

BCCA Protocol Summary for Combined Modality Adjuvant Therapy for Completely Resected Gastric Adenocarcinoma using Fluorouracil + Folinic Acid (Leucovorin) + Radiation Therapy

Protocol Code

GIGAIRT

Tumour Group

Gastrointestinal

Contact Physicians

GI Systemic Therapy

ELIGIBILITY:

- Stage IB – IV M0 adenocarcinoma of the stomach or gastroesophageal junction who have undergone gastric resection with curative intent within 8-10 weeks and who have had a preop CT scan
- ECOG Performance Status 0-1; see Precautions patients with ECOG greater than or equal to 2
- Patients must have a Radiation Oncology consult before proceeding with this treatment

TESTS:

- Baseline: CBC and diff, LFTs,
- **Prior to** each treatment: CBC & diff
- Weekly during radiation therapy: CBC & diff

PREMEDICATIONS:

Treatment is non-emetogenic. See SCNAUSEA protocol.

TREATMENT:

- Chemotherapy is given in 5 cycles: cycle 1 is prior to radiation treatment, cycles 2 and 3 are during radiation treatment, and cycles 4 & 5 are following radiation treatment.

Some patients may experience stomatitis and/or diarrhea during Days 1-5 requiring dose modifications and/or treatment discontinuation due to excessive sensitivity. It is essential that all patients be assessed for stomatitis and diarrhea at each treatment visit and that any signs of these toxicities be reported to the attending physician or designate prior to administering the chemotherapy for that day. Continuing chemotherapy in this setting may result in life threatening toxicity.

Schema:

| CYCLE: WEEK: DAY | CHEMOTHERAPY | | |
|---|------------------|--------------------------------|-------------------------------|
| | Drug | Dose | BCCA Administration Guideline |
| 1:Wk 1:days 1-5 | Leucovorin | 20 mg/m ² /day x5d | IV push prior to Fluorouracil |
| | Fluorouracil | 425 mg/m ² /day x5d | IV push |
| Radiation: 4500 cGy in 25 fractions over 5 weeks (weeks 5-9) | | | |
| 2:Wk 5:days 29-32 (first 4 days of RT) | <i>[deleted]</i> | | |
| | Leucovorin | 20 mg/m ² /day x4d | IV push prior to Fluorouracil |
| 3:Wk 9:days 59-61 (last 3 days of RT) | Fluorouracil | 400 mg/m ² /day x4d | IV push |
| | Leucovorin | 20 mg/m ² /day x3d | IV push prior to Fluorouracil |
| 4*:Wk 14:days 92-96 | Fluorouracil | 400 mg/m ² /day x3d | IV push |
| | Leucovorin | 20 mg/m ² /day x5d | IV push prior to Fluorouracil |
| 5:Wk 18: days 120-124 | Fluorouracil | 425 mg/m ² /day x5d | IV push |
| | Leucovorin | 20 mg/m ² /day x5d | IV push prior to Fluorouracil |

* Cycle 4 starts 28 days after radiation ends

DOSE MODIFICATIONS:

If the radiation therapy is delayed, the chemotherapy should be delayed similarly so that Cycles 2 and 3 are always given during the first and fifth week of radiation therapy.

The dose of Folinic Acid (Leucovorin) is not modified for toxicity but is omitted if Fluorouracil is omitted.

For Cycles 1, 2, 4 and 5:

| | | |
|---|--|---------------------------------|
| 1. <u>ANC (x 10⁹/L)</u> | <u>Platelets (x 10⁹/L)</u> | <u>Fluorouracil Dose</u> |
| greater than or equal to 1.5 | greater than or equal to 100 | 100% |
| less than 1.5 | less than 100 | delay treatment |

For Cycle 3:

| | | |
|--|--|---|
| <u>ANC (x 10⁹/L)</u> | <u>Platelets (x 10⁹/L)</u> | <u>Fluorouracil Dose</u> |
| less than 1.5 | less than 75 | omit treatment RTX at Radiation Oncologist's discretion |

2. Non-hematological Toxicity

(For Cycles 1, 2, 4 and 5)

Inform the attending physician or designate prior to administration of chemotherapy if any signs of stomatitis and/or diarrhea (Grade 1-4) are present.

| Grade | Diarrhea | Stomatitis (if dose not reduced during previous cycle) | Percentage Dose of Fluorouracil for subsequent cycles based on interval toxicity | Dose Fluorouracil + Folinic Acid |
|--------------|---|--|--|--|
| Grade 1 | Increase of 2-3 stools/day or nocturnal stools; or mild increase in loose watery colostomy output | Painless ulcers, erythema or mild soreness | 425 mg/m ² Cycle 1, 4 & 5 or 400 mg/m ² Cycle 2 (or 100% of previous dose) | If greater than or equal to Grade 2 at start of cycle, hold and check weekly, then treat based on interval toxicity. If greater than or equal to Grade 2 after 2 weeks, discontinue. |
| Grade 2 | Increase of 4-6 stools/day, or nocturnal stools or moderate increase in loose watery colostomy output | Painful erythema, edema, or ulcers but can eat | 340 mg/m ² Cycle 1, 4 & 5 or 320 mg/m ² Cycle 2 (or 80% of previous dose) | |
| Grade 3 or 4 | Increase of greater than 7 stools/day or incontinence, malabsorption, severe increase in loose watery colostomy output, grossly bloody diarrhea, may require parenteral support | As above but cannot eat, mucosal necrosis and/or requires enteral support, dehydration | 255 mg/m ² Cycle 1, 4 & 5 or 240mg/m ² Cycle 2 (or 60% of previous dose) | |

(For Cycle 3)

| Toxicity | Action |
|---|--|
| ANC less than 1.5 or Platelets less than 75 | Omit Cycle |
| Stomatitis Grade 2-4 | Omit Cycle |
| Diarrhea Grade 3-4 | Omit Cycle |
| Interruption of Radiation due to diarrhea | Proceed with cycle once radiation resumes if toxicity has resolved. Chemotherapy should always be given on the first 4 days and the last 3 days of radiation therapy |

If toxicity is greater than or equal to Grade 2 after treatment has been held for 2 weeks, **discontinue treatment.**

If multiple toxicities are seen, the dose administered is based on the most severe toxicity experienced. Viral infection, alopecia, fatigue, anorexia and nausea/vomiting controlled by antiemetics require no dose alteration. All other non-hematologic toxicities are managed in the same manner as diarrhea. Dose reductions continue for remaining cycles.

3. **Hepatic dysfunction:** Omit treatment if bilirubin greater than 85 micromol/L unless secondary to biliary obstruction (BCCA Cancer Drug Manual).

PRECAUTIONS:

1. Neutropenia: Fever or other evidence of infection must be assessed promptly and treated aggressively; increased risk of myelosuppression in elderly.
2. Sucking ice chips is recommended, especially at higher doses of Fluorouracil, to reduce stomatitis following chemotherapy. Remove dentures and place ice chips in mouth five minutes before chemotherapy. Continuously swish in mouth for 30 minutes, replenishing as ice melts. This may cause numbness or headaches which subside quickly.
3. A GI syndrome characterized by progression from mild GI symptoms to potentially fatal enterocolitis has been reported. Prompt attention, especially to ensure adequate hydration, is required.
4. Dipyrimidine dehydrogenase deficiency may result in severe and unexpected toxicity – stomatitis, diarrhea, neutropenia, neurotoxicity. This deficiency is thought to be present in about 3% of the population.
5. 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 treatment.
6. Consideration should be given to a dose reduction for elderly patients (greater than 70 years of age, particularly female), patients with poor nutritional status and patients with an ECOG performance status of greater than or equal to 2. Starting Fluorouracil doses should be reduced to 375 mg/m², then increased by 25 mg/m² each cycle until the standard dose for that cycle is reached and there are no side effects at the previous dose.
7. **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: 01 August 2001 (as GIGAI)

Date revised: **1 May 2011 (minor edit in Test Section)**

REFERENCES:

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(10):725-30.