

REVIEW ARTICLE

Progress in the treatment of gastric cancer in Japan over the last 50 years

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Abstract

There have been remarkable changes in gastric cancer treatments in Japan, resulting in superb improvement of prognosis in patients with this disease. In this paper, the last 50 years have been divided into three eras: before 1990; the 1990s; and the era of evidence, which means after 2000. Changes of treatments and prognosis were analyzed by several factors, such as surgery, chemotherapy, informed consent, clinical trials, and others, as improvement of prognosis is not due to one factor but several ones influencing each other.

KEYWORDS

gastric cancer, historical view, treatment

1 | TREATMENT OF GASTRIC CANCER BEFORE 1990

1.1 | Earlier stage at diagnosis

In 1960, the screening test for gastric cancer of upper gastrointestinal (UGI) barium contrast swallow was introduced in the Miyagi prefecture and gradually became adopted in many other parts of the country. In 1983, the Japanese Government issued a law requiring each local government to establish a system of screening for several cancers in their territory, including gastric cancer for citizens over the age of 40 years.¹ Although the actual proportion of people undergoing screening was lower than 30%, the public was well-aware of the elevated risk of gastric cancer in Japan. Because of this increased awareness, people began to seek medical advice very early after the onset of symptoms and were subsequently offered endoscopy. As a result of this increased screening activity, the proportion of early-stage cancers increased year by year (Table 1).² Early detection is likely the most important reason for the improvement of survival for Japanese patients with gastric cancer.

1.2 | Efficacy of chemotherapy treatment

Before 1990, the approved chemotherapeutic agents for gastric cancer included 5-FU (1950s), mitomycin-C (MMC) (1960s), Doxorubicin (1970s), cytarabine (1970s), Etoposide (1970s), and cisplatin (1980s). The combination of 5-FU, adriamycin, and mitomycin-C (FAM) was initially regarded as the standard regimen.³ In the late 1980s, combination chemotherapy using etoposide, adriamycin, and cisplatin (EAP) was demonstrated to have a dramatically high response rate.⁴ This treatment was soon abandoned, however, due to an unacceptably high incidence of treatment-related death rates. In Japan, a combination of 5-FU or several oral derivatives and MMC became the most commonly used regimen.

1.3 | Trends in surgery

With the limited efficacy of non-surgical treatment, surgeons tried to perform more radical surgical procedures in an attempt to improve survival. There was a belief among surgeons that complete resection of all macroscopic tumors, even at distant sites, was the

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TABLE 1 Chronological trends of incidence of early gastric cancer

Period	No. of cases	Proportion of pT1 (%)	5-y OS (%)
1963-1969	1628	22	42
1970-1974	1020	32	56
1975-1979	967	34	58
1980-1984	1165	43	65
1984-1989	1211	53	71

Note: Chronological trends showing increase of T1 and 5-y survival rate of the whole stomach cancer patients undergoing gastrectomy at National Cancer Center Tokyo. Modified from table 1 of Early detection of gastrointestinal cancers: Recent progress in endoscopy and surgical results by Yoshida et al.²

only way to cure gastric cancer. Dr Kajitani reported good results of D2 gastrectomy even for advanced stages.⁵ When performing a D2 total gastrectomy, splenectomy and distal pancreatectomy were routinely performed.⁶ For some advanced tumors with lymphadenopathy involving the celiac trifurcation, en-bloc resection of the stomach, the distal pancreas and spleen, as well as the vascular pedicles of the stomach (i.e., the celiac artery itself with the common hepatic and splenic arteries), was advocated by the Canadian surgeon, Dr Appleby.⁷ This operation, however, showed higher morbidity than a standard total gastrectomy with pancreato-splenectomy and was gradually abandoned in the late 1980s. For large tumors involving the whole stomach like "linitis plastica," an upper abdominal exenteration procedure was advocated by some, which included total gastrectomy, distal pancreatectomy and splenectomy, transverse colectomy with or without left lateral segmentectomy of the liver.⁸ As a retrospective comparison of the patients treated at the National Cancer Center Hospital Tokyo demonstrated better long-term survival results with less morbidity for those whose distal pancreas was preserved than those undergoing radical surgical procedures (i.e., pancreato-splenectomy in case of total gastrectomy) the latter was gradually replaced by the former as advocated by Dr Maruyama.⁹

In some Japanese institutions including the Cancer Institute Hospital, para-aortic node dissection (PAND) was introduced with results showing a relatively high incidence of metastasis in the para-aortic nodes (PAN) and a 5-year survival rate for those having PAN metastasis of 10%-30%.¹⁰⁻¹²

1.4 | Telling the truth and informed consent

As recently as the 1980s in Japan, it was common practice for physicians to withhold information about the disease extent and prognosis from their patients to obtain informed consent from the patients' families. Especially in cases of advanced diseases, doctors were often hesitant to reveal the full extent of the disease to the patients themselves. At universities, medical students were often told not to tell the truth to cancer patients for fear that they would become overwhelmed and distraught and potentially even contemplate

suicide. Informed consent for clinical trials was also often obtained from patients' family members but not from patients themselves.¹³ Compared to the current situation, physician attitudes and practices in this era were, therefore, very paternalistic.

1.5 | Limited knowledge of medical statistics among physicians

As early as the 1980s, many clinical studies of adjuvant chemotherapy in gastric cancer were conducted including a few randomized trials of greater than 1000 patients. Several critical issues about these studies were raised over the next decade including inconsistency in the number of enrolled patients reported in different papers reporting results of the same trials, no consideration of the effects of multiplicity of analysis, no clear statement of hypothesis to justify sample size calculation, no stratification by prognostic factors (e.g. histological stage), and no consideration of quality of surgery.¹⁴ In addition, the quality of data cleaning and monitoring was suboptimal as data was usually collected and handled by busy physicians who had little time to dedicate to the research. Dedicated research nurses were not available in most hospitals. Most importantly, there was a lack of infrastructure for running large clinical studies and the physicians planning and conducting these studies had very limited knowledge of medical statistics, trial design, etc.

1.6 | Establishment of endoscopic treatment (EMR)

After analyzing the data of thousands of patients with early gastric cancer (EGC), it became evident that some types of EGC rarely have nodal metastases.¹⁵ As a result, methods of endoscopic resection for these early cancers were developed by gastroenterologists. The early experience with endoscopic resection involved polypectomy, which could be applied to cancers with a polypoid morphology. Over time, modifications of the polypectomy technique and the introduction of more sophisticated endoscopic instruments led to the development of endoscopic mucosal resection (EMR), which began to be used for flat lesions of limited size in the 1980s.¹⁶

2 | ADVANCES IN THE 1990S

2.1 | Change in physicians attitudes to telling the truth and informed consent

In the 1990s, there were many symposiums organized by different medical societies to discuss the importance of transparency and honesty when dealing with cancer patients, especially with regards to obtaining informed consent. As a result of these often heated discussions, health care professionals and patients themselves gradually accepted the need for transparency and honesty in the practice of medicine. It also became clear that with this change in practice

patterns there would be a need for increased mental health and psychological supports for patients and their families. In situations where the patients could not get such support, there was a tendency towards despair and depression.¹⁷ As of the late 1990s, most physicians became increasingly honest with their patients even in difficult situations like stage IV cancers and palliative conditions. Informed consent was increasingly obtained, not from their family, but directly from the patients themselves in this period.

2.2 | Influence of large international randomized trials

In 1989, the Dutch D1/D2 study commenced following the Medical Research Council trial which had started a few years earlier.^{18,19} The organizers of the Dutch study made attempts to ensure a high level of quality control in both surgical treatment and accurate pathological evaluation, especially with regards to lymph nodal retrieval and reporting.²⁰ The results of the Dutch Trial showed that postoperative hospital mortality was as high as 9.8% in the D2 group, which raised significant concerns about the quality of surgery in this trial. Although efforts had indeed been made to ensure the quality of surgery in this trial, several critical issues were identified: (a) none of participating surgeons except one had ever performed D2 surgery before the study, although an experienced Japanese surgeon performed surgery in the first 30 D2 cases; (b) there was no rigorous vetting process of participating surgeons to ensure the quality of surgery was above a standard level; (c) the treatment of surgical complications was not standardized among institutes, resulting in high mortality rates after anastomotic leakage and pancreatic fistula; (d) the study reported both a high incidence of insufficient nodal dissection (non-compliance) in patients allocated to D2 and a high incidence of over-dissection (contamination) in those allocated to D1; and (e) the data center was not completely independent and allowed frequent access to the survival data for surgical researchers, and (f) alpha spending function concept – an idea to maintain a level of alpha error defined by the study design toward consumption of alpha error by multiple testing during the study – was not applied in this study. Consequently, the survival analysis was carried out several times with little concern about “multiplicity of analysis.”²¹ Yet, despite these limitations, the Dutch Trial was considered as a major step forward in the field of abdominal oncological surgery trials.²²

The author who participated in the Dutch study as surgical quality controller and instructor subsequently went on to initiate clinical studies in the field of gastric cancer surgery in Japan, beginning with Japan Clinical Oncology Group (JCOG) 9501 and 9502. The former was a prospective randomized controlled trial (RCT) comparing D2 (D3) vs that plus PAND for advanced gastric cancer.²³ The latter was a prospective RCT comparing abdominal and transdiaphragmatic dissection (AT) vs left thoracoabdominal (LT) approach for gastric cancer invading the esophagus of 3 cm or less, roughly equivalent to Siewert type 2 and 3 tumors with limited esophageal involvement.²⁴ The JCOG, the first Japanese co-operative group in oncology,

enabled us to perform these studies, providing an independent data center, a data and safety monitoring committee, an independent audit committee, and a framework to lobby for governmental financial support. After these two studies, multiple other phase III studies on gastric cancer surgery were carried out on this group.

2.3 | Evaluation of efficacy of nodal dissection in each station

Before the results of these RCTs to demonstrate the benefit of lymph node dissection became available, the efficacy of nodal dissection was estimated using a new process, multiplying the percentage of metastasis by the 5-year survival rate of those having nodal metastasis in each nodal station, using a large number of patients treated in the National Cancer Center Hospital in Japan.²⁵ Prior to this publication, Japanese surgeons had demonstrated a high incidence of nodal metastasis in the different stations but had never shown the efficacy of surgery by survival rate. After this paper was published, these figures were called “dissection efficacy index” and started to be widely used in other cancer types to evaluate the efficacy of nodal dissection by station.

2.4 | Introduction of the insulation-tipped diathermic knife (IT knife) and endoscopic submucosal dissection (ESD)

In the 1990s, Dr Hosokawa invented the IT knife for ESD, which is now widely used to treat EGC as well as some early colon cancers.²⁶ As the technique of ESD continues to improve, there are increasing indications for the use of ESD.

2.5 | Back to the uncertainty about adjuvant chemotherapy

At the beginning of the 1990s, the majority of Japanese surgeons believed in the efficacy of adjuvant chemotherapy for curatively resected advanced gastric cancer, despite the lack of quality evidence. The majority of clinical studies on adjuvant treatment in the 1980s compared one of the oral fluorouracil derivatives with or without non-specific immunotherapy, such as Bacille-Calmette-Guérin (BCG), Picibanil (OK-432), or polysaccharide Kureha (PSK).¹⁴ In practice, most of the patients treated in Japanese hospitals, except cancer centers, were receiving adjuvant chemotherapy at this time. On the other hand, all studies planned by the JCOG group in the late 1980s and the early 1990s had surgery alone as the control arm and failed to show any significant benefit of adjuvant chemotherapy over surgery alone. JCOG, therefore, advocated a return to high quality surgery alone as the standard of care, arguing that ineffective adjuvant chemotherapy might actually be harmful to some patients without conferring any survival benefit. It was felt that continuing to administer

adjuvant chemotherapy as standard procedure in the absence of any evidence of it being beneficial was therefore unethical and could potentially hamper further trials to establish truly effective adjuvant treatment. Based on this concept, a nationwide RCT on the effect of uracil-tegafur (UFT) as adjuvant treatment for T2N1/2 patients was launched in 1997, but was terminated in 2001 upon the recommendation of the Data Monitoring and Safety Committee due to poor patient accrual.²⁷ The final results of this study published some years later, unexpectedly, showed the significant effect of adjuvant chemotherapy in spite of the small number of enrolled patients. The discussion during this decade changed the mind of surgeons in Japan from accepting surgery followed by adjuvant chemotherapy as the standard of care to accepting surgery alone as the standard treatment for gastric cancer.

2.6 | Additional effective drugs for gastric cancer

In the 1990s, a global phase III study was carried out to evaluate the efficacy and safety of the combination of 5FU, leucovorin, adriamycin, methotrexate (FAMTX) vs etoposide, adriamycin and cisplatin (EAP). This trial showed an improved response rate and median survival time with less toxicity for FAMTX.²⁸ As this regimen turned out, however, intolerable for majority of Japanese patients, the Japan Gastric Cancer Association (JGCA) guideline of 2001²⁹ did not recommend it.

3 | ERA OF EVIDENCE

3.1 | Gastric cancer treatment guidelines by JGCA

In 2001, the first gastric cancer treatment guideline was published by JGCA.²⁹ Before this guideline came out, the level of lymphadenectomy, type of reconstruction, and the chemotherapeutic regimen for both the adjuvant and metastatic setting was quite variable across the country. Since the release of the first set of Guidelines in 2001, regular revisions have been made and the idea of a “gold standard” in gastric cancer treatment has been gradually established.^{30,31}

3.2 | Clinical trials on gastric cancer surgery

After 2000, many important clinical studies have been carried out in the field of gastric cancer surgery. JCOG0110, the first non-inferiority trial conducted by the JCOG Gastric Cancer Surgery Group, evaluated spleen preserving total gastrectomy (D2 without splenic hilum nodes and nodes along the distal splenic artery) vs standard D2 total gastrectomy with splenectomy. In this study, the non-inferiority of spleen preserving total gastrectomy was established in cases where the tumor does not involve the greater curvature.³² Published trials on gastric cancer surgery by JCOG are summarized in Table 2.

3.3 | Minimally invasive surgery

Since 2000, laparoscopic gastrectomy (LG), especially distal gastrectomy (LDG) has been increasingly used for gastric cancer surgery. There is currently sufficient evidence to support the non-inferiority of LG vs open surgery for EGC or stage I gastric cancer.^{33,34} For advanced gastric cancer, a final conclusion about the use of LG should wait for several reasons. Firstly, several prospective trials have shown non-inferiority of LG for advanced tumors but not for stage III, especially IIIC patients.^{35,36} Secondly, exact staging of stage III is not easy, especially discriminating stage IIIA/B from IIIC.³⁷ Thirdly, the principal benefit of the postoperative quality of life could be shown for a relatively short time period. In a large RCT by JCOG for stage I gastric cancer, it was clearly demonstrated that improved quality of life after LG vs OG is limited to just a 3-month postoperative timepoint (unpublished data). One could argue that this very modest improvement is not enough to justify a change in practice until more mature survival data are seen for these patients.

3.4 | Function preserving surgery for EGC

Pylorus preserving gastrectomy (PPG) was initially reported in the 1980s for peptic ulcer treatment. This operation gained popularity in Japan in the 2000s for EGC,^{38,39} but the number of surgeons who continue to perform this surgery has decreased because of the wide application of LG for gastric cancer. Theoretically, laparoscopic PPG is feasible but is much more complicated than standard LDG. As the majority of patients get accustomed to surgical sequela, such as dumping syndrome,³⁸ within a few years, surgeons currently don't adequately weigh the patient benefit of retaining pyloric function against the convenience of the surgeons, to the author's great regret.

The JGCA treatment guidelines propose proximal gastrectomy for small EGC arising near the cardia.³¹ Several methods of reconstruction have been reported for this procedure. The pros and cons of the various techniques are summarized in Table 3. As shown in Table 3, Kamikawa's operation appears to have the best outcomes although this technique might be technically difficult via the laparoscopic approach.⁴⁰ The demonstrated benefits of this technique may justify open surgery when balanced against the time-limited benefit in QOL of other types of LG. The figure of gastroscopy of the remnant stomach is an eloquent demonstration of the potential benefit of Kamikawa's operation (Figure 1A,B).

3.5 | Development of adjuvant therapy

Since S-1, a combination drug of tegafur, gimeracil, and oteracil had shown remarkable efficacy in advanced and metastatic gastric cancer as a single agent and an RCT to evaluate the efficacy of S-1 as adjuvant chemotherapy for stage II/III gastric cancer was launched in 2001. Results of the first interim analysis reported in 2007 already showed significant superiority of this treatment to surgery alone.⁴¹

TABLE 2 Clinical studies on surgical treatment of gastric cancer by JCOG

Study number	Phase	Sample size	Clinical question	Results
JCOG9501	III	520	Superiority of PAND	Negative
JCOG9502	III	265	Superiority of left thoracotomy for EGJ tumors	Negative
JCOG0110	III	500	Non-inferiority of spleen preservation	Positive
JCOG0703	II	170	Feasibility and safety of LADG	Positive
JCOG0912	III	950	Non-inferiority of LADG	Positive
JCOG1001	III	1200	Superiority of bursectomy	Negative
JCOG1401	II	245	Feasibility of LTG/LPG	Positive

Note: Clinical phase 2 and 3 studies on gastric cancer surgery performed by JCOG which have already results of main analysis.

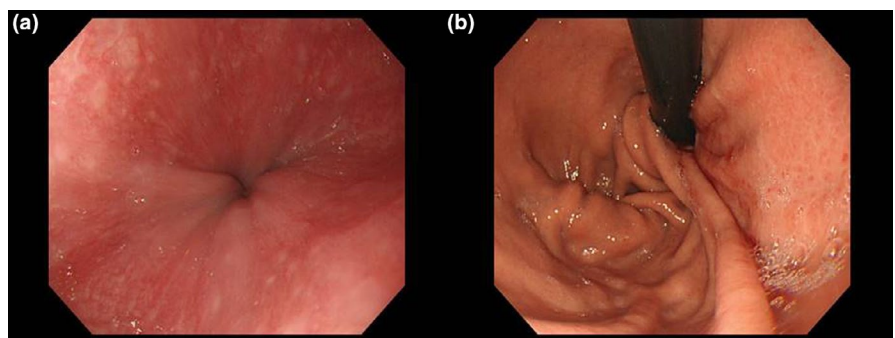
Abbreviations: EGJ, esophago-gastric junctional adenocarcinoma; LADG, laparoscopy assisted distal gastrectomy; LPG, laparoscopic proximal gastrectomy; LTG, laparoscopic total gastrectomy; PAND, para-aortic lymph node dissection.

TABLE 3 Functional aspects by reconstruction type

	Total G-RY	PG-Kamikawa	PG-Double tract	PG-JI
Passage at esophageal end	Eso→jejunum	Eso→stomach	Eso→jejunum	Eso→jejunum
Reservoir function	None	Yes	Low	Yes
Pyloric function	None	Yes	Low	Yes
Anti-reflux	None	Yes	None	None
Reflux esophagitis	Rare	Rare	Occasionally	Occasionally
Technical complexity	Little	High	Moderate	Moderate

Note: Functional aspects according to the type of reconstruction after a proximal gastrectomy including RY reconstruction after a total gastrectomy as reference.

Abbreviations: Eso, esophagus; G-RY, gastrectomy reconstructed by Roux-en Y technique; JI, jejunal interposition; PG, proximal gastrectomy.

FIGURE 1 (left and right): Endoscopic views after Kamikawa's operation. Endoscopic view of the EGJ from proximal side (left) and from remnant stomach (right) at 3 y after Kamikawa's operation

The success in conducting this trial was owing to wide acceptance of the uncertainty of benefit from adjuvant treatment in Japan, allowing the use of the surgery-alone control arm, which was impossible in the 1980s.

In 2009, a Korean RCT, the CLASSIC study, also showed significant benefit of adjuvant chemotherapy using xeloda plus oxaliplatin

(XELOX) for stage II/III gastric cancer.⁴² Recently, after the Japanese Government approved the use of oxaliplatin for gastric cancer, this combination and another combination of S-1 plus oxaliplatin (SOX) were tested for feasibility as adjuvant treatment in Japanese patients. Both treatments were proven to be tolerable by Japanese patients and the *post hoc* survival analysis showed good survival results, although

the number of patients was limited.⁴³⁻⁴⁵ In 2018, a phase III trial comparing S-1 monotherapy with docetaxel plus S-1 (DS), JACCRO GC-07, showed significantly better RFS with DS than with S-1 alone for stage III patients.⁴⁶ On the other hand, the JCOG1104 study, comparing four vs eight courses of S-1 monotherapy, did not demonstrate non-inferiority of four courses treatment for stage II patients.⁴⁷ At the moment, eight courses of S-1 monotherapy remains the standard treatment for stage II disease, but there are several options for stage III as the toxicity profiles, patterns of recurrence, and efficacy by histological type are different (Tables 4 and 5).⁴⁸

3.6 | Evidence for wider application of ESD

The JCOG Endoscopic Treatment Group has performed several prospective confirmatory studies for large-size mucosal cancers of differentiated histology (JCOG0607) and for small (≤ 2 cm)

poorly undifferentiated type including signet ring cell tumors (JCOG1009/1010). Both trials showed adequate overall and relapse-free survival^{49,50} such that ESD is not the first-choice treatment for patients with these lesions.

3.7 | New drugs have become available in this era

After 2000, many drugs have become available under social insurance; irinotecan,⁵¹ S-1,⁵² docetaxel,⁵³ paclitaxel,⁵⁴ capecitabine,⁵⁵ trastuzumab,⁵⁶ ramucirumab,^{57,58} oxaliplatin,⁵⁹ nab-paclitaxel,⁶⁰ nivolumab,⁶¹ and pembrolizumab.^{62,63} In the case of gastric cancer, the proportion of HER2 positive patients in whom trastuzumab is effective is limited to around 20%. With these various drugs, choice of regimens depends first on HER2 status. Ramucirumab is the only molecular targeting agent other than trastuzumab that showed significant efficacy for gastric cancer and is now recommended as the best second-line

TABLE 4 Adverse events of different adjuvant chemotherapy

Toxicity (%)	ACTS-GC		CLASSIC		JACCRO DS		OGSG1002		J-CLASSIC		pII SOX	
	All	G3/4	All	G3/4	All	G3/4	All	G3/4	All	G3/4	All	G3/4
Regimen	S-1 mono		S-1 mono		DS6		DS8		XELOX		SOX	
Neutro/leucopenia	58	1.2	60	22	59	38	65	53	76	33	79	32
Thrombocytopenia	26	0.2	26	8	19	1.2	7	0	43	6	47	4.8
diarrhea	57	3.1	48	2	50	3.3	32	0	67	2	55	1.6
Nausea	35	3.7	66	8	39	4.1	52	2	87	10	42	4.8
Vomiting	21	1.2	39	7	13	1.2	21	0	46	5	14.5	0
Stomatitis	32	0.2	12	<1	40	4.4	11	0	26	0	26	0
Appetite loss	55	6	59	5	63	14	65	18	66	17	57	6.5
Fatigue	58	0.6	31	5	34	1.5	56	10	43	6	31	4.8
Hand foot syndrome	1.4	0	19	1	NA	NA	NA	NA	48	0	NA	NA
Peripheral neuropathy	-	-	56	2	NA	NA	19	0	94	14	86	0
Alopecia	3.4	0	NA	NA	58	0	15	0	NA	NA	NA	NA

Note: Incidence of adverse events during adjuvant chemotherapy of all grade and grade 3/4.

Abbreviations: DS6, 6 courses of DS; DS8, 8 courses of DS; G, grade.

TABLE 5 Cross comparison of 3-y relapse free survival of stage III patients after different adjuvant chemotherapy

pStage	JACCRO GC-07		pII OGSG ⁴⁸	pII SOX	pII J-CLASSIC	ACTS-GC
	S-1	DS6	DS8	SOX	XELOX	S-1
IIIA	149 (32%)	147 (32%)	13 (21%)	17 (27%)	23 (39%)	40 + α^a
IIIB	160 (35%)	158 (35%)	24 (39%)	22 (35%)	16 (27%)	69 + β^a
IIIC	150 (33%)	149 (33%)	23 (37%)	23 (37%)	20 (34%)	78 (30.5%)
3 RFS	49.5%	65.9%	71% ^b	70.9%	67.8%	60.6%

Note: Cross comparison of 3-y relapse free survival rates of Japanese patients with stage III (UICC/AJCC TNM classification version 8) gastric cancer after D2 surgery plus adjuvant chemotherapy with S-1 monotherapy, Docetaxel plus S-1, S-1 plus oxaliplatin, xeloda plus oxaliplatin from three phase 3 and three phase 2 studies.

Abbreviations: DS, docetaxel plus S-1; OGSG, Osaka Gastrointestinal Cancer Chemotherapy Study Group.

^a $\alpha + \beta = 68$, stage IIIB $\geq 27\%$.

^bRFS including 3% of stage II.

treatment in combination with paclitaxel. Immune checkpoint inhibitors are expected to be used more and more, awaiting the results of the studies on efficacy as adjuvant or neo-adjuvant treatment.

4 | SUMMARY

In the last 50 years, treatment of gastric cancer has changed dramatically due to the acceptance of scientific evidence from trials and the development of new chemotherapy drugs. Given the rapid and remarkable aging of the Japanese population, the importance of non-surgical treatments will continue to increase. It seems possible that ESD combined with “gentler” chemotherapy or immunotherapy may enable stomach preserving treatment in more than half of gastric cancer patients. On the other hand, if the phenomenon of increased incidence of signet ring cell cancer among young adults occurs, as in the USA, aggressive multimodal treatment will continue to be necessary, including D2 gastrectomy.

The 3-year RFS of the S-1 arm in the JACCRO GC-07 trial was 10% worse than that of stage III patients of the ACTS-GC and almost as bad as that of the S-1 monotherapy arm in the JCOG0501 study, which included 40% or more stage IV patients. We must be vigilant about maintaining high standards for gastric cancer surgery as this remains the single most important aspect of treatment. It is too early to make light of good local control by D2 surgery since the chemotherapy for this cancer is much less effective than that for breast cancer.

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