

BCCA Protocol Summary for Combined Modality Therapy for Locally Advanced Esophageal Cancer using Cisplatin, Infusional Fluorouracil and Radiation Therapy

Protocol Code

GIEFUPRT

Tumour Group

Gastrointestinal

Contact Physician

GI Systemic Therapy

ELIGIBILITY:

- Locally advanced squamous cell cancer or adenocarcinoma of the esophagus suitable for curative therapy.
- In cases where surgery is not appropriate (e.g by virtue of the high tumour position above the carina), where local surgical clearance is not possible, or where patient is medically unfit or refuses surgery.
- As an alternative to surgery, depending on local Cancer Centre policy and availability of specialized surgical expertise.
- Any age - patients over 69 to be assessed individually
- ECOG 0-2

EXCLUSIONS:

- Distant metastases
- Hearing impairment
- Inadequate renal function (creatinine clearance less than 45 mL/min as calculated by Cockcroft/Gault formula - see page 3).
- Uncontrolled high blood pressure, unstable angina, symptomatic congestive heart failure, myocardial infarction within the preceding 6 months, serious uncontrolled cardiac dysrhythmia.

TESTS:

- Baseline: CBC, diff and platelets, creatinine, serum albumin, bilirubin, SGOT and alkaline phosphatase.
- Prior to each treatment: CBC, diff and platelets, creatinine
- If clinically indicated: bilirubin, liver enzymes

PREMEDICATIONS:

- Antiemetic protocol for High Moderate emetogenic chemotherapy as long as cisplatin dose is not greater than 50 mg. If cisplatin is greater than 50 mg use antiemetic protocol for Highly emetogenic chemotherapy protocols.

TREATMENT:

Chemotherapy

Drug	Dose	BCCA Administration Guideline
Fluorouracil (5FU)	1000 mg/m ² /day for 4 days (total dose = 4000 mg/m ² over 96 h)	IV in D5W to a total volume of 192 mL by continuous infusion at 2 mL/h via appropriate infusor device*
Cisplatin	25 mg/m ² Daily x 3 days **	In 100 mL normal saline, over 30 min

*Inpatients: 1000 mg/m²/day in 1000 mL D5W by continuous infusion daily over 24 h for 4 days.

**For patients with an excellent performance status who are being treated before radiation therapy has begun, the cisplatin total dose may be increased to 100 mg/m² given as 25 mg/m² daily for 4 days (cycles 1-4). In some circumstances the total dose of cisplatin may be given as a single dose with appropriate pre and post hydration.

Radiation Therapy:

5000 cGy in 25 fractions over 5 weeks. Note: Some patients may receive additional brachytherapy as part of a toxicity trial. This does not alter the chemotherapy dosage or schedules.

Duration of chemotherapy: Four cycles of chemotherapy are given as follows:

Week	1	2	3	4	5	6	7	8	9	10	11	12
Radiation	x	x	x	x	x							
Chemo Cycle	1				(2)				3			4

Cycle 1: Given concurrent with the first week of radiation therapy. This is usually started on the first day of the radiation therapy.

Cycle 2: Given concurrent with the fifth week of radiation therapy. This cycle may be eliminated if the patient is experiencing major toxicity.

Cycle 3: Given approximately 3 weeks after the end of radiation therapy.

Cycle 4: Given 3 weeks after day 1 of cycle 3.

Alternative Schedule

Week	1	2	3	4	5	6	7	8	9	10	11	12
Radiation				x	x	x	x	x				
Chemo Cycle	1			2				(3)				4

Cycle 1: Given three weeks prior to initiation of radiation therapy, to allow for planning and wait list for radiation, if this is the best management for the individual patient.

Cycle 2: Given concurrent with the first week of radiation therapy. This is usually started on the first day of the radiation therapy.

Cycle 3: Given concurrent with the fifth week of radiation therapy. This cycle may be eliminated if the patient is experiencing major toxicity.

Cycle 4: Given approximately 3 weeks after the end of radiation therapy.

DOSE MODIFICATIONS:

1. Hematological

Day 1 counts:

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose - Fluorouracil only
greater than 1.5	and	greater than 100	100%
less than 1.5	or	less than 100	Delay x 1 week then reassess

2. Renal

Delay for one week if serum creatinine greater than 3 x ULN. If serum creatinine less than 3 x ULN adjust cisplatin dose as follows:

CrCl (By Cockcroft/Gault formula)	Dose - Cisplatin only
greater than or equal to 60 mL/min	100%
45 – 59 mL/min	50%
less than 45 mL/min	Delay x 1 week then reassess

Cockcroft/Gault formula:

$$CrCl = \frac{N (140 - \text{age}) \times \text{weight (kg)}}{\text{serum creatinine (micromol/L)}}$$

Where N = 1.04 for females, and 1.23 for males

3. **Neurotoxicity:** If clinically significant hearing loss or functionally significant peripheral neuropathy occurs, omit cisplatin and replace with mitomycin 10 mg/m² on day 1 of Cycles 1 and 3 **OR** Cycles 2 and 4 (maximum cumulative dose 20 mg/m²). (See BCCA Cancer Drug Manual for administration guidelines).

4. **GI Toxicity**

- (a) **Nausea and vomiting:** Grade 4 (greater than 10 episodes in 24 h or requires parenteral support, dehydration) - not helped by antiemetics. Decrease cisplatin dose to 80%, or **discontinue therapy.**
- (b) **Stomatitis:** Grade 3-4 (painful erythema, edema or ulcers and cannot eat). Decrease dose of Fluorouracil infusion by 25%.
- (c) **Diarrhea:** Grade 4 (increase of greater than or equal to 10 stools/day or grossly bloody diarrhea; dehydration). dose of Fluorouracil infusion by 25%.

PRECAUTIONS:

- 1. **Nausea and vomiting** are common and patients should be treated with ondansetron and dexamethasone before each dose of cisplatin (see premedication section)
- 2. **Renal toxicity** may occur with a salt and water losing nephropathy. Patients should be encouraged to maintain good oral hydration.
- 3. Myocardial ischemia and angina occurs rarely in patients receiving Fluorouracil. Development of **cardiac symptoms** including signs suggestive of ischemia or of cardiac arrhythmia is an indication to discontinue therapy.
- 4. **CNS toxicity** such as tinnitus, mild high frequency hearing loss and delayed peripheral neuropathy may occur secondary to cisplatin.
- 5. **Nutrition:** It is important to maintain weight if possible and early consultation with a nutritionist to advise about aggressive oral nutritional support and/or an enteral feeding tube is recommended.
- 6. **Possible drug interactions with fluorouracil and warfarin, phenytoin and fosphenytoin** have been reported and may occur at any time. Close monitoring is recommended (eg, for warfarin, monitor INR weekly during fluorouracil therapy and for 1 month after stopping fluorouracil).

Call the GI Systemic Therapy physician at your regional cancer centre or Dr. Sanjay Rao at (250) 712-3900 or 1-888-563-7773 with any problems or questions regarding this treatment program.

Date activated: 22 Sept 1998 (as GIEFUP)

Date revised: 1 June 2011 (Infusion section revised)