NET, GI neuroendocrine tumor; panNET, pancreatic neuroendocrine tumor; PD, progressive disease.

favorably with the PFS outcomes reported in phase III trials, including the three trials that evaluated multitargeted TKIs (sunitinib and surufatinib)^{6,16,17,22} and the RADIANT trials with everolimus.^{7,23} Clearly, PFS outcomes depend not only on the treatment but also on the patient profile, including the disease progression rate, as evidenced by the longer PFS observed in the CLARINET and NETTER-1 trials, both of which included patients with better prognostic factors. In this regard, there is a clear need to design and conduct clinical trials to evaluate the efficacy of treatment strategies in patients with more aggressive tumors and in pretreated patients in whom treatment options are limited.

Several drugs have been evaluated to determine their capacity to revert treatment-resistance to previous molecular-targeted therapies in patients with advanced NETs, but with disappointing results to date. In a non-multikinase pretreated population, PFS in patients treated with pazopanib was similar to sunitinib (11 months), but with an ORR of only 2.1%.²⁴ Although better partial response rates have been reported in patients with panNETs (21.9%), most of the patients in that trial had not received previous treatment with a TA.²⁵ Previously, we reported the results of a phase II trial of pazopanib in advanced NETs.²⁶ Although the findings of that study suggested some

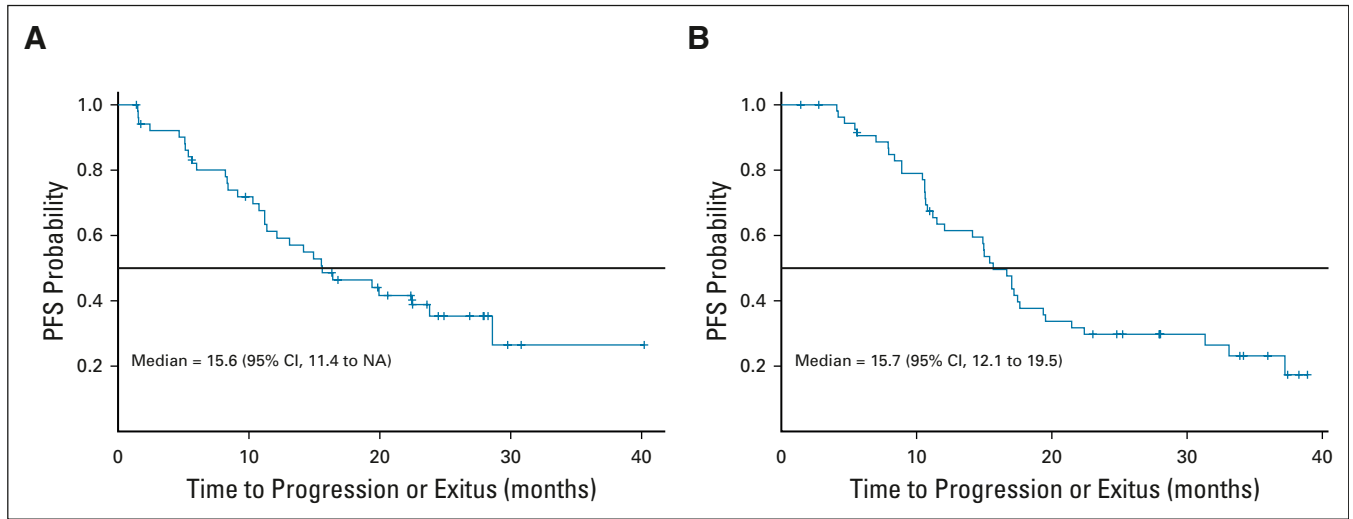


FIG 3. PFS by primary tumor site: (A) patients with panNET; and (B) patients with GI-NET. GI-NET, GI neuroendocrine tumor; panNET, pancreatic neuroendocrine tumor; PFS, progression-free survival.

reversion of resistance to previous TAs, the ORR and PFS were both substantially lower than the values achieved with lenvatinib in the present trial. Cabozantinib has also been investigated in this setting in a phase II trial, in which 15% of patients with panNETs and GI-NETs showed a tumor response.²⁷ The phase III trial with cabozantinib in

pancreatic and extrapancreatic NETs (ClinicalTrials.gov identifier: [NCT03375320](https://clinicaltrials.gov/ct2/show/study/NCT03375320)) is ongoing. Finally, positive results for surufatinib were recently reported in two phase III studies conducted in China. One of those trials was performed to evaluate surufatinib in patients with panNETs, but only 4% of patients were previously treated with

TABLE 3. Most Prevalent Adverse Events According to Toxicity Grade (Common Terminology Criteria for Adverse Events, v.4.03)

Event	PanNETs (n = 55)		GI-NETs (n = 56)	
	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4
Asthenia	28 (50.9)	3 (5.5)	22 (39.3)	9 (16.1)
Hypertension	28 (50.9)	12 (21.8)	30 (53.6)	13 (23.2)
Diarrhea	25 (45.5)	4 (7.3)	28 (50)	8 (14.3)
Dysphonia	22 (40.0)	0 (0)	17 (30.4)	0 (0)
Hypothyroidism	22 (40.0)	0 (0)	18 (32.1)	0 (0)
Nausea	21 (38.2)	1 (1.8)	14 (25.0)	0 (0)
Mucosal inflammation	17 (30.9)	2 (3.6)	11 (19.6)	0 (0)
Pyrexia	16 (29.1)	0 (0)	5 (8.9)	1 (1.8)
Headache	15 (27.3)	0 (0)	14 (25.0)	0 (0)
Abdominal pain	14 (25.5)	4 (7.3)	21 (37.5)	2 (3.6)
Vomiting	14 (25.5)	5 (9.1)	9 (16.1)	1 (1.8)
Palmar-plantar erythrodysesthesia syndrome	13 (23.6)	2 (3.6)	9 (16.1)	2 (3.6)
Arthralgia	12 (21.8)	0 (0)	6 (10.7)	0 (0)
Constipation	12 (21.8)	0 (0)	7 (12.5)	1 (1.8)
Decreased appetite	12 (21.8)	0 (0)	19 (33.9)	2 (3.6)
Proteinuria	11 (20.0)	0 (0)	9 (16.1)	2 (3.6)
Rash	9 (16.4)	1 (1.8)	7 (12.5)	0 (0)
Abdominal pain upper	8 (14.6)	0 (0)	4 (7.1)	0 (0)
Alkaline phosphatase increased	8 (14.6)	0 (0)	1 (1.8)	0 (0)
Epistaxis	8 (14.6)	0 (0)	2 (3.6)	1 (1.8)

NOTE. Data are presented as No. (%).

Abbreviations: GI-NET, GI neuroendocrine tumor; panNET, pancreatic neuroendocrine tumor.

sunitinib. The centrally assessed ORR was 14%. Similarly, in the extrapancreatic cohort, most patients had been pretreated with chemotherapy (only 34% of patients with SSAs), with a centrally assessed ORR of 8%. Several trials have been planned in western countries to evaluate the role of surufatinib in patients with advanced NETs and different pretreatment backgrounds (ClinicalTrials.gov identifier: [NCT04579679](https://clinicaltrials.gov/ct2/show/study/NCT04579679)).

In terms of safety outcomes with lenvatinib, our findings are consistent with previous reports.²⁸ Dose reductions or interruptions were required in most (> 90%) patients, but dose density was maintained in 20 mg QD and definitive treatment discontinuation was necessary for 14% of patients, similar to other targeted therapies in the same setting.^{7,29}

The main limitation of this phase II trial is the lack of randomization comparing lenvatinib with an alternative

treatment option. By contrast, the independent central review is an important strength that should be underscored. Finally, this is the first trial to evidence antitumor activity in patients with advanced GEP-NETs with progressive disease after treatment with other TAs, including MKIs in the same drug family.

In summary, lenvatinib was associated with clinically meaningful activity in patients with advanced and heavily pretreated GEP-NETs. Lenvatinib was well-tolerated, and the safety findings were consistent with previous experience in other cancers. Crucially, this study provides evidence, for the first time, of the efficacy of an MKI in patients with disease progression following treatment with other TAs. These findings support the potential for lenvatinib to produce significant tumor shrinkage and to revert drug resistance data that strongly suggest that lenvatinib merits further development in this setting.

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PRIOR PRESENTATION

Presented in part as oral and poster presentations at the ESMO Congress, Munich, Germany, October 19-23, 2018; ENETS Annual Conference, Barcelona, Spain, March 6-8, 2019; and the ASCO Annual Meeting, Chicago, IL, May 31-June 4, 2019.

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CLINICAL TRIAL INFORMATION

[NCT02678780](https://clinicaltrials.gov/ct2/show/study/NCT02678780)

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI <https://doi.org/10.1200/JCO.20.03368>.

DATA SHARING STATEMENT

This was an investigator-initiated study by the multidisciplinary Spanish Task Force for Neuroendocrine and Endocrine Tumors (GETNE), who owns all study data. Deidentified participant data supporting the results reported in this article will be made available on a case-by-case basis. For data access, requestors should submit a proposal to the corresponding author. All proposals will be reviewed by GETNE.

AUTHOR CONTRIBUTIONS

Conception and design: Jaume Capdevila

Provision of study materials or patients: All authors

Collection and assembly of data: All authors

Data analysis and interpretation: Jaume Capdevila, Nicola Fazio, Juan W. Valle, Salvatore Tafuto, Enrique Grande, Rocio García-Carbonero, Xavier Merino, Toni Ibrahim

Manuscript writing: All authors

Final approval of manuscript: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**Lenvatinib in Patients With Advanced Grade 1/2 Pancreatic and Gastrointestinal Neuroendocrine Tumors: Results of the Phase II TALENT Trial (GETNE1509)**

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