and Cancer Center, Division of Gastroenterology, Kasama, Japan; [11] *University of Fukui, Department of Gastroenterological Surgery, Fukui, Japan;* [12] *Kanto Rosai Hospital, Department of Surgery, Kawasaki, Japan;* [13] *Tokyo Metropolitan Tama Medical Center, Department of Surgery, Fuchu, Japan;* [14] *Gunma University Hospital, Integrative Center of General Surgery-Division of Gastroenterological Surgery, Maebashi, Japan;* [15] *National Kyushu Medical Center, Department of Gastroenterological Surgery and Clinical Research Institute Cancer Research Division, Fukuoka, Japan;* [16] *Kitano Hospital- Tazuke-Kofukai Medical Research Institute, Department of Gastroenterological Surgery and Oncology, Osaka, Japan;* [17] *Aichi Medical University, Department of Gastroenterological Surgery, Nagakute, Japan;* [18] *The University of Tokyo Graduate School of Medicine, Department of Gastroenterology, Tokyo, Japan;* [19] *Jichi Medical University, Department of Clinical Oncology, Shimotsuke, Japan;* [20] *Jichi Medical University, Support Center for Clinical Investigation, Shimotsuke, Japan*

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.

67

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

B. Van Der Wilk [1], L.K.A. Neijenhuis [1], B.J. Noordman [1], G.A.P. Nieuwenhuijzen [2], M.N. Sosef [3], M.I. van Berge Henegouwen [4], S.M. Lagarde [1], B.P.L. Wijnhoven [1], A. van der Gaast [5], J.J.B. van Lanschot [1]. [1] *Erasmus MC, Surgery, Rotterdam, Netherlands;* [2] *Catharina Cancer Center, Surgery, Eindhoven, Netherlands;* [3] *Zuyderland MC, Surgery, Heerlen, Netherlands;* [4] *Academic Medical Center, Surgery, Amsterdam, Netherlands;* [5] *Erasmus MC, Medical Oncology, Rotterdam, Netherlands*

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.

68

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)

K. Kataoka [2], C.I. Caballero [1], T. Suto [3], O. Masayuki [4], C.K. Hyunseon [5], R. Troisi [6], T. Yasumasa [7], H. Uetake [8], T. Nobuhiro [9], Y. Kazuhiro [10], O. Hitoshi [11], Y. Kishi [12], A. Shiomi [13], M. Ducreux [14], B. Bonhomme [15], L. Collette [16], L. Rubbia-Brandt [17], G. Brown [18], M. Shiozawa [19], S. Evrard [20]. On behalf of EORTC GITCG and JCOG investigators and ESSO Clinical Research Committee[1] *EORTC, Medical, Brussel, Belgium;* [2] *Hyogo College of Medicine, Colorectal Cancer Surgery, Hyogo, Japan;* [3] *Yamagata Prefectural Central Hospital, Surgery, Yamagata, Japan;* [4] *Osaka Medical Center for Cancer and Cardiovascular Diseases, Surgery, Osaka, Japan;* [5] *The University of Texas MD Anderson Cancer Center, Radiology, Houston, USA;* [6] *Universitair Ziekenhuis Gent, Hepatobiliary Surgery, Gent, Belgium;* [7] *Niigata Prefectural Cancer Center Hospital, Surgery, Nigata, Japan;* [8] *Tokyo Medical and Dental University, Surgery, Tokyo, Japan;* [9] *Chiba Cancer Center, Surgery, Chiba, Japan;* [10] *Gifu University Hospital, Surgery, Gifu, Japan;* [11] *Gunma Cancer Center, Surgery, Gunma, Japan;* [12] *National Cancer Center, Surgery, Tokyo, Japan;* [13] *Shizuoka Cancer Center, Surgery, Shizuoka, Japan;* [14] *Gustave Roussy, Oncology, Villejuif, France;* [15] *Institut Bergonie, Pathology, Bordeaux, France;* [16] *EORTC, Statistics, Brussel, Belgium;* [17] *Hôpitaux Universitaires de Genève, Pathology, Geneva, Switzerland;* [18] *Royal Marsden NHS Foundation, Radiology, Sutton, United Kingdom;*

[19] *Kanagawa Cancer Center, Colorectal Cancer Surgery, Yokohama, Japan;* [20] *Institut Bergonie, Digestive Surgery, Bordeaux, France*

For patients with initially unresectable colorectal liver metastases (CRLM) with good clinical response to chemotherapy, the presence of disappearing liver metastases (DLMs) diagnosed by CT is a major independent prognostic factor. However, correlation between radiological and pathological complete response has not been fully investigated using the latest imaging and pathology techniques. DW-MRI and contrast enhanced (CE)-MRI are recommended to detect and characterise CRLM. Our main aim is to demonstrate the added value of DW-MRI, CE-MRI and CT scan to provide precise assessment of the viability of DLMs. In addition, we aim to improve prognostication and treatment strategies for CRLM patients using parenchymal sparing surgery (PSS). No large scale study has been conducted to date to determine the predictive value of DW-MRI combined with CE-MRI in confirming sites of DLMs and assessing their true status. This is the first collaborative study between EORTC, ESSO and JCOG with an integrated quality assurance (QA) program for imaging, surgery and pathology. Together, we also developed an infrastructure for surgical QA in clinical trials (SURCARE) to advance the surgical oncology research agenda in Europe and Asia.

Patients with unresectable CRLM will receive standard systemic therapy & liver resection once resectable. CT scan and MRI (DW-MRI, CE-MRI and T1/T2) will be used to identify confirmed DLMs (cDLMs). Treatment (surgery or clinical follow-up) and outcome (either based on pathology or follow-up imaging) of cDLMs will be documented until 2 years after surgery to evaluate the true status of the cDLM. Primary endpoint is negative predictive value (NPV) of DW-MRI, CE-MRI, T1/T2 and CT scan in confirming the status of cDLM using histopathology or follow-up imaging as comparators. The study aims to exclude a NPV$\leq$0.85 and is powered under the alternative that the NPV$\geq$0.95. The planned sample size is 92 evaluable (resected or left behind) cDLMs, with a 1-sided alpha of 5% and a power of 90% adjusting for within-patient correlation between cDLMs of 0.2 and an average number of 2 cDLMs per patient. Around 400 patients will be registered from Europe, Japan and US over 3 years. The sample size will be adapted based on updated estimates of the correlation and average number of cDLMs pr patient.Through SURCARE, a retrospective central review of clinical data from imaging, surgery and pathology will be performed. An imaging platform to store DICOM images, pathology reports and standardized liver surgery template has been developed for DREAM (NCT02781935) & will be reviewed by an independent multidisciplinary team of experts.

As of April 2018, 88 patients have been registered: 69 from JPN; 9 from FR; 6 from US; 4 from BE. Outcome of the central review will be used to improve the PSS strategy for CRLM surgery. SURCARE will be implemented in future EORTC studies.

Conflict of interest: No conflict of interest.