Therapeutic response to ramucirumab + folfiri in patients with metastatic gastric cancer

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Abstract

Background: Gastric tumors are important gastrointestinal malignancies, and the prediction of therapeutic responses and related factors are important to improve the prognosis. Hence the aim of this study was to determine the therapeutic response to ramucirumab + folfiri in patients with metastatic gastric cancer. Methods and Materials: In this prospective cohort, 13 consecutive patients with metastatic gastric cancer attending Taleghani Hospital that underwent ramucirumab + folfiri therapy were enrolled, and the therapeutic response among them was determined. Results: The results in this study demonstrated that initial therapeutic response was 92.3% and the Progression-free Survival (PFS) was 16.2 months (84.6%) (CI95%:13.2-19.3). The nine-month PFS was 69.2%. Total survival was 16.7 months (CI95%:13.5-19.9). Conclusion: Ultimately, according to the obtained results, it may be concluded that the therapeutic response to ramucirumab + folfiri in a patient with metastatic gastric cancer is good, and the use of this regimen is recommended.

Keywords: Folfiri, gastric cancer, ramucirumab, treatment
some controversies in this era and the high prevalence rate of advanced gastric cancer, this study was carried out to determine the therapeutic response to ramucirumab + folfox in patients with metastatic gastric cancer.

**Materials and Methods**

In this prospective cohort, 13 consecutive patients with metastatic gastric cancer attending Taleghani Hospital I in 2018 and 2019 were enrolled, including those that underwent ramucirumab + folfox therapy, and the therapeutic response among them was determined. Inclusion criteria were gastric adenocarcinoma, metastasis, optimal functional status, and appropriate renal and hepatic function. The exclusion criteria were inappropriate functional status, loss to follow-up, previous treatment, severe background disease or infection, brain metastasis, and neuropathy. The study was approved by the local ethical committee in Shahid-Beheshti University of Medical Sciences.

The patients with established gastric adenocarcinoma with metastasis (approved by physical examination beside spiral CT scan and bone scan) with optimal functional status (FIGO score of 0 to 2) were enrolled. An informed consent form was received from patients. Ramucirumab was prescribed biweekly, and after the first three doses, the patients were assessed by clinical and imaging modalities. In responsive/stable cases, maximally six and occasionally eight courses were used. In cases experiencing adverse effects or disease progression, the treatment was discontinued earlier than six months. Patients that received minimally two treatment cycles were enrolled. Total response rate, Progression Free Survival (PFS), Overall Survival (OS), and adverse drug effects were recorded. After the third cycle, the response was assessed by RECIST criteria. Complete response, defined as the absence of all tumoral lesions, was assessed by endoscopy, biopsy, and CT scan. Partial response was defined as a minimal 30% reduction in tumoral lesions as compared to the initial size. The stable disease in patients was defined as a lack of the change in the size of the tumor in comparison with the smallest size at initiation or after 1–2 new lesions are present.

Data analysis was carried out by SPSS version 13.0 software among 13 patients. The utilized tests were ANOVA, Independent-Sample-T, and Kaplan-Meyer tests, and the P-values under 0.05 were considered statistically significant.

**Results**

Initial therapeutic response was seen in 12 out of 13 patients (92.3%). PFS was 84.6%, and nine-month PFS was also calculated as 69.2%. As shown in Figure 1, the mean duration of PFS was 16.2 months (CI: 95%: 13.2–19.3 months).

As shown in Figure 2, the mean duration of overall survival was 16.7 months (CI: 95%: 13.5–19.9 months).

Duration of PFS was 17 and 15.3 months in female and male patients, respectively, showing a significant difference \((P = 0.001)\). Duration of overall survival was 19 and 15.3 months in female and male patients, respectively, showing a significant difference \((P = 0.001)\). The age was not related to survival \((P = 0.676; r = 0.128)\). As shown in Tables 1 and 2, the PFS and OS were not differed according to the metastasis location \((P > 0.05)\).

**Discussion**

Chemotherapy is the main therapeutic method in gastric cancer patients. Further efficacy and a lower rate of adverse effects develop a good prognosis and quality of life in the patients. In this study, the efficacy and safety of a regimen including ramucirumab plus folfox was assessed in patients with metastatic gastric cancer. The overall and progression-free survival rates of 92 and 85 percent were encouraging outcomes with a mean duration of 16 and 17 months, respectively. Lorenzen S et al. demonstrated good efficacy for Ramucirumab plus Folfiri regimen as well as our study.

Moore et al. also compared the efficacy of Folfox-6 plus ramucirumab versus irucumab. They reversely reported no optimal efficacy for both regimens. Tabernero J et al. compared efficacy of Folfiri plus ramucirumab versus placebo in colorectal cancer patients. The overall survival was 13.3 versus 7.7 months in intervention and placebo groups, respectively. Neutropenia was seen in 38 and 23 percent of the cases, respectively. But the side effects had a lower rate in our study.

Al-Batran et al. compared the quality of life and survival after the use of Folfiri plus ramucirumab versus placebo. They reported better quality of life and longer survival in the intervention group. It is congruent with our findings. Attarian et al. reported mortality rate of 65 percent in 19-month follow-up by various chemotherapy regimens, including cisplatin and docetaxel plus Folfiri. The mean overall survival was ten months. However, the efficacy and outcomes were better in our study.
It has been demonstrated that the incidence of cancer and cancer mortality are growing rapidly worldwide. Malignancies of the gastrointestinal (GI) tract such as the esophagus, pancreas, stomach, colon, rectum, anus, liver, biliary system, and small intestine are among the five most common cancers in both men and women worldwide. GI cancers are overall the most common causes of cancer-related death in men. A recent study showed that FOLFIRI is an active and well-tolerated regimen after the failure of a fluoropyrimidine/platinum regimen in patients with advanced gastroesophageal adenocarcinoma. Population with poor prognostic features was well represented. Efficacy outcomes were similar to the ones reported for the paclitaxel/ramucirumab combination RAINBOW trial. Previous studies reported that the use of ramucirumab in combination with FOLFIRI showed favourable progression-free survival and overall survival in patients with prior treatments with platinum and/or taxane-based agents and allowed further treatment lines after progression. In patients with taxane pretreatment or persistent high-grade PNP, the combination of FOLFIRI-R might be promising. Finally, according to the obtained results, it may be concluded that therapeutic response to
ramucirumab + folfiri in a patient with metastatic gastric cancer is good, and the use of this regimen is recommended. However, further studies with a larger sample size and longer follow-up in multiple centers are required for more definite results.

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**Conflicts of interest**

There are no conflicts of interest.

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