Appendix 1 Subgroup survival analysis of patients with different doses of medication

Because only one patient in each group was considered to have a final stable daily dose of 40 mg, in the dose-survival subgroup analysis, only the survival prognosis of the final stable daily dose of 80, 120, and 160 mg subgroups was compared. The results in the monotherapy group showed a mPFS of 5.2 months (95% CI: 3.6–NA) for 80 mg, 5.7 months (95% CI: 5.1–NA) for 120 mg, and 9.5 months (95% CI: 7.7–NA) for 160 mg, with no significant difference in PFS between the three subgroups (P=0.45) (*Figure S1A*). In addition, the mOS of patients in the monotherapy group was 11.2 months (95% CI: 8.3–NA) for 80 mg, 14.3 months (95% CI: 13.7–NA) for 120 mg and 20.4 months (95% CI: 13.6–NA) for 160 mg, which was a significant difference in OS between the three subgroups (P=0.005) (*Figure S1B*). In the combination group, the results showed mPFS of 6.7 months (95% CI: 5.6–NA) for patients on 80 mg, 9.7 months (95% CI: 7.6–NA) for patients on 120 mg and 13.5 months (95% CI: 12.5–NA) for patients on 160 mg, with no significant difference in PFS between the three subgroups (P=0.12) (*Figure S1C*). mOS was 14.7 months (95% CI: 10.9–NA) for patients treated with 80 mg, 25.4 months (95% CI: 20.8–NA) for patients treated with 120 mg and 27.6 months (95% CI: 27.6–NA) for patients treated with 160 mg in the combination group, which was a significant difference in OS between the three subgroups (P=0.003) (*Figure S1D*).

To further investigate the survival differences between the monotherapy and ICI combination groups with different final daily stable doses, the survival curves showed no significant difference between the 80 mg monotherapy subgroup and the 80 mg combination subgroup (PFS, P=0.48; OS, P=0.26) (*Figure S2A,S2B*). The PFS of the 120 mg monotherapy subgroup and combination subgroup was not significantly different, but there was a significant difference in OS (PFS, P=0.28; OS, P=0.02) (*Figure S2C,S2D*). There was a significant difference in PFS and no significant difference in OS (PFS, P=0.01; OS, P=0.051) between the 160 mg monotherapy combination subgroups (*Figure S2E,S2F*).

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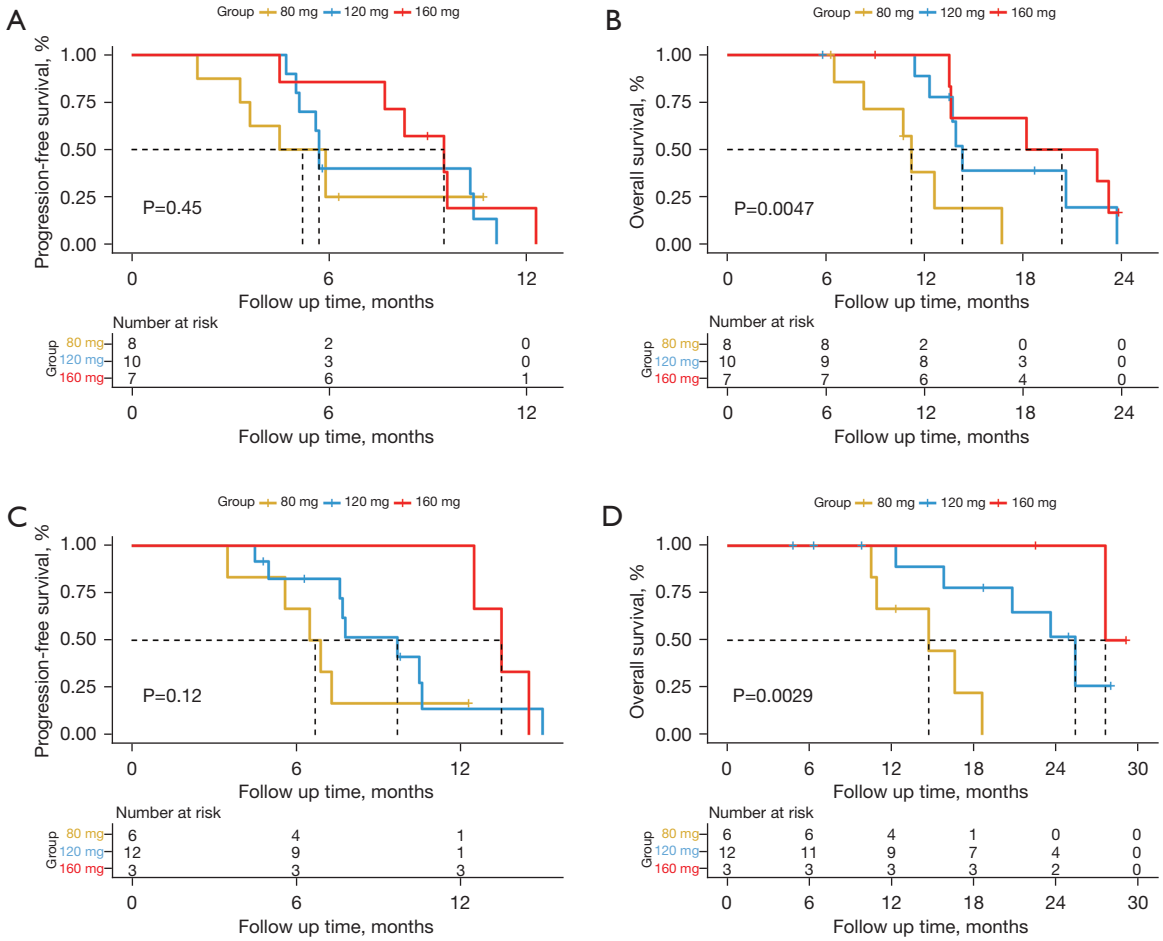

Figure S1 Comparison of survival curves for patients with different final daily stable doses in the regorafenib and regorafenib + ICI groups. (A) Comparison of PFS survival curves for daily stable doses of 80, 120, and 160 mg in the regorafenib group (P=0.45). (B) Comparison of OS survival curves for daily stable doses of 80, 120, and 160 mg in the regorafenib group (P=0.005). (C) Comparison of PFS survival curves for daily stable doses of 80, 120, and 160 mg in the regorafenib + ICI group (P=0.12). (D) Comparison of OS survival curves for daily stable doses of 80 mg, 120 mg, and 160 mg in the regorafenib + ICI group (P=0.003). ICI, immune checkpoint inhibitor; PFS, progression-free survival; OS, overall survival.

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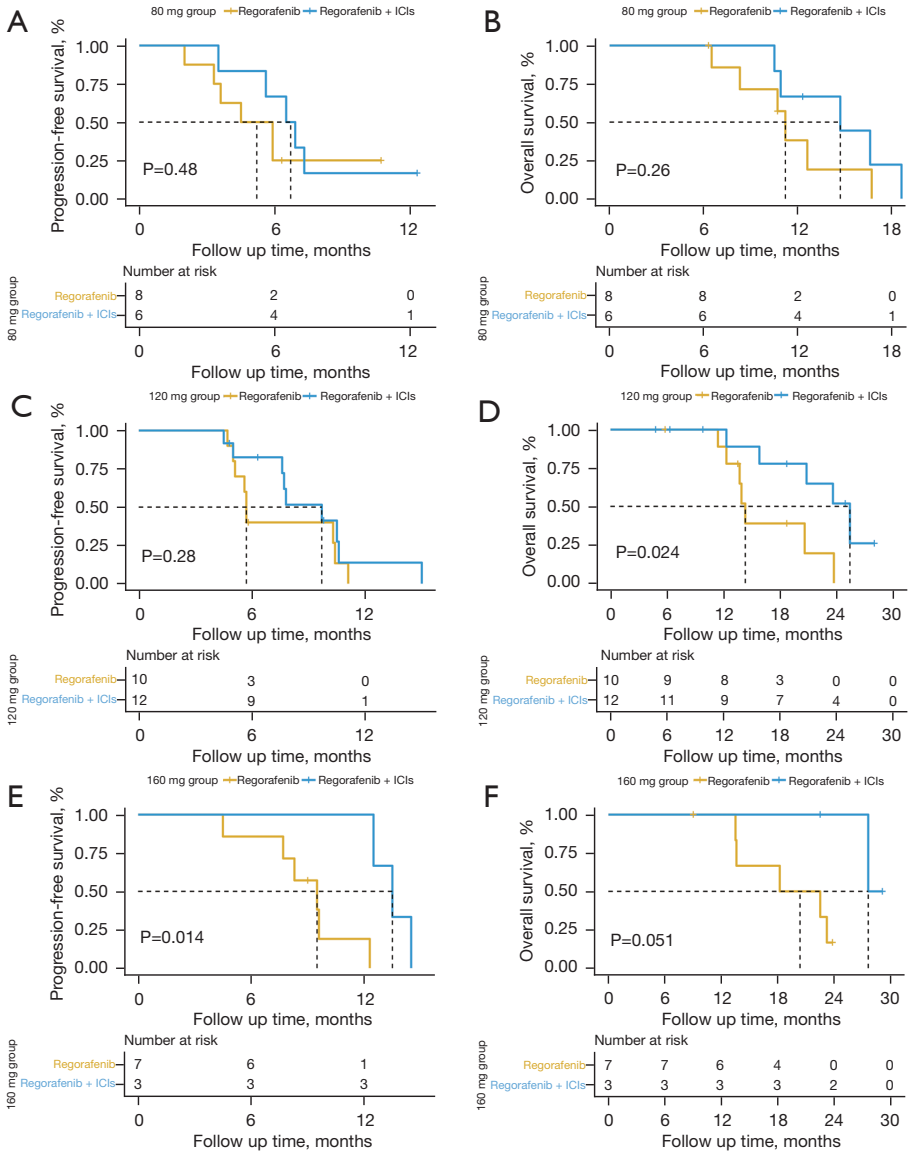

Figure S2 Comparison of survival curves for patients with different daily stable doses in the regorafenib and regorafenib + ICI groups. (A,B) Comparison of PFS and OS survival curves for a daily stable dose of 80 mg in the regorafenib and regorafenib + ICI groups (PFS, P=0.48; OS, P=0.26). (C,D) Comparison of PFS and OS survival curves for a daily stable dose of 120 mg in the regorafenib and regorafenib + ICI groups (PFS, P=0.28; OS, P=0.02). (E,F) Comparison of PFS and OS survival curves for a daily stable dose of 160 mg in the regorafenib and regorafenib + ICI groups (PFS, P=0.01; OS, P=0.051). ICI, immune checkpoint inhibitor; PFS, progression-free survival; OS, overall survival.

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