Managing Side-effects of Cancer Drugs

Breast and Colorectal Cancer

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Disclosure statement

I have/had an affiliation with the following:

Janssen	as a speaker
Astra-Zeneca	as a reviewer for scientific content
Pear Healthcare	
Solutions/Pfizer	as a reviewer for scientific content
Merck	as a speaker, consultant

Presentation

- Case presentations in breast and colon cancer.
- Define solutions for managing side effects of cancer drugs.
- Define useful tools for helping in decision making for side effect management.

Breast cancer case #1: Mrs AB

Mrs AB is a 67 year old with metastatic ER+, PR+, Her2+ breast cancer previously treated with anthracycline, taxane, trastuzumab based chemotherapies and hormonal therapy.

Her medical oncologist decides to start lapatinib and capecitabine. After a few weeks of therapy, she calls the clinic complaining of painful redness and peeling of the skin on soles of hands and feet.

Breast cancer case #1: Mrs AB

Your recommendation is to:

1- Do nothing.

2- Take some acetaminophen and call us in a week if still not better.

3- Call oncologist, get Dilaudid rx and fax to pharmacy.

4- Soak hands, feet in lukewarm water, apply hydrating cream, consider dose adjustment of capecitabine at next cycle.

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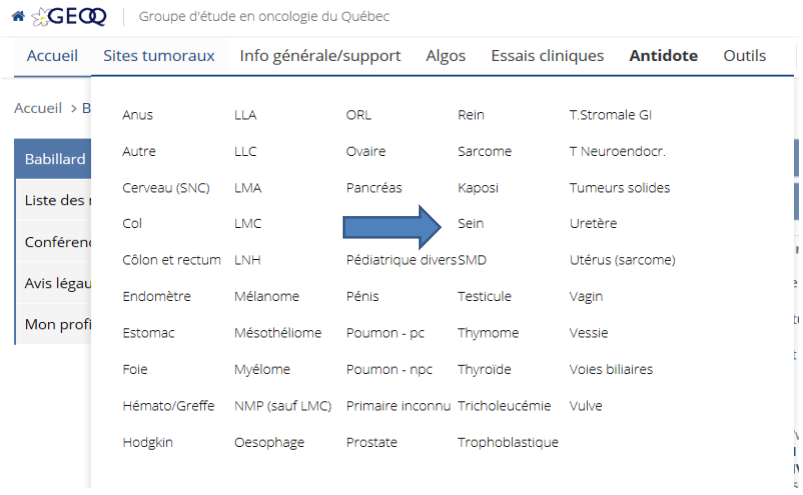

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Her2+					
Pertuzumab + trastuzumab + docétaxel					4%
Pertuzumab + trastuzumab + paclitaxel					1%
Trastuzumab + paclitaxel hebdomadaire					1%
Trastuzumab + docétaxel					1%
Trastuzumab + vinorelbine					1%
Trastuzumab + capécitabine					1%
T-DM1 (trastuzumab emtansine)					5%
Lapatinib + capécitabine					1%

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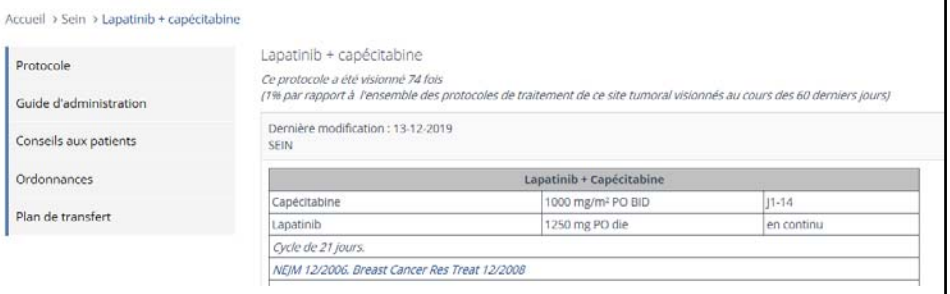

Accueil › Sein › Lapatinib + capécitabine

- Protocole
- Guide d'administration
- Conseils aux patients
- Ordonnances
- Plan de transfert

Lapatinib + capécitabine

Ce protocole a été visionné 74 fois
(1% par rapport à l'ensemble des protocoles de traitement de ce site tumoral visionnés au cours des 60 derniers jours)

Dernière modification : 13-12-2019
SEIN

Lapatinib + Capécitabine		
Capécitabine	1000 mg/m² PO BID	J1-14
Lapatinib	1250 mg PO die	en continu
Cycle de 21 jours.		
NEJM 12/2006. Breast Cancer Res Treat 12/2008		

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Guide d'administration

Protocole *: Capecitabine/Lapatinib*
(Xeloda^{md} / Tykerb^{md})

- **Le syndrome mains-pieds (érythrodysesthésie palmoplantaire)** est apparu chez 53% des patientes qui ont reçu l'association lapatinib/capécitabine. L'apparition de ce syndrome nécessite plus souvent l'interruption temporaire qu'une réduction de dose[1,2,5] (voir section 3 : Guide d'ajustement posologique).

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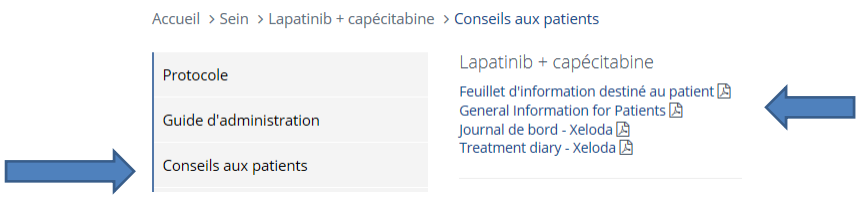

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ADVERSE EFFECTS	MANAGEMENT
Hand and foot syndrome may appear during your treatment. You may experience numbness, tingling, swelling, redness on your hands and feet. Pain, blisters, desquamation may accompany these symptoms.	**To prevent this syndrome:** • Avoid wearing tight clothes or shoes. • Wear absorbent sponge rubber soles,and/or gel pads to relieve pressure points. • Pat dry your hands and feet rather than rubbing them. • Wear light clothing or keep skin free of clothing to avoid perspiring. • Wear rubber gloves while washing dishes. • Wash your hands and feet in lukewarm water; avoid hot water. • Keep your skin well hydrated by regurlarly using a non perfumed emollient and thick cream. • Avoid strenuous exercises or activities that put too much of an ordeal on your hands and feet. **If symptoms occur:** • If these symptoms occur and affect your daily activities, stop taking the medication and notify a member of your healthcare team as soon as possible.

Breast cancer case #1: Mrs AB

Your recommendation is to:

1- Do nothing.

2- Take some acetaminophen and call us in a week if still not better.

3- Call oncologist, get Dilaudid rx and fax to pharmacy.

4- Soak hands, feet in lukewarm water, apply hydrating cream, consider dose adjustment of capecitabine at next cycle.

Colon cancer case #1: Mr CD

Mr CD is a 74 year old diagnosed with metastatic colon cancer. His disease is RAS wild-type. He is DYPD negative. He is to start on palliative combination chemotherapy of FOLFIRI-Panitumumab q2wks.

Mr CD receives his first cycle and calls you back 3 days later complaining of diarrhea, many episodes in the last 24 hours.

Colon cancer case #1: Mr CD

Your recommendation is:

1- Go to ER where they will give you Methylprednisolone 1 mg/kg iv q6h.

2- Budesonide 6 mg po bid.

3- Loperamide 4 mg po stat then 2 mg po q2h until 12 hrs free of diarrhea.

4- Octreotide 100 mg sc q8h.

5- Atropine 0.4 mg sc stat x 1 dose.

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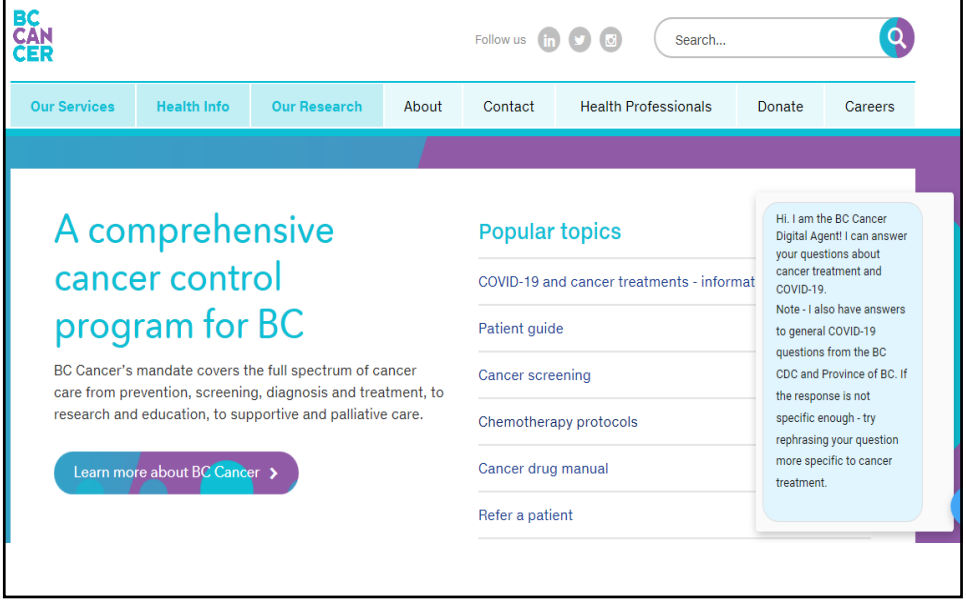

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Cancer Drug Manual

The Cancer Drug Manual® provides concise, evaluative information on drugs used in oncology. Inclusion in this index is not an indication of the funding status of a drug through BC Cancer. To determine drug coverage, see Benefit Drug List.

Go to the Drug Index >

Go to Immunotherapy >

Go to Biosimilar Drugs >

Introduction

User's Guide

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Irinotecan Liposome Monograph >

Irinotecan Monograph >

Irinotecan Patient Handout >

Irinotecan Patient Handout (Chinese)

Irinotecan Patient Handout (Punjabi)

Ixabepilone Monograph

DRUG NAME: Irinotecan

SYNONYM: Irinotecan hydrochloride trihydrate, CPT-11

COMMON TRADE NAME(S): CAMPTOSAR®

CLASSIFICATION: Topoisomerase I inhibitor

Special pediatric considerations are noted when applicable,

MECHANISM OF ACTION:

Irinotecan is a semisynthetic, water-soluble derivative of camptothecin, v
plants such as *Camptotheca acuminata*.[1] Irinotecan and its active metab
topoisomerase I, an enzyme that produces reversible single-strand breal
single-strand breaks relieve torsional strain and allow DNA replication to
topoisomerase I-DNA complex and prevent religation of the DNA strand,
and cell death. The precise contribution of SN-38 to the activity of irinote
cell cycle phase-specific (S-phase).[3]

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Late onset diarrhea: This occurs more than 24 hours after administration of irinotecan and can be prolonged, leading to potentially life-threatening dehydration and electrolyte imbalance.[1] The diarrhea has a median onset of 5 and 11 days after the 3-weekly[30] and weekly[34] dosing schedule of irinotecan, respectively. The median duration of diarrhea for the one-weekly schedule was 3 days, with severe diarrhea (grades 3-4) lasting for 7 days.[1] Late onset diarrhea is thought to be related to abnormal ion transport in the injured intestinal mucosa, leading to increased secretion of water and electrolytes into the intestinal lumen.[35] Management of diarrhea should include prompt treatment with high dose loperamide. Patients with severe diarrhea should be carefully monitored for dehydration and given fluid and electrolyte replacement as needed. Premedication with loperamide prior to irinotecan treatment is not required. However, patients should be instructed to have loperamide on hand and start the following treatment at the first poorly formed or loose stool, or earliest onset of more frequent bowel movement than usual (NB, loperamide dose used is higher than recommended by the manufacturer):

- loperamide 4 mg immediately
- then 2 mg every 2 hours until diarrhea-free for 12 hours
- may take 4 mg every 4 hours at night.[1,36]

An alternative regimen of loperamide 4 mg every 3 hours plus diphenhydramine 25 mg every 6 hours has also been used in a limited number of patients.[12] Laxatives may increase the risk of severe diarrhea[1] and patients should be counselled about laxative use during irinotecan treatment.

BC Cancer Agency www.bccancer.bc.ca

Chemotherapy Protocols

BC Cancer Systemic Therapy Program has placed summaries of specific treatment protocols on the website.

Gastrointestinal

Protocols | T

- Resectable Colorectal (Adjuvant)
- Unresectable Colorectal (Advanced)
- Esophagus, Stomach
- Pancreas, Gall Bladder, Biliary Tract
- Liver
- Carcinoid & Neuroendocrine Tumours
- Others

UGIFFIRPAN

Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan, Fluorouracil, Leucovorin, and PANitumumab

- UGIFFIRPAN Protocol
- UGIFFIRPAN Preprinted order
- UGIFFIRPAN Patient Handout

BC Cancer Agency www.bccancer.bc.ca

PRECAUTIONS

1. **Diarrhea:** may be life threatening and requires prompt, aggressive treatment.
   - **Early diarrhea** or abdominal cramps occurring within the first 24 hours is treated with **atropine** 0.3 to 1.2 mg IV or SC. Prophylactic atropine may be required for subsequent treatments.
   - **Late diarrhea** has an onset of 5 to 11 days post-treatment, a duration of 3 to 7 days and must be treated promptly with **loperamide** (eg, IMODIUM®). The loperamide dose is higher than recommended by the manufacturer. Instruct patient to have loperamide on hand and start treatment at the first poorly formed or loose stool, or earliest onset of more frequent stool than usual:
     - **4 mg stat**
     - **then 2 mg every 2 hours until diarrhea-free for 12 hours**
     - may take 4 mg every 4 hours at night

Colon cancer case #1: Mr CD

Your recommendation is:

1- Go to ER where they will give you Methylprednisolone 1 mg/kg iv q6h.

2- Budesonide 6 mg po bid.

3- Loperamide 4 mg po stat then 2 mg po q2h until 12 hrs free of diarrhea.

4- Octreotide 100 mg sc q8h.

5- Atropine 0.4 mg sc stat x 1 dose.

Breast cancer case #2: Mrs EL

Mrs EL is a 68 year old with metastatic breast cancer which is ER+/PR+ but Her2-. She has started a new regimen of a combination of oral agents, Everolimus and Exemestane. She calls you at her community pharmacy and mentions she has painful mouth sores and would like to know what she can do.

Breast cancer case #2: Mrs EL

Your call her oncologist with the following recommendation:

1- Salt and bicarbonate rinses qid.

2- Magic mouthwash 15-30 ml po qid prn.

3- Dexamethasone mouthwash 0.5 mg/5 ml 10 ml po qid.

4- Lidocaine viscous 2% 15 ml po qid prn.

https://ontargetonco.com/en

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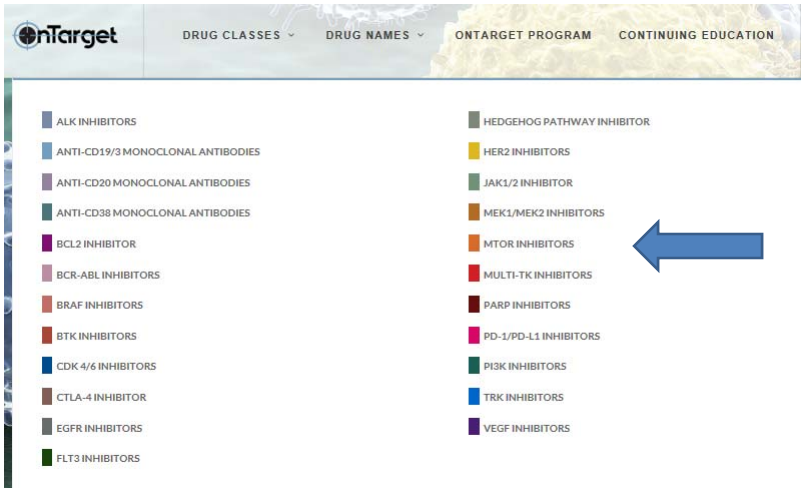

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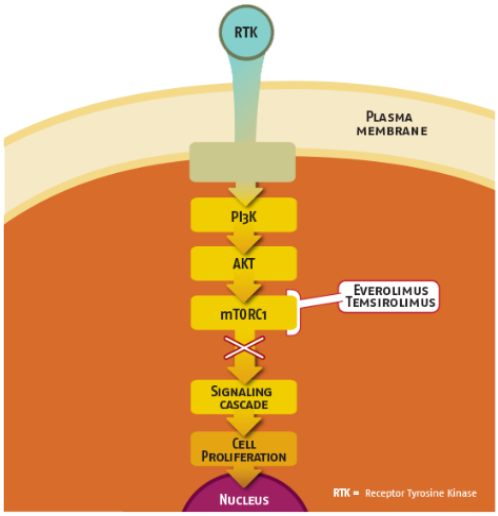
Drugs and Mechanism of Action

Within the cell, **everolimus** and **temsirolimus** bind to a specific protein, FKBP-12, to produce a protein-drug complex. This complex binds to the mTOR kinase to neutralize its activity.[1,2,4,5]

Because the mTOR pathway is dysfunctional in many cancers, mTOR has become an important target for therapy.[3] In cancer cells, deactivation of the mTOR signaling network by mTOR inhibitors induces cell death and suppresses:[3,4]

- Protein synthesis (cell growth)
- Cell proliferation
- Angiogenesis
- Spread of cancer cells



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mTOR Inhibitors

Everolimus (Afinitor®) - Temsirolimus (Torisel®)

- The Target
- The Drugs
- Drug Administration
- Interesting Facts
- When to Refer
- Adverse Events
- Management of AEs
- References
- Quiz

mTOR in cancer

In the 1970s, rapamycin, a natural product with antiproliferative effects, was discovered in the soil of Easter Island. Two decades later, the mammalian target of rapamycin (mTOR) was identified as a serine-threonine protein kinase that regulates a cell-signaling pathway that controls cell-cycle progression, cell proliferation, and angiogenesis.[3,4]

The mTOR signaling pathway is incredibly complex, but one of its essential functions is to balance growth factor and nutrient signals. Growth factors activate mTOR, whereas low nutrient availability, e.g., low glucose or oxygen supplies, inhibits mTOR. When well regulated, this signaling network ensures that cell growth occurs under favourable conditions. When conditions are unfavorable, mTOR slows growth.[4]

The mTOR pathway acts like an on-off switch to regulate cell-cycle progression (cell division) in response to growth signals. It regulates the:[4]

- Cellular machinery that controls protein synthesis
- Proteins that control cell division
- Tumor suppressor functions that control new blood-vessel growth and cell survival

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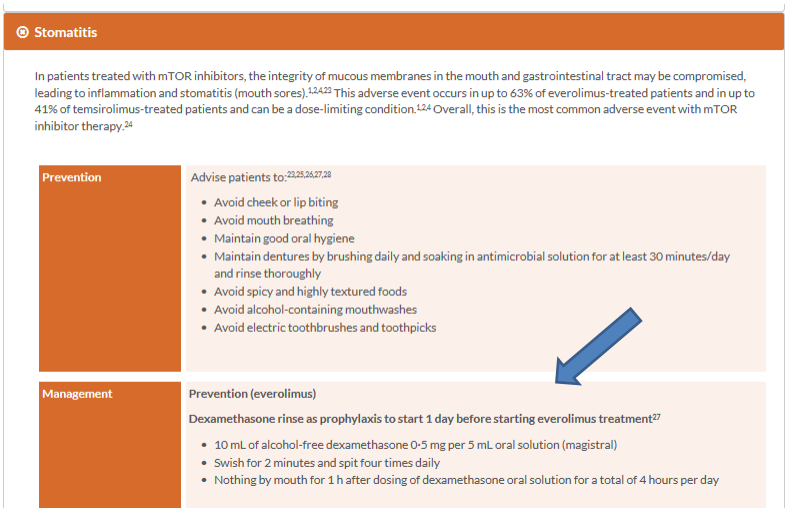


Breast cancer case #2: Mrs EL

Your call her oncologist with the following recommendation:

1- Salt and bicarbonate rinses qid.

2- Magic mouthwash 15-30 ml po qid prn.

3- Dexamethasone mouthwash 0.5 mg/5 ml 10 ml po qid.

4- Lidocaine viscous 2% 15 ml po qid prn.

Colon cancer case #2: Mr EF

Mr EF is a 57 year old diagnosed with metastatic colon cancer. Over many years he has received many lines of chemotherapy regimens with variable degrees of success. He is now offered a palliative regimen and shows up at your community pharmacy with the following prescription:

Lonsurf 35 mg/m^2 po bid

What is wrong with this prescription?

Colon cancer case #2: Mr EF

You call back the prescriber with the following recommendation; your order should be:

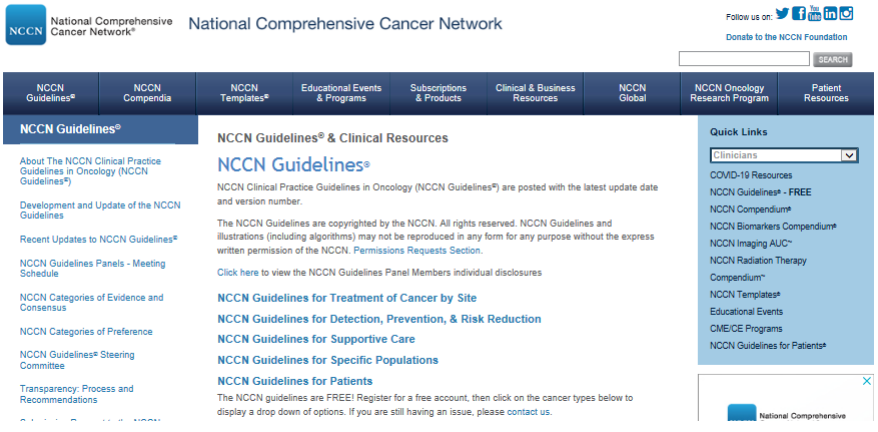
1- Lonsurf 1000 mg/m^2 po bid x 14 days q21d

2- Lonsurf 35 mg/m^2 po bid x 14 days q21d

3- Lonsurf 35 mg/m^2 po bid d1-5, 8-12 q28d

4- Lonsurf 70 mg/m^2 po die x 21d q28d

www.nccn.org



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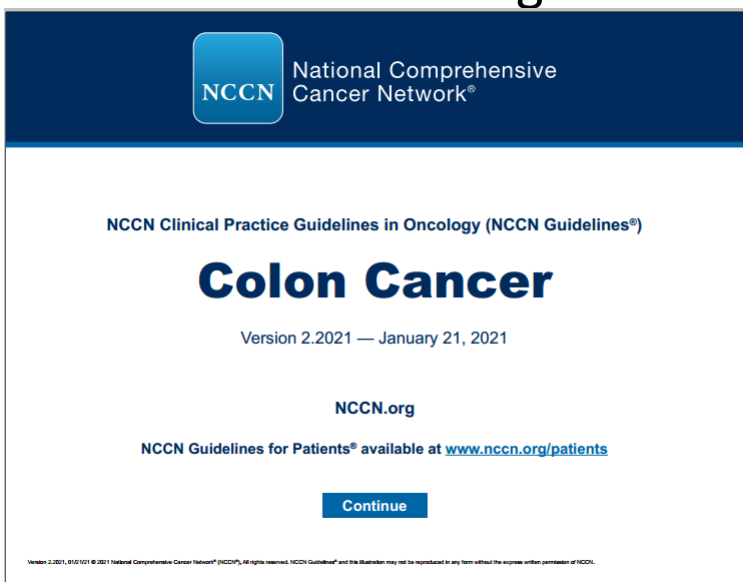

National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Colon Cancer

Version 2.2021 — January 21, 2021

NCCN.org

NCCN Guidelines for Patients® available at www.nccn.org/patients

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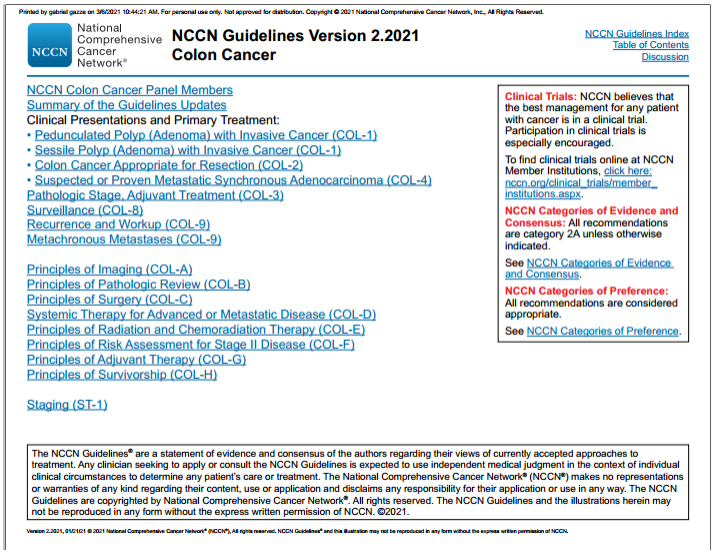

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Clinical Trials: NCCN believes that the best management for any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

To find clinical trials online at NCCN Member Institutions, click here: nccn.org/clinical_trials/member_institutions.aspx.

NCCN Categories of Evidence and Consensus: All recommendations are category 2A unless otherwise indicated.

See NCCN Categories of Evidence and Consensus.

NCCN Categories of Preference: All recommendations are considered appropriate.

See NCCN Categories of Preference.

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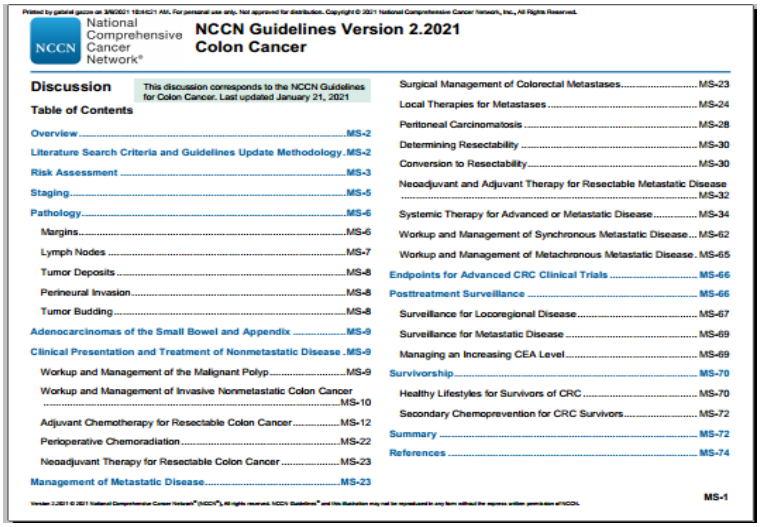

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This discussion corresponds to the NCCN Guidelines for Colon Cancer. Last updated January 21, 2021

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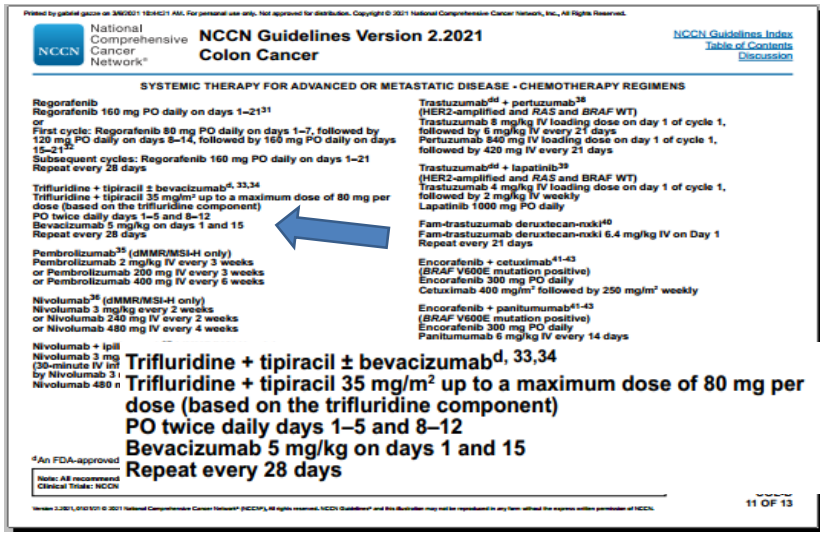

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SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE • CHEMOTHERAPY REGIMENS

Regorafenib
Regorafenib 160 mg PO daily on days 1–21[31]
or
First cycle: Regorafenib 80 mg PO daily on days 1–7, followed by 120 mg PO daily on days 8–14, followed by 160 mg PO daily on days 15–21[32]
Subsequent cycles: Regorafenib 160 mg PO daily on days 1–21
Repeat every 28 days

Trifluridine + tipiracil ± bevacizumab[d, 33,34]
Trifluridine + tipiracil 35 mg/m² up to a maximum dose of 80 mg per dose (based on the trifluridine component)
PO twice daily days 1–5 and 8–12
Bevacizumab 5 mg/kg on days 1 and 15
Repeat every 28 days

Pembrolizumab[35] (dMMR/MSI-H only)
Pembrolizumab 2 mg/kg IV every 3 weeks
or Pembrolizumab 200 mg IV every 3 weeks
or Pembrolizumab 400 mg IV every 6 weeks

Nivolumab[36] (dMMR/MSI-H only)
Nivolumab 3 mg/kg every 2 weeks
or Nivolumab 240 mg IV every 2 weeks
or Nivolumab 480 mg IV every 4 weeks

Nivolumab + ipili
Nivolumab 3 mg
(30-minute IV inf
by Nivolumab 3
Nivolumab 480 n

Trastuzumab[dd] + pertuzumab[38]
(HER2-amplified and *RAS* and *BRAF* WT)
Trastuzumab 8 mg/kg IV loading dose on day 1 of cycle 1, followed by 6 mg/kg IV every 21 days
Pertuzumab 840 mg IV loading dose on day 1 of cycle 1, followed by 420 mg IV every 21 days

Trastuzumab[dd] + lapatinib[39]
(HER2-amplified and *RAS* and BRAF WT)
Trastuzumab 4 mg/kg IV loading dose on day 1 of cycle 1, followed by 2 mg/kg IV weekly
Lapatinib 1000 mg PO daily

Fam-trastuzumab deruxtecan-nxki[40]
Fam-trastuzumab deruxtecan-nxki 6.4 mg/kg IV on Day 1
Repeat every 21 days

Encorafenib + cetuximab[41-43]
(*BRAF* V600E mutation positive)
Encorafenib 300 mg PO daily
Cetuximab 400 mg/m² followed by 250 mg/m² weekly

Encorafenib + panitumumab[41-43]
(*BRAF* V600E mutation positive)
Encorafenib 300 mg PO daily
Panitumumab 6 mg/kg IV every 14 days

Trifluridine + tipiracil ± bevacizumab[d, 33,34]
Trifluridine + tipiracil 35 mg/m² up to a maximum dose of 80 mg per dose (based on the trifluridine component)
PO twice daily days 1–5 and 8–12
Bevacizumab 5 mg/kg on days 1 and 15
Repeat every 28 days

[d] An FDA-approved

Note: All recommend
Clinical Trials: NCCN

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Colon cancer case #2: Mr EF

You call back the prescriber with the following recommendation; your order should be:

1- Lonsurf 1000 mg/m^2 po bid x 14 days q21d

2- Lonsurf 35 mg/m^2 po bid x 14 days q21d

3- Lonsurf 35 mg/m^2 po bid d1-5, 8-12 q28d

4- Lonsurf 70 mg/m^2 po die x 21d q28d

Other useful tools

- https://www.cancercareontario.ca/en
- https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs
- https://www.asco.org
- https://www.mascc.org/

original reports

The Randomized AMBORA Trial: Impact of Pharmacological/Pharmaceutical Care on Medication Safety and Patient-Reported Outcomes During Treatment With New Oral Anticancer Agents

Pauline Dürr[1,2]; Katja Schlichtig[2,3]; Carolin Kelz[2,3]; Birgit Deutsch, MD[2,3]; Renke Maas, MD[2,3]; Michael J. Eckart, MD[4]; Jochen Wilke, MD[5]; Harald Wagner, MD[5]; Kerstin Wolff, MD[2,6]; Caroline Preuß, MD[2,7]; Valeska Brückl, MD[2,8]; Norbert Meidenbauer, MD[2,8]; Christian Staerk, PhD[9]; Andreas Mayr, PhD[9]; Rainer Fietkau, MD[2,10]; Peter J. Goebell, MD[2,11]; Frank Kunath, MD[2,11]; Matthias W. Beckmann, MD[2,7]; Andreas Mackensen, MD[2,6]; Markus F. Neurath, MD[2,6]; Marianne Pavel, MD[2,6]; Frank Dörje, PhD, MBA[1,2]; and Martin F. Fromm, MD[2,3]

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