American College of Radiology
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RESECTABLE STOMACH CANCER

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Summary of Literature Review

Introduction/Background

In 2013, approximately 21,600 new cases of gastric cancer will occur in the United States, with an estimated 10,990 deaths from the disease [1]. Although 2000–2009 data demonstrated that gastric cancer is among the top 4 cancers with the largest annual decline in death rates in the United States [1], it remains the second leading cause of death worldwide, with an annual estimated 989,600 new cases, with the highest incidences in eastern Asia, Europe, and South America [2]. Although surgery remains the mainstay of management in gastric cancer, due to the high rate of locoregional and distant relapse, curative treatment generally requires a multimodality approach. Outcomes data from Surveillance, Epidemiology, and End Results (SEER) analysis demonstrate an overall 5-year survival of approximately 30%, largely due to the fact that most patients present with locally advanced disease [3]. Although the 5-year survival for patients with localized disease at diagnosis is 62.3%, patients with lymph-node positive disease (27.7%) or metastatic disease (3.7%) have a much worse prognosis [3].

Previously, the classification of gastric carcinomas included tumors arising at the gastroesophageal junction (GEJ) or tumors originating in the stomach at 5 cm or less from and crossing the GEJ. However, the seventh edition American Joint Committee on Cancer (AJCC) gastric cancer staging system defines gastric carcinomas as tumors either arising in the distal stomach or those originating in the proximal 5 cm of the stomach, but not crossing the GEJ [4]. This revision is mainly due to the prognostic implication of inappropriately including GEJ tumors in gastric tumor staging, since the outcomes for GEJ tumors after resection differ from gastric cancers [5].

Prognostic Factors

Histological tumor type can correlate with prognosis. The diffuse type/signet cell histology correlates to poorer outcomes, with a predilection for intraperitoneal metastases when compared to the intestinal type [6,7]. Disease location also has a prognostic implication and, generally, outcomes are worse for proximal tumors of the cardia compared with distal gastric lesions [8,9]. Distal gastric tumors are more common in Asia and tend to have a more favorable 5-year overall survival rate of up to 60%, compared with gastric cardia tumors, which are more common in the United States, with 5-year overall survival rates of approximately 20% [9,10]. Although this difference in outcomes may be due to genetic variations between the 2 populations, it may also be associated with the presence of widespread screening programs in countries such as Japan, which permit earlier detection of gastric cancer [9]. In addition, it is believed that the superior outcomes in Asia may be due to an increased utilization of more comprehensive yet potentially morbid D2 lymph node dissections, which remove additional lymph node basins as compared to D1 nodal dissections, which only evaluate the perigastric nodal regions [11].

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Although several studies have shown no survival advantage with a D2 resection, a recent study demonstrated a significant benefit in cancer specific survival in long-term follow up [12-14].

Treatment

Surgery

Surgical resection is an essential component of the management of gastric cancer and may involve various approaches including endoscopic mucosal resection for early stage (Tis, T1a) disease and minimally invasive laparoscopic resection or open gastrectomy for more advanced disease [15]. Minimally invasive approaches are becoming increasingly popular due to technological advances and the publication of data from randomized studies, which demonstrate equivalent outcomes with laparoscopic procedures compared with open techniques [15,16]. Commonly, a total gastrectomy is utilized for proximal or middle third lesions, and a partial gastrectomy is recommended for lesions in the distal third of the stomach [15]. The goal of resection is to obtain a negative margin (R0) resection since a microscopically positive (R1) resection is associated with a worse prognosis, and typically a wide resection margin (4–6 cm) around the primary gastric cancer is desired for potentially curative surgery. Due to the propensity for mucosal spread, "simple" or "close" gross negative margins are not sufficient. [15]. Given the significant disease-specific survival benefit with a more comprehensive nodal resection, a D2 nodal dissection with a minimum of 15 lymph nodes is preferred in large volume centers [14,17] The number of involved nodes reflects the burden of disease, and AJCC stage group survival estimates are thought to be best represented when at least 15 nodes are examined [17]. However, the concept of lymph node ratio, described as the ratio of positive lymph nodes to total number of retrieved lymph nodes, has been recently proposed as a more accurate indicator of lymph node metastasis. Based on several studies, use of lymph node ratio offers an independent prognostic factor that can reduce the influence of the extent of lymphadenectomy [18].

Chemotherapy

In an autopsy-based series used to examine patterns of relapse, 80%–93% of patients showed locoregional relapse after resection, with 49% demonstrating distant relapse [15]. Considering the high local and distant relapse rates with surgery alone, multiple studies have focused on efforts to improve outcomes with adjuvant treatment. Although initial studies did not seem to indicate a benefit to adjuvant chemotherapy over surgery alone for resectable stage II-III gastric cancer, 2 large randomized Asian trials (Adjuvant Chemotherapy Trial of TS-1 for Gastric Cancer and The Capecitabine and Oxaliplatin Adjuvant Study in Stomach Cancer trials) demonstrated a significant benefit in survival with postoperative chemotherapy after D2 resection [19,20]. Although the benefit of postoperative chemotherapy has been questioned in patients treated with D1 gastrectomy in Western countries, the recent Global Advanced/Adjuvant Stomach Tumor Research International Collaboration meta-analysis of 17 worldwide randomized trials of postoperative chemotherapy versus surgery alone demonstrated a significant improvement in both overall survival and disease-free survival, with a significant improvement in median survival from 4.9 years with surgery alone to 7.8 years with adjuvant 5-fluorouracil (5-FU) based chemotherapy [21].

Studies have investigated the role of preoperative chemotherapy in gastric cancer. The MRC Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial was a phase III design that randomized 503 patients with locally advanced, resectable adenocarcinoma of the stomach (74%), GEJ (14%), and distal esophagus (12%) to perioperative chemotherapy (epirubicin, cisplatin and 5-FU [ECF]) versus surgery alone [22]. Although none of the patients in the chemotherapy group demonstrated a pathological complete response, the 5-year overall survival rate was significantly improved with perioperative chemotherapy (36%) as compared to surgery alone (23%), with no difference in postoperative morbidity between the 2 groups. However, the relative contribution of preoperative and postoperative chemotherapy in the study is unclear as only 42% of patients assigned to perioperative chemotherapy completed protocol therapy, and 34% of patients completing preoperative chemotherapy and surgery did not receive postoperative chemotherapy [22]. A smaller phase III trial including 224 patients with esophageal (13%), GEJ (62%), and gastric (25%) cancer noted a benefit in R0 resection rate and disease-free and overall survival using a perioperative platinum/fluorinated pyrimidine combination [23] (see Variant 2).

The European Organization for Research and Treatment of Cancer (EORTC) conducted a study comparing preoperative chemotherapy (cisplatin, 5-FU) followed by surgery to surgery alone. The results showed a significant improvement in R0 resection rate (82% versus 67%) and a 7.1% rate of pathological complete response, but failed to demonstrate an overall survival benefit [24]. The discrepancy in outcomes of the MAGIC and the EORTC studies may be attributed to differences between the 2 studies including earlier stage disease, higher statistical power, and postoperative chemotherapy in the MAGIC trial. In addition, patients in the EORTC

trial were possibly more accurately staged with endoscopic ultrasound (EUS), whereas the MAGIC trial did not routinely utilize EUS-based staging.

Radiation Therapy

Many studies have examined the role of radiation therapy (RT), both in the preoperative and postoperative setting, in efforts to achieve a benefit over surgery alone. Among these, a randomized controlled trial by the British Stomach Cancer Group examined the benefit of postoperative RT or postoperative chemotherapy to surgery alone. Although there was a significant reduction in locoregional recurrence with postoperative RT (10% with RT versus 27% with surgery alone), there was no benefit in survival with either adjuvant treatment [25]. The role of preoperative RT was evaluated in a large randomized trial from China that found that the addition of preoperative RT versus surgery alone led to a significant improvement in overall survival (30% versus 20%), with a benefit to local recurrence (39% versus 52%), reduction in regional nodal metastases, and tumor downstaging, as well as a higher resection rate (89.5% versus 79%) [26]. A recent meta-analysis of 9 trials was conducted to examine the benefit of RT (postoperative, preoperative, or intraoperative) over surgery alone or surgery and chemotherapy. Results indicated a significant benefit in 5-year overall survival (relative risk = 1.39 by intent to treat analysis) with the addition of preoperative RT [27]. Of note, the meta-analysis included trials utilizing both preoperative RT alone, and in combination with chemotherapy, making it difficult to distinguish the relative benefit of preoperative RT alone in this setting. The Quality Research in Radiation Oncology (QRRO) patterns of care survey notes that 19% of patients receiving RT as a component of treatment for stage IB-IV (nonmetastatic) gastric cancer did so in the preoperative setting [28].

Combined Modality Treatment

Definitive Chemoradiotherapy

The majority of phase III studies for unresectable gastric cancer showed an advantage for combined-modality treatment over either RT or chemotherapy alone. Among these studies, Moertel et al [29] showed a significant improvement in 5-year survival from 0% with RT alone (35–37.5 Gy) to 12% with 5-FU chemoradiotherapy for locally advanced gastric cancer without surgery. The Gastrointestinal Tumor Study Group compared combination chemotherapy with 5-FU and lomustine to chemoradiotherapy with 5-FU and 50 Gy split-course RT, followed by maintenance chemotherapy and found a significant benefit in 4-year survival (18% versus 7%) with chemoradiotherapy [30] (see Variant 3).

Preoperative Chemoradiotherapy

The Radiation Therapy Oncology Group® (RTOG®) conducted phase II study RTOG 9904 studying the benefit of preoperative chemoradiotherapy consisting of induction chemotherapy (leucovorin, 5-FU, and cisplatin) followed by 45 Gy of RT with concurrent chemotherapy (5-FU and paclitaxel). The results demonstrated a 26% pathological complete response rate and a 77% R0 resection rate [31]. Walsh et al [32] conducted a randomized study of surgery alone versus neoadjuvant concurrent chemoradiotherapy (5-FU and cisplatin and 40 Gy RT) followed by surgery in patients mainly with esophageal adenocarcinoma (65%), including a proportion of patients with adenocarcinoma of the gastric cardia (35%). Results indicated that preoperative chemoradiotherapy resulted in a statistically significant improvement in median survival (16 months versus 11 months) and overall survival rates (32% versus 6%) over surgery alone. There have been several other promising small prospective trials examining the role of preoperative chemoradiotherapy [33,34]. It is important to note that one of the major benefits of the preoperative approach may be in the ability to select patients that may develop metastases and are therefore spared the morbidity of surgery, considering that approximately 12–17% of patients in prospective trials developed distant disease during preoperative chemoradiotherapy [35]. In addition, this approach has the potential benefit of improved adherence to treatment (see Variant 5).

Postoperative Chemoradiotherapy

Among the initial studies demonstrating a benefit to adjuvant chemoradiotherapy in patients with locally advanced gastric cancer, Moertel et al [36] randomized patients to surgery alone versus surgery plus adjuvant RT (37.5 Gy) concurrent with 5-FU chemotherapy. The results of the trial demonstrated a significant improvement in 5-year overall survival (23% versus 4%) with postoperative chemoradiotherapy. The landmark phase III Intergroup 0116 trial by Macdonald et al [37] examined the benefit of postoperative chemoradiotherapy in resectable gastric cancer and lower GEJ tumors (20%). This study included patients with stage IB-IV disease (AJCC 1988, 3rd ed.) randomized to surgery alone versus surgery followed by adjuvant chemoradiotherapy with 5-FU and leucovorin. The study demonstrated a significant benefit with adjuvant chemoradiotherapy with an improvement in median survival (36 months versus 27 months) and 3-year overall survival rates (50% versus

41%). A recent 10-year update of the INT-0116 demonstrated unchanged significance in the benefit for both overall survival (hazard ratio [HR] 1.32) and progression-free survival (HR 1.52) with postoperative chemoradiotherapy, in addition to a significant improvement in locoregional recurrence with adjuvant chemoradiotherapy (24%) as compared to surgery alone (47%) [38] (see Variant 1). The Eastern Cooperative Oncology Group E7296 Phase II trial of 3 cycles of preoperative paclitaxel and cisplatin and adjuvant RT (45 Gy) with concurrent and postoperative 5-FU and leucovorin included 38 patients, 42% of whom had gastric tumors and 58% had GEJ tumors. This regimen was difficult to tolerate as 8% were able to receive all assigned treatment, and 66% of patients had grade 3 and 4 toxicity, so this regimen was not recommended to undergo further development [39].

Only 10% of patients in the 0116 trial had a D2 resection, suggesting that the benefit of adjuvant chemoradiotherapy may possibly be limited to cases with less extensive lymph node dissections. Dikken et al [40] performed an analysis of phase I/II trials utilizing adjuvant chemoradiotherapy and studies from the Dutch Gastric Cancer Group Trial randomizing patients to D1 or D2 surgery alone. The analysis demonstrated that although chemoradiotherapy resulted in an overall significant decrease in local recurrence as compared to surgery alone trials (17% versus 5%), on subgroup analysis the local recurrence benefit of chemoradiotherapy was limited to D1 resected patients (8% with D1 surgery alone versus 2% with D1 plus chemoradiotherapy), with no improvement in local recurrence with the addition of postoperative chemoradiotherapy after D2 resection [40]. In contrast, Kim et al [41] conducted a study supporting the benefit to adjuvant chemoradiotherapy following D2 lymphadenectomy showing a significant benefit in overall survival and progression-free survival with adjuvant chemoradiotherapy as compared to surgery alone in patients undergoing D2 resection. The Adjuvant Chemoradiation Therapy in Stomach Cancer (ARTIST) trial examined the role of adjuvant treatment in patients with D2 resection followed by postoperative chemotherapy (cisplatin and capecitabine) or chemoradiotherapy, with the results demonstrating no benefit in disease-free survival with the addition of RT. However, subgroup analysis revealed a significant improvement in patients with lymph-node positive disease, highlighting a role for postoperative chemoradiotherapy in D2 resected patients with node-positive disease [42] (see Variant 4).

Based on the data above, resectable gastric cancer treatment may include lymph node resection followed by postoperative chemoradiotherapy with 5-FU and leucovorin chemotherapy (alternatively infusional 5-FU or capecitabine) concurrently with 45 Gy external beam RT. Alternatively, perioperative chemotherapy as per the MAGIC trial can be considered in the management of gastric cancer [43]. For resected cases with positive or close margins, adjuvant chemoradiation should be employed.

Radiation Therapy Technique

The Intergroup 0116 trial utilized external beam RT with at least 4 MV photons, in a conventional anteroposterior/posteroanterior (AP/PA) field arrangement. Although the results of the trial contributed to the current standard of care, chemoradiotherapy treatment resulted in significant grade 3 or greater treatment-related morbidity, with 54% and 33% of patients experiencing hematologic and gastrointestinal toxicity, respectively [37]. With advances in technology and techniques for conformal radiation delivery such as intensity-modulated radiation therapy (IMRT), it has become possible to attempt to spare normal tissues in an effort to decrease treatment-related toxicity. Several studies have investigated the possible advantage of IMRT in the treatment of gastric cancer. Ringash et al [44] compared 3-D conformal radiation therapy (3D-CRT) with IMRT planning in 20 patients. Evaluation of plans demonstrated improved target volume coverage with IMRT in 86% of cases, in addition to improved sparing of spinal cord (74%), kidneys (69%), liver (71%), and heart (69%). Minn et al [45] from Stanford suggested better preservation of kidney function with significantly lower median postradiation serum creatinine levels with IMRT compared to 3D-CRT. However, dosimetric evaluation of the kidneys showed nonsignificant improvements in the V20 but higher mean doses to the kidneys with IMRT. A recent study from MD Anderson utilizing preoperative IMRT concurrent with chemotherapy demonstrated excellent target coverage and organ sparing with IMRT but failed to demonstrate a significant difference in rates of acute toxicity, hospitalization, or feeding tube use as compared to a group of patients treated with 3D-CRT [46]. Although IMRT may lead to improved organ sparing, currently there is insufficient clinical evidence regarding its role in decreasing treatment-related toxicity as compared to 3D-CRT.

A survey of practice patterns by the QRRO attempted to analyze the penetration of multiple clinical performance measures and use of modern treatment planning approaches as a partial surrogate of quality. The 3 clinical performance measures included the following: use of CT-based treatment planning, generation of dose–volume histograms (DVH) to specifically evaluate dose to the kidneys and liver, and timely completion of prescribed

postoperative RT. Of the institutions surveyed over a 24-month time period within the last decade (2005–2007), almost all postoperative gastric cancer patients received CT-based treatment planning, 75% underwent kidney DVH analysis, and nearly the same percentage completed RT as prescribed. The QRRO survey also showed that IMRT and image-guided radiation therapy were used in nearly one-fifth of patients [28].

Ongoing Studies

Current data support a role for both combined modality treatment with postoperative chemoradiotherapy and perioperative chemotherapy in resectable gastric cancer, based on the results on the Intergroup INT-0116 and MAGIC trial, respectively. Current studies are underway to further define the role of chemotherapy and RT in management of gastric cancer. In the multicenter phase III Dutch CRITICS trial, patients are treated with 3 cycles of chemotherapy (epirubicin, cisplatin, capecitabine) followed by surgery and randomization to 3 additional cycles of the same chemotherapy versus concurrent chemoradiotherapy (45 Gy, cisplatin and capecitabine). The randomized phase III MAGIC-B study will examine the benefit of the addition of the anti-VEGF antibody bevacizumab to the original perioperative MAGIC regimen. The ARTIST-2 trial will study the role of D2 lymphadenectomy alone to D2 lymphadenectomy followed by chemoradiotherapy in patients with pathologically involved lymph nodes. Currently in active accrual, the phase II/III international Trial of Preoperative Therapy for Gastric and Esophagogastric Junction Adenocarcinoma will examine the role of neoadjuvant chemoradiotherapy (45 Gy RT, concurrent 5-FU or capecitabine) compared to neoadjuvant chemotherapy (ECF) for resectable disease, to determine any improvement in the endpoints of pathological complete response and overall survival. The results of these studies and future trials will further delineate optimal management of gastric cancer in efforts to improve outcomes in this disease.

Summary of Recommendations

- After gastric cancer resection, adjuvant chemotherapy combined with chemoradiation (INT-0116) are standard treatments and should be considered particularly for D0 lymph node dissection, positive regional lymph nodes, poor clinical response to induction chemotherapy, or positive margins.
- A standard treatment option for resectable gastric cancer is perioperative chemotherapy, with 3 cycles of epirubicin, cisplatin, and 5-FU (or other appropriate alternatives) given before and after surgery.
- For patients who have undergone D2 lymph node dissection, especially those with negative regional lymph nodes, adjuvant chemotherapy alone could be considered.
- Induction chemotherapy followed by surgery is a less studied treatment option. Little data exist comparing preoperative chemotherapy alone to preoperative chemoradiation regimens with surgery for gastric cancer.
- For unresectable gastric cancer, standard treatment options include chemoradiation, preferably for the patient who can tolerate such a regimen. Alternatively, radiation therapy alone or chemotherapy alone is a viable treatment option for a patient with a compromised performance status.

Summary of Evidence

Of the 46 references cited in the *ACR Appropriateness Criteria® Resectable Stomach Cancer* document, all of them are categorized as therapeutic references including 22 well designed studies and 3 good quality studies. There are 21 references that may not be useful as primary evidence.

The 46 references cited in the *ACR Appropriateness Criteria® Resectable Stomach Cancer* document were published between 1965-2014.

While there are references that report on studies with design limitations, 25 well designed or good quality studies provide good evidence.

Supporting Documents

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Clinical Condition: **Resectable Stomach Cancer**

Variant 1: **54-year-old man with EUS uT2NxM0 gastric cardia adenocarcinoma status post total gastrectomy, final pathology, pT3N0M0, negative margins, D0 lymph node dissection. No neoadjuvant therapy given. KPS 80.**

Treatment	Rating	Comments
Chemoradiotherapy + chemotherapy	8	
Chemotherapy alone	5	
RT alone	3	
Observation	2	
Sequencing of Therapy		
Induction chemotherapy × 1 cycle + chemoradiotherapy + chemo x 3 cycles	8	
Induction chemotherapy × 4 cycles + chemoradiotherapy	6	
Chemoradiotherapy + chemotherapy × 4 cycles	6	
Type of Chemotherapy Before/After and During Chemoradiotherapy		
5-FU +/- leucovorin	8	Leucovorin is generally not used in practice.
Capecitabine alone	6	It is unclear if capecitabine is absorbed properly after gastrectomy.
5-FU + oxaliplatin	5	5-FU + cisplatin may be a reasonable alternative as per the ARTIST trial [42].
Dose to Tumor Bed		
45 Gy/1.8 Gy	9	
50.4 Gy/1.8 Gy	7	
54 Gy/1.8 Gy	3	
RT Technique		
AP/PA photons	5	
4–5 field photon conformal plan	8	
IMRT	7	
RT Volume Needed		
Operative and tumor bed, anastomotic sites, adjacent pancreas, left hemidiaphragm, perigastric, periesophageal (3–5 cm of esophagus), celiac lymph node beds	8	
Operative and tumor bed, anastomotic sites, adjacent pancreas, left hemidiaphragm, periesophageal (3–5 cm of esophagus)	5	
Operative and tumor bed, anastomotic sites	3	

Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**

Clinical Condition: **Resectable Stomach Cancer**

Variant 2: **60-year-old man with uT3N1M0 gastric body adenocarcinoma status post 3 cycles ECF chemotherapy, followed by total gastrectomy, pT3N2M0, with residual bulky tumor at surgery, D1 lymph node dissection, negative margins. KPS ≥70.**

Treatment	Rating	Comments
Chemoradiotherapy + chemotherapy	8	
Chemotherapy alone with different (not ECF regimen)	6	
Chemotherapy alone with continuation of ECF	4	It may not be appropriate to continue ECF if there is no significant response.
RT alone	3	
Observation	1	
Sequencing of Therapy		
Induction chemotherapy × 1 cycle + chemoradiotherapy + chemo x 3 cycles	6	
Induction chemotherapy × 4 cycles + chemoradiotherapy	6	
Chemoradiotherapy + chemotherapy × 4 cycles	6	
Type of Chemotherapy Before/After Chemoradiotherapy		
Continuous infusion 5-FU +/- leucovorin	7	Leucovorin is generally not used in practice.
5-FU + oxaliplatin	5	5-FU + cisplatin may be a reasonable alternative as per the ARTIST trial [42].
Type of Chemotherapy During Chemoradiotherapy		
Continuous infusion 5-FU +/- leucovorin	8	
Capecitabine Monday–Friday	6	
Dose to Tumor Bed		
45 Gy/1.8 Gy	8	
50.4 Gy/1.8 Gy	7	
54 Gy/1.8 Gy	6	
RT Technique		
AP/PA photons	5	
4–5 field photon conformal plan	8	
IMRT	7	
RT Volume Needed		
Tumor bed + anastomoses + celiac LN + perigastric LN + splenic + suprapancreatic + pancreaticoduodenal + porta hepatis	8	
Tumor bed + anastomoses + celiac LN + perigastric LN+ splenic+ suprapancreatic	7	
Tumor bed + anastomoses + celiac LN + perigastric LN	6	
Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**		

Clinical Condition: **Resectable Stomach Cancer**

Variant 3: **80-year-old woman with uT3N1M0 gastric body adenocarcinoma. Patient is not a surgical candidate due to KPS 60 and 15% weight loss over 6 months.**

Treatment	Rating	Comments
Chemoradiotherapy alone	8	
RT alone	6	
Chemotherapy alone	6	
Dose to Tumor Bed		
45 Gy/1.8 Gy	7	
50.4 Gy/1.8 Gy	8	
54 Gy/1.8 Gy	6	
RT Technique		
AP/PA photons	5	
4–5 field photon conformal plan	8	
IMRT	7	
RT Volume Needed		
Stomach + involved LN	7	
Whole stomach + involved LN + celiac LN + perigastric LN + splenic + suprapancreatic + pancreaticoduodenal + porta hepatis	5	
Tumor + involved LN	4	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Resectable Stomach Cancer**

Variant 4: **63-year-old woman with uT2N1 antral adenocarcinoma status post partial gastrectomy, final pathology T2N1M0, with positive distal margin, D2 lymph node dissection. KPS ≥80.**

Treatment	Rating	Comments
Chemoradiotherapy + chemotherapy	8	
RT alone	3	
Chemotherapy alone	3	
Observation	1	
Sequencing of Therapy		
Induction chemotherapy × 1 cycle + chemoradiotherapy + chemo x 3 cycles	8	
Chemoradiotherapy + chemotherapy × 4 cycles	7	
Induction chemotherapy × 4 cycles + chemoradiotherapy	6	
Type of Chemotherapy Before/After and During Chemoradiotherapy		
5-FU +/- leucovorin	8	
Capecitabine alone	6	
5-FU + oxaliplatin	5	5-FU + cisplatin may be a reasonable alternative as per the ARTIST trial [42].
Dose to Tumor Bed		
45 Gy/1.8 Gy	7	
50.4 Gy/1.8 Gy	8	
54 Gy/1.8 Gy	7	
RT Technique		
AP/PA photons	5	
4–5 field photon conformal plan	8	
IMRT	7	
RT Volume Needed		
Tumor bed + anastomosis with boost to distal anastomosis + perigastric + pancreaticoduodenal + porta hepatis + celiac + suprapancreatic LN	8	
Tumor bed + anastomosis with boost to distal anastomosis + perigastric + pancreaticoduodenal + porta hepatis LN	7	
Tumor bed + anastomosis with boost to distal anastomosis	5	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Resectable Stomach Cancer**

Variant 5: **57-year-old man with uT4N2M0 gastric body adenocarcinoma. KPS 80.**

Treatment	Rating	Comments
Chemoradiotherapy then surgery	8	
Chemotherapy alone then surgery	7	
Chemotherapy then chemoradiotherapy then surgery	6	
Surgery then chemoradiotherapy and chemotherapy	5	
If Preoperative Chemoradiotherapy: Dose to Tumor Bed		
45 Gy/1.8 Gy	7	
50.4 Gy/1.8 Gy	7	
54 Gy/1.8 Gy	4	
RT Technique		
AP/PA photons	5	
4–5 field photon conformal plan	8	
IMRT	7	
If Preoperative Chemoradiotherapy: RT Volume Needed		
Tumor + involved LN + celiac LN + perigastric LN + splenic + suprapancreatic + pancreaticoduodenal + porta hepatis	7	
Whole stomach + involved LN + celiac LN + perigastric LN + splenic + suprapancreatic + pancreaticoduodenal + porta hepatis	7	
Stomach + involved LN	6	
Tumor + involved LN	5	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		