Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

MFOLFOX6+PEMB+TRAS Regimen

Oxaliplatin-Fluorouracil-Leucovorin-Pembrolizumab-Trastuzumab

Disease Site
Gastrointestinal
Gastric / Stomach

Intent
Palliative

Regimen Category
Evidence-informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

This **Regimen Abstract** is an **abbreviated** version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Rationale and Uses
Treatment of patients with locally advanced unresectable or metastatic HER2 positive gastric or gastroesophageal junction (GEJ) adenocarcinoma, whose tumours express PD-L1

Supplementary Public Funding
trastuzumab
New Drug Funding Program (Trastuzumab (Biosimilar) - Advanced Gastric,

Gastroesophageal, or Esophageal Cancer) (NDFP Website)

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B - Drug Regimen

Pembrolizumab every 6 weeks:

pembrolizumab[1,2]	400 mg	IV	Day 1; q6 weeks

(This drug is not currently publicly funded for this regimen and intent)

AND mFOLFOX6+Trastuzumab every 2 weeks:

trastuzumab	6 mg /kg	IV	Day 1 (Cycle 1 only)
trastuzumab	4 mg /kg	IV	Day 1; q2 weeks (Cycle 2 and onwards)
oxaliplatin	85 mg /m²	IV	Day 1
leucovorin	400 mg /m²	IV (concurrently with oxaliplatin)	Day 1
fluorouracil	400 mg /m²	IV bolus, after leucovorin	Day 1

Then,

fluorouracil	2400 mg /m²	IV continuous infusion over 46 hours (single dose)	Start on Day 1

[1]Alternative pembrolizumab dosing schedule is 200 mg IV q3 weeks.

[2]Administer pembrolizumab prior to trastuzumab and chemotherapy when given on the same day.

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C - Cycle Frequency

MFOLFOX6+TRAS: Repeat every 2 weeks
PEMBROLIZUMAB: Repeat every 6 weeks (400mg dose)†

Until disease progression or unacceptable toxicity^, or up to a maximum of 2 years, whichever occurs first

†Alternative pembrolizumab dosing schedule is 200 mg IV every 3 weeks.

^If chemotherapy is discontinued after at least 1 cycle due to intolerance, pembrolizumab and trastuzumab may be continued (PEMB+TRAS(MNT)) for up to 2 years, unless disease progression or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate
Minimal ((pembrolizumab-only days))

Other Supportive Care:

- **Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.
- Also refer to CCO Antiemetic Recommendations.
- Patients should be counselled about cold avoidance prior to receiving oxaliplatin, since cold temperatures can precipitate or exacerbate acute neurological symptoms.
- Avoid the use of corticosteroids or immunosuppressants before starting pembrolizumab treatment.

Premedication (prophylaxis for infusion reactions):

Pembrolizumab:

- Routine pre-medication is not recommended.
- May consider antipyretic and H1-receptor antagonist in patients who experienced a grade 1-2 infusion reaction.

Oxaliplatin

- There is insufficient evidence that routine prophylaxis with pre-medications reduces IR rates.
- Consider corticosteroids and H1-receptor antagonists ± H2-receptor antagonists in high-risk patients (i.e. ≥ cycle 6, younger age, female gender, prior platinum exposure, platinum-free interval ≥ 3 years).

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J - Administrative Information

Approximate Patient Visit	4 to 5 hours
Pharmacy Workload (average time per visit)	49.195 minutes
Nursing Workload (average time per visit)	89.167 minutes

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K - References

Al-Batran SE, 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(9):1435-42.

Fluorouracil drug monograph, Ontario Health (Cancer Care Ontario).

Janjigian YY, Kawazoe A, Bai Y, et al; KEYNOTE-811 Investigators. Pembrolizumab plus trastuzumab and chemotherapy for HER2-positive gastric or gastro-oesophageal junction adenocarcinoma: interim analyses from the phase 3 KEYNOTE-811 randomised placebo-controlled trial. Lancet 2023 Dec 9;402(10418):2197-208.

Leucovorin drug monograph, Ontario Health (Cancer Care Ontario).

Montagnani F, et al. Effectiveness and safety of oxaliplatin compared to cisplatin for advanced, unresectable gastric cancer: a systematic review and meta-analysis. Gastric Cancer 2011;14(1):50-55.

Oxaliplatin drug monograph, Ontario Health (Cancer Care Ontario).

Pembrolizumab drug monograph, Ontario Health (Cancer Care Ontario).

Soularue É, Cohen R, Tournigand C, et al. Efficacy and safety of trastuzumab in combination with oxaliplatin and fluorouracil-based chemotherapy for patients with HER2-positive metastatic gastric and gastro-oesophageal junction adenocarcinoma patients: a retrospective study. Bull Cancer 2015 Apr;102(4):324-31.

Ter Veer E, et al. Comparing cytotoxic backbones for first-line trastuzumab-containing regimens in human epidermal growth factor receptor 2-positive advanced oesophagogastric cancer: A meta-analysis. Int J Cancer 2018;143:438-448.

Trastuzumab drug monograph, Ontario Health (Cancer Care Ontario).

April 2024 new ST-QBP regimen

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L - Other Notes

DPD Deficiency Testing and Guidance

Patients should be tested for DPD deficiency before starting treatment with fluorouracil. Refer to the DPD Deficiency Guidance for Clinicians for more information.

In patients with unrecognized DPD deficiency, acute, life-threatening toxicity may occur; if acute grade 2-4 toxicity develops, treatment should be stopped immediately and permanent discontinuation considered based on clinical assessment of the toxicities.

Antidote for Fluorouracil Overdose:

Uridine triacetate is a prodrug of uridine and is a specific antidote for treating fluorouracil overdose or severe early onset toxicities. If available, consider administering as soon as possible (i.e. within 96 hours) for suspected overdose. If not available, treatment is symptomatic and supportive.

For usage approval and supply, contact Health Canada's Special Access Program (SAP) (Phone: 613-941-2108. On-call service is available for emergencies). Uridine triacetate (Vistogard®) is supplied by its manufacturer in the United States.

The recommended dosing and administration for **uridine triacetate** in patients ≥18 years is:

- 10 grams (1 packet of coated granules) orally every 6 hours for 20 doses in total, without regards to meals.
- Granules should not be chewed. They should be mixed with 3 to 4 ounces of soft foods such as applesauce, pudding or yogurt.
- The dose should be ingested within 30 minutes of preparation, followed by at least 4 ounces of water.
- Refer to the prescribing information on dose preparation for NG-tube or G-tube use.

Additional resources on the management of fluorouracil infusion overdose:

- Management of Fluorouracil Infusion Overdose Guideline (Alberta Health Services)

- Management of Fluorouracil Infusion Overdose at the BCCA - Interim Guidance (BC Cancer Agency)

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M - Disclaimer

Regimen Abstracts

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Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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