

# ESOPHAGEAL CANCER

## COMBINED MODALITY THERAPY

### CISPLATIN – 5-FLUOROURACIL – RADIATION (DEFINITIVE THERAPY)

5-Fluorouracil	1000 mg/m <sup>2</sup> /day	CIVI	Days 1 – 4, weeks 1, 5, 8 and 11
Cisplatin	75 mg/m <sup>2</sup>	IV*	Day 1, weeks 1, 5, 8 and 11

*Concurrent with*

Radiation therapy                      50 Gy starting on Day 1, week 1 of chemotherapy

\*Administer at a rate of 1 mg/minute with routine pre- and post-hydration.

References: [Herskovic A, et al. \*N Engl J Med\* 1992;326:1593 – 8](#); [Cooper JS, et al. \*JAMA\* 1999;281:1623 – 7](#).

### CISPLATIN-5-FLUOROURACIL-RADIATION (NEOADJUVANT)

5-Fluorouracil	1000 mg/m <sup>2</sup> /day	CIVI	Days 1 – 4 and 29 –32
Cisplatin	100 mg/m <sup>2</sup>	IV*	Days 1 and 29

*Concurrent with*

Radiation therapy                      50.4 Gy starting on Day 1, week 1 of chemotherapy

*Followed by*

Surgery                                      Upon recovery from chemoradiotherapy

\*Routine pre- and post-hydration required.

Reference: [Tepper JE, et al. \*J Clin Oncol\* 2006;24\(18S\). Abstract 4012](#).

### CISPLATIN – PACLITAXEL – HYPERFRACTIONATED RADIATION (NEOADJUVANT)

Cisplatin	75 mg/m <sup>2</sup>	IV*	Day 1
Paclitaxel <sup>‡</sup>	60 mg/m <sup>2</sup>	IV**	Days 1, 8, 15 and 22
Radiation therapy	1.5 Gy twice per day on Days 1 – 5, Days 8 – 12, and Days 15 – 19, for a total dose of 45 Gy (minimal interfraction interval = 6 hours).		
Filgrastim	5 micrograms/kg	SQ	Day 23 until ANC recovery

*Followed by*

Surgery                                      Transhiatal esophagectomy performed on approximately Day 50

<sup>‡</sup>Routine premedication required; \*Administer over 2 hours with routine pre- and post-hydration;

\*\*Administer over 3 hours.

Reference: [Urba SG, et al. \*Cancer\* 2003;98:2177 – 83](#).

### **5-FLUOROURACIL – LEUCOVORIN – RADIATION (MACDONALD ADJUVANT REGIMEN)**

5-Fluorouracil	425 mg/m <sup>2</sup> /day	IV*	Days 1 – 5
Leucovorin	20 mg/m <sup>2</sup> /day	IV*	Days 1 – 5

*The above treatment was initiated on Day 1. On Day 29 the following chemoradiotherapy is started:*

Radiation	45 Gy (1.8 Gy per day) five days per week for 5 weeks plus		
5-Fluorouracil	400 mg/m <sup>2</sup> /day	IV*	On the first four and last 3 days of radiation
Leucovorin	20 mg/m <sup>2</sup> /day	IV*	On the first 4 and last 3 days of radiation

*One month following completion of chemoradiotherapy the following is initiated*

5-Fluorouracil	425 mg/m <sup>2</sup> /day	IV*	Days 1 – 5
Leucovorin	20 mg/m <sup>2</sup> /day	IV*	Days 1 – 5

Repeat this cycle every 28 days for 2 cycles.

\*Administer as an IV bolus.

NOTE: Regimen indicated for GE-junction adenocarcinoma only.

Reference: [Macdonald JS, et al. N Engl J Med 2001;345:725 – 30.](#)

### **PACLITAXEL – CARBOPLATIN – 5-FLUOROURACIL – RADIATION (NEOADJUVANT)**

Paclitaxel‡	200 mg/m <sup>2</sup>	IV*	Days 1 and 22
Carboplatin	AUC 6**	IV	Days 1 and 22
5-Fluorouracil	225 mg/m <sup>2</sup> /day	CIVI	Days 1 – 42
Radiation therapy	5 days per week for 5 weeks beginning Day 1 of chemotherapy. Administered as 1.8 Gy single daily fractions, to a total dose of 45 Gy.		

*Followed by*

Surgery Esophagectomy 4 – 8 weeks after completion of therapy

*OR*

Additional cycle of carboplatin/paclitaxel and additional radiation boost to a total of 54 – 60 Gy.

‡Routine premedication required; \*Administer over 1 hour; \*\*Dose calculated using the Calvert formula.

Reference: [Meluch AA, et al. Cancer J 2003;9:251 – 60.](#)

## ESOPHAGEAL CANCER CHEMOTHERAPY

### CAPECITABINE – OXALIPLATIN

Capecitabine	1000 mg/m <sup>2</sup>	BID	PO	Days 1 – 14
Oxaliplatin	130 mg/m <sup>2</sup>		IV*	Day 1

\*Administer over 2 hours.

NOTE: Capecitabine to be ingested with water every 12 hours, approximately 30 minutes after a meal, starting the evening of day 1. Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

DOSE MODIFICATION: Persistent ( $\geq 14$  days) paresthesia or temporary (7 – 14 days) painful paresthesia or functional impairment resulted in a 25% dose reduction of oxaliplatin. In cases of persistent ( $\geq 14$  days) painful paresthesia or functional impairment, oxaliplatin had to be omitted until recovery and then restarted at 50% of the dose. Capecitabine was reduced by 25% in cases of grade 2 hand-foot syndrome.

Repeat cycle every 21 days. Continue treatment to a maximum of eight cycles.

Reference: [van Meerten E, et al. Br J Cancer 2007;96:1348 – 52.](#)

### CARBOPLATIN – PACLITAXEL

#### CYCLE 1

Paclitaxel <sup>‡</sup>	200 mg/m <sup>2</sup>		IV*	Day 1
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*Followed by*

Carboplatin	AUC 5**		IV	Day 1
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#### CYCLE 2 ONWARDS<sup>#</sup>

Paclitaxel <sup>‡</sup>	225 mg/m <sup>2</sup>		IV*	Day 1
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*Followed by*

Carboplatin	AUC 6**		IV	Day 1
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<sup>‡</sup>Routine premedication administered; \*Administer over 3 hours; \*\*Calculated using the Calvert Formula; <sup>#</sup>Doses escalated in cycle 2 if the ANC nadir was  $1 \times 10^9/L$  or greater, and the platelet nadir was  $100 \times 10^9/L$  or greater.

Repeat cycle every 21 days until best response.

Reference: [El-Rayes BF, et al. Ann Oncol 2004;15:960 – 5.](#)

### **CISPLATIN – 5-FLUOROURACIL**

Cisplatin	100 mg/m <sup>2</sup>	IV*	Day 1
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*Followed by*

5-Fluorouracil	1000 mg/m <sup>2</sup> /day	CIVI	Days 1 – 5
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\*Administer over 1 hour with routine pre- and post-hydration.

Repeat every 21 days for three cycles, and then follow with surgery or radiation therapy.

References: [Kies MS, et al. \*Cancer\* 1987;60:2156 – 60](#); [Bleiberg H, et al. \*Eur J Cancer\* 1997;33:1216 – 20](#).

### **CISPLATIN – 5-FLUOROURACIL (NEOADJUVANT)**

Cisplatin	80 mg/m <sup>2</sup>	IV*	Day 1
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5-Fluorouracil	1000 mg/m <sup>2</sup> /day	CIVI	Days 1 – 4
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\*Administer over 4 hours with routine pre- and post-hydration.

Repeat cycle every 21 days for 2 cycles, then surgical resection 3 – 5 weeks after starting cycle number 2.

Reference: [Medical Research Council Oesophageal Cancer Working Party. \*Lancet\* 2002;359:1727 – 33](#).

### **CISPLATIN – IRINOTECAN**

Cisplatin	30 mg/m <sup>2</sup>	IV	Days 1 and 8
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*Followed by*

Irinotecan	65 mg/m <sup>2</sup>	IV*	Days 1 and 8
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\*Administer over 30 minutes.

Repeat cycle every 21 days.

References: [Ilson DH, et al. \*ASCO GI Symposium\* 2004; \[abstract 13\]](#); [Ilson DH, et al. \*J Clin Oncol\* 1999;17:3270 – 5](#).

### **DCF (DOCETAXEL – CISPLATIN – 5-FLUOROURACIL)**

Docetaxel <sup>‡</sup>	75 mg/m <sup>2</sup>	IV	Day 1
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Cisplatin	75 mg/m <sup>2</sup>	IV*	Day 1
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5-Fluorouracil	750 mg/m <sup>2</sup> /day	CIVI	Days 1 – 5
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<sup>‡</sup>Routine premedication required; \*Routine pre- and post-hydration required.

NOTE: Adenocarcinoma of the GE-junction only.

Repeat cycle every 21 days.

Reference: [Van Cutsem E, et al. \*J Clin Oncol\* 2006;24:4991 – 7](#).

### **ECF (EPIRUBICIN-CISPLATIN-5-FLUOROURACIL)**

Epirubicin	50 mg/m <sup>2</sup>	IV	Day 1
Cisplatin	60 mg/m <sup>2</sup>	IV*	Day 1
5-Fluorouracil	200 mg/m <sup>2</sup> /day	CIVI	Day 1 onwards up to 6 months

\*Routine pre- and post-hydration required.

NOTE: Adenocarcinoma of the GE-junction only.

Repeat cycle every 21 days to a maximum of 8 cycles. For peri-operative use, administer only 3 cycles pre-surgery and 3 cycles post-surgery (6 total).

References: [Ross P, et al. \*J Clin Oncol\* 2002;20:1996 - 2004](#); [Waters JS, et al. \*Br J Cancer\* 1999;80:269 - 72](#); [Cunningham D, et al. \*N Engl J Med\* 2006;355:11 - 20](#).

### **EOX (EPIRUBICIN - OXALIPLATIN - CAPECITABINE) - ADENOCARCINOMA ONLY**

Epirubicin	50 mg/m <sup>2</sup>	IV	Day 1
Oxaliplatin	130 mg/m <sup>2</sup>	IV*	Day 1
Capecitabine	650mg/m <sup>2</sup> BID	PO	Day 1 onwards continuously

\*Administer over 2 hours.

NOTE: Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

Repeat cycle every 21 days to a maximum of 8 cycles.

Reference: [Sumpter K, et al. \*Br J Cancer\* 2005;92:1976 - 83](#).

# GASTRIC CANCER

## CAPECITABINE

Capecitabine	1250 mg/m <sup>2</sup> BID	PO	Days 1 - 14
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NOTE: Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

Repeat cycle every 21 days for up to 6 cycles.

Reference: [Hong YS, et al. \*Ann Oncol\* 2004;15:1344 - 7.](#)

## CAPECITABINE - CISPLATIN

Capecitabine	1000 mg/m <sup>2</sup> BID	PO	Days 1 - 14
Cisplatin	80 mg/m <sup>2</sup>	IV*	Day 1

\*Routine pre- and post-hydration required.

NOTE: Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

Repeat cycle every 21 days until disease progression or unacceptable toxicity.

Reference: [Kang Y, et al. \*Proc Am Soc Clin Oncol\* 2006;24\(18S\):934s; Abstract LBA4018.](#)

## CAPECITABINE - OXALIPLATIN

Capecitabine	1000 mg/m <sup>2</sup> BID	PO	Days 1 - 14
Oxaliplatin	130 mg/m <sup>2</sup>	IV*	Day 1

\*Administer over 2 hours.

NOTE: Capecitabine to be ingested with water every 12 hours, approximately 30 minutes after a meal, starting the evening of day 1. Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

DOSE MODIFICATION: Persistent ( $\geq 14$  days) paresthesia or temporary (7 - 14 days) painful paresthesia or functional impairment resulted in a 25% dose reduction of oxaliplatin. In cases of persistent ( $\geq 14$  days) painful paresthesia or functional impairment, oxaliplatin had to be omitted until recovery and then restarted at 50% of the dose. Capecitabine was reduced by 25% in cases of grade 2 hand-foot syndrome.

Repeat cycle every 21 days. Continue treatment to a maximum of eight cycles.

Reference: [van Meerten E, et al. \*Br J Cancer\* 2007;96:1348 - 52.](#)

**DCF (DOCETAXEL – CISPLATIN – 5-FLUOROURACIL)**

Docetaxel <sup>‡</sup>	75 mg/m <sup>2</sup>	IV	Day 1
Cisplatin	75 mg/m <sup>2</sup>	IV*	Day 1
5-Fluorouracil	750 mg/m <sup>2</sup> /day	CIVI	Days 1 – 5

<sup>‡</sup>Routine premedication required; \*Routine pre- and post-hydration required.

Repeat cycle every 21 days.

Reference: [Van Cutsem E, et al. \*J Clin Oncol\* 2006;24:4991 – 7.](#)

**DOCETAXEL – CAPECITABINE**

Docetaxel <sup>‡</sup>	75 mg/m <sup>2</sup>	IV	Day 1
Capecitabine	825 mg/m <sup>2</sup> BID	PO	Days 1 – 14

<sup>‡</sup>Routine premedication required.

NOTE: Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

Repeat cycle every 21 days until progression.

Reference: [Giordano KF, et al. \*Ann Oncol\* 2006;17:652 – 6.](#)

**ECF (EPIRUBICIN – CISPLATIN – 5-FLUOROURACIL)**

Epirubicin	50 mg/m <sup>2</sup>	IV	Day 1
Cisplatin	60 mg/m <sup>2</sup>	IV*	Day 1
5-Fluorouracil	200 mg/m <sup>2</sup> /day	CIVI	Day 1 onwards up to 6 months

\*Routine pre- and post-hydration required.

Repeat cycle every 21 days to a maximum of 8 cycles. For peri-operative use, administer only 3 cycles pre-surgery and 3 cycles post-surgery (6 total).

References: [Ross P, et al. \*J Clin Oncol\* 2002;20:1996 – 2004](#); [Waters JS, et al. \*Br J Cancer\* 1999;80:269 – 72](#); [Cunningham D, et al. \*N Engl J Med\* 2006;355:11 – 20.](#)

### **ELF (ETOPOSIDE – LEUCOVORIN – 5-FLUOROURACIL)**

Leucovorin	300 mg/m <sup>2</sup> /day	IV*	Days 1 – 3
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*Followed immediately by*

Etoposide	120 mg/m <sup>2</sup> /day	IV**	Days 1 – 3
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*Followed by*

5-Fluorouracil	500 mg/m <sup>2</sup> /day	IVB	Days 1 – 3
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\*Administer over 10 minutes; \*\*Administer over 50 minutes.

Repeat cycle every 22 days.

Reference: [Vanhoef U, et al. J Clin Oncol 2000;18:2648 – 57.](#)

### **EOX (EPIRUBICIN – OXALIPLATIN – CAPECITABINE)**

Epirubicin	50 mg/m <sup>2</sup>	IV	Day 1
Oxaliplatin	130 mg/m <sup>2</sup>	IV*	Day 1
Capecitabine	650mg/m <sup>2</sup> BID	PO	Day 1 onwards continuously

\*Administer over 2 hours.

NOTE: Capecitabine dose should be rounded to the nearest 150 mg or 500 mg tablet size.

Repeat cycle every 21 days to a maximum of 8 cycles.

Reference: [Sumpter K, et al. Br J Cancer 2005;92:1976 – 83.](#)

**FAMTX (5-FLUOROURACIL – METHOTREXATE – LEUCOVORIN – DOXORUBICIN)**

Methotrexate*	1500 mg/m <sup>2</sup>	IV	Day 1
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*Followed 1 hour later by*

5-Fluorouracil	1500 mg/m <sup>2</sup> **	IV	Day 1
Leucovorin	30 mg Q6H***	PO	Days 2 and 3
Doxorubicin	30 mg/m <sup>2</sup>	IV	Day 15

\*Ensure the patient has alkaline urine (i.e., pH greater than 7), and is well hydrated prior to methotrexate, and check each urine void to ensure pH is 7 and greater. If not increase bicarbonate or consider acetazolamide; \*\*Start 1 hour after the methotrexate on Day 1; \*\*\*Leucovorin begins 24 hours after methotrexate dose. Plasma levels of methotrexate are evaluated at 24 hours and 48 hours after the methotrexate dose, and leucovorin rescue at 30 – 60 mg every 6 hours was administered until the plasma levels were less than  $2.5 \times 10^6$  mol/L.

Repeat cycle every 29 days.

References: [Wils JA, et al. J Clin Oncol 1991;9:827 – 31](#); [Vanhoefer U, et al. J Clin Oncol 2000;18:2648 – 57](#).

**FUP (5-FLUOROURACIL – CISPLATIN)**

5-Fluorouracil	1000 mg/m <sup>2</sup> /day	CIVI	Days 1 – 5
Cisplatin	100 mg/m <sup>2</sup>	IV*	Day 2

\*Administer over 1 hour with routine pre- and post-hydration.

Repeat cycle every 29 days.

Reference: [Vanhoefer U, et al. J Clin Oncol 2000;18:2648 – 57](#).

**5-FLUOROURACIL – LEUCOVORIN**

Leucovorin	200 mg/m <sup>2</sup> /day	IVB	Days 1 – 5
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*Followed immediately afterwards by*

5-Fluorouracil	370–400 mg/m <sup>2</sup> /day*	IV**	Days 1 – 5
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\*Initially administered at a dose of 370 mg/m<sup>2</sup>, increased to 400 mg/m<sup>2</sup> if toxicity was absent at the 370 mg/m<sup>2</sup> dosing level; \*\*Administer over 15 minutes.

Repeat cycle every 26 days.

Reference: [Machover D, et al. J Clin Oncol 1986;4:685 – 96](#).

### **5-FLUOROURACIL – LEUCOVORIN – IRINOTECAN**

Leucovorin	200 mg/m <sup>2</sup> /day	IV*	Days 1 and 2
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*Followed by*

5-Fluorouracil	400 mg/m <sup>2</sup> /day	IVB**	Days 1 and 2
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*Then*

5-Fluorouracil	600 mg/m <sup>2</sup> /day	CIVI***	Days 1 and 2
Irinotecan	180 mg/m <sup>2</sup>	IV#	Day 1

\*Administer over 2 hours; \*\*Administer as an IV bolus over 2 – 4 minutes; \*\*\*Administer as a 22 hour continuous infusion; #Administer over 90 minutes.

Repeat cycle every 14 days until disease progression or toxicity.

Reference: [Bouche O, et al. J Clin Oncol 2004;22:4319 – 28.](#)

### **FOLFOX 6 (OXALIPLATIN – 5-FLUOROURACIL – LEUCOVORIN)**

Oxaliplatin	100 mg/m <sup>2</sup>	IV*	Day 1
Leucovorin	400 mg/m <sup>2</sup>	IV*	Day 1

*Followed by*

5-Fluorouracil	400 mg/m <sup>2</sup>	IV**	Day 1
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*Followed immediately by*

5-Fluorouracil	3000 mg/m <sup>2</sup>	CIVI***	Day 1
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\*Administer over 2 hours simultaneously in D<sub>5</sub>W; \*\*IV bolus administered over 10 minutes; \*\*\*Administer as a CIVI of 5-Fluorouracil over 46 hours, following the bolus dose.

Repeat cycle every 14 days (for at least 6 cycles, except in the event of disease progression).

Reference: [Louvret C, et al. J Clin Oncol 2002;20:4543 – 8.](#)

## GASTRIC CANCER ADJUVANT TREATMENT

### 5-FLUOROURACIL-LEUCOVORIN-RADIATION (MACDONALD ADJUVANT REGIMEN)

5-Fluorouracil	425 mg/m <sup>2</sup> /day	IV*	Days 1 - 5
Leucovorin	20 mg/m <sup>2</sup> /day	IV*	Days 1 - 5

*The above treatment was initiated on Day 1. On Day 29 the following chemoradiotherapy is started:*

Radiation	45 Gy (1.8 Gy per day) five days per week for 5 weeks		
5-Fluorouracil	400 mg/m <sup>2</sup> /day	IV*	On the first four and last 3 days of radiation
Leucovorin	20 mg/m <sup>2</sup> /day	IV*	On the first 4 and last 3 days of radiation

*One month following completion of chemoradiotherapy the following is initiated*

5-Fluorouracil	425 mg/m <sup>2</sup> /day	IV*	Days 1 - 5
Leucovorin	20 mg/m <sup>2</sup> /day	IV*	Days 1 - 5

Repeat this cycle every 28 days for 2 cycles.

\*Administer as an IV bolus.

Reference: [Macdonald JS, et al. N Engl J Med 2001;345:725 - 30.](#)

### ECF (EPIRUBICIN-CISPLATIN-5-FLUOROURACIL)

Epirubicin	50 mg/m <sup>2</sup>	IV	Day 1
Cisplatin	60 mg/m <sup>2</sup>	IV*	Day 1
5-Fluorouracil	200 mg/m <sup>2</sup> /day	CIVI	Day 1 onwards up to 6 months

\*Routine pre- and post-hydration required.

Repeat cycle every 21 days. Administer 3 cycles pre-surgery and 3 cycles post-surgery (6 total).

Reference: [Cunningham D, et al. N Engl J Med 2006;355:11 - 20.](#)