Prolonged survival with quality of life can come true by using low-dose pazopanib maintenance

Currently, pazopanib is used as a second- or third-line adjuvant chemotherapeutic in patients with soft tissue sarcoma, given at a fixed dose of 800 mg once a day. However, pazopanib has many side effects, and there is no consensus on the optimal dosing schedule of pazopanib. The purpose of this study was to evaluate the dose and side effects as well as treatment outcomes of pazopanib in patients treated at our institution, and to find a better dosage method. This study was a retrospective cohort study.

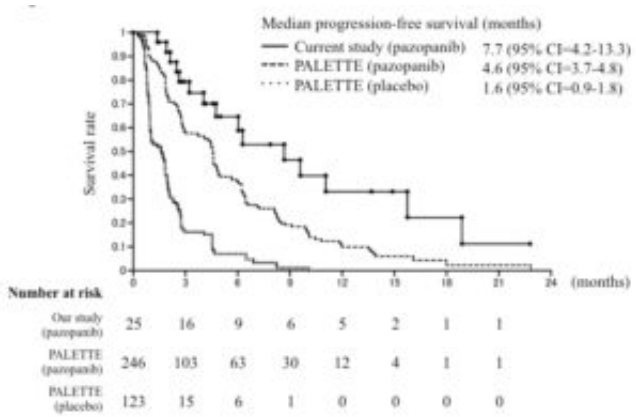

Fig. 1. Progression-free survival of patients in the current study and the PALETTE study, as determined by the Kaplan–Meier method.

Twenty-five patients (14 males, 11 females; malignant fibrous histiocytoma/undifferentiated pleomorphic sarcoma (MFH/UPS) 11 cases, the most) that were prescribed pazopanib between 2012 and 2015 were included in this retrospective analysis. All patients had distant metastases and had previously undergone treatment. Initial pazopanib doses were 800, 600, 400, 200, and 100 mg in 3, 3, 8, 7, and 4 patients, respectively. The dose of pazopanib was adjusted based on side effects during the course of treatment. Pazopanib doses above 400 mg were defined as high-dose and those below 400 mg were defined as low-dose. The mean treatment duration was 7.6 (1.3-21.6) months, and the pazopanib dose was decreased in 72% of the cases. Almost all patients complained of fatigue, which was not severe enough for discontinuation of pazopanib. Other common side effects included hypertension in 13 patients (4 with grade 3), thrombocytopenia in 10 patients (2 with grade 3), hepatological abnormalities in 8 patients (2 with grade 3) and dermatological side effects in 7 patients (2 with grade 3). We defined the dose that could be tolerated the longest by patients as the maintenance dose. Consequently, the maintenance pazopanib doses of 600, 400, 200, and 100 mg were administered to 3, 10, 8, and 4 patients, respectively. The median progression-free survival (PFS) time was 7.7 months (95% confidence

interval, 4.2-13.3) (Fig. 1). The log-rank test revealed that there were no significant differences in the PFS times between the low and high-dose pazopanib groups during the initial (P = 0.79) or maintenance (P = 0.19) periods (Fig. 2). Moreover, PFS time in our study (various dose) was similar to that achieved by high-dose pazopanib in the PALETTE study (Fig. 1). Partial response (PR) and stable disease (SD) were achieved in 6% and 67% of the cases in the PALETTE trial, respectively. In contrast, in our study, PR and SD were achieved in 17% and 58% of the patients by first radiographic assessment and in 5% and 19% of the patients by final radiographic assessment.

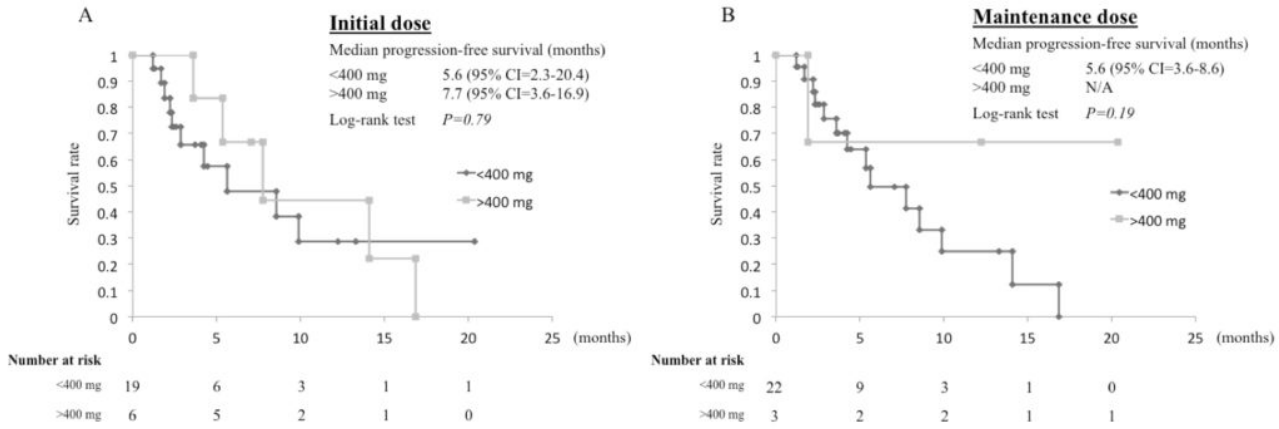

Fig. 2. Comparison of progression-free survival between the low-dose and high-dose pazopanib groups in this study. (A) Initial period, (B) maintenance period.

These findings suggested that pazopanib was similar in efficacy in our study to that observed in the PALETTE trial, despite its use at lower doses. Moreover, majority of patients received a maintenance dose of 400 mg, and there were no significant differences in the PFS time between the low- and high-dose pazopanib groups, indicating that controlling the side effects might be more critical than administering higher doses. From the above, pazopanib has in fact provided benefits. However, patients on pazopanib suffer from many associated side effects that significantly impact their quality of life (QoL). Thus, it is critical to provide a balance between the life-prolonging effects of pazopanib and QoL. This study suggested that pazopanib should be started from a low dose with careful increase to avoid pazopanib-related side effects, which is necessary to provide a balance between the life-prolonging effects of pazopanib and quality of life of patients.

Kensaku Abe *and* ***Hiroyuki Tsuchiya***
Department of Orthopaedic Surgery, Graduate School of Medical Science, Kanazawa University, Kanazawa, Japan

Publication

Balancing Prolonged Survival with QoL Using Low-dose Pazopanib Maintenance: A Comparison with the PALETTE Study.

Abe K, Yamamoto N, Hayashi K, Takeuchi A, Miwa S, Inatani H, Higuchi T, Taniguchi Y, Tsuchiya H

Anticancer Res. 2016 Jun