progression at the end of three courses. The median number of first-line chemotherapy courses was 4.5 cycles, five cases (17.9%) had received seven or more courses, and the maximum number of first-line chemotherapy courses was 13 cycles. Nineteen (67.9%) patients received cisplatin-based chemotherapy at the start of first-line chemotherapy. A total of 16 cases (57.1%) had visceral metastases, of which seven (25.0%) had liver metastases.

Ten patients (35.7%) received focal therapy for disease control before or after first-line chemotherapy. Details of focal therapy are shown in Table II. External beam radiotherapy was performed in seven cases, radiofrequency ablation was performed in two cases and primary lesion or lymph node resection was performed in two cases. Twenty-five patients (89.3%) received second-line chemotherapy or immunotherapy.

The therapeutic effect was CR in 1 case, PR in 11 cases and SD in 16 cases at the end of three courses. Figure 1 shows the PFS and OS of patients. Median PFS and OS were 7.1 and 27.1 months, respectively. A comparison of OS between patients with fewer than six courses and those with six or more courses of first-line chemotherapy showed 36.2 and 23.0 months, respectively. Moreover, OS was compared for ECOG-PS, albumin, NLR and liver metastases. OS of patients with ECOG-PS 0-1 and PS ≥2 was 27.1 and 15.2 months, respectively (p=0.834, log-rank test). OS of patients with albumin level of 3.5 g/dL or more and below 3.5 g/dL was 36.2 and 15.2 months, respectively (p=0.100 log-rank test). OS of patients with an NLR of 5 or more and below 5 was 36.2 and 23.0 months, respectively (p=0.886, log-rank test). OS of patients with and without liver metastasis was 31.4 and 15.2 months, respectively (p=0.780, log-rank test). Figure 2 shows a comparison of OS of patients with and without focal therapy for disease control. OS was significantly longer in patients with focal therapy than in those without focal therapy (p=0.019, log-rank test).

Discussion

Chemotherapy with GC has been widely selected as the first-line treatment since it became the standard for UC (2). Recently, the advent of ICI has provided new treatment options. Various reports have been made on the effectiveness of ICI, including first-line treatment of cases unsuitable for cisplatin, second-line treatment and maintenance therapy after first-line chemotherapy (4-7). However, no conclusions have been reached as to what treatment strategy is best for metastatic UC yet.

In this study, the OS of patients with metastatic UC who had more than SD after three courses of first-line chemotherapy was 27.1 months. In the JAVELIN Bladder 100 trial, patients were assigned to the avelumab maintenance therapy with BSC group or the BSC-only group at intervals of 4-10 weeks after four to six courses of primary chemotherapy. The OS in the avelumab maintenance therapy with BSC group was 21.4 months, and the OS in the BSC-only group was 14.3 months (7). Although it is not possible to directly compare this study and the JAVELIN Bladder 100 trial because of the differing start time of OS measurement, we compared these by subtracting the time to start measuring OS in JAVELIN Bladder 100 from that in this study. Specifically, we subtracted the duration of primary chemotherapy (112-168 days for 4-6 courses over 28 days per course) and the time to randomization [4-10 weeks (28-70 days)], for a total of 140-238 days. The result was 19.3-22.5 months, which was equivalent to that of the avelumab with the BSC group. The results may have been related to the high rate of focal treatment for disease control and the high rate of second-line chemotherapy without large intervals in this study.

Although there are some reports showing that focal therapies, including metastasectomy, radiation therapy and radiofrequency therapy are effective for metastatic UC, the role of focal therapy and its impact on survival remains controversial. Several studies on metastasectomy reported that patients who underwent...