Neoadjuvant or Adjuvant Therapy for Resectable Esophageal Cancer: Is There a Standard of Care?

Khaldoun Almhanna, MD, MPH, Ravi Shridhar, MD, PhD, and Kenneth L. Meredith, MD, FACS

**Background:** Carcinoma of the esophagus is an aggressive and lethal disease with an increasing incidence worldwide. Despite changes in the treatment approach over the past two decades and even following complete resection, most patients will eventually relapse and die as a result of their disease. Several clinical trials evaluated different modalities in treating locally advanced esophageal cancer; however, because of stage migration and the changes in disease epidemiology, applying these trials to clinical practice has become a daunting task.

**Methods:** We searched Medline and conference abstracts for randomized studies published in the past three decades. We restricted our search to articles published in English.

**Results:** Neoadjuvant chemoradiotherapy followed by surgical resection is an accepted standard of care in the United States for patients with locally advanced esophageal cancer. Esophagectomy remains an essential component of treatment and can lead to improved overall survival, especially when performed at high-volume institutions. The role of adjuvant chemotherapy following curative resection in patients who underwent neoadjuvant chemoradiotherapy remains unclear.

**Conclusions:** Several questions still need to be answered regarding the use of neoadjuvant or adjuvant therapy for patients with resectable esophageal cancer. The optimal chemotherapy regimen has not yet been identified for these patients, although newer therapies show promise.

**Introduction**
Carcinoma of the esophagus is an aggressive disease with a poor overall outcome. In 2012 in the United States, approximately 17,360 new cases were diagnosed and 15,070 patients died of the disease. The incidence of adenocarcinoma of the esophagus is rising dramatically worldwide, whereas the incidence of squamous cell carcinoma (SqCC) is decreasing. Survival rates in metastatic esophageal cancer remain low, and outcomes in patients with locoregional resectable esophageal cancer have slightly improved since incorporating multimodality therapy in the treatment of this patient population.

Multiple clinical trials have addressed the preferred treatment sequence in managing locally advanced esophageal cancer (LAEC); however, no standard therapy has been established. While esophagectomy remains the cornerstone treatment of clinically localized esophageal
carcinoma, the systemic nature of the disease attributes to the failure of surgery alone. Systemic chemotherapy, with or without radiotherapy, could lead to improved outcomes. Several authors have addressed the role of chemotherapy and radiation therapy, before and/or after surgery; however, their data have yielded conflicting results. The heterogeneous patient populations, tumor biology (pathological response to therapy), and lack of a standard approach to esophagectomy may explain the discrepancies in results among institutions.

The majority of the studies published in the past three decades have included mostly patients with SqCC, and a distinction between the two subtypes has not always been made. However, it remains unclear as to whether histology should dictate the treatment approach. Extrapolating from these data when treating patients is acceptable until further data in adenocarcinoma are available. Enrollment in clinical trials should be encouraged.

In this article, we review the literature on treating LAEC as well as present our own treatment approach. Most of the trials reviewed excluded patients with SqCC of the cervical esophagus, and therefore interpretation of this review is limited to more distal tumors.

**Treatment With Surgery Alone**

Less than half of patients with esophageal cancer have resectable disease at presentation, based on staging positron emission tomography (PET) scans and esophageal ultrasonography. Surgical resection remains the standard treatment of early-stage disease. Endoscopic mucosal resection (EMR) is recommended for T1a disease if negative margins can be achieved. Upfront esophagectomy is recommended if EMR is not feasible in patients with positive margins following EMR or in patients with T1b disease.

Several clinical trials have used surgery alone as a control arm. For example, in the Radiation Therapy Oncology Group (RTOG) 8911 trial, patients who were randomized to surgery alone had a median survival of 1.3 years.³ In surgery-only series, 5-year survival rates were less than 50% for patients with stage II or higher disease.⁴ ⁵ ⁶ Therefore, it is currently recommended that patients with locally advanced disease (T2 or greater or node positive) receive neoadjuvant therapy (chemotherapy or chemoradiation).

Although there is great debate among surgeons regarding the technique of esophagectomy, median overall and disease-free survival rates have not been shown to differ statistically based on the surgical approach (extended transthoracic resection vs limited transthiatal resection).⁴ In the 1980s, the overall survival rate after esophagectomy was 4%, with a surgical mortality rate of 25%. Currently, mortality rates after esophagectomy have decreased significantly. Higher-volume institutions have lower operative mortality rates for esophagectomy (more than a 12% absolute reduction in mortality compared with low-volume centers).⁷ Referring patients with resectable esophageal cancer to a high-volume institution for surgical resection is crucial.

**Preoperative Radiotherapy**

Several randomized trials comparing neoadjuvant radiotherapy and surgery vs surgery alone in patients with LAEC have been reported.⁸ ⁹ ¹⁰ ¹¹ ¹² ¹³ Investigators used different radiation doses and techniques. No statistically significant difference was seen in overall survival with preoperative radiotherapy compared with surgery alone. These trials are summarized in Table 1.⁸ ⁹ ¹³

**Postoperative Radiotherapy**

To improve local tumor recurrence, several randomized trials compared surgery alone with surgery followed by radiation therapy. Studies enrolled a heterogeneous population, including patients with

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**Table 1. — Randomized Trials of Preoperative Radiotherapy (RT) and Surgery vs Surgery Alone**

<table>
<thead>
<tr>
<th>Study</th>
<th>Yr</th>
<th>No. of Patients</th>
<th>Pathology</th>
<th>Median Survival (mos)</th>
<th>5-yr Survival Rate* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+RT</td>
<td>–RT</td>
</tr>
<tr>
<td>Fok³</td>
<td>1994</td>
<td>79</td>
<td>SqCC</td>
<td>11</td>
<td>22</td>
</tr>
<tr>
<td>Launois⁹</td>
<td>1981</td>
<td>124</td>
<td>SqCC</td>
<td>4.5</td>
<td>8.2</td>
</tr>
<tr>
<td>Gignoux¹⁰</td>
<td>1987</td>
<td>229</td>
<td>SqCC</td>
<td>12.3</td>
<td>12</td>
</tr>
<tr>
<td>Wang¹¹</td>
<td>1989</td>
<td>206</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Nygaard¹²</td>
<td>1992</td>
<td>108</td>
<td>SqCC</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Arnott¹³</td>
<td>1992</td>
<td>196</td>
<td>SqCC + Adenocarcinoma</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

*Not statistically significant.
SqCC = squamous cell carcinoma.
positive celiac nodes\textsuperscript{14,15} (M1a per the American Joint Committee on Cancer [AJCC] Cancer Staging, 6th ed) and R1 resection.\textsuperscript{16} Investigators used higher doses of radiation with different fractionation. Radiation was delivered from 6 to 12 weeks following surgery. These trials had conflicting results, with three studies failing to demonstrate any survival benefits to adjuvant radiation\textsuperscript{14,15,17} and one trial\textsuperscript{16} showing a worse survival in patients who received radiation therapy. Another trial showed improvement in quality of life in the surgery-only arm compared with the adjuvant radiation arm.\textsuperscript{15}

A pooled analysis of the five adjuvant radiation trials\textsuperscript{18} showed no significant difference in survival following adjuvant radiotherapy compared with surgery alone. Improvement in local tumor recurrence was reported in some of these trials but at the expense of toxicity. Preoperative radiotherapy was compared with postoperative radiotherapy in a small randomized trial; no difference in survival was detected between the two arms.\textsuperscript{18} Patients receiving preoperative radiotherapy had a higher rate of morbidity.\textsuperscript{18}

**Preoperative Chemotherapy**

Multiple randomized trials compared preoperative chemotherapy and surgery with surgery alone for the treatment of resectable esophageal cancer (Table 2).\textsuperscript{12,19-26} Of the seven earlier trials summarized, four showed no survival benefit to neoadjuvant chemotherapy and three did show a survival benefit with neoadjuvant chemotherapy compared with esophagectomy alone.

Larger, more recent studies have shown improved benefits for patient receiving neoadjuvant therapy. In the Medical Research Council (MRC) study,\textsuperscript{19} 802 patients with resectable esophageal cancer were randomly allocated to either 2 cycles of cisplatin and 5-fluorouracil (5-FU) followed by surgical resection or resection alone. Postoperative complications were similar in both groups. Overall survival was prolonged in the chemotherapy group, with a median survival of 16.8 months vs 13.3 months in the surgery-only group. In the MAGIC trial,\textsuperscript{20} 503 patients with resectable adenocarcinoma of the stomach, esophagogastric junction, or lower esophagus were randomly assigned to either perioperative chemotherapy or surgery alone. Chemotherapy consisted of 3 preoperative and 3 postoperative cycles of intravenous epirubicin, cisplatin, and continuous intravenous infusion of 5-FU. With a median follow-up of 4 years, the overall survival rate was significantly improved in the perioperative chemotherapy arm (36% vs 23%).

In an update of the MRC trial,\textsuperscript{27} there were 655 deaths, 335 in the surgery arm and 320 in the chemotherapy arm. The survival benefit has been maintained, with a hazard ratio (HR) of 0.84 (95% confidence interval [CI], 0.72–0.98; \(P = .03\)); in absolute terms, this represents a 5-year survival rate of 23.0% for chemotherapy and surgery compared with 17.1% for surgery alone. The treatment effect is consistent in both adenocarcinoma and SqCC.

Several pooled and meta-analyses addressed the role of neoadjuvant chemotherapy followed by sur-

<table>
<thead>
<tr>
<th>Study</th>
<th>Yr</th>
<th>No. of Patients</th>
<th>Chemotherapy</th>
<th>Pathology</th>
<th>Median Survival (mos)</th>
<th>3-yr Survival Rate (%)</th>
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</thead>
<tbody>
<tr>
<td>R  \textsuperscript{26}</td>
<td>1988</td>
<td>39</td>
<td>Cisplatin/bleomycin/vindesine</td>
<td>SqCC</td>
<td>&gt;20\textsuperscript{*}</td>
<td>8.6</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>–</td>
</tr>
<tr>
<td>N  \textsuperscript{12}</td>
<td>1992</td>
<td>112</td>
<td>Cisplatin/bleomycin</td>
<td>SqCC</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>S  \textsuperscript{21}</td>
<td>1992</td>
<td>46</td>
<td>Cisplatin/5-FU</td>
<td>SqCC</td>
<td>7.5</td>
<td>5</td>
</tr>
<tr>
<td>M  \textsuperscript{23}</td>
<td>1994</td>
<td>46</td>
<td>Cisplatin/bleomycin</td>
<td>SqCC</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>L  \textsuperscript{22}</td>
<td>1997</td>
<td>147</td>
<td>Cisplatin/5-FU</td>
<td>SqCC</td>
<td>16.8</td>
<td>13</td>
</tr>
<tr>
<td>K  \textsuperscript{25}</td>
<td>1998</td>
<td>440</td>
<td>Cisplatin/5-FU</td>
<td>55% Adenocarcinoma</td>
<td>14.9</td>
<td>16.1</td>
</tr>
<tr>
<td>A  \textsuperscript{24}</td>
<td>2001</td>
<td>94</td>
<td>Cisplatin/5-FU</td>
<td>–</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>MRC\textsuperscript{19}</td>
<td>2002</td>
<td>802</td>
<td>Cisplatin/5-FU</td>
<td>67% Adenocarcinoma</td>
<td>16.8</td>
<td>13.3</td>
</tr>
<tr>
<td>MAGIC\textsuperscript{20}</td>
<td>2006</td>
<td>503</td>
<td>ECF</td>
<td>Adenocarcinoma</td>
<td>–</td>
<td>79</td>
</tr>
</tbody>
</table>

\*Median survival for responders.

ECF = epirubicin, cisplatin, 5-FU, 5-FU = 5-fluorouracil, SqCC = squamous cell carcinoma.

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surgery compared with surgery alone. Malthaner et al\textsuperscript{18} included six studies in their meta-analysis.\textsuperscript{12,19,21-24} No significant difference in outcome was detected (relative risk, 1.00; 95% CI, 0.83–1.19; \( P = .98 \)).

A meta-analysis published in 2002 included 11 randomized clinical trials (RCTs) comparing surgery alone with preoperative chemotherapy.\textsuperscript{28} Again, no statistically significant difference was reported in 3-year survival in patients who received preoperative chemotherapy compared with those who underwent upfront surgical resection. Two additional meta-analyses demonstrated survival benefits for preoperative chemotherapy; the first was a Cochrane Review, which pooled 11 RCTs. A statistically significant difference in survival favoring preoperative chemotherapy was detected only at 5 years.\textsuperscript{29} An updated meta-analysis\textsuperscript{30} comparing survival after neoadjuvant chemotherapy or surgery alone in 9 RCTs (total of 1,981 patients) for resectable esophageal cancer found strong evidence of a survival benefit to neoadjuvant chemotherapy over surgery alone; there was a pooled HR of 0.87 (0.79–0.96; \( P = .005 \)), which corresponded to an absolute survival difference at 2 years of 5.1%.

**Postoperative Chemotherapy**

A small number of randomized trials evaluated postoperative chemotherapy and surgery compared with surgery alone. Pouliquen et al\textsuperscript{31} found no improvement in survival with postoperative chemotherapy (cisplatin/5-FU) in patients with SqCC. The duration of dysphagia was similar for both groups as well.

Another randomized trial conducted in Japan compared surgery alone vs surgery followed by adjuvant cisplatin/5-FU in 242 patients with SqCC.\textsuperscript{32} The disease-free survival rate at 5 years favored the adjuvant therapy arm (55% vs 45%); however, the overall survival rate did not reach statistical significance (61% vs 52%). The study included only patients with SqCC, the duration of adjuvant therapy was suboptimal, and about 25% of patients in the chemotherapy arms failed to receive the full course of adjuvant therapy.

**Preoperative Chemoradiotherapy**

The poor outcome associated with surgery alone and the high locoregional tumor recurrence rate with definitive chemoradiotherapy provided the rationale behind evaluating neoadjuvant chemoradiotherapy in patients with resectable esophageal cancer. At least 10 randomized trials compared neoadjuvant chemoradiotherapy followed by surgery with other modalities. These trials are summarized in Table 3.\textsuperscript{12,33-41} The majority of patients included in these studies had SqCC, except in the more recent trials. Most trials did not have appropriate pre-enrollment staging. The Irish trial\textsuperscript{33} and the Dutch trial\textsuperscript{34} showed statistically significant improvement in overall survival with combined preoperative chemoradiotherapy, but the Irish study was criticized for a lack of appropriate staging, premature closure, and an unusually poor survival rate in the surgery-alone arm.

The recently published phase III Dutch study\textsuperscript{34} (the CROSS study) randomized patients with resectable esophageal cancer to receive surgery alone or

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**Table 3. — Randomized Trials of Preoperative Chemoradiotherapy (CRT) and Surgery vs Surgery Alone**

<table>
<thead>
<tr>
<th>Study</th>
<th>Yr</th>
<th>No. of Patients</th>
<th>Chemotherapy</th>
<th>Pathology</th>
<th>Median Survival (mos)</th>
<th>3-yr Survival Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+CRT</td>
<td>−CRT</td>
</tr>
<tr>
<td>Nygaard\textsuperscript{12}</td>
<td>1992</td>
<td>103</td>
<td>Cisplatin/bleomycin</td>
<td>SqCC</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Le Prise\textsuperscript{35}</td>
<td>1994</td>
<td>86</td>
<td>Cisplatin/5-FU</td>
<td>SqCC</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Apinop\textsuperscript{36}</td>
<td>1994</td>
<td>69</td>
<td>Cisplatin/5-FU</td>
<td>SqCC</td>
<td>9.7</td>
<td>7.4</td>
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<td>Walsh\textsuperscript{35}</td>
<td>1996</td>
<td>113</td>
<td>Cisplatin/5-FU</td>
<td>Adenocarcinoma</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Bosset\textsuperscript{37}</td>
<td>1997</td>
<td>282</td>
<td>Cisplatin</td>
<td>SqCC</td>
<td>18.6</td>
<td>18.6</td>
</tr>
<tr>
<td>Urba\textsuperscript{38}</td>
<td>2001</td>
<td>100</td>
<td>Cisplatin/vinblastine/5-FU</td>
<td>75% Adenocarcinoma</td>
<td>17.6</td>
<td>16.9</td>
</tr>
<tr>
<td>Lee\textsuperscript{40}</td>
<td>2004</td>
<td>101</td>
<td>Cisplatin/5-FU</td>
<td>SqCC</td>
<td>28.2</td>
<td>27.3</td>
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<td>Burmeister\textsuperscript{39}</td>
<td>2005</td>
<td>257</td>
<td>Cisplatin/5-FU</td>
<td>63% Adenocarcinoma</td>
<td>22</td>
<td>19</td>
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<tr>
<td>Tepper\textsuperscript{41}</td>
<td>2008</td>
<td>56</td>
<td>Cisplatin/5-FU</td>
<td>−</td>
<td>53</td>
<td>21</td>
</tr>
<tr>
<td>van Hagen\textsuperscript{34}</td>
<td>2012</td>
<td>366</td>
<td>Carboplatin/paclitaxel</td>
<td>75% Adenocarcinoma</td>
<td>49</td>
<td>24</td>
</tr>
</tbody>
</table>

5-FU = 5-fluorouracil, SqCC = squamous cell carcinoma.
weekly administration of carboplatin and paclitaxel for 5 weeks and concurrent radiotherapy followed by surgery. A total of 75% of patients had adenocarcinoma. R0 resection was achieved in 92% of patients in the chemoradiotherapy-surgery group vs 69% in the surgery group (P < .001). A pathological complete response (pCR) was achieved in 29% of patients who underwent resection after chemoradiotherapy. Postoperative complications were similar in both groups, as was in-hospital mortality. The median overall survival was 49.4 months in the chemoradiotherapy-surgery group vs 24.0 months in the surgery group (HR, 0.657; 95% CI, 0.495–0.871; P = .003).

Several meta-analyses have addressed the benefit of trimodality therapy over surgery alone for esophageal cancer. The first meta-analysis by Fiorica et al42 pooled six RCTs comparing preoperative chemoradiation and surgery with surgery alone. Chemoradiotherapy followed by surgery significantly decreased mortality (odds ratio [OR], 0.53; 95% CI, 0.31–0.93; P = .03). However, the risk of postoperative mortality was higher in the multimodality arm.

A second meta-analysis, by Urschel and Vasan,43 pooled nine RCTs including 1,116 patients. A statistically significant survival difference was found at 3 years in favor of preoperative chemoradiotherapy given concurrently (OR, 0.66; 95% CI, 0.47–0.92; P = .016). Neoadjuvant chemoradiotherapy was associated with a lower rate of resection but a higher rate of complete (R0) resection. A nonsignificant trend toward increased treatment mortality with neoadjuvant chemoradiotherapy was reported.

A third meta-analysis, by Gebski et al,44 pooled 10 RCTs comparing neoadjuvant chemoradiotherapy vs surgery alone, with a total of 1,209 patients. A significant survival benefit was evident for preoperative chemoradiotherapy, with an HR of 0.81 (95% CI, 0.70–0.93; P = .002), corresponding to a 13% absolute difference in survival at 2 years. The results applied for SqCC demonstrated an HR of 0.84 (0.71–0.99; P = .04) and for adenocarcinoma, an HR of 0.75 (0.59–0.95; P = .02).

The most recent meta-analysis, by Sjoquist et al,30 included 12 RCTs of neoadjuvant chemoradiotherapy vs surgery alone (1,854 patients). The updated analysis contained 4,188 patients, whereas the previous publication included 2,933 patients. This updated meta-analysis contained about 3,500 events, compared with about 2,230 in the previous meta-analysis (estimated 57% increase). The HR for all-cause mortality for neoadjuvant chemoradiotherapy was 0.78 (95% CI, 0.70–0.88; P < .0001); the HR for SqCC was 0.78 (95% CI, 0.69–0.89; P < .0001); and for adenocarcinoma only was 0.75 (0.59–0.95; P = .02). This analysis also compared neoadjuvant chemoradiotherapy with chemotherapy, where a survival benefit was evident for neoadjuvant chemoradiotherapy but was not statistically significant 0.88 (0.76–1.01; P = .07).

**Neoadjuvant Chemotherapy vs Neoadjuvant Chemoradiotherapy**

Two randomized trials compared neoadjuvant chemotherapy with neoadjuvant chemoradiotherapy; both trials included patients with adenocarcinoma, were closed early, and were underpowered to show a survival advantage. In the Australian trial,45 75 patients were randomized to receive preoperative cisplatin and 5-FU or preoperative chemoradiotherapy with the same drugs with a lower dose of 5-FU. The pathological response rate was higher in the chemoradiotherapy arm (31% vs 8%; P = .01). The median progression-free survival for the two groups was 14 and 26 months, also favoring the chemoradiotherapy arm (P = .37). The median overall survival was 29 months vs 32 months for the chemoradiotherapy arm, but it did not reach statistically significance (P = .83).

In the Preoperative Chemotherapy or Radiochemotherapy in Esophago-gastric Adenocarcinoma Trial (POET),46 126 patients with gastroesophageal junction adenocarcinoma were randomly assigned to receive chemotherapy alone (cisplatin/5-FU/leucovorin) for 15 weeks vs 12 weeks of the same regimen followed by low-dose radiotherapy concurrent with cisplatin and etoposide. The pCR rate was significantly higher in the induction arm (16% vs 2%), with a nonsignificant trend toward a better 3-year survival rate as well (47% vs 28%; P = .07). A meta-analysis of the two trials40 favored chemoradiotherapy, but it was not statistically significant.

**Institutional Experience**

The majority of the previously mentioned studies found that pCR in the surgical specimen indicated a better overall outcome, which may make it tempting to intensify preoperative therapy by increasing the number and potency of chemotherapeutic agents and/or radiation therapy (including targeted therapy). However, we believe that profiling genetic alterations in individual tumors combined with drug sensitivity assays is a better way to develop a tailored approach to treating patients in the neoadjuvant setting.

We have previously investigated (and published on47–49) the impact of response to neoadjuvant therapy in our own series of patients with esophageal cancer who underwent neoadjuvant therapy. We assessed the impact of pCR, partial pathological response (pPR), and no response (NR) in patients who underwent esophagectomy.

Among the 347 patients who underwent esophagectomy, 262 (75.5%) were treated with neoadjuvant therapy. A response to neoadjuvant therapy, including
Adverse Effects and Surgical Complications

In the previously reviewed studies, adverse effects and surgical complications were inconsistently reported. Patients who underwent perioperative chemotherapy and/or radiation therapy experienced treatment-related toxicity more frequently compared with patients who underwent surgical resection alone. Data on toxicities and complications were not always reported in the meta-analyses either. With the newer surgical technique and the advances in supportive care, these complications are expected to decrease, especially if surgery is performed in a high-volume institution, where a multidisciplinary approach is followed in treating this patient population.
than single-agent therapy concurrent with radiation therapy, based on our clinical pathway. Another option is weekly carboplatin/paclitaxel treatment (from the CROSS trial\(^4\)), especially in patients with renal insufficiency or in those who are not interested in a continuous infusion.

Data on adjuvant therapy after resection are lacking. For patients with completely resected node-negative disease who have not received neoadjuvant therapy, we suggest postoperative adjuvant therapy with chemoradiotherapy, based on the INT-0016 trial.\(^49\) Patients who have residual node-positive completely resected disease following neoadjuvant therapy (nonresponders) have had poor outcomes, and the potential benefits of adjuvant therapy in this setting are not clear. Our clinical pathway recommends close monitoring.

Conclusions

Several questions still need to be answered, as the majority of patients in the previously mentioned trials had squamous cell carcinoma, which is currently the less common histologic type in the United States, and patients did not have appropriate staging per current standards (ie, positron emission tomography scan or endoscopic ultrasonography). Furthermore, the optimal chemotherapy regimen has not been established; cisplatin has been the backbone of the previously used regimen, although newer regimens have shown promising results. Future trials in locally advanced esophageal cancer should include platinum-based chemoradiotherapy as a control arm, based on the CROSS study; secondary endpoints should include local disease control and quality of life.

Treatment decisions for individual patients should be based on comorbidities and the effects of neoadjuvant therapy on the patient’s performance status and quality of life. Moving beyond TNM staging and incorporating a tumor’s molecular biology could allow us to develop individualized therapy, which would potentially reduce treatment morbidity. Incorporating targeted therapy into adjuvant therapy treatment based on tumor profiles will help identify patients who may be likely to benefit from certain treatment modalities, which may improve outcomes in this disease.

References

33. Pouliquen X, Levard H, Hay JM, et al. 5-Fluorouracil and cisplatin


