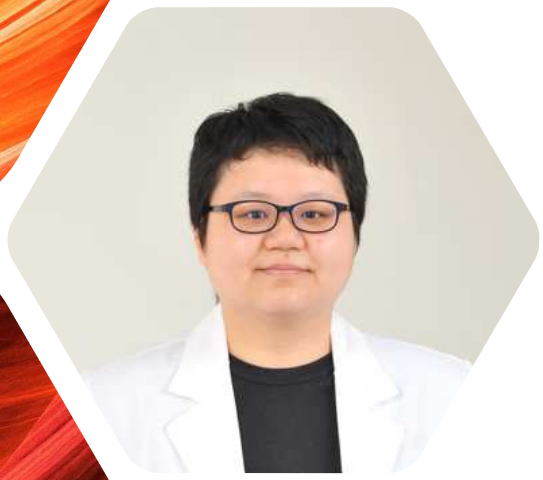


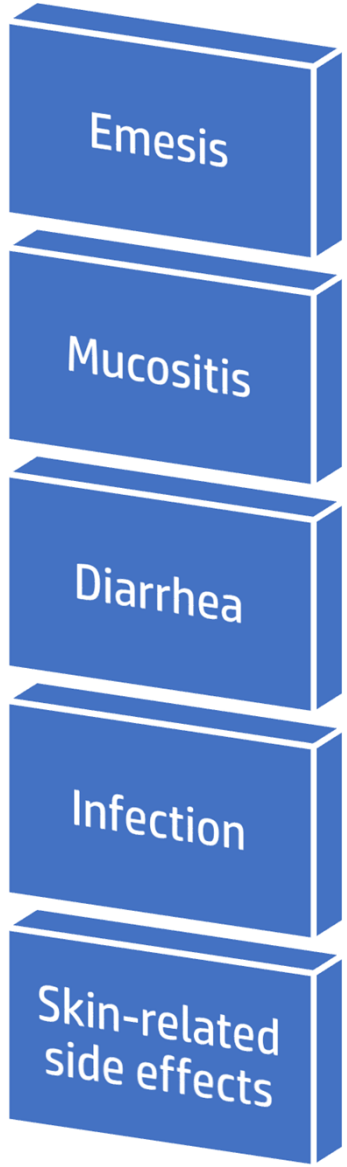
How to Make Chemotherapy A Little Easier

Division of Hematology-Oncology,
Department of Internal Medicine,
Chang-Gung Memorial Hospital,
Linkou branch

Pei-Wei Huang, M.D.

Outline

- Adverse events grading system: CTCAE
- Clinical parameters that may affect the severity
- Brief algorism for chemotherapy-related Side effects prevention/management
- Prevention/manage most common symptoms (right-side list)



Common Terminology Criteria for Adverse Events (CTCAE)

	Description	ADL	Intervention
Grade 1	**Mild**: asymptomatic or mild symptoms		not indicated
Grade 2	**Moderate** symptoms	limiting age-appropriate instrumental ADL.	minimal, local or noninvasive intervention
Grade 3	**Severe** but not immediately life-threatening	disabling; limiting self-care ADL.	**Hospitalization**
Grade 4	**Life threatening**		**Urgent**
Grade 5	**Death** related to AE		

Clinical Parameters That May Affect the Severity

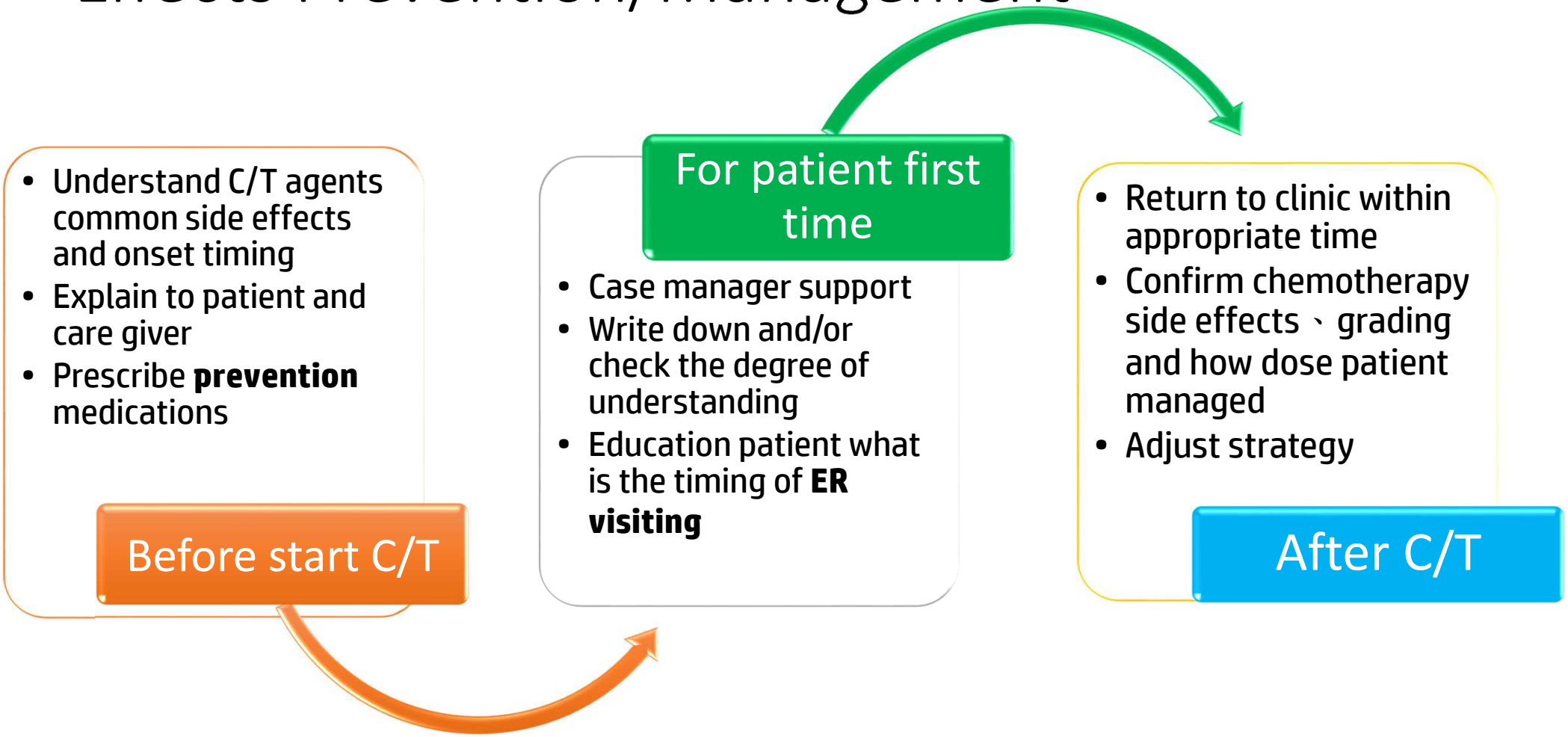
Patient-related

- ECOG、BMI、Nutrition status
- Individual difference
  - Ex: UGT1A1 genotyping
- Comorbidity
- Social economic supports
- Basic knowledge to medical

Chemotherapy-related

- Kinds of drugs
- Combination or not
- Dose
- Schedule
- Supportive medication
  - Ex: GCSF

Brief Algorism for Chemotherapy-related Side Effects Prevention/Management



Emesis

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2021
Antiemesis

EMETOGENIC POTENTIAL OF PARENTERAL ANTICANCER AGENTS[a]

LEVEL	AGENT		
High emetic risk (>90% frequency of emesis)[b,c,d]	• AC combination defined as any chemotherapy regimen that contains an anthracycline and cyclophosphamide • Carboplatin AUC ≥4 • Carmustine >250 mg/m²	• Cisplatin • Cyclophosphamide >1,500 mg/m² • Dacarbazine • Doxorubicin ≥60 mg/m² • Epirubicin >90 mg/m² • Ifosfamide ≥2 g/m² per dose	• Mechlorethamine • Melphalan ≥140 mg/m² • Sacituzumab govitecan-hziy • Streptozocin
Moderate emetic risk (>30%–90% frequency of emesis)[b,c,d]	• Aldesleukin >12–15 million IU/m² • Amifostine >300 mg/m² • Azacitidine • Bendamustine • Busulfan • Carboplatin AUC[e] <4 • Carmustine[e] ≤250 mg/m² • Clofarabine • Cyclophosphamide[e] ≤1500 mg/m² • Cytarabine >200 mg/m² • Dactinomycin[e]	• Daunorubicin[e] • Dual-drug liposomal encapsulation of cytarabine and daunorubicin • Dinutuximab • Doxorubicin[e] <60 mg/m² • Epirubicin[e] ≤90 mg/m² • Fam-trastuzumab deruxtecan-nxki • Idarubicine • Ifosfamide[e] <2 g/m² per dose • Irinotecan[e] • Irinotecan (liposomal)	• Lurbinectedin • Melphalan <140 mg/m² • Methotrexate[e] ≥250 mg/m² • Oxaliplatin[e] • Temozolomide • Trabectedin[e]

Patterns and Definition of Emesis

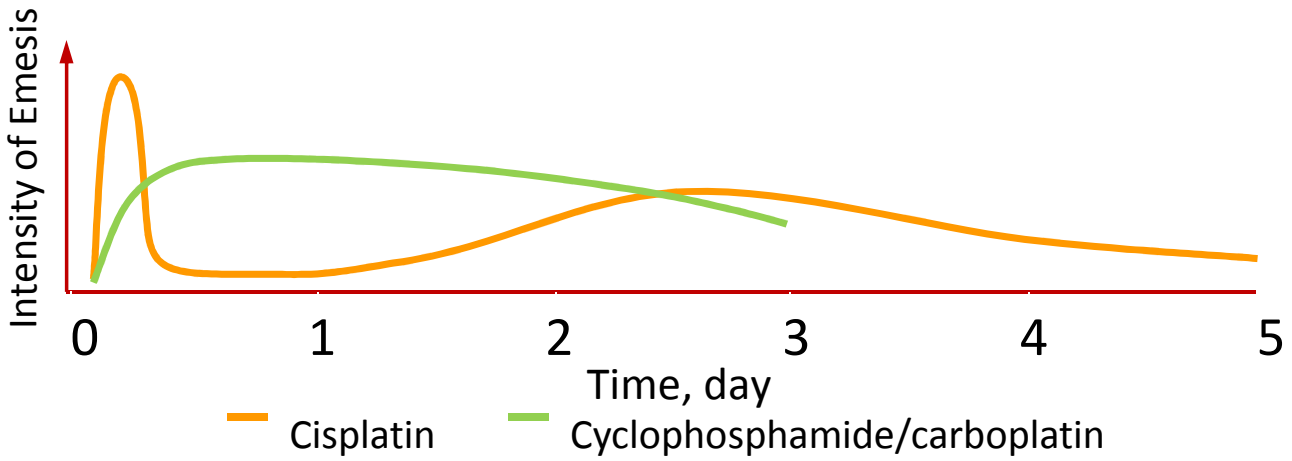


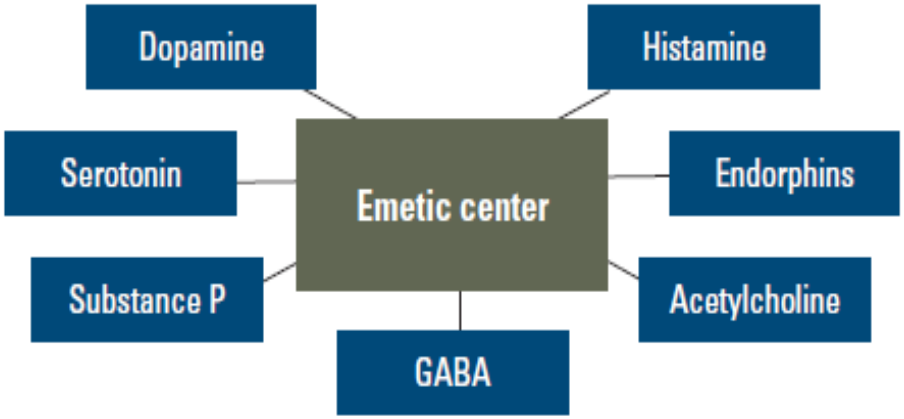
Table 1. Classes of Chemotherapy-Induced Nausea and Vomiting.

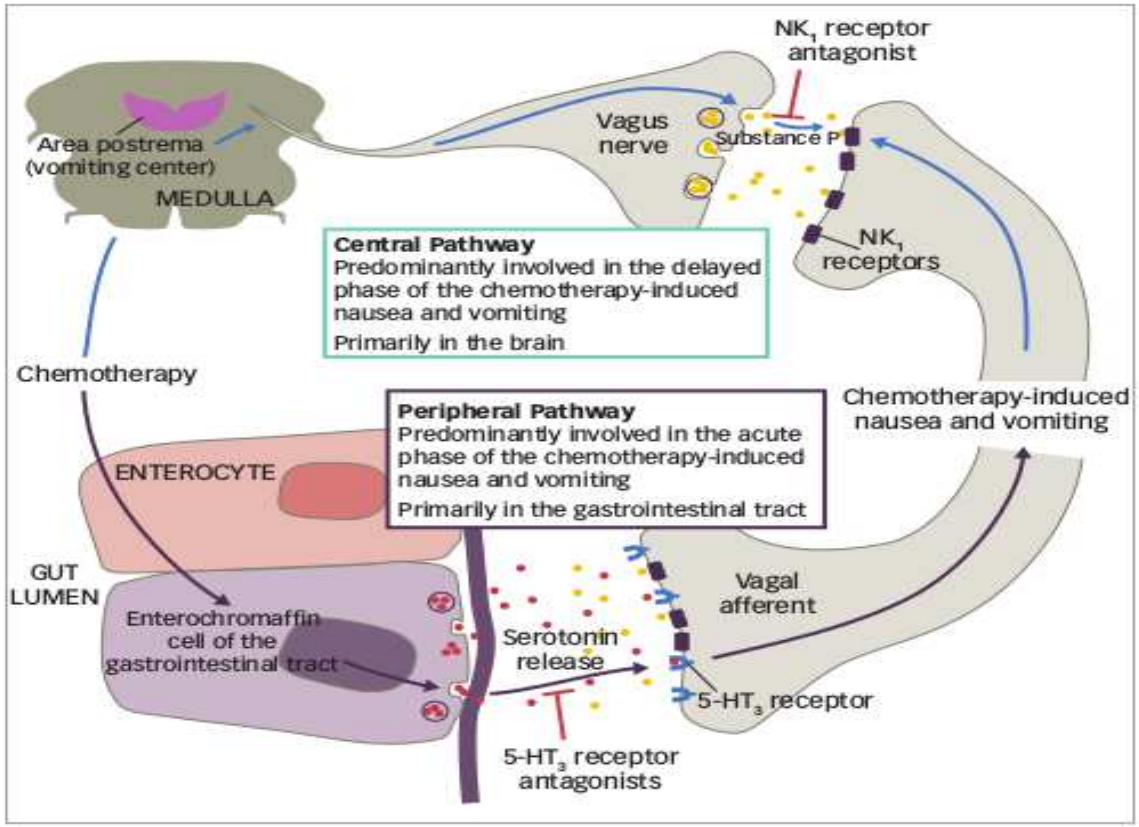
Classification	Definition
Acute	Occurring within the first 24 hours after initiation of chemotherapy[10]; generally peaks after 5 to 6 hours[11]
Delayed	Occurring from 24 hours to several days (days 2 to 5) after chemotherapy[12]
Breakthrough	Occurring despite appropriate prophylactic treatment[13]
Anticipatory	Occurring before a treatment as a conditioned response to the occurrence of chemotherapy-induced nausea and vomiting in previous cycles[14]
Refractory	Recurring in subsequent cycles of therapy, excluding anticipatory chemotherapy-induced nausea and vomiting[13]

Martin M. Oncology. 1996;53(suppl 1):26–31

Navari. RM., et al. N Engl J Med 2016

Chemotherapy-induced Nausea and Vomiting Pathophysiological Aspects

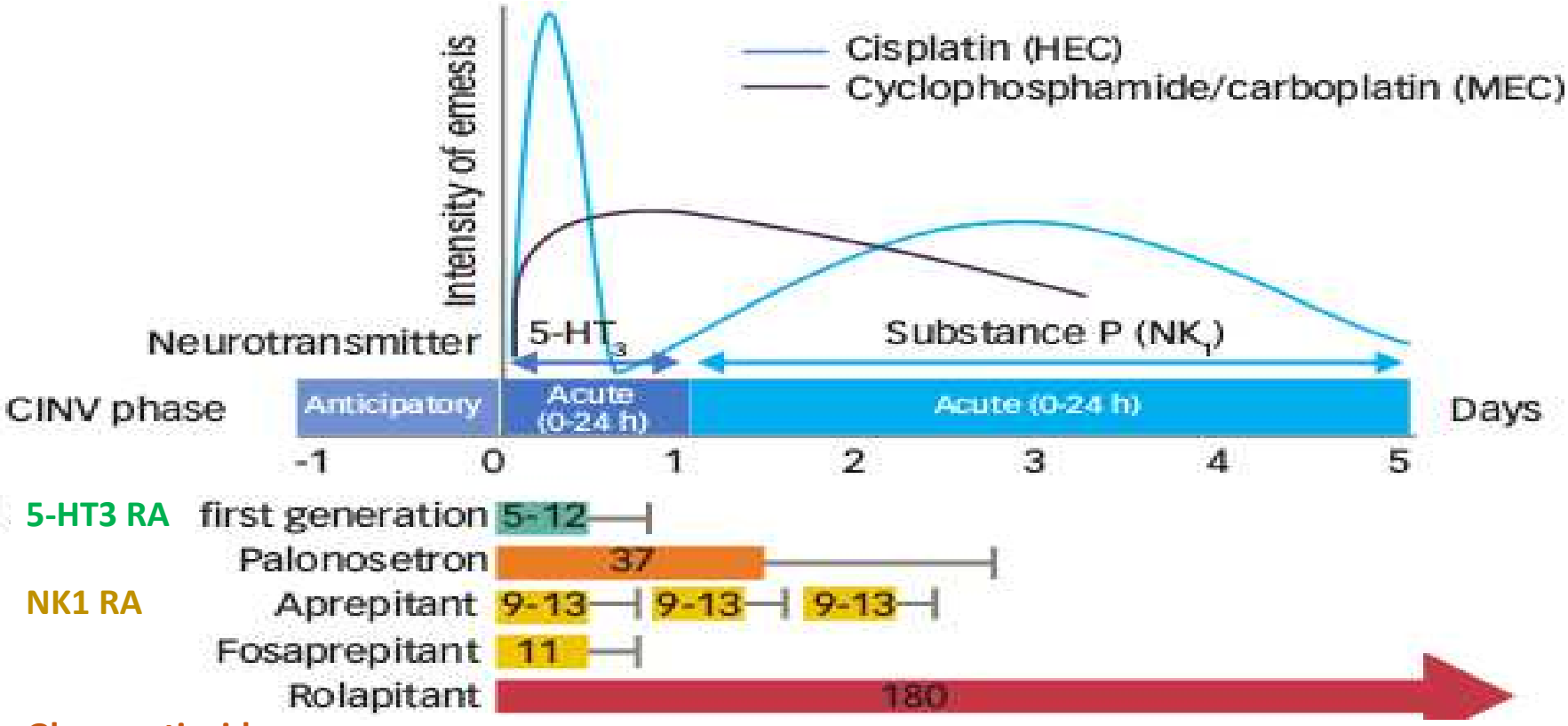




5-HT3 = 5-hydroxytryptamine type 3; NK1 = neurokinin 1. Reproduced with permission from Navari et al., 2016.[12]

Navari. RM. Oncology (Williston Park) 2018

Rapoport BL., et al. European Oncology & Haematology 2017



Glucocorticoids

Dopamine RA Olanzapine

Dopamin-2/-5-HT3 receptor antagonist Metoclopramide/Prochlorperazine

GABA RA Lorazepam

Proton-pump inhibitors (personal experience)

Modified from Rapoport BL., et al. European Oncology & Haematology 2017

Mucositis

Grading System and Common C/T Drug Cause Mucositis

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Asymptomatic or mild symptoms; intervention not indicated	Moderate pain or ulcer that does not interfere with oral intake; modified diet indicated	Severe pain; interfering with oral intake	Life-threatening consequences; urgent intervention indicated	Death

- Methotrexate.
- Doxorubicin.
- 5-FU.
- Bleomycin.
- The platinum coordination complexes, including cisplatin and carboplatin.

How to Approach?

Step 1: Assess risk

⇩

Step 2: Refer to dental professional

⇩

Step 3: Basic oral care

⇩

Step 4: Consider Other interventions

Patient Factors	Disease Factors
Smoking	Head and neck cancer
Baseline oral hygiene	Treatment plan (chemotherapy *v* radiation *v* combined)
Age	Planned duration of treatment
Female sex	Dose of therapy
Pretreatment nutritional status	Frequency of therapy

- Brush all tooth surfaces for at least 90 seconds, at least twice daily by a soft toothbrush.
- Floss at least once daily or as advised by clinician.
- Rinse mouth four times daily with a bland rinse.
- Avoid tobacco, alcohol, irritating foods (acidic, hot, rough, and spicy).
- Use water-based moisturizers to protect lips.
- Maintain adequate hydration.

Brown TJ.,et al. JCO Oncol Pract. 2020

MASCC/ISOO Clinical Practice Guidelines

Basic oral care	Anti-inflammatory agents	Others	Effective under specific circumstances
• Patient education • Multiagent combination oral care protocols • Professional oral care • Saline/sodium bicarbonate mouth rinses	• Benzydamine mouthwash	• Cryotherapy • Topical morphine 0.2% mouthwash • Oral glutamine • Honey	• Photobiomodulation • KGF-1 (cytokines)

Elad S., et al. Cancer 2020

Diarrhea

Grading System and Common C/T Drug Cause Diarrhea

NCI CTCAE v5.0 diarrhea

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Increase of <4 stools per day over baseline; mild increase in ostomy output compared with baseline	Increase of four to six stools per day over baseline; moderate increase in ostomy output compared with baseline; limiting instrumental ADL*	Increase of seven or more stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared with baseline; limiting self-care ADL*	Life-threatening consequences; urgent intervention indicated	Death

Diarrhea is characterized by an increase in frequency and/or loose or watery bowel movements.

- Common C/T Drugs cause diarrhea
  - Fluoropyrimidines (ex: Xeloda, S-1)
  - Irinotecan
  - Taxotere
  - Combinations

ChT	Incidence of grade 3 and 4 diarrhoea (%)
CapeIRI	47
FOLFOXIRI	20
mIFL	19
Bolus fluorouracil with folinic acid	16
Irinotecan with fluorouracil and folinic acid	15
Docetaxel with capecitabine	14
FOLFIRI	14
FLOX	10

Diarrhea in adult cancer patients: ESMO Clinical Practice Guidelines 2018

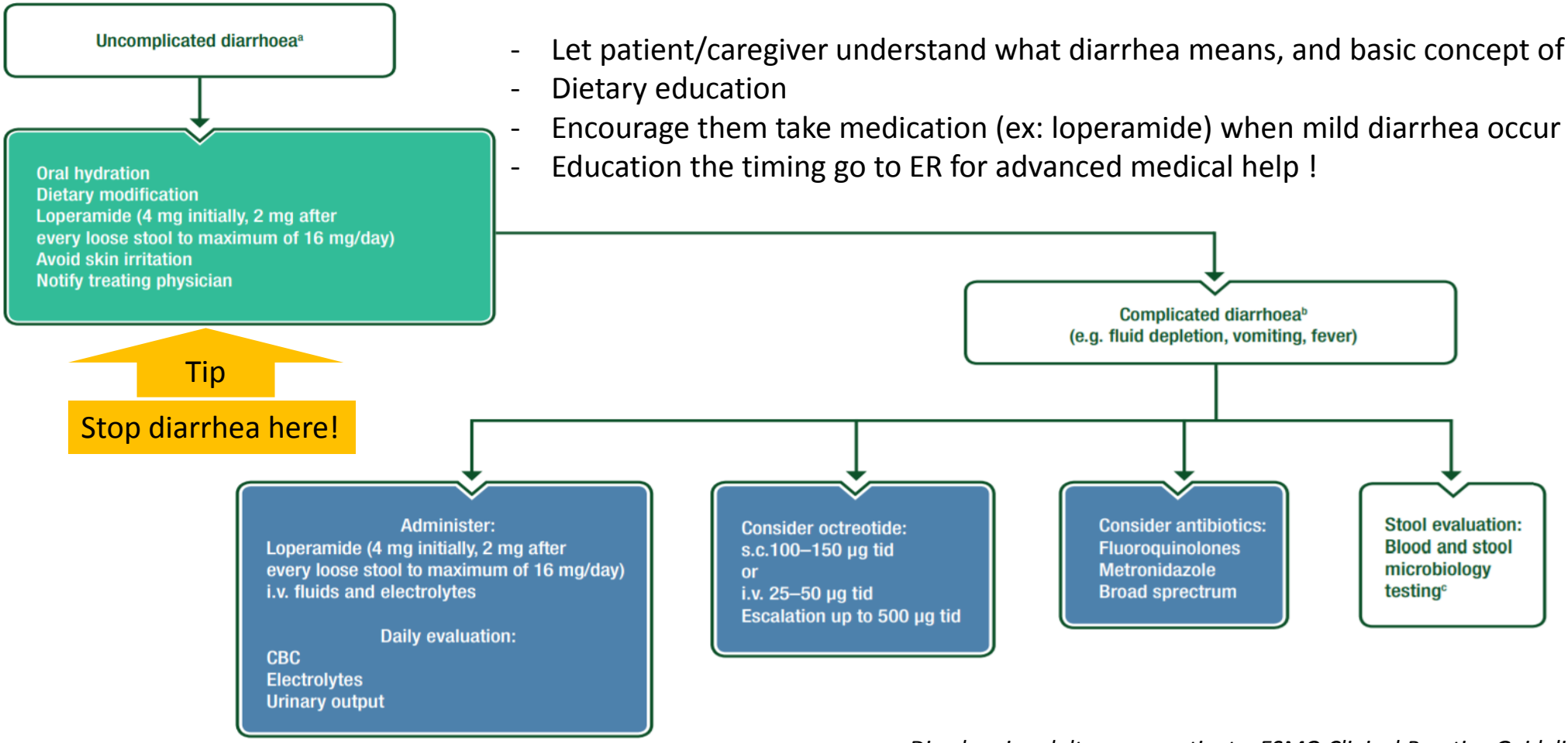
Foods and Medications need to be avoided

Food products	Medications
Milk and dairy products	Bulk laxatives
Spicy foods	Stool softeners
Alcohol	Promotility drugs
Caffeine-containing products	High-osmolarity drugs
High fiber and high fat foods	
Some fruit juices	

Remind patient before start C/T.

Management of acute chemotherapy-related diarrhea 2021 UpToDate

How to Manage C/T-related Diarrhea



- Let patient/caregiver understand what diarrhea means, and basic concept of severity
- Dietary education
- Encourage them take medication (ex: loperamide) when mild diarrhea occur
- Education the timing go to ER for advanced medical help !

Diarrhea in adult cancer patients: ESMO Clinical Practice Guidelines 2018

Prevention and Treatment for Cancer-related Infections

National Comprehensive Cancer Network®

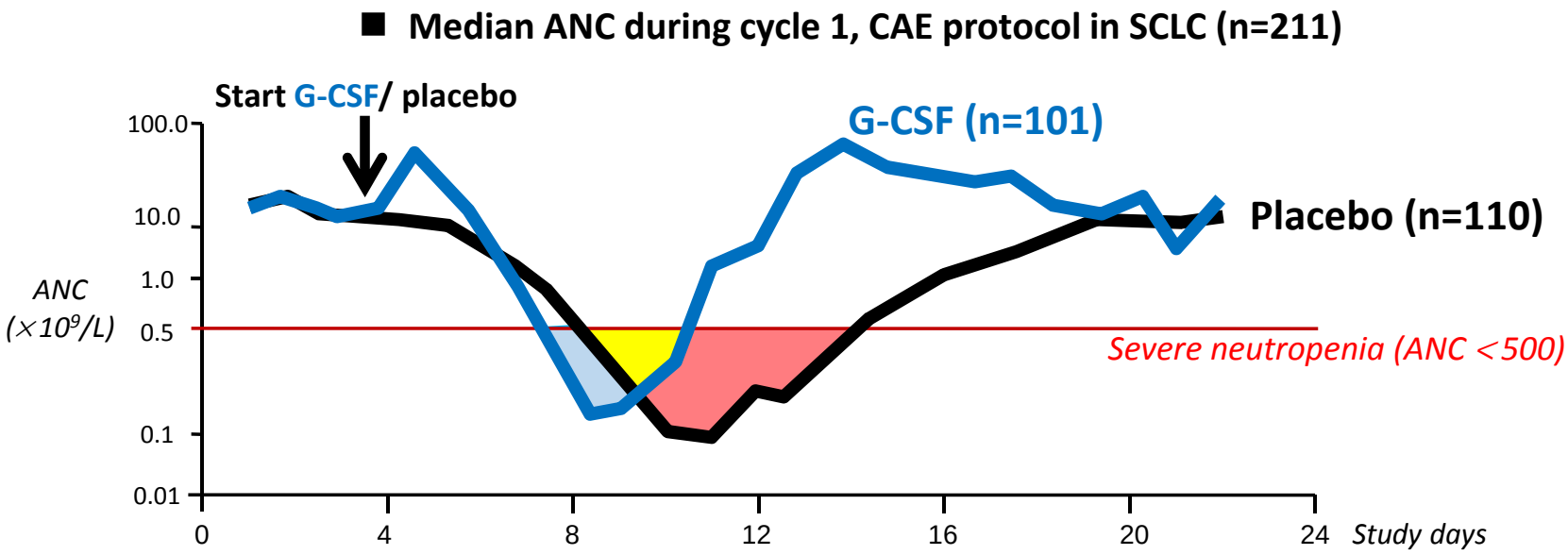
NCCN Guidelines Version 1.2021
Prevention and Treatment of Cancer-Related Infections

ANTIMICROBIAL PROPHYLAXIS BASED ON OVERALL INFECTION RISK IN PATIENTS WITH CANCER

Overall Infection Risk in Patients with Cancer[a]	Disease/Therapy Examples	Antimicrobial Prophylaxis[d]
Low	• Standard chemotherapy regimens for most solid tumors • Anticipated neutropenia less than 7 days	• Bacterial - None • Fungal - None • Viral - None unless prior HSV episode
Intermediate	• Autologous HCT • Lymphoma[c] • Multiple myeloma[c] • CLL[c] • Purine analog therapy (ie, fludarabine, clofarabine, nelarabine, cladribine) • Anticipated neutropenia 7–10 days	• Bacterial - Consider fluoroquinolone prophylaxis during neutropenia[e] • Fungal - Consider prophylaxis during neutropenia and for anticipated mucositis (See INF-2); consider PJP prophylaxis (See INF-6) • Viral - During neutropenia and longer depending on risk (See INF-3, INF-4, INF-5)
High[b]	• Allogeneic HCT including cord blood • Acute leukemia ▸ Induction ▸ Consolidation/maintenance • Alemtuzumab therapy • Moderate to severe GVHD • Anticipated neutropenia greater than 10 days	• Bacterial - Consider fluoroquinolone prophylaxis during neutropenia[e] • Fungal - Consider prophylaxis during neutropenia (See INF-2); consider PJP prophylaxis (See INF-6) • Viral - During neutropenia and longer depending on risk (See INF-3, INF-4, INF-5)

Exception: Combinations such as TPF (Induction C/T in head and neck cancer)

With the help from G-CSF:

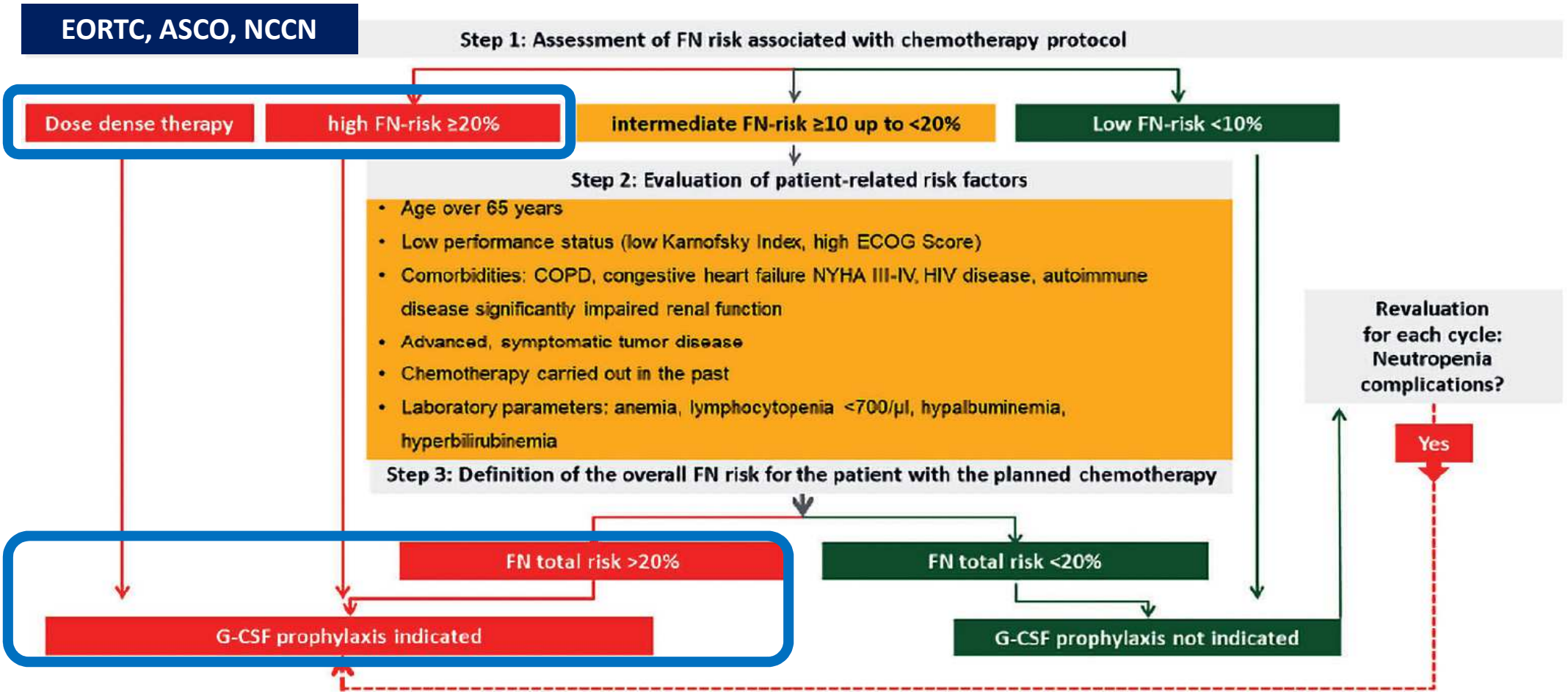


add G-CSF

Category 1 evidence	Category 2A evidence
↓ Febrile Neutropenia	↓ Infection-related mortality
↓ Days of hospitalization	
↓ IV Antibiotics usage	

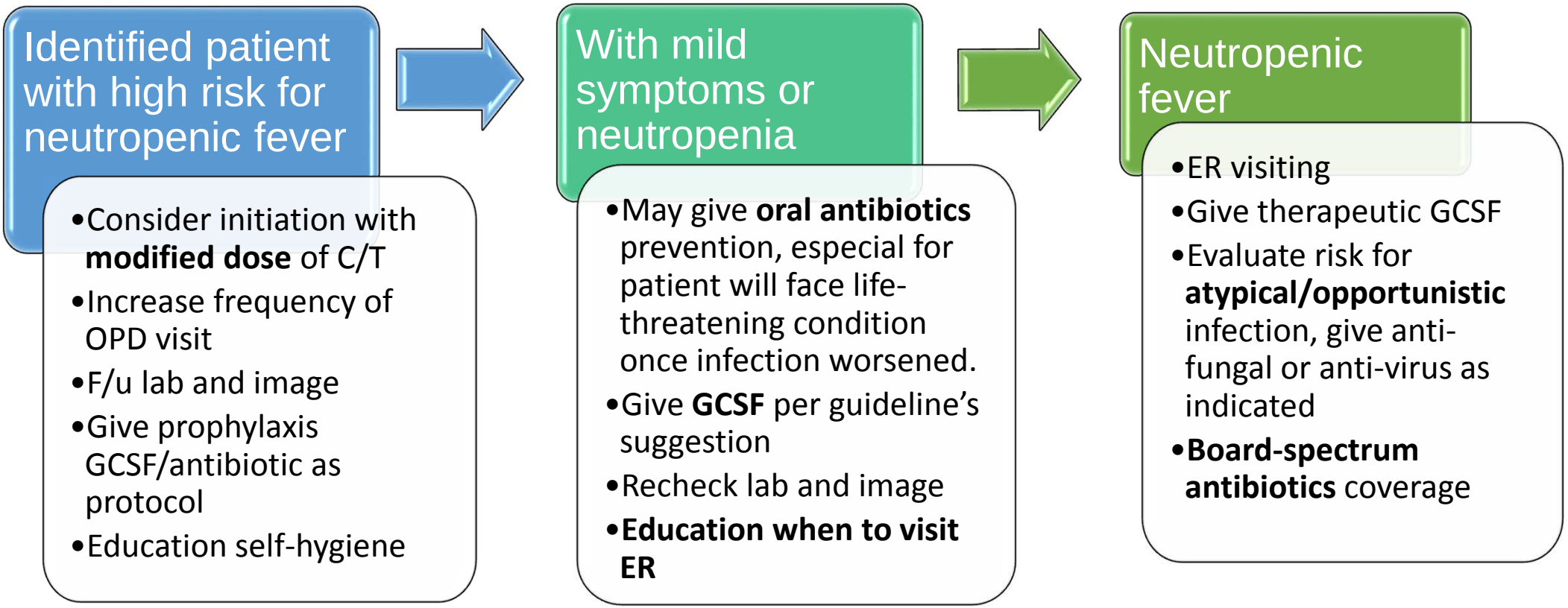
Crawford J, et al. N Engl J Med 1991;325:164-170

International Guidelines: Prophylactic G-CSF



Hematopoietic Growth Factors in the Management of Anemia and Febrile Neutropenia. Breast Care 2019

My Algorism for C/T-related Neutropenic Fever



Skin-related Side Effects

Hand-foot-syndrome/
Skin or nail changes

Symptoms and C/T Drugs Related to Hand-foot Syndromes

Frequently implicated drugs	Capecitabine, cytarabine, doxorubicin, 5-fluorouracil, taxanes[4] , pegylated liposomal doxorubicin
Histopathologic findings	Hyperkeratosis, parakeratosis Spongiosis Focal vacuolization and pyknosis in basal cell layer Dermis with ectatic blood vessels, mild perivascular lymphohistiocytic infiltrate[4,15,16]
Clinical appearance	Edema, erythema, and scale with or without blisters and erosions[4,5]
Distribution	Symmetrical and diffuse over the palms, soles, and digits[4,5]
Onset	24 h to 10 mo after initiation of therapy[2,4] (median, 79 d[12])

Hoesly FJ., et al. Arch Dermatol. 2011

Preventative measures

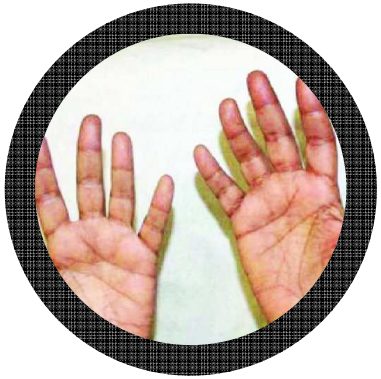
- Avoid mechanical stress/trauma
- Avoid exposure to high temperatures around administration
- Maintenance of good hygiene
- Moisturizing with urea-based cream three times per day
- **Local hypothermia** at time of administration
  (only for short-term infusions of pegylated liposomal doxorubicin and docetaxel)
- Referral to dermatologist for treatment of pre-existing dermatologic conditions

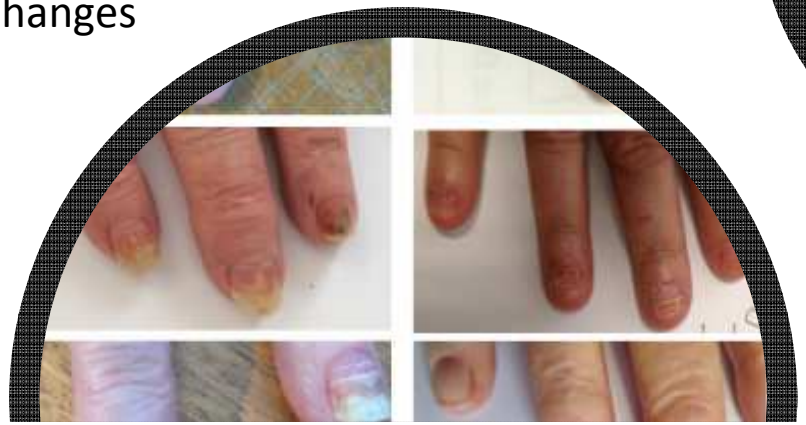
Kwakman J., et al. Oncology Reviews 2020

Other Common Cutaneous Side Effects

Informed patient earlier to make them have prepared for these changes

- Alopecia
- Rash
- Sores
- Light sensitivity
- Pigmentation changes
- Nail changes






Thank You !