Randomized phase II trial of oral doxifluoridine plus leucovorin versus intravenous bolus 5-fluorouracil plus leucovorin in patients with previously untreated, advanced colorectal cancer (CRC)

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Background Combination of 5-FU and leucovorin in IV route has been a standard first-line treatment for the patients with advanced CRC. Doxifluoridine(5-dFUR), a fluoropyrimidine derivative, is known to be well absorbed in oral route and activated preferentially in tumor to normal tissue. We conducted a randomized phase II study to evaluate the efficacy and toxicities of oral doxifluoridine plus leucovorin by comparing them with those of IV 5-FU plus leucovorin in patients with previously untreated advanced CRC with measurable lesion.

Methods Previously untreated metastatic CRC patients with measurable lesion were randomized to receive either an IV bolus of leucovorin 20 mg/m2 plus 5-FU 400 mg/m2 on days 1 to 5(group A), or orally administered leucovorin 15 mg twice daily plus doxifluoridine 1,000 mg/m2 per day divided by 3, on days 1 to 7 and 15 to 21(group B), with the cycles repeated every 4 weeks.

Results Between July 1998 and May 2000, 65 patients were enrolled; 31 in group A and 34 in group B. Median age was 58 years(range 21-78). Response rate was 12.9%(4 PR, 95% CI, 0-25) in group A, and 26.5%(9 PR, 95% CI, 11-42) in group B on an intention-to-treat analysis. The median response duration was 5.5 and 5.6 months; median time to progression was 4.2(range 1-15.5), and 5.7 months(range 1-14.8), respectively. With a median follow-up of 21.8 months, median survival time was 13.8(95% CI, 10.0-17.5) and 11.7 months(95% CI, 7.9-15.5), respectively. Hematologic toxicities greater than grade II did not occur in both groups. Grade III stomatitis and diarrhea were observed in 12 cycles of group A, but grade III diarrhea was observed only in 1 cycle of group B.

Conclusion This trial showed that a combination of oral doxifluoridine plus leucovorin could be an active and safe first-line treatment for the patients with advanced CRC.