Prospective Phase II Trial of Combination Treatment of Whole Hepatic Irradiation and Hyperthermia in Chemorefractory Numerous Hepatic Metastases of Gastrointestinal Malignancy

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Introduction: The present prospective phase II trial was conducted to evaluate the effectiveness and toxicity of whole hepatic irradiation (WHI) and hyperthermia in chemorefractory numerous hepatic metastasis of gastrointestinal (GI) tract malignancies.

Methods: All patients were required to have pathologically confirmed GI tract carcinoma with unresectable and chemorefractory numerous hepatic metastases. Patients with less than eight weeks expected survival, previously received upper abdominal RT, uncontrolled ascites, or unstable respiration related with pleural effusion or chronic obstructive pulmonary disease were excluded. Patients who had Eastern Cooperative Oncology Group performance status four were also excluded. Total five sessions of hyperthermia and seven fractions of 3 gray (Gy) WHI were planned. Health related quality of life (HRQoL) using the Korean version of European Organization for Research and Treatment of Cancer Quality of Life C-30 and Functional Assessment of Cancer Therapy—Hepatobiliary version 4.0 (FACT-Hep v4.0), and degree of current pain status using the Visual Analog Scale for Pain (VAS) were assessed at baseline, and at one, two and three months after treatment. The objective response was evaluated with the Revised Response Evaluation Criteria in Solid Tumors (RECIST version 1.1). The pain response was evaluated with International Bone Metastases Consensus Group (BMCG) criteria. Patients’ toxicity levels were assessed with the Common Terminology Criteria for Adverse Events, version 4.0. The present study was approved by the institutional review board at Samsung Medical Center, and registered at clinicaltrials.gov (NCT01963117). All patients provided written informed consent before study enrollment.

Results: A total 12 patients were consent to the present trial, and ten patients who received WHI and hyperthermia were analyzed. The median number of chemotherapy cycles administered before WHI and hyperthermia was 23 (range, 1 to 46). WHI in nine and hyperthermia in eight were completed as planned. Follow-up was assessable in all at one month, five at two months, and four patients at three months after treatment (Fig 1). According to RECIST criteria, partial response in three patients (30.0%), and stable disease in four patients was achieved at one month follow-up. Pain response was partial in four and stable in four patients. During the follow-up, one patient died at one month after treatment because of the respiratory failure related with pleural metastasis progression. Other grade III or higher toxicities were detected in three patients; however, all these severe toxicities were related with disease progression rather than treatment. There was no significant difference of HRQoL according to the timing of assessment in the patients who were assessable to questionnaire.

Conclusion: Combined WHI and hyperthermia was well tolerated without severe treatment related toxicities in chemorefractory numerous hepatic metastasis of gastrointestinal malignancies. Early follow-up loss was a problem to evaluate the real effectiveness of the treatment. Well-designed larger scale prospective studies are warranted.