## ESOPHAGEAL AND ESOPHAGOGASTRIC JUNCTION CANCER TREATMENT REGIMENS (Part 1 of 7)

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are provided only to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

whatsoever regarding their content, use	e, or application and disclaims any responsibility for their application or use in any way.
Preoperative Chemoradiation	ր!
Note: All recommendations are c	ategory 2A unless otherwise indicated.
Preferred Regimens	
REGIMEN	DOSING
Paclitaxel + carboplatin (Category 1) <sup>2</sup>	<b>Day 1:</b> Paclitaxel 50mg/m² IV + carboplatin AUC 2mg·min/mL IV. Repeat weekly for 5 weeks (Days 1, 8, 15, 22, and 29).
Cisplatin + 5-fluorouracil (5-FU) (Category 1) <sup>3,4</sup>	Days 1 and 29: Cisplatin 75–100mg/m² IV Days 1-4 and 29-32: 5-FU 750–1,000mg/m² IV continuous infusion over 24 hours on a 35-day cycle.  OR Days 1-5: Cisplatin 15mg/m² IV daily Days 1-5 and Days 22-26: 5-FU 800 mg/m² IV continuous infusion over 24 hours. Cycled every 21 days for 2 cycles.
Oxaliplatin + 5-FU + leucovorin <sup>5</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m² and leucovorin 200mg/m² followed by 5-FU 400mg/m² bolus, then 1,600mg/m² 46-hour continuous infusion; the first 3 cycles were delivered during radiotherapy (RT), the other 3 after RT for 6 bimonthly (14 days) cycles.
Cisplatin + capecitabine (Category 1) <sup>6</sup>	Day 1: Cisplatin 30mg/m² IV Days 1-5: Capecitabine 800mg/m² orally twice daily Repeat cycle weekly for 5 weeks.
Oxaliplatin + 5-FU (Category 1) <sup>7</sup>	Days 1, 15, and 29: Oxaliplatin 85mg/m² IV Days 1-33: 5-FU 180mg/m²/day continuous IV infusion.
Oxaliplatin + capecitabine (Category 1) <sup>8</sup>	Days 1, 15, and 29: Oxaliplatin 85mg/m² IV Days 1-5: Capecitabine 625mg/m² orally twice daily for 5 weeks.
Other Regimens	
rinotecan + cisplatin (Category 2B) <sup>9</sup>	Days 1, 8, 22, and 29: Irinotecan 65mg/m² IV plus cisplatin 30mg/m² IV.
Paclitaxel + 5-FU (Category 2B) <sup>10</sup>	Day 1: Paclitaxel 45mg/m² IV weekly Days 1-5: 5-FU 300mg/m²/day continuous IV infusion. Repeat cycle weekly for 5 weeks.
Paclitaxel + capecitabine (Category 2B) <sup>10</sup>	Day 1: Paclitaxel 45–50mg/m² IV Days 1-5: Capecitabine 625–825mg/m² orally twice daily. Repeat cycle weekly for 5 weeks.
Perioperative Chemotherapy	(including esophagogastric junction)¹
ECF (epirubicin + cisplatin + 5-FU) (Category 3) <sup>11a</sup>	Day 1: Epirubicin 50mg/m² IV bolus and cisplatin 60mg/m² IV Days 1-21: 5-FU 200mg/m² IV continuous infusion over 24 hours daily. Repeat cycle every 21 days for 3 cycles preoperatively and 3 cycles postoperatively.
ECF modifications (Category 3) <sup>12</sup>	Day 1: Epirubicin 50mg/m² IV; cisplatin 60mg/m² IV Days 1-21: 5-FU 200mg/m² IV continuous infusion once daily; cycled every 21 days for 3 cycles preoperatively and 3 cycles postoperatively.  OR Day 1: Epirubicin 50mg/m² IV; oxaliplatin 130mg/m² IV Days 1-21: 5-FU 200mg/m² IV continuous infusion over 24 hours; cycled every 21 days for 3 cycles preoperatively and 3 cycles postoperatively.  OR Day 1: Epirubicin 50mg/m² IV; oxaliplatin 130mg/m² IV Days 1-21: Capecitabine 625mg/m² orally twice daily. Cycled every 21 days for 3 cycles preoperatively and 3 cycles postoperatively.
5-FU + cisplatin (Category 1) <sup>13</sup>	Day 1: Cisplatin 100mg/m² IV Days 1-5: 5-FU 800mg/m² IV continuous infusion over 24 hours daily; cycled every 28 days for 2-3 cycles preoperatively and 3-4 cycles postoperatively for a total of 6 cycles.
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# ESOPHAGEAL AND ESOPHAGOGASTRIC JUNCTION CANCER TREATMENT REGIMENS (Part 2 of 7)

Definitive Chemoradiation (N	onsurgical)¹
Preferred Regimens	
REGIMEN	DOSING
Cisplatin + 5-FU (Category 1) <sup>14</sup>	Day 1: Cisplatin 75–100mg/m² IV Days 1-4: 5-FU 750–1,000mg/m²/day continuous IV infusion over 24 hours daily. Repeat cycle every 28 days for 2-4 cycles for 2 cycles with radiation followed by 2 cycles without radiation.
Oxaliplatin + 5-FU (Category 1) <sup>7,15</sup>	Days 1, 15, and 29: Oxaliplatin 85mg/m² IV for 3 doses Days 1-33: 5-FU 180mg/m² IV daily. OR Day 1: Oxaliplatin 85mg/m² IV Day 1: Leucovorin 400mg/m² IV Day 1: 5-FU 400mg/m² IVP Days 1 and 2: 5-FU 800mg/m² continuous IV over 24 hours daily. Repeat cycle every 14 days for 3 cycles with radiation followed by 3 cycles without radiation.
Cisplatin + capecitabine (Category 1) <sup>6</sup>	<b>Day 1:</b> Cisplatin 30mg/m² IV <b>Days 1–5:</b> Capecitabine 800mg/m² orally twice daily. Repeat cycle weekly for 5 weeks.
Oxaliplatin + capecitabine (Category 1) <sup>8</sup>	Days 1, 15, and 29: Oxaliplatin 85mg/m² IV Days 1-5: Capecitabine 625mg/m² orally twice daily for 5 weeks.
Paclitaxel + carboplatin <sup>2</sup>	<b>Day 1:</b> Paclitaxel 50mg/m² IV and carboplatin 2mg·min/mL IV once weekly for 5 weeks.
Other Regimens	
Paclitaxel + cisplatin <sup>16</sup>	Days 1, 8, 15, and 22: Paclitaxel 60mg/m² IV Day 1: Cisplatin 75mg/m² IV given for 1 cycle.
Docetaxel + cisplatin <sup>17,18</sup>	Days 1 and 22: Docetaxel 60mg/m² IV Days 1 and 22: Cisplatin 60-80mg/m² IV given for 1 cycle.  OR Day 1: Docetaxel 20-30mg/m² IV Day 1: Cisplatin 20-30mg/m² IV given for weekly for 5 weeks.
Irinotecan + cisplatin (Category 2B) <sup>9</sup>	Days 1, 8, 22, and 29: Irinotecan 65mg/m² IV Days 1, 8, 22, and 29: Cisplatin 30mg/m² IV.
Paclitaxel + 5-FU (Category 2B) <sup>10</sup>	<b>Day 1:</b> Paclitaxel 45mg/m² IV weekly <b>Days 1–5:</b> 5-FU 300mg/m² IV continuous infusion daily. Repeat cycle weekly for 5 weeks.
Paclitaxel + capecitabine (Category 2B) <sup>10</sup>	<b>Day 1:</b> Paclitaxel 45–50mg/m² IV <b>Days 1–5:</b> Capecitabine 625–825mg/m² PO twice daily. Repeat cycle weekly for 5 weeks.
Postoperative Chemoradiation	n (for adenocarcinoma or gastroesophageal junction only)¹
5-FU + leucovorin (Category 1) <sup>18,19</sup>	Days 1–5: 5-FU 425mg/m²/day IV and leucovorin 20mg/m²/day IV, followed by chemoradiotherapy beginning 4 weeks after the start of the initial cycle of chemotherapy. Chemoradiotherapy: 4,500cGy of radiation at 180cGy/day, 5 days/week for 5 weeks, with 5-FU 400mg/m²/day IV and leucovorin 20mg/m²/day IV on the first 4 and the last 3 days of radiotherapy. At 1 month following completion of radiotherapy, two 5-day cycles of 5-FU 425mg/m²/day IV and leucovorin 20mg/m²/day IV; given 1 month apart. NOTE: The NCCN panel acknowledges that the Intergroup 0116 Trial formed the basis for postoperative adjuvant chemoradiation strategy. However, the panel does not recommend the above specified doses or schedule of cytotoxic agents because of concerns regarding toxicity. The panel recommends one of the following modifications instead:
Capecitabine <sup>20,21</sup>	<b>Days 1–14:</b> Capecitabine 750–1000mg/m² orally twice daily; cycled every 28 days; 1 cycle before and 2 cycles after chemoradiation.
5-FU + leucovorin <sup>22</sup>	<b>Days 1, 2, 15, and 16:</b> Leucovorin 200mg/m² IV as 2-hour infusion followed by 5-FU 400mg/m² IV push and a 22-hour infusion of 5-FU 600mg/m².
5-FU with radiation <sup>23</sup>	$\label{eq:days} \textbf{1-5 OR Days 1-7:} \ 5\text{-FU } 200\text{-}250\text{mg/m}^2 \ \text{IV continuous infusion over } 24 \ \text{hours} \\ \text{daily, once weekly for 5 weeks.}$
Capecitabine with radiation <sup>6</sup>	$\label{eq:Days 1-5 or Days 1-7:} \textbf{Capecitabine 625-825mg/m}^2 \ \text{orally twice daily, once} \\ \text{weekly for 5 weeks.}$
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# ESOPHAGEAL AND ESOPHAGOGASTRIC JUNCTION CANCER TREATMENT REGIMENS (Part 3 of 7)

Metastatic or Locally Advanced Cancer (where local therapy is not indicated) <sup>1</sup>		
First-line therapy		
REGIMEN	DOSING	
Trastuzumab + chemotherapy (for HER2-neu malignancies) <sup>24</sup>	Day 1: Trastuzumab 8mg/kg IV loading dose (Cycle 1 only); followed by trastuzumab 6mg/kg IV every 3 weeks, plus chemotherapy (Category 2B).  OR Day 1 of Cycle 1: Trastuzumab 6mg/kg IV loading dose, then 4mg/kg IV every 14 days Day 1: Cisplatin 80mg/m² IV, plus Days 1-14: Capecitabine 1000mg/m² orally twice daily OR Days 1-5: 5-FU 800mg/m² continuous IV infusion (Category 1). Repeat cycle every 21 days for 6 cycles.	
Preferred Regimens	Tropout dyale drain 2 days for a dyaloc.	
DCF (docetaxel + leucovorin + cisplatin + 5-FU) <sup>25</sup>	Day 1: Docetaxel 40mg/m² IV + leucovorin 400mg/m² IV + 5-FU 400mg/m² IV, plus Days 1 and 2: 5-FU 1000mg/m² IV continuous infusion over 24 hours (total 2000mg/m²), followed by Day 3: Cisplatin 40mg/m² IV. Repeat cycle every 14 days.	
Modified DCF (docetaxel + oxaliplatin + leucovorin + 5-FU) <sup>26</sup>	<b>Day 1:</b> Docetaxel 50mg/m² IV + leucovorin 200mg/m² IV + oxaliplatin 85mg/m² IV + 5-FU 2600mg/m² IV continuous infusion over 24 hours. Repeat cycle every 14 days.	
Modified DCF (docetaxel + oxaliplatin + 5-FU) <sup>27</sup>	Day 1: Docetaxel 50mg/m² IV + oxaliplatin 85mg/m² IV Days 1 and 2: 5-FU 1200mg/m² IV continuous infusion over 24 hours. Repeat cycle every 14 days.	
Modified DCF (docetaxel + carboplatin + 5-FU) (Category 2B) <sup>28</sup>	Day 1: Docetaxel 75mg/m² IV Day 2: Carboplatin AUC 6mg·min/mL IV Days 1-3: 5-FU 1200mg/m² IV continuous infusion over 24 hours daily. Repeat cycle every 21 days.	
Fluoropyrimidine and cisplatin (5-FU + cisplatin) (Category 1) <sup>29b</sup>	Day 1: Cisplatin 100mg/m² IV Days 1-4: 5-FU 1,000mg/m² IV continuous infusion over 24 hours daily doses of 250mg/m² IV over 60 minutes.	
Fluoropyrimidine and cisplatin (5-FU + cisplatin + leucovorin) (Category 1) <sup>26,30b</sup>	Day 1: Cisplatin 50mg/m² IV Day 1: Leucovorin 200mg/m² IV Day 1: 5-FU 2,000mg/m² IV continuous infusion over 24 hours. Repeat cycle every 14 days.	
Fluoropyrimidine and cisplatin (capecitabine + cisplatin) (Category 1) <sup>31</sup>	Day 1: Cisplatin 80mg/m² IV Day 1-14: Capecitabine 1,000mg/m² orally twice daily. Repeat cycle every 3 weeks	
Fluoropyrimidine and oxaliplatin (oxaliplatin + leucovorin + 5-FU) <sup>31,32</sup>	Day 1: Oxaliplatin 85mg/m² IV plus leucovorin 400mg/m² IV plus 5-FU 400mg/m² IVP Days 1 and 2: 5-FU 1200mg/m² IV continuous infusion over 24 hours daily. Repeat cycle every 14 days.  OR  Day 1: Oxaliplatin 85mg/m² IV plus leucovorin 200mg/m² IV plus 5-FU 400mg/m² IVP plus 5-FU 2600mg/m² IV continuous infusion over 24 hours daily. Repeat cycle every 14 days.	
Fluoropyrimidine and oxaliplatin (oxaliplatin + capecitabine) <sup>33</sup>	Day 1: Oxaliplatin 130mg/m² IV Days 1-14: Capecitabine 1000mg/m² orally twice daily. Repeat cycle every 21 days.	
Other Regimens		
Paclitaxel + cisplatin or carboplatin <sup>34-36</sup>	Day 1: Paclitaxel 135–200mg/m² IV Day 2: Cisplatin 75mg/m² IV Repeat cycle every 21 days. OR Day 1: Paclitaxel 90mg/m² IV plus cisplatin 75mg/m² IV Repeat cycle every 14 days. OR Day 1: Paclitaxel 200mg/m² IV plus carboplatin 5mg·min/mL. Repeat cycle every 21 days.	
Docetaxel + cisplatin <sup>37,38</sup>	<b>Day 1:</b> Docetaxel 70–85mg/m² IV plus cisplatin 70–75mg/m² IV. Repeat cycle every 21 days.	
Docetaxel + irinotecan (Category 1) <sup>39</sup>	Days 1 and 8: Docetaxel 35mg/m² IV plus irinotecan 50mg/m² IV. Repeat cycle every 21 days.	
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## **ESOPHAGEAL AND ESOPHAGOGASTRIC JUNCTION CANCER TREATMENT REGIMENS** (Part 4 of 7)

Other Regimens (continued)	
DECIMEN	DOCINO
REGIMEN 40.42	DOSING
Fluoropyridimine <sup>40-42</sup>	Day 1: Leucovorin 400mg/m² IV plus 5-FU 400mg/m² IVP Days 1 and 2: 5-FU 1200mg/m² IV continuous infusion over 24 hours daily. Repeat cycle every 14 days. OR
	Days 1-5: 5-FU 800mg/m² IV continuous infusion over 24 hours daily. Repeat cycle every 28 days.  OR
	<b>Days 1–14:</b> Capecitabine 1000–1250mg/m² orally twice daily. Repeat cycle every 21 days.
Taxane <sup>43-45</sup>	Day 1: Docetaxel 75–100mg/m² IV. Repeat cycle every 21 days. OR
	Day 1: Paclitaxel 135–250mg/m² IV. Repeat cycle every 21 days.  OR
	<b>Days 1, 8, 15, and 22:</b> Paclitaxel 80mg/m <sup>2</sup> IV once weekly. Repeat cycle every 28 days.
ECF (epirubicin + cisplatin + 5-FU) (Category 1) <sup>46,47</sup>	Day 1: Epirubicin 50mg/m² IV bolus + cisplatin 60mg/m² IV Days 1-21: 5-FU 200mg/m² IV continuous infusion over 24 hours daily. Repeat cycle every 21 days.
ECF modifications (epirubicin + oxaliplatin + 5-FU) (Category 1) <sup>47</sup>	Days 1: Epirubicin 50mg/m² IV + oxaliplatin 130mg/m² IV Days 1-21: 5-FU 200mg/m² IV continuous infusion over 24 hours. Repeat cycle every 21 days.
ECF modifications (epirubicin + cisplatin + capecitabine) (Category 1) <sup>47</sup>	Day 1: Epirubicin 50mg/m² IV + cisplatin 60mg/m² IV Days 1-21: Capecitabine 625mg/m² IV orally twice daily. Repeat cycle every 21 days.
ECF modifications (epirubicin + oxaliplatin + capecitabine) (Category 1) <sup>47</sup>	Day 1: Epirubicin 50mg/m² IV + oxaliplatin 130mg/m² IV Days 1-21: Capecitabine 625mg/m² IV orally twice daily. Repeat cycle every 21 days.
5-FU and irinotecan (irinotecan + leucovorin + 5-FU) (Category 1) <sup>40,48,49</sup>	Day 1: Irinotecan 80mg/m² IV + Ieucovorin 500mg/m² IV + 5-FU 2000mg/m² IV continuous infusion over 24 hours, weekly for 6 weeks followed by 1 week off treatment OR weekly for 6 weeks followed by 2 weeks off treatment.  OR  Day 1: Irinotecan 180mg/m² IV + Ieucovorin 400mg/m² IV + 5-FU 400mg/m² IVP  Day 1-2: 5-FU 1200mg/m² IV continuous infusion over 24 hours.  Repeat cycle every 14 days.
Second-line Therapy¹	
Preferred Regimens	
Ramucirumab + paclitaxel (for adenocarcinoma) (Category 1 for EGJ adenocarcinoma; Category 2A for esophageal adenocarcinoma) <sup>50</sup>	
Ramucirumab (for adeno- carcinoma) (Category 1 for EGJ adenocarcinoma; Category 2A for	<b>Days 1 and 15:</b> Ramucirumab 8mg/kg IV. Repeat cycle every 28 days.
esophageal adenocarcinoma) <sup>51</sup>	Day 1: Docetaxel 75-100mg/m² IV
Docetaxel (Category 1) <sup>43</sup>	Repeat cycle every 21 days.
	Repeat cycle every 21 days.  Day 1: Paclitaxel 135-250mg/m² IV Repeat cycle every 21 days.  OR
Docetaxel (Category 1) <sup>43</sup>	Repeat cycle every 21 days. <b>Day 1:</b> Paclitaxel 135–250mg/m² IV Repeat cycle every 21 days.

## ESOPHAGEAL AND ESOPHAGOGASTRIC JUNCTION CANCER TREATMENT REGIMENS (Part 5 of 7)

Second-line Therapy1 (continu	ed)	
Preferred Regimens (continued)		
REGIMEN	DOSING	
Irinotecan (Category 1) <sup>52-54</sup>	Day 1: Irinotecan 250-350mg/m² IV Repeat cycle every 21 days.  OR Day 1: Irinotecan 150-180mg/m² IV Repeat cycle every 14 days.  OR Days 1 and 8: Irinotecan 125mg/m² IV. Repeat cycle every 21 days.	
Other Regimens		
Irinotecan + cisplatin <sup>32,55</sup>	<b>Days 1 and 8:</b> Irinotecan 65mg/m² IV plus cisplatin 25–30mg/m² IV. Repeat cycle every 21 days.	
Irinotecan + fluoropyridimine (Category 2B) <sup>56</sup>	Day 1: Irinotecan 250mg/m² IV Days 1-14: Capecitabine 1000mg/m² PO BID daily. Repeat cycle every 21 days.	
Irinotecan + fluoropyridimine (Category 2B) <sup>48,57</sup>	Day 1: Irinotecan 180mg/m² IV plus leucovorin 400mg/m² IV plus 5-FU 400mg/m² IVP Days 1 and 2: 5-FU 600-1200mg/m²/day IV continuous infusion on days 1 and 2. Repeat cycle every 14 days.	
Docetaxel + irinotecan (Category 2B) <sup>39</sup>	<b>Days 1 and 8:</b> Docetaxel 35mg/m² IV plus irinotecan 50mg/m² IV. Repeat cycle every 21 days.	

#### Second-line Therapy<sup>1</sup>

#### General Treatment Notes<sup>1</sup>

Chemotherapy regimens should be chosen in the context of performance status, medical comorbidities, toxicity profile, and HER2-neu expression (for adenocarcinoma only). Two-drug cytotoxic regimens are preferred for patients with advanced disease because of lower toxicity, Three-drug cytotoxic regimens should be reserved for medically fit patients with good PS and access to frequent toxicity evaluation. Doses and schedules for any regimen that is not derived from category 1 evidence is a suggestion, and subject to appropriate modifications depending on the circumstances, Infusional fluorouracil and capecitabine may be used interchangeably (except as indicated). Cisplatin and oxaliplatin may be used interchangeably depending on toxicity profile.

- a Modified regimens substituting oxaliplatin and/or capecitabine are also acceptable.
- b May be coupled with cetuximab administered as an initial dose of cetuximab 400 mg/m² IV on Day 1 over 120 minutes; followed by weekly doses of 250 mg/m² IV over 60 minutes.

#### References

- Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology™. Esophageal Cancer. v 2.2016. Available at: http://www.nccn.org/professionals/physician\_gls/ pdf/esophageal.pdf. Accessed August 30, 2016.
- van Hagen P, Hulshof MC, van Lanschot JJ, et al; CROSS Group. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med. 2012;366:2074–2084.
- Tepper J, Krasna MJ, Niedzwiecki D, et al. Phase III trial of trimodality therapy with cisplatin, fluorouracii, radiotherapy, and surgery compared with surgery alone for esophageal cancer: CALGB 9781. J Clin Oncol. 2008;26:1086–1092.
- Bedenne L, Michel P, Bouché O, et al. Chemoradiation followed by surgery compared with chemoradiation alone in squamous cancer of the esophagus: FFCD 9102. J Clin Oncol. 2007;25: 1160-1168.
- Conroy T, Galais M-P, Raoul JL, et al; UNICANCER-GI/FFCD PRODIGE Intergroup. Phase III randomized trial of definitive chemoradiotherapy (CRT) with FOLFOX or cisplatin and fluorouracil in esophageal cancer (EC): Final results of the PRODIGE 5/ACCORD 17 trial [abstract]. J Clin Oncol. 2012;30 (Suppl 18):LBA4003.
- Lee HS, Choi Y, Hur WJ, et al. Pilot study of postoperative adjuvant chemoradiation for advanced gastric cancer: adjuvant 5-FU/cisplatin and chemoradiation with capecitabine. World J Gastroenterol. 2006;12:603–607.

- Khushalani NI, Leichman CG, Proulx G, et al. Oxaliplatin in combination with protracted-infusion fluorouracil and radiation: report of a clinical trial for patients with esophageal cancer. J Clin Oncol. 2002;20:2844–2850.
- Javle MM, Yang G, Nwogu CE, et al. Capecitabine, oxaliplatin and radiotherapy: a phase 1B neoadjuvant study for esophageal cancer with gene expression analysis. *Cancer Invest.* 2009:27:193–200.
- Cunningham D, Allum WH, Stenning SP, et al. MAGIC Trial Participants. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med. 2006;355:11–20.
- Sumpter K, Harper-Wynne C, et al. Report of two protocol planned interim analyses in a randomised multicentre phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophagogastric cancer receiving ECF. Br J Cancer. 2005;92:1976–1983.
- Sharma R, Yang GY, Nava HR, et al. A single institution experience with neoadjuvant chemoradiation (CRT) with irinotecan (I) and cisplatin (C) in locally advanced esophageal carcinoma (LAEC). J Clin Oncol. 2009;27 (suppl 15): Abstract e15619.
- Ajani JA, Winter K, Okawara GS, et al. Phase II trial of preoperative chemoradiation in patients with localized gastric adenocarcinoma (RTOG 9904): quality of combined modality therapy and pathologic response. J Clin Oncol. 2006;24:3953-3958.

## ESOPHAGEAL AND ESOPHAGOGASTRIC JUNCTION CANCER TREATMENT REGIMENS (Part 6 of 7)

#### References (continued)

- Hihara J, Yoshida K, Hamai Y, et al. Phase I study of docetaxel (TXT) and 5-fluorouracil (5-FU) with concurrent radiotherapy in patients with advanced esophageal cancer. Anticancer Res. 2007;27:2597–2603.
- Minsky BD, Pajak TF, Ginsberg RJ, et al. INT 0123 (Radiation Therapy Oncology Group 94-05) phase III trial of combined-modality therapy for esophageal cancer: high-dose versus standard-dose radiation therapy. J Clin Oncol. 2002;20:1167-1174.
- Conroy T, Galais P, Raoul JL, et al. Phase III randomized trial of definitive chemoradiotherapy (CRT) with FOLFOX or cisplatin and fluorouracil in esophageal cancer (EC): Final results of the PRODIGE 5/ACCORD 17 trial. J Clin Oncol. 30, 2012 (suppl; abstr LBA4003).
- Urba SG, Orringer MB, Ianettonni M, et al. Concurrent cisplatin, paclitaxel, and radiotherapy as preoperative treatment for patients with locoregional esophageal carcinoma. Cancer. 2003;98:2177-2183.
- Li QQ, Liu MZ, Hu YH, et al. Definitive concomitant chemoradiotherapy with docetaxel and cisplatin in squamous esophageal carcinoma. Dis Esophagus. 2010;23:253–259.
- Day FL, Leong T, Ngan S, et al. Phase I trial of docetaxel, cisplatin, and concurrent radical radiotherapy in locally advanced esophageal cancer. Br J Cancer. 2011;104:265–271.
- Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med. 2001;345:725-730.
- Jansen EP, Boot H, Saunders MP, et al. A phase I-II study of postoperative capecitabine-based chemoradiotherapy in gastric cancer. Int J Radiat Oncol Biol Phys. 2007;69:1424–1428.
- Chua YJ, Barbachano Y, Cunningham D, et al. Neoadjuvant capecitabine and oxaliplatin before chemoradiotherapy and total mesorectal excision in MRI-defined poor-risk rectal cancer: a phase 2 trial. *Lancet Oncol.* 2010;11:241-248.
- André T, Quinaux E, Louvet C, et al. Phase III study comparing a semimonthly with a monthly regimen of fluorouracil and leucovorin as adjuvant treatment for stage II and III colon cancer patients: final results of GERCOR C96.1. J Clin Oncol. 2007;25:3732–3738.
- Leong T, Joon DL, Willis D, et al. Adjuvant chemoradiation for gastric cancer using epirubicin, cisplatin, and 5-fluorouracil before and after three-dimensional conformal radiotherapy with concurrent infusional 5-fluorouracil: a multicenter study of the Trans-Tasman Radiation Oncology Group. Int J Radiat. Oncol Biol Phys. 2011;79:690-695.
- 24. Bang YJ, Van Cutsem E, Feyereislova A, et al; ToGA Trial Investigators. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. *Lancet*. 2010; 376(9742):687-697.
- Shah MA, Shibata S, Stoller RG, et al; MSKCC Gastric Cancer Consortium. Random assignment multicenter phase II study of modified docetaxel, cisplatin, fluorouracil (mDCF) versus DCF with growth factor support (GCSF) in metastatic gastroesophageal adenocarcinoma (GE). J Clin Oncol. 2010;28 (Suppl 15):4010.
- Al-Batran S-E, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol. 2008;26:1435–1442.
- 27. Shankaran V, Mulcahy MF, Hochster HS, et al. Docetaxel, oxaliplatin and 5-fluorouracil for the treatment of metastatic or unresectable gastric or gastroesophageal junction (GEJ) adenocarcinomas: preliminary results of a phase II study [abstract]. Presented at the Gastrointestinal Cancers Symposium 2009; Abstract 47.
- Elkerm YM, Elsaid A, Al-Batran S, et al. Final results of a phase Il trial of docetaxel-carboplatin-FU in locally advanced gastric carcinoma [abstract]. Presented at the 2008 Gastrointestinal Cancers Symposium. Abstract 38.

- Lorenzen S, Brucher B, Zimmermann F, et al. Neoadjuvant continuous infusion of weekly 5-fluorouracil and escalating doses of oxaliplatin plus concurrent radiation in locally advanced oesophageal squamous cell carcinoma: results of a phase I/II trial. Br J Cancer. 2008;99:1020-1026.
- Bouché O, Raoul JL, Bonnetain F, et al; Fédération Francophone de Cancérologie Digestive Group. Randomized multicenter phase II trial of a biweekly regimen of fluorouracii and leucovorin (LV5FU2), LV5FU2 plus cisplatin, or LV5FU2 plus irinotecan in patients with previously untreated metastatic gastric cancer: a Federation Francophone de Cancerologie Digestive Group Study—FFCD 9803. J Clin Oncol. 2004;22:4319–4328.
- Kang YK, Kang WK, Shin DB, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III noninferiority trial. Ann Oncol. 2009;20:666-673.
- Enzinger PC, Burtness B, Hollis D, et al. CALGB 80403/ECOG 1206: A randomized phase II study of three standard chemotherapy regimens (ECF, IC, FOLFOX) plus cetuximab in metastatic esophageal and GE junction cancer [abstract 4006]. J Clin Oncol. 2010; 28 (suppl 15):4007.
- Kim GM, Jeung HC, Rha SY, et al. A randomized phase II trial of S-1-oxaliplatin versus capecitabine-oxaliplatin in advanced gastric cancer. Eur J Cancer. 2012;48:518–526.
- Ilson DH, Forastiere A, Arquette M, et al. A phase II trial of paclitaxel and cisplatin in patients with advanced carcinoma of the esophagus. Cancer J. 2000;6:316-323.
- Petrasch S, Welt A, Reinacher A, et al. Chemotherapy with cisplatin and paclitaxel in patients with locally advanced, recurrent or metastatic oesophageal cancer. Br J Cancer. 1998;78:511–514.
- Gadgeel SM, Shields AF, Heilbrun LK, et al. Phase II study of paclitaxel and carboplatin in patients with advanced gastric cancer. Am J Clin Oncol. 2003;26:37–41.
- Ajani JA, Fodor MB, Tjulandin SA, et al. Phase II multiinstitutional randomized trial of docetaxel plus cisplatin with or without fluorouracil in patients with untreated, advanced gastric, or gastroesophageal adenocarcinoma. J Clin Oncol. 2005;23:5660–5667.
- Kim JY, Do YR, Park KU, et al. A multi-center phase II study of docetaxel plus cisplatin as first-line therapy in patients with metastatic squamous cell esophageal cancer. Cancer Chemother Pharmacol. 2010;66:31–36.
- Burtness B, Gibson M, Egleston B, et al. Phase II trial of docetaxel-irinotecan combination in advanced esophageal cancer. Ann Oncol. 2009;20:1242–1248.
- André T, Louvet C, Maindrault-Goebel F, et al. CPT-11 (irinotecan) addition to bimonthly, high-dose leucovorin and bolus and continuous-infusion 5-fluorouracil (FOLFIRI) for pretreated metastatic colorectal cancer. GERCOR. Eur J Cancer. 1999; 35:1343-1347.
- 41. Ohtsu A, Shimada Y, Shirao K, et al. Randomized phase III trial of fluorouracil alone versus fluorouracil plus cisplatin versus uracil and tegafur plus mitomycin in patients with unresectable, advanced gastric cancer: The Japan Clinical Oncology Group Study (JCOG9205). J Clin Oncol. 2003;21:54–59.
- Hong YS, Song SY, Lee SI, et al. A phase II trial of capecitabine in previously untreated patients with advanced and/or metastatic gastric cancer. Ann Oncol. 2004;15:1344–1347.
- Albertsson M, Johansson B, Friesland S, et al. Phase II studies on docetaxel alone every third week, or weekly in combination with gemcitabine in patients with primary locally advanced, metastatic, or recurrent esophageal cancer. Med Oncol. 2007;24(4):407–412.
- Ajani JA, Ilson DH, Daugherty K, et al. Activity of taxol in patients with squamous cell carcinoma and adenocarcinoma of the esophagus. J Natl Cancer Inst. 1994;86:1086–1091.
- Ilson DH, Wadleigh RG, Leichman LP, et al. Paclitaxel given by a weekly 1-h infusion in advanced esophageal cancer. Ann Oncol. 2007;18:898–902.

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#### References (continued)

- Ross P, Nicolson M, Cunningham D, et al. Prospective randomized trial comparing mitomycin, cisplatin, and protracted venousinfusion fluorouracil (PVI 5-FU) With epirubicin, cisplatin, and PVI 5-FU in advanced esophagogastric cancer. J Clin Oncol. 2002;20:1996–2004.
- Cunningham D, Starling N, Rao S, et al. Capecitabine and oxaliplatin for advanced esophagogastric cancer. N Engl J Med. 2008;358:36-46.
- 48. Dank M, Zaluski J, Barone C, et al. Randomized phase III study comparing irinotecan combined with 5-fluorouracil and folinic acid to cisplatin combined with 5-fluorouracil in chemotherapy naive patients with advanced adenocarcinoma of the stomach or esophagogastric junction. Ann Oncol. 2008;19:1450–1457.
- 49. Wolff K, Wein A, Reulbach U, et al. Weekly high-dose 5-fluorouracil as a 24-h infusion and sodium folinic acid (AlO regimen) plus irinotecan in patients with locally advanced nonresectable and metastatic adenocarcinoma or squamous cell carcinoma of the oesophagus: a phase II trial. Anticancer Drugs. 2009;20:165–173.
- Wilke H, Muro K, Van Cutsem E, et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-esophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. *Lancet Oncol.* 2014;1224–1235.
- Fuchs CS, Tomasek J, Yong CJ, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastroesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. *Lancet*. 2014;383:31–39.

- 52. Ueda S, Hironaka S, Yasui H, et al; West Japan Oncology Group. Randomized phase III study of irinotecan (CPT-11) versus weekly paclitaxel (wPTX) for advanced gastric cancer (AGC) refractory to combination chemotherapy (CT) of fluoropyrimidine plus platinum (FP): WJOG4007 trial. J Clin Oncol. 2012;30:15s (suppl; abstr 4002).
- 53. Thuss-Patience PC, Kretzschmar A, Deist T, et al. Irinotecan versus best supportive care (BSC) as second-line therapy in gastric cancer: A randomized phase III study of the Arbeitsgemeinschaft Internistische Onkologie (AIO). J Clin Oncol. 2009;27:15s (suppl; abstr 4540)
- Fuchs CS, Moore MR, Harker G, et al. Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer. J Clin Oncol. 2003;21:807–814.
- Ilson DH. Phase II trial of weekly irinotecan/cisplatin in advanced esophageal cancer. Oncology (Williston Park). 2004;18(14 Suppl 14):22–25.
- 56. Leary A, Assersohn L, Cunningham D, et al. A phase II trial evaluating capecitabine and irinotecan as second line treatment in patients with oesophago-gastric cancer who have progressed on, or within 3 months of platinum-based chemotherapy. Cancer Chemother Pharmacol. 2009; 64:455–462.
- Di Lauro L, Fattoruso SI, Giacinti L, et al. Second-line chemotherapy with FOLFIRI in patients with metastatic gastric cancer (MGC) not previously treated with fluoropyrimidines. *J Clin Oncol*. 2009;27:15s (suppl; abstr 4549).

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