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A randomized, double-blind, placebo-controlled, Phase III study of pazopanib in patients with soft tissue sarcoma: results from the Japanese subgroup

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Abstract

Objective: This analysis of the Japanese subpopulation of the PALETTE Phase III, randomized, placebo-controlled study investigated efficacy and safety of pazopanib in patients with metastatic soft tissue sarcoma after failure of standard chemotherapy.

Methods: Patients were randomly assigned in a 2:1 ratio to receive either pazopanib 800 mg once daily or placebo, with no subsequent cross-over. Primary endpoint was progression-free survival. Secondary endpoints included overall survival and overall response rate. Efficacy analysis was by intent-to-treat. Safety was also investigated.

Results: Forty-seven patients received either pazopanib ($n = 31$) or placebo ($n = 16$). Median progression-free survival was 7.0 weeks (95% confidence interval: 4.0–11.7) for placebo and 24.7 weeks (95% confidence interval: 8.6–28.1) for pazopanib (hazard ratio = 0.41 [95% confidence interval: 0.19–0.90]; $P = 0.002$). Median overall survival was 14.9 months (95% confidence interval: 6.8—not calculable) for placebo and 15.4 months (95% confidence interval: 7.9–28.8) for pazopanib (hazard ratio = 0.87 [95% confidence interval: 0.41–1.83]; $P = 0.687$). More patients receiving pazopanib experienced best response of stable disease versus placebo. Adverse events were similar to the global population; those leading to dose reduction were more common and mean daily dose was lower in the Japanese population versus the global population (45 vs. 32% and 624.4 vs. 700.4 mg, respectively).

Conclusions: The efficacy and safety of pazopanib observed in the Japanese subpopulation of PALETTE were similar to those in the global population. Pazopanib is a new treatment option for Japanese patients with metastatic non-adipocytic soft tissue sarcoma after chemotherapy.

Clinical trial Registration number: NCT00753688; GSK study ID: VEG110727; http://www.gsk-clinicalstudyregister.com/study/VEG110727#ps.

Key words: randomized controlled trial, pazopanib, soft tissue sarcoma

Introduction

Until the introduction of orally available multi-tyrosine kinase inhibitors, doxorubicin and ifosfamide were the only approved treatments for soft tissue sarcoma (STS) in Japan. However, if these options failed, there was no universally agreed standard of care across all STS subtypes, which remained a highly unmet medical need.

Pazopanib is an orally available multi-tyrosine kinase inhibitor approved in Japan for the treatment of STS in September 2012 (1). Approval was based on results from the PALETTE study, a pivotal Phase III, randomized, double-blind, placebo-controlled study conducted in 72 institutions, across 13 countries, involving 369 patients (ClinicalTrials.gov: NCT00753688). PALETTE was designed to investigate the efficacy and safety of once-daily pazopanib 800 mg in patients with advanced STS who had failed prior chemotherapy (2).

In the PALETTE study, median progression-free survival (PFS; primary endpoint) was significantly longer for pazopanib compared with placebo {median 20.0 [95% confidence interval (CI): 17.9–21.3] weeks vs. 7.0 [95% CI: 4.4–8.1] weeks; hazard ratio [HR] = 0.35 [95% CI: 0.26–0.48]; $P < 0.001$} as determined by an independent radiologist. Overall survival (OS; the principal secondary endpoint) did not differ significantly between groups (median 12.5 months [95% CI: 10.6–14.8] for pazopanib, compared with median 10.7 months [95% CI: 8.7–12.8] for placebo; HR = 0.86 [95% CI: 0.67–1.11]; $P = 0.25$). The range of adverse events (AEs) reported was consistent with those observed for pazopanib in a previous study in patients with renal cell cancer, although a higher proportion of all grade AEs occurred in those with STS (2,3).

Here we report results from the Japanese patients enrolled in the PALETTE study.

Patients and methods

Full details of patients and methods for the PALETTE study, including full inclusion and exclusion criteria, have been published previously (2).

Study design

PALETTE was a randomized, double-blind, placebo-controlled, multicenter, Phase III study, conducted by GlaxoSmithKline in cooperation with the Soft Tissue and Bone Sarcoma Group of the European Organization for Research and Treatment of Cancer (EORTC) between October 2008 and February 2010.

Patients

Eligible patients were 18 years of age or older with metastatic STS and progressive disease according to Response Evaluation Criteria in Solid Tumors (RECIST, v1.0) (4) during the 6 months before the start of study drug (or 12 months for previous adjuvant treatment). Full details of inclusion and exclusion criteria for histology subtypes are included in the Supplementary material. Patients had a World Health Organization (WHO) performance status (PS) of 0 or 1, and had received ≥1 regimen containing anthracycline and ≤4 previous lines of systemic therapy for metastatic disease (≤2 lines of combination regimens). Patients were randomly assigned by an interactive voice randomization system in a 2:1 ratio in permuted blocks (with block sizes of six) to receive either pazopanib 800 mg or placebo, with no subsequent cross-over.

Study procedures and endpoints

Study drug was taken orally once daily. Disease and safety assessments were carried out at baseline, at Weeks 4, 8, 12 and then at 8-week intervals thereafter. Treatment was continued until disease progression according to RECIST criteria, unacceptable toxic effects, withdrawal of consent or death.

The primary endpoint was PFS. Secondary efficacy endpoints evaluated for the Japanese population were OS and overall response rate. Due to the limited number of patients, other secondary endpoints of the PALETTE study could not be evaluated in the Japanese population.

Safety endpoints examined included AEs, deaths and serious AEs (SAEs). Other safety investigations included AEs of special interest (liver chemistry abnormalities and AEs, hypertension, cardiac and vascular events, hemorrhagic events, thyroid function abnormalities and proteinuria), dose modification of the investigational product and permanent discontinuation of study treatment due to AEs. Laboratory values, vital signs, 12-lead electrocardiogram, left ventricular ejection fraction and WHO PS were also investigated.

All AEs occurring between the initial administration of the investigational product and 28 days after the last administration were investigated, regardless of their causal relationship with the investigational product. AEs were recorded according to the Common Terminology Criteria for Adverse Events v3.0 (5) and encoded with the Medical Dictionary for Regulatory Activities v13.1 (6).

Statistical analysis

Efficacy analyses were carried out on the intent-to-treat population, which included all patients who were randomized to treatment. All patients who received at least one dose of pazopanib were included in the safety population.

PFS was defined as time from randomization to either first disease progression (based on independent radiologic assessment of tumor measurements, according to RECIST v1.0 criteria) or death from any cause. Patients alive at the time of analysis were censored at the date of last disease assessment. OS was measured from the date of randomization to the date of death (from any cause). Overall response rate was defined as the percentage of patients who achieved either a confirmed complete response or partial response (according to RECIST v1.0) as their best confirmed response.

For analyses of PFS and OS, two-sided log-rank tests stratified for WHO PS and number of prior lines of systemic treatment for advanced disease were used, and tested at the significance level of 0.05. The Pike estimators (7) of the treatment HRs were provided, together with a 95% CI. For each treatment group, the Kaplan–Meier estimates for the median PFS and OS were presented. Greenwood's formula (8) was used to calculate the standard error of the estimates from the Kaplan–Meier curves.

The PALETTE study was powered to detect a 15% difference in PFS at 6 months for the global population, but was not powered for any subgroup analysis.

Results

Patients

Baseline demographics and characteristics of the Japanese subgroup are presented in Table 1. A total of 47 patients (pazopanib arm, $n = 31$; placebo arm, $n = 16$) were enrolled. The mean (standard deviation) daily dose of pazopanib was 624.4 mg (165.9); median treatment duration was 21.9 weeks for the pazopanib arm and 8.5 weeks for the placebo arm. All 16 patients in the placebo arm and 29 (94%) patients in the pazopanib arm had permanently discontinued the study treatment at the time of data cutoff (24 October 2011) (Fig. 1).

Efficacy

Median PFS as determined by independent radiologist was 7.0 weeks (95% CI: 4.0–11.7) in the placebo arm and 24.7 weeks (95%

Table 1. Demographics and baseline disease characteristics

	Japanese population		Global population	
	Placebo ($n = 16$)	Pazopanib ($n = 31$)	Placebo ($n = 123$)	Pazopanib ($n = 246$)
Mean (SD) age, years	50.1 (16.26)	53.5 (17.14)	51.7 (13.77)	54.0 (14.92)
Male, *n* (%)	7 (44)	18 (58)	54 (44)	99 (40)
Mean (SD) weight, kg	58.2 (9.68)	61.3 (18.10)	75.0 (17.23)	71.5 (16.88)
WHO PS, *n* (%)				
0	10 (63)	19 (61)	60 (49)	118 (48)
1	6 (38)	12 (39)	63 (51)	128 (52)
Histology, *n* (%)				
Leiomyosarcoma	5 (31)	8 (26)	49 (40)	109 (44)
Undifferentiated sarcoma (not otherwise specified)	0	4 (13)	5 (4)	15 (6)
Undifferentiated pleomorphic sarcoma	0	4 (13)	11 (9)	20 (8)
Alveolar soft part sarcoma	2 (13)	3 (10)	4 (3)	6 (2)
Solitary fibrous tumor	0	3 (10)	4 (3)	8 (3)
Synovial sarcoma	3 (19)	2 (6)	13 (11)	25 (10)
Epithelioid sarcoma	1 (6)	2 (6)	5 (4)	7 (3)
Desmoplastic small cell round tumor	0	1 (3)	1 (<1)	3 (1)
Extra-renal cell rhabdoid tumor	0	1 (3)	0	1 (<1)
Clear cell sarcoma	2 (13)	0	2 (2)	1 (<1)
Myxofibrosarcoma	2 (13)	0	6 (5)	8 (3)
Malignant peripheral nerve sheath tumor	1 (6)	0	4 (3)	8 (3)
Other soft tissue sarcoma histologies	0	3 (10)	10 (8)	22 (9)
Prior anti-cancer therapy, *n* (%)[a]				
Systemic therapy, any[b]	16 (100)	31 (100)	123 (100)	246 (100)
Systemic therapy, neo-adjuvant	7 (44)	10 (32)	19 (15)	31 (13)
Systemic therapy, adjuvant	6 (38)	7 (23)	26 (21)	43 (17)
Systemic therapy, advanced (first line)	12 (75)	25 (81)	110 (89)	232 (94)
Systemic therapy, advanced (second line)	5 (31)	7 (23)	67 (54)	132 (54)
Systemic therapy, advanced (3rd line)	1 (6)	1 (3)	28 (23)	51 (21)
Surgery	14 (88)	27 (87)	114 (93)	224 (91)
Radiotherapy	7 (44)	16 (52)	75 (61)	128 (52)
Other therapy[c]	6 (38)	3 (10)	15 (12)	11 (4)

PS, performance status; SD, standard deviation; WHO, World Health Organization.

[a]Each participant may have had more than one type of prior therapy.

[b]'Systemic therapy, any' includes systemic therapy for neo-adjuvant, adjuvant, maintenance and advanced disease.

[c]'Other therapy' includes major hormonal therapy, immunotherapy or other Investigational agent.

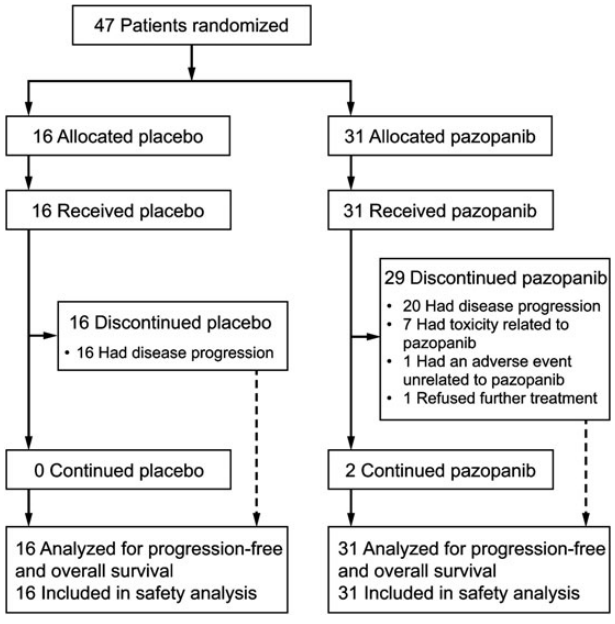

Figure 1. Patient disposition.

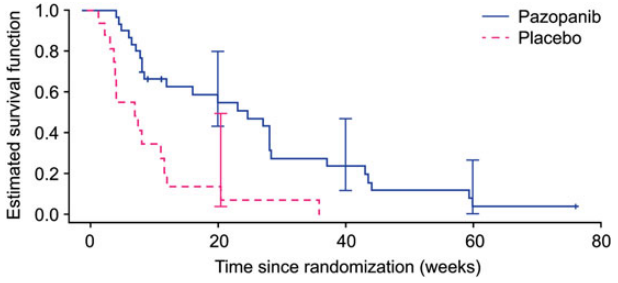

Figure 2. Progression-free survival (ITT population, assessed by independent radiologist). ITT, intent-to-treat.

CI: 8.6–28.1) in the pazopanib arm (HR = 0.41; 95% CI: 0.19–0.90; $P = 0.002$) (Fig. 2). Median OS was 14.9 months (95% CI: 6.8–not specified) in the placebo arm and 15.4 months (95% CI: 7.9–28.8) in the pazopanib arm (HR = 0.87 [95% CI: 0.41–1.83]; $P = 0.687$) (Fig. 3).

In the pazopanib arm, 1 (3%) patient by independent radiology and 5 (16%) patients by investigator assessment, experienced a confirmed partial response as their best objective response. No confirmed partial responses were reported in the placebo arm. No confirmed complete responses were reported in either arm. A greater proportion

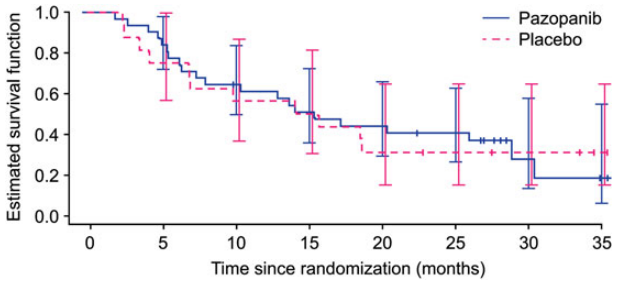

Figure 3. Overall survival (ITT population). ITT, intent-to-treat.

of patients in the pazopanib arm experienced a best response of stable disease as compared with patients in the placebo arm (58 vs. 31% by independent radiology, 65 vs. 38% by investigator assessment).

Safety

Incidence of any on-therapy AE was higher in the pazopanib arm than in the placebo arm (100 vs. 75%). In the pazopanib arm, 5 (16%) patients experienced AEs leading to permanent discontinuation of study treatment or early withdrawal from the study, 14 (45%) patients experienced AEs leading to a dose reduction, and 17 (55%) patients experienced AEs leading to dose interruption or delay (Table 2 and Supplementary Material). No AEs leading to dose interruption or delay were reported in the placebo arm. Over a third of patients (35%) in the pazopanib arm experienced an SAE compared with 19% in the placebo arm.

The most commonly reported AEs included decreased weight, nausea, fatigue, hair color changes (observed in pazopanib arm only) and decreased appetite (Table 3). Most AEs were of Grade 1 or 2. Left ventricular dysfunction (Grade 1 or 2) was observed in 3 (10%) patients in the pazopanib arm. Five (16%) patients in the pazopanib arm experienced Grade 3 hypertension. Other commonly reported (>10% in either treatment arm) Grade 3 AEs were fatigue (observed in pazopanib arm only) and tumor pain (10% pazopanib arm vs. 6% placebo arm). No pneumothorax was reported in either arm of the Japanese population.

Eleven (69%) patients in the placebo arm and 21 (68%) patients in the pazopanib arm died. In all cases, the primary cause of death, as attributed by the investigator, was disease progression. An investigator designated disease progression as a fatal SAE for one patient in the pazopanib arm because the time to disease progression was 'faster than expected'. This patient had been diagnosed with undifferentiated pleomorphic sarcoma with metastasis to the lungs and liver. Pazopanib was initiated ~12 months after initial diagnosis. Treatment was discontinued after ~5 months because of suspicion of disease progression. Subsequent magnetic resonance imaging (MRI) of the brain showed suspicion of meningioma or dural metastasis and MRI of the lumbar vertebrae showed multiple spine metastases, and the patient died due to disease progression 15 days after the last dose of study treatment. According to the investigator, the disease progression was not considered to be related to study treatment.

Most laboratory abnormalities observed were Grade 1 or 2 (Table 4). Alanine transaminase was elevated in 16 (52%) patients in the pazopanib arm and 2 (13%) patients in the placebo arm. Of these, elevation greater than three times the upper limit of normal (ULN) was observed in seven (23%) patients in the pazopanib arm and one (6%) patient in the placebo arm, all within the first 18 weeks of treatment, all resolved. No Japanese patients demonstrated an ALT exceeding eight times the ULN.

Table 2. Adverse events (AEs), safety population

AE, *n* (%)	Japanese population		Global population	
	Placebo (*n* = 16)	Pazopanib (*n* = 31)	Placebo (*n* = 123)	Pazopanib (*n* = 240)
Any on-therapy AE	12 (75)	31 (100)	110 (89)	237 (99)
AEs related to study treatment	7 (44)	29 (94)	78 (63)	219 (91)
AEs leading to dose interruption, delay	0	17 (55)	12 (10)	120 (50)
AEs leading to dose reduction	0	14 (45)	1 (<1)	77 (32)
AEs leading to permanent discontinuation of study treatment or early withdrawal from study	0	5 (16)	6 (5)	48 (20)
Any serious AE (SAE)	3 (19)	11 (35)	29 (24)	99 (41)
Fatal SAEs	0	1 (3)	6 (5)	8 (3)
Fatal SAEs related to study treatment	0	0	0	1 (<1)

Discussion

Prior to the introduction of pazopanib, there were no approved drugs for STS that progressed after chemotherapy with doxorubicin or ifosfamide indicated in Japan. In our investigation of the efficacy and safety of pazopanib in the Japanese cohort of the PALETTE study, pazopanib demonstrated significantly longer PFS compared with placebo. Although analysis of OS did not show a significant benefit for pazopanib, there was a trend toward longer OS in the pazopanib arm than in the placebo arm. These results are similar to those observed in the PALETTE global population.

Although the results in the global and Japanese PALETTE study population were similar, some differences were observed. There was a trend towards longer survival (both PFS and OS) in both arms of the Japanese population compared with the PALETTE global population. This trend could be related to differences in baseline disease characteristics between the Japanese and global populations. The majority (62%) of the Japanese population were asymptomatic (WHO PS = 0), compared with 48% of the global PALETTE population. In addition, fewer Japanese patients had received two or more lines of prior systemic therapy for advanced disease (26 vs. 54% for the global population). In a multivariate analysis of the global PALETTE population, good PS (WHO PS = 0) and fewer than two lines of prior systemic therapy were identified as favorable prognostic factors for PFS (2).

Although AEs that were frequently found in the Japanese population were similar to those in the global population, differences in the frequency of certain events were observed. AEs leading to dose reduction were more common in the Japanese population (45%) compared with the global population (32%). Hypertension was the most common reason for dose reduction in the Japanese population (19 vs. 7% in the global population), whereas fatigue was the most common reason in the global population (9%). Decreased weight and decreased appetite were more frequent in the pazopanib arm of the Japanese population (65 and 58%, respectively) compared with the pazopanib arm of the global population (48 and 40%, respectively). The mean

Table 3. Common (>10%) AEs, safety population

Event, *n* (%)	Japanese population						Global population					
	Placebo (*n* = 16)			Pazopanib (*n* = 31)			Placebo (*n* = 123)			Pazopanib (*n* = 240)		
	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Decreased weight	3 (19)	0	0	20 (65)	1 (3)	0	18 (15)	0	0	116 (48)	9 (4)	0
Nausea	5 (31)	0	0	18 (58)	0	0	27 (22)	2 (2)	0	135 (56)	8 (3)	0
Fatigue	5 (31)	0	0	18 (58)	1 (3)	0	59 (48)	5 (4)	1 (<1)	157 (65)	32 (13)	1 (<1)
Hair color changes	0	0	0	18 (58)	0	0	3 (2)	0	0	93 (39)	0	0
Decreased appetite	6 (38)	0	0	18 (58)	2 (6)	0	23 (19)	0	0	97 (40)	14 (6)	0
Diarrhea	4 (25)	0	0	17 (55)	2 (6)	0	19 (15)	1 (<1)	0	141 (59)	11 (5)	0
Hypertension	3 (19)	0	0	16 (52)	5 (16)	0	7 (6)	0	0	101 (42)	16 (7)	0
Dysgeusia	1 (6)	0	0	13 (42)	0	0	4 (3)	0	0	66 (28)	0	0
Vomiting	3 (19)	0	0	11 (35)	0	0	14 (11)	1 (<1)	0	80 (33)	8 (3)	0
Exfoliative rash	2 (13)	0	0	11 (35)	0	0	11 (9)	0	0	44 (18)	1 (<1)	0
Constipation	2 (13)	0	0	9 (29)	0	0	21 (17)	3 (2)	0	38 (16)	1 (<1)	0
Skin disorder	0	0	0	9 (29)	1 (3)	0	1 (<1)	0	0	27 (11)	4 (2)	0
Musculoskeletal pain	1 (6)	0	0	8 (26)	1 (3)	0	24 (20)	2 (2)	0	56 (23)	5 (2)	0
Myalgia	0	0	0	8 (26)	1 (3)	0	11 (9)	0	0	56 (23)	5 (2)	0
Alopecia	0	0	0	7 (23)	0	0	1 (<1)	0	0	28 (12)	0	0
Headache	0	0	0	7 (23)	0	0	10 (8)	0	0	56 (23)	2 (<1)	0
Chest pain	1 (6)	0	0	6 (19)	1 (3)	0	7 (6)	0	0	25 (10)	4 (2)	0
Cough	2 (13)	1 (6)	0	6 (19)	0	0	15 (12)	1 (<1)	0	41 (17)	1 (<1)	0
Gastrointestinal pain	0	0	0	6 (19)	0	0	11 (9)	5 (4)	0	55 (23)	6 (3)	0
Nasopharyngitis	4 (25)	0	0	6 (19)	0	0	7 (6)	0	0	12 (5)	0	0
Tumor pain	3 (19)	1 (6)	0	6 (19)	3 (10)	0	26 (21)	8 (7)	2 (2)	70 (29)	20 (8)	0
Peripheral edema	2 (13)	0	0	5 (16)	2 (6)	0	11 (9)	2 (2)	0	33 (14)	5 (2)	0
Stomatitis	0	0	0	5 (16)	0	0	4 (3)	0	0	27 (11)	1 (<1)	0
Skin hypopigmentation	0	0	0	5 (16)	0	0	0	0	0	27 (11)	0	0
Pruritus	1 (6)	0	0	5 (16)	0	0	3 (2)	0	0	10 (4)	0	0
Anxiety	0	0	0	4 (13)	0	0	8 (7)	1 (<1)	0	20 (8)	2 (<1)	0
Peripheral sensory neuropathy	0	0	0	4 (13)	0	0	10 (8)	1 (<1)	0	22 (9)	1 (<1)	0
Dyspepsia	0	0	0	3 (10)	0	0	2 (2)	0	0	17 (7)	0	0
Dysphonia	1 (6)	0	0	3 (10)	0	0	3 (2)	0	0	18 (8)	0	0
Abnormal ear, nose, throat examination	0	0	0	3 (10)	0	0	3 (2)	0	0	29 (12)	4 (2)	0
Abnormal hair growth	0	0	0	3 (10)	0	0	0	0	0	3 (1)	0	0
Left ventricular dysfunction	0	0	0	3 (10)	0	0	5 (4)	0	0	19 (8)	3 (1)	1 (<1)
Pyrexia	1 (6)	0	0	3 (10)	0	0	12 (10)	1 (<1)	0	25 (10)	0	0
Somnolence	0	0	0	3 (10)	0	0	0	0	0	8 (3)	0	0

daily dose of pazopanib was also slightly lower in the Japanese population compared with the global population (624.4 vs. 700.4 mg). As discussed above, AEs leading to dose reduction were more common in the Japanese population compared with the global population, and this is likely to explain the observed difference in mean daily dose. The reason for the difference in the frequency of AEs is unclear. It could be related to the lower average body weight of the Japanese population (61.3 vs. 71.5 kg in the global population), although the statistical significance of this difference has not been tested. However, as previously reported, the pharmacokinetic profile of pazopanib in Japanese patients is similar to that in non-Japanese patients (9). Furthermore, it is important to note that pazopanib is approved for use in Japan at a dosage of 800 mg once daily, although the dose may be adjusted based on clinical judgement of a patient's individual symptoms (1). Overall, despite the difference in mean daily dose, the efficacy and safety of pazopanib in the Japanese population was similar to that in the global population.

In the PALETTE global population, pneumothorax occurred in eight (3%) patients in the pazopanib arm and one (1%) patient in the placebo arm (2). A recent retrospective review of 32 patients with STS treated with pazopanib in a Japanese institute reported five events of pneumothorax in 3 (9.4%) patients, equating to an incidence of 1.53 per 1000 pazopanib-treatment days (10). However, no cases of pneumothorax occurred in the PALETTE Japanese subpopulation. Nevertheless, it will be important to continue to monitor the incidence and course of pneumothorax in patients treated with pazopanib in clinical practice in Japan based on prior experience with the drug.

Table 4. Common (>30%) laboratory abnormalities, safety population

Abnormality, *n* (%)	Japanese population						Global population					
	Placebo (*n* = 16)			Pazopanib (*n* = 31)			Placebo (*n* = 123)			Pazopanib (*n* = 240)		
	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
White blood cells decreased	3 (19)	0	0	21 (68)	1 (3)	0	18 (15)	0	0	106 (44)	3 (1)	0
Aspartate transaminase increased	2 (13)	1 (6)	0	20 (65)	2 (6)	0	27 (22)	2 (2)	0	122 (51)	13 (5)	6 (3)
Lymphocytes decreased	6 (38)	2 (13)	0	17 (55)	4 (13)	0	44 (36)	11 (9)	2 (2)	102 (43)	23 (10)	0
Alanine transaminase increased	2 (13)	1 (6)	0	16 (52)	5 (16)	0	22 (18)	3 (2)	1 (<1)	110 (46)	18 (8)	5 (2)
Neutrophils decreased	2 (13)	0	0	15 (48)	5 (16)	0	8 (7)	0	0	79 (33)	10 (4)	0
Platelets decreased	2 (13)	0	0	15 (48)	2 (6)	0	7 (6)	0	0	86 (36)	7 (3)	2 (<1)
Total bilirubin increased	1 (6)	0	0	13 (42)	0	0	9 (7)	2 (2)	0	68 (29)	3 (1)	0
Albumin decreased	2 (13)	0	0	13 (42)	1 (3)	0	26 (21)	0	0	81 (34)	2 (<1)	0
Hyperglycemia	3 (19)	0	0	13 (42)	1 (3)	0	43 (35)	2 (2)	0	106 (45)	1 (<1)	0

It is important to note that this analysis of the Japanese subpopulation of the PALETTE study is limited by the small sample size—the PALETTE study was not powered for subgroup analyses, and the statistical significance of the differences described here has not been tested.

In summary, the efficacy and safety of pazopanib observed in the Japanese cohort of PALETTE were similar to those for the global population. The interpretation that pazopanib is a new treatment option for patients with metastatic STS after previous chemotherapy, is valid for the Japanese cohort.

Supplementary data

Supplementary data at http://www.jjco.oxfordjournals.org.

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Conflict of interest statement

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