At the cut-off date, OS data were immature with a median follow-up of 8.5 months for avapritinib. In patients without D842V mutations (n=230 vs n=233), ORR was higher for avapritinib (16%; 95% CI 11–23) compared with regorafenib (7%; 95% CI 4–11; Table 1). Avapritinib demonstrated clinical activity in patients whose tumors harbor active activating mutations in the PDGFRA kinase domain, including D816V (n=67 vs n=68), D816I (n=4 vs n=5), and D842G (n=10 vs n=14). Across tumor subtypes, ORR was higher for avapritinib (22% vs 12%; 95% CI 15–29) compared with regorafenib (7%; 95% CI 4–11; Table 1). The majority of patients were evaluable for DCR (97%; 95% CI 96–98) across both treatment arms (Table 1).

Efficacy

Progression-free survival

The primary endpoint for this study was not met, as there was no significant difference in median PFS between avapritinib and regorafenib (HR 1.25; 95% CI 0.99–1.57; median PFS 4.2 vs 5.6 months; Table 3, Figures 2 and 3). In the ITT population, ORR was higher for avapritinib (17%; 95% CI 13–22), compared with regorafenib (7%; 95% CI 4–11; Table 2). Response rates were similar across tumor subtypes, with ORR ≥15% in patients with D842V and ≥10% in patients with D816I and D816V mutations (Table 1). Among patients with PDGFRA exon 17 or PDGFRA exon 18 mutations, ORR was higher for avapritinib (16% vs 7%; 95% CI 4–12; all PR) compared with regorafenib (Table 3).

Safety

The AE profile lacked some typical AEs associated with regorafenib, including diarrhea (7% vs 16%), hand-foot skin reaction (1% vs 8%), and hypertension (0% vs 7%). Serious adverse events (SAEs; requiring hospitalization) occurred in 41% and 36% of patients treated with avapritinib and regorafenib, respectively. Treatment-related SAEs occurred in 23% of patients treated with avapritinib and 15% of patients treated with regorafenib. The most common treatment-related SAEs were intracranial bleeding comprised pooled terms of intracranial hemorrhage, subdural hematoma, and cerebral hemorrhage (n=9; 9.2%) and any grade proteinuria (n=10; 10.4%) (Table 3).

Conclusions

The primary endpoint for this study was not met, as there was no significant difference in median PFS between avapritinib and regorafenib (HR 1.25; 95% CI 0.99–1.57). ORR was higher for avapritinib versus regorafenib in patients with D842V mutations (17% vs 7%; 95% CI 13–22; all PR). Treatment-related SAEs were similar between the two treatment arms; the most common treatment-related SAEs were intracranial bleeding comprised pooled terms of intracranial hemorrhage, subdural hematoma, and cerebral hemorrhage (9.2%) and any grade proteinuria (10.4%). Avapritinib AE profile lacked some typical AEs associated with regorafenib, including diarrhea (7% vs 16%), hand-foot skin reaction (1% vs 8%), and hypertension (0% vs 7%). Serious adverse events (SAEs; requiring hospitalization) occurred in 41% and 36% of patients treated with avapritinib and regorafenib, respectively. Treatment-related SAEs occurred in 23% of patients treated with avapritinib and 15% of patients treated with regorafenib. The most common treatment-related SAEs were intracranial bleeding comprised pooled terms of intracranial hemorrhage, subdural hematoma, and cerebral hemorrhage (9.2%) and any grade proteinuria (10.4%).