Updated Survival Analysis of the Randomized Phase III Trial of S-1 Versus Capecitabine in the First-Line Treatment of Metastatic Colorectal Cancer by the Dutch Colorectal Cancer Group

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We previously reported the results of a multicenter, open-label phase III trial (ClinicalTrials.gov: NCT01918852) in which 161 metastatic colorectal cancer patients, in whom first-line fluoropyrimidine monochemotherapy was indicated, were randomized between capecitabine (n = 81) or S-1 (n = 80) treatment.[1] Patients received capecitabine twice daily on day 1 to 14 at a dose of 1250 mg/m^2 for patients younger than 70 years or 1000 mg/m^2 for patients 70 years of age and older, or S-1 twice-daily on day 1 to 14 at a dose of 30 mg/m^2, irrespective of age. Co-treatment with bevacizumab, 7.5 mg/kg intravenously on day 1, was left to the discretion of the local investigator, and was administered to 59% of patients in both arms. Cycles were repeated every 3 weeks. The primary objective, a lower incidence of hand-foot syndrome for S-1, was met (all grade 58 patients [73%] in the capecitabine group vs. 36 patients [45%] in the S-1 group; odds ratio, 0.31 [95% confidence interval (CI), 0.16-0.60], P = .0005; Grade 3 17 patients [21%] in the capecitabine group and 3 patients [4%] in the S-1 group, P = .003). There was no significant difference in median progression-free survival (PFS), and data on overall survival (OS) were immature. Herein we present updated results on survival.

At data cutoff on August 6, 2018, after a median follow-up of 40.3 months (interquartile range, 36.5-43.5), 71 patients (88%) in the capecitabine group and 68 patients (85%) in the S-1 group had died. Median PFS was 8.2 months (95% CI, 6.4-10.3) for treatment with capecitabine and 8.4 months (95% CI, 6.4-10.6) for treatment with S-1 (hazard ratio [HR], 1.02; 95% CI, 0.75-1.40; P = .89). Median OS was 17.1 months (95% CI, 14.3-23.5) for treatment with capecitabine and 17.0 months (13.0-20.1) for treatment with S-1 (HR, 1.07; 95% CI, 0.76-1.49; P = .70; Figure 1). Exploratory survival analysis of treatment with or without bevacizumab showed a median PFS of 8.7 versus 6.6 months, and median OS of 17.8 versus 15.1 months, respectively.

Forty patients (49%) in the capecitabine group and 41 patients (51%) in the S-1 group received 1 or more subsequent treatments (P = .88).

To our knowledge, our study is the first to compare the safety of S-1 with capecitabine in Western metastatic colorectal cancer

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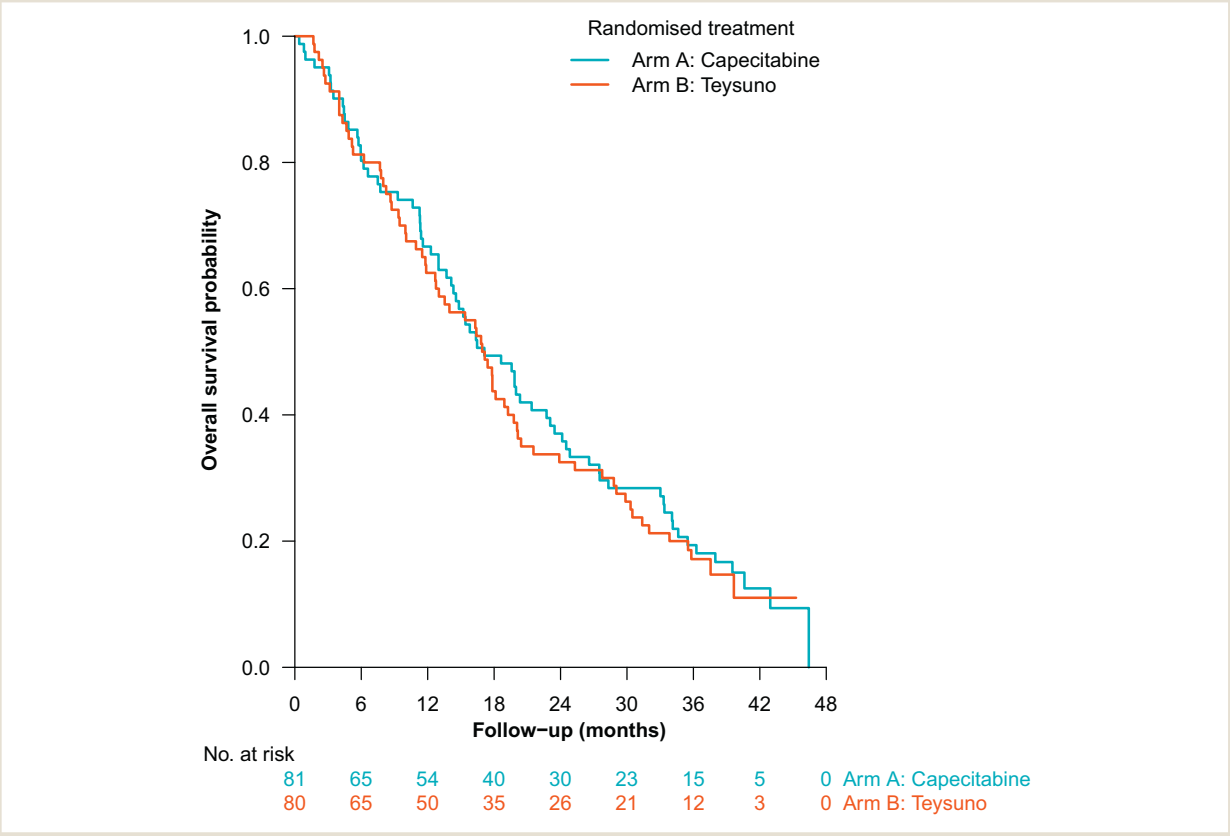
Figure 1 Kaplan–Meier Curves of Overall Survival



patients, and the results show that treatment with S-1 is associated with a significantly lower incidence of hand-foot syndrome. Although our study was not powered to show noninferiority, our survival data suggest comparable efficacy of S-1 and capecitabine in terms of PFS and OS, which is in line with studies in Asian patients.[2,3] Therefore, S-1 should be considered as a valid alternative to capecitabine, and appears to be indicated in patients with intolerance to capecitabine.[4,5]

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Disclosure

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