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**Citation**

Wagner, A. J., Kindler, H., Gelderblom, H., Schoffski, P., Bauer, S., Hohenberger, P., ... Rutkowski, P. (2017). A phase II study of a human anti-PDGFR alpha monoclonal antibody (olaratumab, IMC-3G3) in previously treated patients with metastatic gastrointestinal stromal tumors. *Annals Of Oncology*, 28(3), 541-546. doi:10.1093/annonc/mdw659

Version: Not Applicable (or Unknown)  
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**Note:** To cite this publication please use the final published version (if applicable).

## ORIGINAL ARTICLE

# A phase II study of a human anti-PDGFR $\alpha$ monoclonal antibody (olaratumab, IMC-3G3) in previously treated patients with metastatic gastrointestinal stromal tumors

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**Background:** This study evaluated tumor response to olaratumab (an anti-PDGFR $\alpha$  monoclonal antibody) in previously treated patients with metastatic gastrointestinal stromal tumor (GIST) with or without PDGFR $\alpha$  mutations (cohorts 1 and 2, respectively).

**Patients and methods:** Patients received olaratumab 20 mg/kg intravenously every 14 days until disease progression, death, or intolerable toxicity occurred. Outcome measures were 12-week tumor response, progression-free survival (PFS), overall survival (OS), and safety.

**Results:** Of 30 patients enrolled, 21 patients received  $\geq 1$  dose of olaratumab. In the evaluable population (cohort 1,  $n = 6$ ; cohort 2,  $n = 14$ ), no complete response (CR) or partial response (PR) was observed. Stable disease (SD) was observed in 3 patients (50.0%) in cohort 1 and 2 patients (14.3%) in cohort 2. Progressive disease (PD) was observed in 3 patients (50.0%) in cohort 1 and 12 patients (85.7%) in cohort 2. The 12-week clinical benefit rate (CR + PR + SD) (90% CI) was 50.0% (15.3–84.7%) in cohort 1 and 14.3% (2.6–38.5%) in cohort 2. SD lasted beyond 12 weeks in 5 patients (cohort 1,  $n = 3$ ; cohort 2,  $n = 2$ ). Median PFS (90% CI) was 32.1 (5.0–35.9) weeks in cohort 1 and 6.1 (5.7–6.3) weeks in cohort 2. Median OS was not reached in cohort 1 and was 24.9 (14.4–49.1) weeks in cohort 2. All patients in cohort 1 and 9 (64.3%) in cohort 2 experienced an olaratumab-related adverse event (AE), most commonly fatigue (38.1%), nausea (19.0%), and peripheral edema (14.3%). Two grade  $\geq 3$  olaratumab-related events were reported (cohort 1, syncope; cohort 2, hypertension).

**Conclusions:** Olaratumab had an acceptable AE profile in patients with GIST. While there was no apparent effect on PFS in patients without PDGFR $\alpha$  mutations, patients with PDGFR $\alpha$ -mutant GIST (all with D842V mutations) treated with olaratumab had longer disease control compared with historical data for this genotype.

**ClinicalTrials.gov Identifier:** NCT01316263.

**Key words:** gastrointestinal stromal tumor, platelet-derived growth factor receptor  $\alpha$ , IMC-3G3, mutation, monoclonal antibody

## Introduction

Most gastrointestinal stromal tumors (GIST) are driven by activating mutations in the KIT tyrosine kinase receptor. These also confer sensitivity to the small molecule kinase inhibitors imatinib, sunitinib, and regorafenib. A small proportion (5–10%) of metastatic GIST have activating mutations in the related kinase platelet-derived growth factor receptor  $\alpha$  (PDGFR $\alpha$ ). Although most GIST are initially sensitive to first-line imatinib, some never respond (primary resistance) and most ultimately progress on therapy as a result of additional mutations in the KIT kinase domain or activation loop (secondary resistance). Most tumors that harbor PDGFR $\alpha$  mutations are primarily resistant since the most common variant, D842V [1–3], is not inhibited by approved therapies. The median progression-free survival (PFS) of unselected patients with GIST on placebo is <6 weeks [4, 5]; the PFS for patients with PDGFR $\alpha$  mutations has not been prospectively defined but was reported to be 2.8 months in a retrospective study of patients with tumors with D842V mutations [6]. New therapies are needed for patients with metastatic GIST resistant to tyrosine kinase inhibitors (TKIs) [7, 8].

Olaratumab (LY3012207; formerly IMC-3G3) is an immunoglobulin G, subclass 1 (IgG1) monoclonal antibody that binds to PDGFR $\alpha$  with high affinity, blocks ligand-induced cell mitogenesis, and inhibits receptor autophosphorylation and ligand-induced phosphorylation of the downstream signaling molecules protein kinase B (Akt) and mitogen-activated protein kinase [9]. In preclinical studies, olaratumab induced growth inhibition in sarcoma xenograft models and led to reduced levels of total and phosphorylated PDGFR $\alpha$  in glioblastoma xenografts [9]; PDGFR $\alpha$ -mutant GIST models are not available for preclinical testing. Olaratumab also promotes internalization/downmodulation of surface PDGFR and thus may be active in the context of a growth-driving mutation affecting the internal kinase domain [10]. Furthermore, KIT-mutant GIST also express PDGFR $\alpha$ , which may in turn provide a target for antibody-directed therapy and a potential therapeutic approach to tumors resistant to small-molecule kinase inhibitors.

The primary objective of this phase II study was to evaluate the clinical benefit of olaratumab in terms of tumor response at 12 weeks per Response Evaluation Criteria In Solid Tumors (RECIST) 1.1 in two separate cohorts representing molecularly distinct subsets of previously treated patients with GIST (i.e. tumors with or without PDGFR $\alpha$  mutations). Secondary objectives were to evaluate PFS, radiographic objective response rate (ORR) and disease control rate (DCR) per RECIST 1.1, overall survival (OS), and safety.

## Methods

This study (ClinicalTrials.gov NCT01316263) was performed in accordance with applicable laws and regulations, good clinical practices, and the Declaration of Helsinki. The protocol and consent forms were reviewed and approved by each study site's institutional review board or independent ethics committee. Written informed consent was obtained from each subject before participation in the study.

## Subjects

Eligible subjects were  $\geq 18$  years old with histologically or cytologically confirmed, unresectable and/or metastatic GIST with investigator-assessed

objective progression after, or intolerance to, treatment with at least both imatinib and sunitinib; measurable disease (RECIST 1.1); and Eastern Cooperative Oncology Group performance status 0–2.

## Study design and procedures

This was an open-label, 2-stage, multicenter, multinational phase II trial in which patients received olaratumab 20 mg/kg by intravenous infusion every 14 days (1 cycle) based on the results of a phase I study in patients with advanced solid tumors [11]. The drug was supplied in single-use 500 mg/50 ml vials containing 10 mg/ml of olaratumab in sterile, preservative-free histidine buffer (10 mM histidine, 100 mM glycine, 50 mM sodium chloride, 75 mM mannitol, and 0.02% polysorbate-20, pH 5.5).

Patients were assessed for tumor response according to RECIST 1.1 every 6 weeks. All patients received treatment until radiographic documentation of disease progression, death, or intolerable toxicity occurred or until other withdrawal criteria were met.

This study utilized a Simon 2-stage optimal design and two cohorts: patients with PDGFR $\alpha$ -mutant GIST (cohort 1) and patients with GIST without a PDGFR $\alpha$  mutation (cohort 2). Tumor genotype was determined by the local institutions and centrally reviewed for cohort assignment. The statistical design assumed for each cohort improvement in the proportion of patients with a response of stable disease (SD) or better at 12 weeks from 35% to 59%, a type I error of 0.1, and a power of 90%. The plan was to enroll eight evaluable patients in each cohort during stage I. If at least three patients in a cohort had SD for at least 12 weeks, then the plan was to enroll an additional 24 patients during stage II to a total of at least 32 evaluable patients in each cohort (i.e. a total maximal sample size of 64).

## Efficacy analysis

The clinical benefit rate (CBR) (CR + PR + SD) at 12 weeks (primary efficacy endpoint) and PFS, OS, ORR, and DCR were analyzed statistically. The CBR at 12 weeks and its 90% exact confidence interval (CI) were estimated for each cohort.

The Kaplan–Meier method was used to estimate the median PFS time and PFS rate at 12 weeks and 90% CIs. Analysis of PFS was performed according to prespecified rules for censoring outcomes of disease progression and death.

Median overall survival was estimated by the Kaplan–Meier method and a 90% CI was provided. The number of patients achieving a best overall response of partial or complete response (PR + CR) according to RECIST 1.1 was divided by the total number of patients treated to yield the ORR and corresponding 90% CI. The number of patients achieving a best overall response of CR, PR, or SD was divided by the total number of patients treated to yield the DCR and 90% CI.

The stage-I stopping rule for efficacy was based on the evaluable population (i.e. all eligible patients who had received at least one dose of study drug and had adequate tumor assessment at 12 weeks, including any patients discontinuing early due to progressive disease or death). The primary efficacy endpoint was also analyzed for all patients included in the modified intent-to-treat (mITT) population (i.e. all patients who received any quantity of study drug). All other efficacy analyses were based on the mITT population.

## Safety analysis

Safety outcomes included adverse events (AEs), physical examinations, electrocardiograms (ECGs), and clinical/laboratory tests. Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 15.0, and graded using the National Cancer Institute–Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 4.0. Clinical laboratory toxicity was graded using NCI-CTCAE, version 4.0. Safety analyses were based on the safety population (i.e. all patients who received any quantity of study drug), which was identical to the mITT population.

**Table 1. Patient demographics and baseline characteristics (mITT population)**

	<b>Cohort 1 (PDGFR<math>\alpha</math> mutant) (N=7)</b>	<b>Cohort 2 (PDGFR<math>\alpha</math> wild-type) (N=14)</b>	<b>Total (N=21)</b>
Sex, n (%)			
Male	5 (71.4)	7 (50.0)	12 (57.1)
Female	2 (28.6)	7 (50.0)	9 (42.9)
Race, n (%)			
White	7 (100)	14 (100)	21 (100)
Ethnicity, n (%)			
Not Hispanic or Latino	7 (100)	14 (100)	21 (100)
Age, years			
Median (range)	67 (51–74)	49 (33–61)	57 (33–74)
KIT mutation present <sup>a</sup>	0	11 (78.6)	11 (52.4)
Prior TKI therapy, n (%)			
Dasatinib	3 (42.9)	0	3 (14.3)
Imatinib	7 (100)	14 (100)	21 (100)
Nilotinib	1 (14.3)	7 (50.0)	8 (38.1)
Sorafenib	3 (42.9)	5 (35.7)	8 (38.1)
Sunitinib	7 (100)	14 (100)	21 (100)

mITT, modified intent-to-treat; PDGFR $\alpha$ , platelet-derived growth factor receptor  $\alpha$ ; TKI, tyrosine kinase inhibitor.

<sup>a</sup>As confirmed by central mutation analysis.

## Results

### Demographics and disposition

The study was conducted at 11 sites in 6 countries. Thirty patients were enrolled between 29 August 2011 and 13 November 2012. Of these, eight patients were considered screen failures and did not receive olaratumab, and one patient died of complications of GIST (retroperitoneal hemorrhage, hepatic failure, and sepsis) before beginning study treatment. The remaining 21 patients received at least one dose of olaratumab (cohort 1,  $N=7$ ; cohort 2,  $N=14$ ). All patients in cohort 1 had GIST with PDGFR $\alpha$  D842V mutations. Cohort 1 enrollment was stopped before the planned treatment of eight patients because of slow accrual and strategic reasons. Reasons for study discontinuation included radiographically documented progressive disease (PD) (18 patients, 85.7%); symptomatic deterioration/clinical progression (2 patients, 9.5%); and death (1 patient, 4.8%). No patients discontinued study treatment due to AEs. All 21 patients were included in the mITT and safety populations. Twenty patients were included in the evaluable population (cohort 1,  $N=6$ ; cohort 2,  $N=14$ ); one patient in cohort 1 did not have restaging studies performed at 12 weeks and was excluded from the evaluable population. The study was terminated by the Sponsor earlier than planned for strategic reasons.

Key baseline demographics are presented in Table 1.

### Efficacy

**Primary efficacy.** No responses were observed in the evaluable population (Table 2). SD at 12 weeks was observed in three

**Table 2. Clinical benefit rate at 12 weeks (evaluable population)**

	<b>Cohort 1 (PDGFR<math>\alpha</math> mutant) (N=6)</b>	<b>Cohort 2 (PDGFR<math>\alpha</math> wild-type) (N=14)</b>
Tumor response at 12 weeks, n (%)		
CR	0	0
PR	0	0
SD	3 (50.0)	2 (14.3)
PD	3 (50.0)	12 (85.7)
Not evaluable	0	0
Clinical benefit rate (CR+PR+SD) n (%)	3 (50.0)	2 (14.3)
90% CI	15.3, 84.7	2.6, 38.5

CI, confidence interval; CR, complete response; PD, progressive disease; PDGFR $\alpha$ , platelet-derived growth factor receptor  $\alpha$ ; PR, partial response; SD, stable disease.

**Table 3. Progression-free survival estimated by Kaplan–Meier method (mITT population)<sup>a</sup>**

	<b>Cohort 1 (PDGFR<math>\alpha</math> mutant) (N=7)</b>	<b>Cohort 2 (PDGFR<math>\alpha</math> wild-type) (N=14)</b>
Median (90% CI), weeks	32.1 (5.0–35.9)	6.1 (5.7–6.3)
12-week PFS rate (90% CI), %	51.4 (17.0–77.9)	14.3 (3.4–32.7)
24-week PFS rate (90% CI), %	51.4 (17.0–77.9)	NE

<sup>a</sup>This analysis censored data from two patients in cohort 1 who had no documented progressive disease during the study.

CI, confidence interval; mITT, modified intent-to-treat; NE, not evaluable; PDGFR $\alpha$ , platelet-derived growth factor receptor  $\alpha$ ; PFS, progression-free survival.

patients (50.0%) in cohort 1 and two patients (14.3%) in cohort 2. PD in the first 12 weeks was observed in 3 patients (50.0%) in cohort 1 and 12 patients (85.7%) in cohort 2. The CBR at 12 weeks was 50.0% (90% CI, 15.3–84.7%) in cohort 1 and 14.3% (90% CI, 2.6–38.5%) in cohort 2. SD was maintained beyond 12 weeks in five patients overall, including three patients in cohort 1 (32.1, 17.9, and 35.9 weeks) and two patients in cohort 2 (17.9 and 14.4 weeks).

Results in the mITT population were similar.

**Secondary efficacy.** All secondary efficacy analyses were based on the mITT population.

**Progression-free survival:** Median PFS was 32.1 weeks (90% CI, 5.0–35.9 weeks) in cohort 1 and 6.1 weeks (90% CI, 5.7–6.3 weeks) in cohort 2 (Table 3). In cohort 1, the 12- and 24-week PFS rates were both 51.4% (90% CI, 17.0–77.9%). In cohort 2, the 12-week

**Table 4. Summary of treatment-emergent adverse events (safety population)**

Patients with event, n (%)	Cohort 1 (PDGFR $\alpha$ mutant) (N=7)	Cohort 2 (PDGFR $\alpha$ wild-type) (N=14)	Overall (N=21)
AE	7 (100)	13 (92.9)	20 (95.2)
Treatment-related	7 (100)	9 (64.3)	16 (76.2)
Grade $\geq 3$ AE	2 (28.6)	6 (42.9)	8 (38.1)
Treatment-related	1 (14.3)	1 (7.1)	2 (9.5)
SAE	2 (28.6)	3 (21.4)	5 (23.8)
Treatment-related	1 (14.3)	0	1 (4.8)

AE, adverse event; PDGFR $\alpha$ , platelet-derived growth factor receptor  $\alpha$ ; SAE, serious adverse event.

PFS rate was 14.3% (90% CI, 3.4–32.7%); the 24-week PFS rate was not evaluable.

**Overall survival:** In cohort 1, median OS was not reached, and 6-month survival was 71.4% (90% CI, 33.9–90.1%). In cohort 2, median OS was 24.9 weeks (90% CI, 14.4–49.1 weeks), and 6-month survival was 50.0% (90% CI, 27.1–69.2%).

**Overall response rate:** In the mITT population, no CR or PR was observed. As best response, SD was observed in five patients (71.4%) in cohort 1 and four patients (28.6%) in cohort 2. PD was observed in 2 patients (28.6%) in cohort 1 and 10 patients (71.4%) in cohort 2.

**Disease control rate:** The DCR was 71.4% (90% CI, 34.1–94.7%) in cohort 1 and 28.6% (90% CI, 10.4–54.0%) in cohort 2.

## Safety

**Adverse events.** All patients in cohort 1 and 13 patients (92.9%) in cohort 2 experienced at least 1 treatment-emergent AE (TEAE). The most commonly reported TEAEs overall were fatigue (42.9%); abdominal pain (28.6%); nausea (23.8%); constipation, peripheral edema, and headache (19.0% each); decreased appetite and infusion-related reaction (14.3% each); and cough, abdominal discomfort, and decreased weight (9.5% each).

Overall, 16 patients (76.2%) experienced at least 1 olaratumab-related TEAE (Table 4), and most of these events were mild or moderate in severity. The most commonly reported olaratumab-related TEAEs were fatigue (38.1%); nausea and headache (19.0% each); infusion-related reaction and peripheral edema (14.3% each); and blood alkaline phosphatase increased, constipation, decreased appetite, dyspnea, hypertension, pyrexia, and rash (9.5% each) (Table 5). Two patients experienced a grade  $\geq 3$  olaratumab-related event (grade 3 syncope in cohort 1 and grade 3 hypertension in cohort 2). Three patients experienced infusion-related reactions (all grade 2 or less) in cohort 2; none did in cohort 1.

**Deaths and serious adverse events.** In cohort 1, no patient died while on olaratumab therapy or within 30 days of last dose. In

**Table 5. Summary of olaratumab-related treatment-emergent adverse events occurring in  $\geq 2$  patients overall (safety population)**

Preferred/consolidated term (%)	Cohort 1 (PDGFR $\alpha$ mutant) (N=7)	Cohort 2 (PDGFR $\alpha$ wild-type) (N=14)	Overall (N=21)
Any olaratumab-related adverse event	7 (100)	9 (64.3)	16 (76.2)
Fatigue <sup>a</sup>	4 (57.1)	4 (28.6)	8 (38.1)
Nausea	1 (14.3)	3 (21.4)	4 (19.0)
Headache	0	4 (28.6)	4 (19.0)
Infusion-related reaction	0	3 (21.4)	3 (14.3)
Peripheral edema	1 (14.3)	2 (14.3)	3 (14.3)
Blood alkaline phosphatase increased	1 (14.3)	1 (7.1)	2 (9.5)
Constipation	2 (28.6)	0	2 (9.5)
Decreased appetite	1 (14.3)	1 (7.1)	2 (9.5)
Dyspnea	1 (14.3)	1 (7.1)	2 (9.5)
Hypertension <sup>b</sup>	1 (14.3)	1 (7.1)	2 (9.5)
Pyrexia	1 (14.3)	1 (7.1)	2 (9.5)
Rash <sup>c</sup>	2 (28.6)	0	2 (9.5)

<sup>a</sup>Consolidated term including fatigue and asthenia.

<sup>b</sup>Consolidated term including hypertension and blood pressure increased.

<sup>c</sup>Consolidated term including rash, dermatitis, dermatitis acneiform, rash macular, and rash pruritic.

AE, adverse event; SAE, serious adverse event.

cohort 2, two patients died within 30 days of last olaratumab dose due to disease progression.

Two patients in cohort 1 and three patients in cohort 2 experienced at least one treatment-emergent serious adverse event (SAE). The only SAE reported in both cohorts was abdominal pain. One patient in cohort 1 experienced an olaratumab-related SAE of  $\geq$  grade 3 syncope. Although no definite cause was determined, the clinical workup suggested that the syncope was likely due to orthostatic hypotension.

## Discussion

Most GIST are driven by activating mutations in the tyrosine kinase receptors KIT or PDGFR $\alpha$  and while most GIST are initially sensitive to inhibitors, resistance ultimately develops, or some tumors, notably those harboring PDGFR $\alpha$  D842V mutations, are inherently resistant to all approved therapies. In this study, we explored the effects of the anti-PDGFR $\alpha$  antibody olaratumab in patients with advanced GIST. This approach has the potential to provide antitumor activity by targeting neoplastic or stromal cells that may be dependent on PDGFR signaling, either through inhibition of ligand-induced receptor activation or possibly through receptor internalization and downmodulation. Although olaratumab is capable of binding Fc $\gamma$  receptors by virtue of its human IgG1 Fc backbone, its binding to cell-associated PDGFR $\alpha$  is unlikely to elicit an antibody-dependent cellular cytotoxicity (ADCC) response, as preclinical studies did not detect ADCC activity on tumor cells expressing high PDGFR $\alpha$  (unpublished observations).



This study was conducted to determine the efficacy of single-agent olaratumab in two molecularly distinct subsets of previously treated patients with refractory unresectable and/or metastatic GIST. Cohort 1 included 7 patients with GIST harboring D842V PDGFR $\alpha$  mutations; cohort 2 included 14 patients with GIST not harboring PDGFR $\alpha$  mutations, and 11 of these patients had tumors with KIT mutations. The primary outcome measure of CBR was evaluated at 12 weeks. In patients with PDGFR $\alpha$ -mutant tumors (cohort 1), the PFS rates at 12 and 24 weeks were 51.4%; in patients with tumors without PDGFR $\alpha$  mutations (cohort 2), the PFS rate at 12 weeks was 14.3%. All patients in cohort 2 came off study by 24 weeks, most because of disease progression. Median PFS was 32.1 weeks for cohort 1 and 6.1 weeks for cohort 2. Median OS was not reached for cohort 1 and was 24.9 weeks for cohort 2.

The outcomes in cohorts 1 and 2 differed strikingly. Despite the small sample numbers, this difference is unlikely to have been observed by chance and is more likely due to a treatment effect or to the different biology of the two patient cohorts. This outcome may be a direct effect of olaratumab on the tumors that are dependent on constitutive PDGFR $\alpha$  signaling, or potentially reflect differential effects of olaratumab on tumor-associated stroma in PDGFR $\alpha$  wild-type and mutant GIST subtypes. Although no objective disease responses were observed, the disease stabilization observed over 24 weeks in patients with D842V PDGFR $\alpha$ -mutant GIST, a highly refractory population having no standard therapeutic options, is of interest. There is limited published evidence on the natural disease course for this rare subtype of GIST. A retrospective study of 32 patients with metastatic GIST with PDGFR $\alpha$  D842V mutations reported a median PFS of 2.8 months and median OS of 14.7 months [6]. A registry-based report demonstrated a significantly lower risk of recurrence of 18 resected tumors with PDGFR $\alpha$  mutations; while this may be accounted for in part by an indolent behavior, it may also reflect a lower metastatic potential associated with this genotype [12]. Our present observation of a median PFS of 32.1 weeks and an unreached median OS is strikingly different, although the small sample size, differing study designs, and potential for variability in patient selection limit the ability to reach definitive conclusions.

PDGFR $\alpha$ -mutant GIST is rare, and there is no known effective therapy for the most common mutation, D842V. Despite being conducted at 11 sites in six countries, this study highlights the challenges in accruing enough patients to evaluate the efficacy of a novel treatment. PDGFR-mutant GIST reportedly accounts for >10% of primary tumors; however, patients whose tumors have these mutations constitute <5% of enrollment in typical studies of advanced disease [13], which suggests a lower prevalence and risk of recurrence. At the time of this study, another clinical trial in patients with PDGFR $\alpha$ -mutant GIST (ClinicalTrials.gov NCT01243346) was ongoing, further limiting the available patient population. Although markedly prolonged disease control compared with historical data was achieved in patients with D842V PDGFR $\alpha$ -mutant GIST, this observation could have been strengthened by the inclusion of additional patients. Unfortunately, enrollment challenges and strategic considerations led to the decision to stop the study earlier than initially planned.

The present study is notable for having been enriched for patients with PDGFR $\alpha$ -mutant tumors, thereby allowing the study of PDGFR $\alpha$ -mutant patients in one dedicated trial arm. In other

reports of outcomes of patients with GIST, PDGFR $\alpha$ -mutant tumors were typically included in 'wild type' or non-KIT-mutant cohorts, or represented a small proportion of the total study population. For example, in a phase III study of first-line imatinib, only 10 of 377 tumors exhibited mutations in PDGFR $\alpha$  [14]. Three of the 10 patients bearing such tumors achieved PR, and 3 patients had SD of unreported duration. In a phase II study of second-line sunitinib for GIST, only 4 of 78 evaluable tumors contained PDGFR $\alpha$  mutations [1]. None of the 4 patients bearing such tumors achieved PR or disease control for at least 6 months on sunitinib. In the present study's cohort of 7 patients with PDGFR $\alpha$ -mutant tumors treated with olaratumab, median PFS exceeded 24 weeks. While the small sample sizes and interstudy heterogeneity limit the ability to reach definitive conclusions, these results provide interest for further study of PDGFR $\alpha$ -mutant GIST in a larger study.

In summary, olaratumab had an acceptable safety profile in patients with pretreated GIST. There was no apparent effect of olaratumab in patients with GIST without PDGFR $\alpha$  mutations. Patients with PDGFR $\alpha$ -mutant GIST treated with olaratumab had prolonged disease control compared with historical data for this genotype, although the small sample size of patients with this mutant subtype of GIST limited reaching any definitive conclusions.

## Acknowledgements

Jude Richard, ELS (INC Research, Austin, TX) assisted with the writing of this article.

## Funding

This work was supported by Eli Lilly and Company. No grant numbers apply.

## Disclosure

AJW has received clinical research support provided to the Dana-Farber Cancer Institute from Eli Lilly and Company, Novartis, and Pfizer, and has served as a member of an advisory board for Eli Lilly and Company. AQ and RLI are employees of Eli Lilly and Company. JN is an employee of Merck KGaA (formerly ImClone Medical). PRu has received honoraria from Novartis and Bayer and has served as a member of the advisory boards for these companies. All other authors have declared no conflicts of interest.

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