Regimen Reference Order – GAST – TNT (PRODIGE23)

ARIA: GAST - [FOLFIRINOX (PRODIGE23)]
GAST - [cape + RT (PRODIGE23)]
GAST - [cape (ADJ – PRODIGE23)]
GAST - [mFOLFOX6 (ADJ – PRODIGE23)]

Planned Course: **Neo-Adjuvant Phase: FOLFIRINOX every 14 days for 6 cycles, followed by:**
Concurrent Chemoradiation (CRT) Phase: capecitabine with radiation (25 fractions of radiation over 5 to 6 weeks), followed by surgery, then:
Adjuvant Phase: capecitabine for 4 cycles (1 cycle = 21 days) OR mFOLFOX6 for 6 cycles (1 cycle = 14 days)

Indication for Use: **Rectal Cancer; Total Neoadjuvant Therapy (TNT)**

CVAD: Required (Ambulatory Pump) for FOLFIRINOX and mFOLFOX6

Proceed with treatment if:
ANC equal to or greater than 1.5 x 10^9/L AND Platelets equal to or greater than 75 x 10^9/L
- ***Contact Physician if parameters are not met***

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – GAST – TNT (PRODIGE23)

Neo-Adjuvant Phase – FOLFIRINOX every 14 days for 6 cycles

Establish primary solution 500 mL of: D5W

Drug	Dose	CCMB Administration Guideline
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
oxaliplatin	85 mg/m^2	IV in D5W 500 mL over 2 hours
atropine	0.6 mg	IV Push over 2-3 minutes pre-irinotecan May be repeated once if diarrhea occurs during irinotecan infusion
irinotecan	180 mg/m^2	IV in D5W 500 mL over 90 minutes **Nursing Alert: irinotecan and leucovorin may be infused over the same 90-minute period using a Y-site connector*
leucovorin	400 mg/m^2	IV in D5W 500 mL over 90 minutes

fluorouracil	2400 mg/m^2	IV in D5W continuously over 46 hours by ambulatory infusion device

Concurrent Chemoradiation (CRT) Phase – capecitabine with radiation

Drug	Dose	CCMB Administration Guideline
capecitabine	800 mg/m^2	Orally twice daily on days of radiation only Take with food. Swallow whole **(Self-administered at home)**

Adjuvant Phase

Option #1: capecitabine every 21 days for 4 cycles

Drug	Dose	CCMB Administration Guideline
capecitabine	1250 mg/m^2	Orally twice daily on **Days 1 to 14**, followed by 7 days off Take with food. Swallow whole **(Self-administered at home)**

OR

Option #2: mFOLFOX6 every 14 days for 6 cycles

Establish primary solution 500 mL of: D5W

Drug	Dose	CCMB Administration Guideline
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
oxaliplatin	85 mg/m^2	IV in D5W 500 mL over 2 hours **Nursing Alert: oxaliplatin and leucovorin may be infused over the same 2-hour period using a Y-site connector*
leucovorin	400 mg/m^2	IV in D5W 500 mL over 2 hours
fluorouracil	400 mg/m^2	IV push over 5 minutes
fluorouracil	2400 mg/m^2	IV in D5W continuously over 46 hours by ambulatory infusion device

capecitabine (XELODA®) available dosage strengths: 150 mg and 500 mg tablets
Classification: Cytotoxic, Hazardous

All doses will be automatically rounded that fall within CCMB Approved Dose Bands. See Dose Banding document for more information

In the event of an infusion-related hypersensitivity reaction, refer to the **'Hypersensitivity Reaction Standing Order'**

REQUIRED MONITORING

FOLFIRINOX (Neo-Adjuvant Phase)

All Cycles

- CBC, serum creatinine, urea, electrolytes, liver enzymes and total bilirubin as per Physician Orders

Concurrent Chemoradiation (CRT) Phase

Prior to start of radiation

- CBC, serum creatinine, urea, electrolytes, liver enzymes and total bilirubin as per Physician Orders

During radiation

- CBC once weekly as per Physician Orders

capecitabine OR mFOLFOX6 (Adjuvant Phase)

All Cycles

- CBC, serum creatinine, urea, electrolytes, liver enzymes and total bilirubin as per Physician Orders

Recommended Support Medications – GAST – TNT (PRODIGE23)

Drug	Dose	CCMB Administration Guideline
Neo-Adjuvant Phase – FOLFIRINOX		
dexamethasone	8 mg	Orally once daily on Days 2 and 3
prochlorperazine	10 mg	Orally every 6 hours as needed for nausea and vomiting
loperamide	2 – 4 mg	Orally as directed in Discharge Instructions below
Concurrent Chemoradiation (CRT) Phase – capecitabine with radiation		
prochlorperazine	10 mg	Orally every 6 hours as needed for nausea and vomiting
Adjuvant Phase		
Option #1: capecitabine		
prochlorperazine	10 mg	Orally every 6 hours as needed for nausea and vomiting
Option #2: mFOLFOX6		
dexamethasone	8 mg	Orally once daily on Days 2 and 3
prochlorperazine	10 mg	Orally every 6 hours as needed for nausea and vomiting

DISCHARGE INSTRUCTIONS

All Treatment Phases

- Instruct patient to continue taking anti-emetic(s) at home
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

FOLFIRINOX (Neo-Adjuvant Phase)

- If diarrhea occurs within 24 hours of irinotecan administration:
    - Return to cancer care clinic or go to the emergency department. A second dose of intravenous atropine may be required
- If cramping or diarrhea occurs more than 24 hours after irinotecan administration:
    - Take loperamide 4 mg (two 2 mg tablets) orally STAT; then
    - During the day: Take 2 mg (one 2 mg tablet) orally every 2 hours
    - During the night: Take 4 mg (two 2 mg tablets) orally at bedtime and then every 4 hours until morning
    - STOP loperamide once no bowel movement has occurred (e.g. diarrhea-free) for 12 hours
    - If diarrhea has not stopped despite taking **12 tablets (24 mg) of loperamide over a 24-hour period**, please contact your clinic for further instructions. If this occurs after clinic hours, please call the Medical Oncologist on-call and/or report to the nearest emergency room/urgent care centre. Please note that 24 mg per 24 hours is higher than the usual "over the counter" dose for loperamide
- Ensure patient has received a home chemotherapy spill kit and instructions for use

Concurrent Chemoradiation (CRT) Phase

- Inform patient to start capecitabine on the first day of radiation and to take capecitabine every day that they receive radiation. If patient will run out of capecitabine supply before the end of radiation, patient should contact medical oncologist's clinic to discuss whether an additional prescription is required

capecitabine OR mFOLFOX6 (Adjuvant Phase)

- For patients prescribed mFOLFOX6:
    - Ensure patient has received a home chemotherapy spill kit and instructions for use

ADDITIONAL INFORMATION

FOLFIRINOX (Neo-Adjuvant Phase)

- Nurse to provide patient with 30 tablet supply of loperamide 2 mg, labelled by Pharmacy, to take home with Cycle 1
- oxaliplatin causes cold intolerance and laryngopharyngeal dysesthesia
    - no ice chips or cold drinks
- oxaliplatin may cause progressive, irreversible neuropathy
    - dose modification may be required

Concurrent Chemoradiation (CRT) Phase

- capecitabine can cause diarrhea, hand-foot syndrome and neuropathy
- capecitabine with concurrent radiation starts 1 to 3 weeks after last cycle of FOLFIRINOX
- capecitabine should start on the first day of radiation and continue on the days of radiation until the last day of radiation (radiation is given on Mondays through Fridays for 25 fractions of radiation). capecitabine is not taken on Saturdays and Sundays or any other day without radiation treatment (e.g. statutory holidays, radiation machine maintenance days)

capecitabine OR mFOLFOX6 (Adjuvant Phase)

- Adjuvant treatment starts 5 to 12 weeks following surgery
- capecitabine can cause diarrhea, hand-foot syndrome and neuropathy
- oxaliplatin causes cold intolerance and laryngopharyngeal dysesthesia
    - no ice chips or cold drinks
- oxaliplatin may cause progressive, irreversible neuropathy
    - dose modification may be required