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Background: Intraperitoneal (ip) chemotherapy is a promising treatment option for peritoneal malignancy. However, even with cytoreductive surgery and hyperthermia, bolus ip chemotherapy for 30–60 minutes may not be sufficiently effective for gastric cancer with peritoneal metastasis. We have developed a new multidisciplinary treatment with long-term normothermic ip and systemic chemotherapy, using paclitaxel (PTX) or docetaxel (DOC) for ip administration via an ip port, combined with gastrectomy after response to chemotherapy. These drugs have pharmacokinetic properties that allow high local concentration, and rarely cause adhesions in the peritoneal cavity. Here we report the results of 10 clinical trials completed between 2006 and 2018 and a retrospective study of surgery after response to chemotherapy.

Material and methods: We performed phase I clinical trials of five combination chemotherapy regimens: S-1/PTX plus ip PTX, S-1/oxaliplatin plus ip PTX, S-1/cisplatin plus ip PTX, capecitabine/cisplatin plus ip DOC, and FOLFOX plus ip PTX. We completed single- or multicenter phase II clinical trials of the first three regimens and a multicenter phase III PHOENIX-GC trial comparing S-1/PTX plus ip PTX with standard systemic chemotherapy. Additionally, we retrospectively evaluated the safety and efficacy of gastrectomy in three multicenter phase II and III trials.

Results: In phase I trials, recommended doses of weekly ip PTX and ip DOC were determined to be 20–40 mg/m^2 and 10 mg/m^2, respectively, with systemic dose-limiting toxicities. In phase II trials, the median durations of protocol treatment were 18–33 weeks. The 1-year overall survival rates were 72%–78%, and the negative conversion rates on peritoneal cytology were 68%–86%. The common grade 3/4 adverse events were leukopenia (8%–28%), neutropenia (21%–50%), anemia (9%–29%), and anorexia (0%–25%). PHOENIX-GC trial narrowly failed to show statistical superiority of S-1/PTX plus ip PTX over S-1 plus cisplatin (p=0.080; hazard ratio [HR] 0.72, 95% confidence interval [CI] 0.49–1.04). However, the exploratory analysis adjusting for the baseline imbalance in the amount of ascites between the arms suggested clinical benefits (HR 0.59, 95% CI 0.39–0.87). Out of 222 patients treated with ip chemotherapy in three multicenter trials, 93 patients (42%) underwent gastrectomy after disappearance or marked shrinkage of peritoneal metastasis. The median survival times of patients with and without surgery were 26.3 months (95% CI 21.3–34.2 months) and 12.3 months (95% CI 11.3–13.1 months), respectively. Postoperative complications of Clavien-Dindo grade II–IVa occurred in 10 patients, with no treatment-related deaths.

Conclusions: Multidisciplinary treatment with long-term ip and systemic chemotherapy combined with gastrectomy is safe and effective for gastric cancer patients with peritoneal metastasis.

Conflict of interest Other Substantive Relationships: Drugs were provided by Nippon Kayaku Co.,Ltd., Sawai Pharmaceutical Co.,Ltd., Yakult Honsha Co.,Ltd., and Kyowa Hakko Kirin Co.,Ltd. in some of the clinical trials.

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ACTIVE SURVEILLANCE VERSUS SURGERY IN CLINICALLY COMPLETE RESPONDERS AFTER NEOADJUVANT CHEMORADIOTHERAPY FOR ESOPHAGEAL CANCER: A PROPENSITY-MATCHED STUDY

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Background. Nearly one third of esophageal cancer patients show a pathologically complete response in their resection specimens after neoadjuvant chemoradiotherapy (nCRT) according to CROSS regimen. This raises questions whether all patients benefit from surgery or if active surveillance can be applied to patients with a clinically complete response (cCR) after nCRT. This retrospective-multicenter propensity matched study compared outcomes of patients with a cCR after nCRT undergoing active surveillance or standard surgery.

Material and Methods. Patients that refused surgery after nCRT between 2012-2017 from 4 hospitals were included. For the standard surgery group, patients from the preSANO trial were enrolled. A cCR was defined as endoscopies with multiple (bite-on-bite) biopsies, EUS-FNA and PET-CT showing no residual disease 6 and 12 weeks after completion of nCRT.

Optimal propensity-score matching generated a matched cohort (1:2) matched for age, comorbidities, cT, cN, histology of the tumor and biopsy type. For comparison of severity of complications according to Clavien-Dindo (CD) classification, a separate optimal propensity-score matching cohort was generated (1:2) for all patients in the active surveillance group that underwent surgery.

Primary outcome was overall survival, secondary outcomes were rate of radically resected tumors, distant dissemination rate and rate of postoperative complications according to the CD-classification.

Results. 75 patients were identified of whom 50 patients underwent standard surgery and 25 patients underwent active surveillance. 13 of 25 patients in the active surveillance group underwent surgery for locoregional recurrent disease. Median follow-up was 23.7 months for the standard surgery group and 18.8 months for the active surveillance group. There was no statistically significant difference between the groups in overall survival (HR=0.48, 95%C.I. 0.10–2.2,P=0.96). In both groups, all tumors were radically resected. There were no statistically significant differences in distant dissemination rate between the active surveillance and standard surgery group (16.0% versus 22.0%,*P=0.76*) or in severity of complications (CD≥3;46.2% versus 23.1%,*P=0.16*).

Conclusion. There was no statistically significant difference in overall survival, distant dissemination rate and severity of complications between patients undergoing standard surgery or active surveillance after nCRT. However, since sample sizes were small, especially for the severity of complications, these results should be interpreted with caution.

Conflict of interest: No conflict of interest.

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IMPLEMENTING INTEGRATED QUALITY ASSURANCE (SURCARE) FOR EORTC-JCOG 1527 / ESSO 02: DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING (DW-MRI) ASSESSMENT OF LIVER METASTASIS TO IMPROVE SURGICAL PLANNING (DREAM)

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