Chemotherapy 101

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Learning Objectives

1. Identify the different classes of anti-cancer medications
2. Identify the common toxicities and side effects of anti-cancer medications
3. Understand basic interventions for managing treatment toxicities

Disclosures

- No relevant financial relationships with any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients

Patient Case

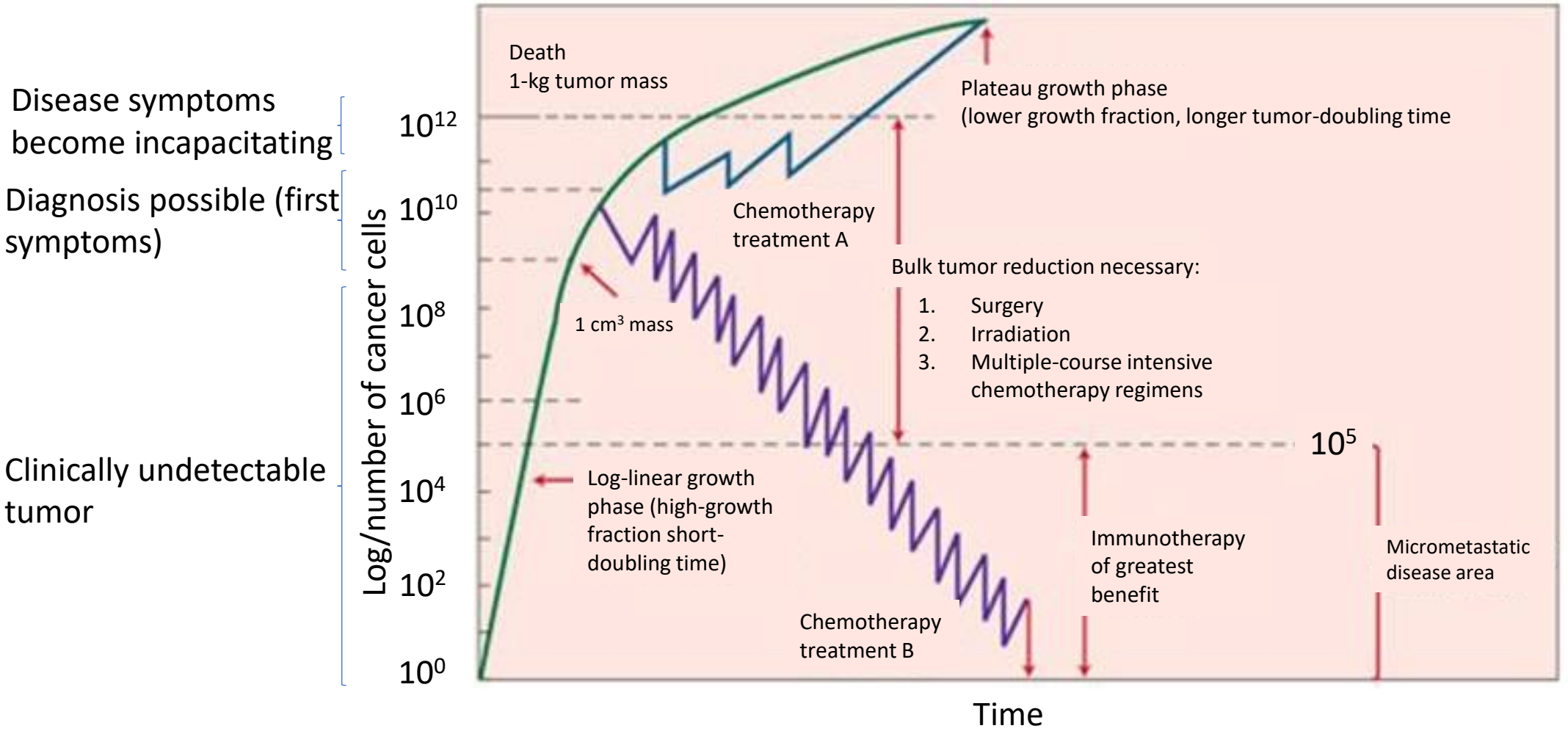
- MS is a 45 year old female with cervical cancer
- She is starting treatment with cisplatin + paclitaxel + pembrolizumab + bevacizumab

Principles of Chemotherapy

Principles of Chemotherapy

- Tumor Growth: Gompertzian
  - Early stages: tumor growth is exponential
  - Growth fraction declines as tumors expand in size
  - Larger tumors harbor higher numbers of nonproliferating cells

Gompertzian Growth Curve



Brundage D. Cancer Therapy and Treatments. Pharmacotherapy Principles and Practice (Chisholm-Burns, Pharmacotherapy), 2nd Ed.

Kinetic Principles

Non-phase specific:

- Fixed percentage of cells killed at a given dose
- Dose-dependent

Phase-specific:

- Plateau in concentration dependent effects since only a subset of proliferating cells remain fully sensitive to cytotoxic effects
- Schedule-dependent

Takimoto CD, et al. Principles of Oncologic Pharmacotherapy. 2009.

Rationale for Combination Chemotherapy

A number of active drugs from different classes used in combination

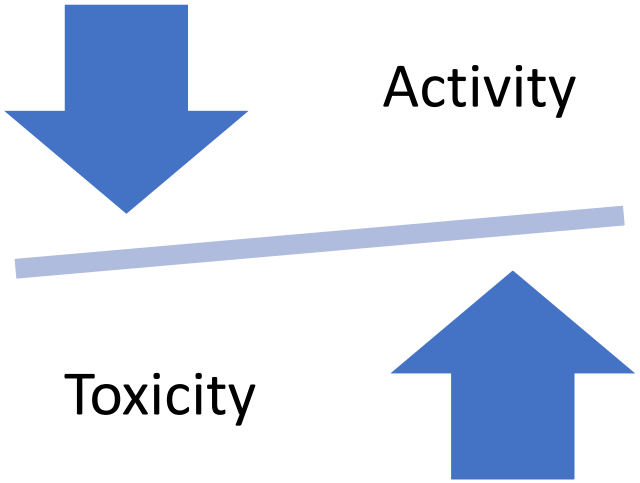
1. Provides maximal cell kill within the range of toxicity tolerated by the host

2. Provides a broader range of interaction between drugs & (heterogeneous) tumor cells

3. May prevent or slow the development of cellular drug resistance

Principles of Combination Chemotherapy

- Use only drugs known to be effective against the tumor when used alone
- Use drugs with different mechanisms
- When choosing from a particular class, use a drug without toxicities that overlap with other agents in the combination (assumes equal efficacy)
- Use drugs with different patterns of resistance
- Use drugs at their optimal dose & schedule
- Give at consistent interval



Dosing of Chemotherapy

- Flat
- Weight based: BSA, mg/kg
- Capped dosing
  - Vincristine 2mg
  - Brentuximab vedotin 120mg
  - Gemtuzumab ozogamicin 4.5mg
  - Tisotumab vedotin 200mg
- Unique: Carbo AUC calculation – based on weight and SCr

Dosing in Obesity

- Underdosing
  - 20% relative reduction in survival in adjuvant breast cancer patients as a result of underdosing
  - Cure rate of cisplatin-based chemo for testicular cancer reduced by 10% by underdosing

- ASCO Recommendation is to use actual body weight

Griggs JJ, et al. J Clin Oncol 2021; 39(18):2037-2048.

Anticancer Therapy

Hallmarks of Cancer

- Self sufficiency in growth signals
- Insensitivity to growth-inhibitor signals
- Evasion of apoptosis
- Limitless replicative potential
- Sustained angiogenesis
- Tissue invasion coupled with metastasis

Weinberg RA. The Biology of Cancer, 2nd ed. 2014. New York: Garland Science

Chemotherapy

Non-Cell Cycle Specific

- Alkylating agents
- Platinum analogs
- Hypomethylators
- Anthracyclines

Cell Cycle Specific

- Antimetabolites
- Microtubule inhibitors
- Topoisomerase inhibitors
- Anthracyclines

Chemotherapy

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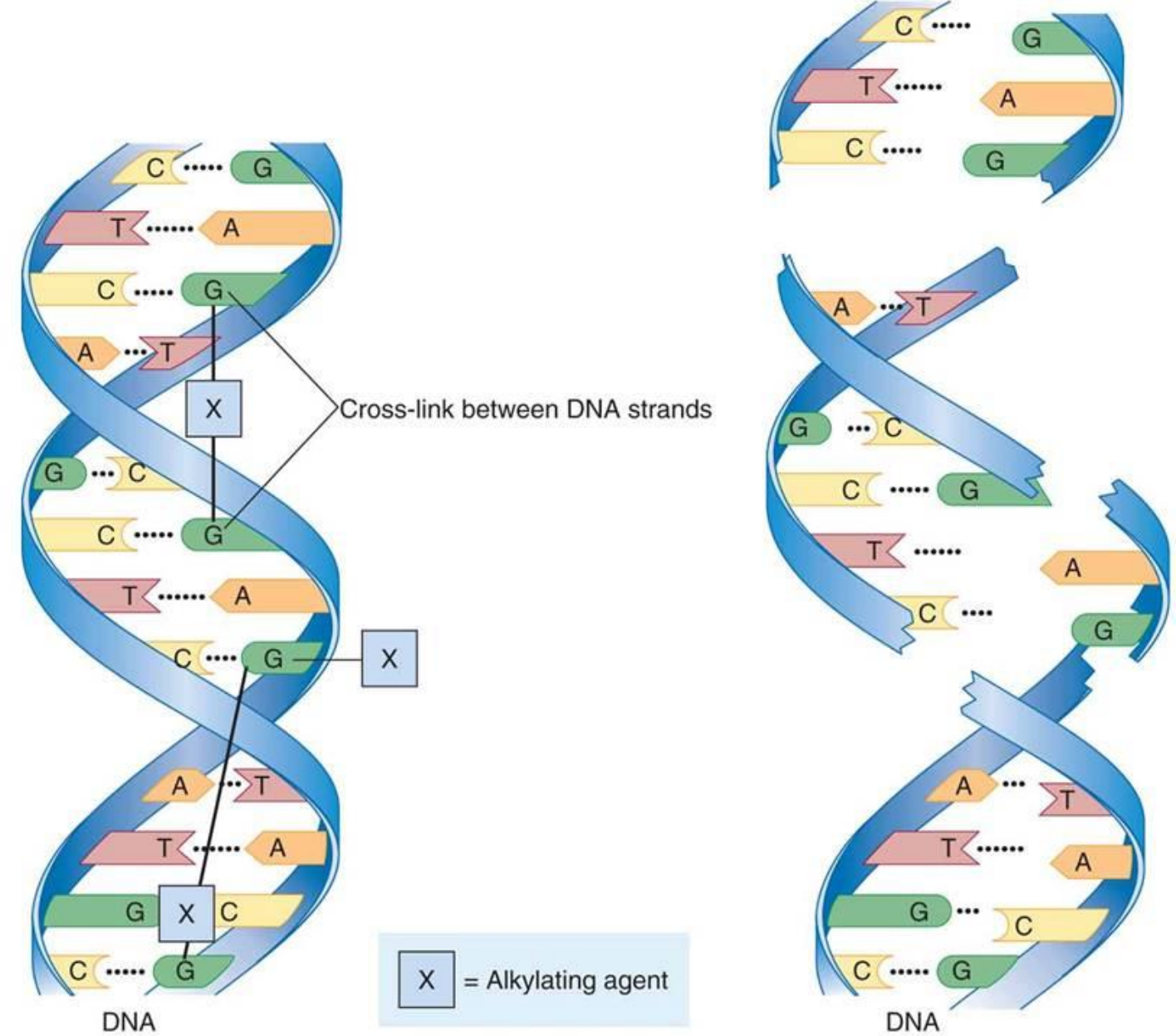
Alkylating Agents

- Forms covalent bonds in DNA and RNA to prevent cell replication
- Some of the earliest anticancer agents



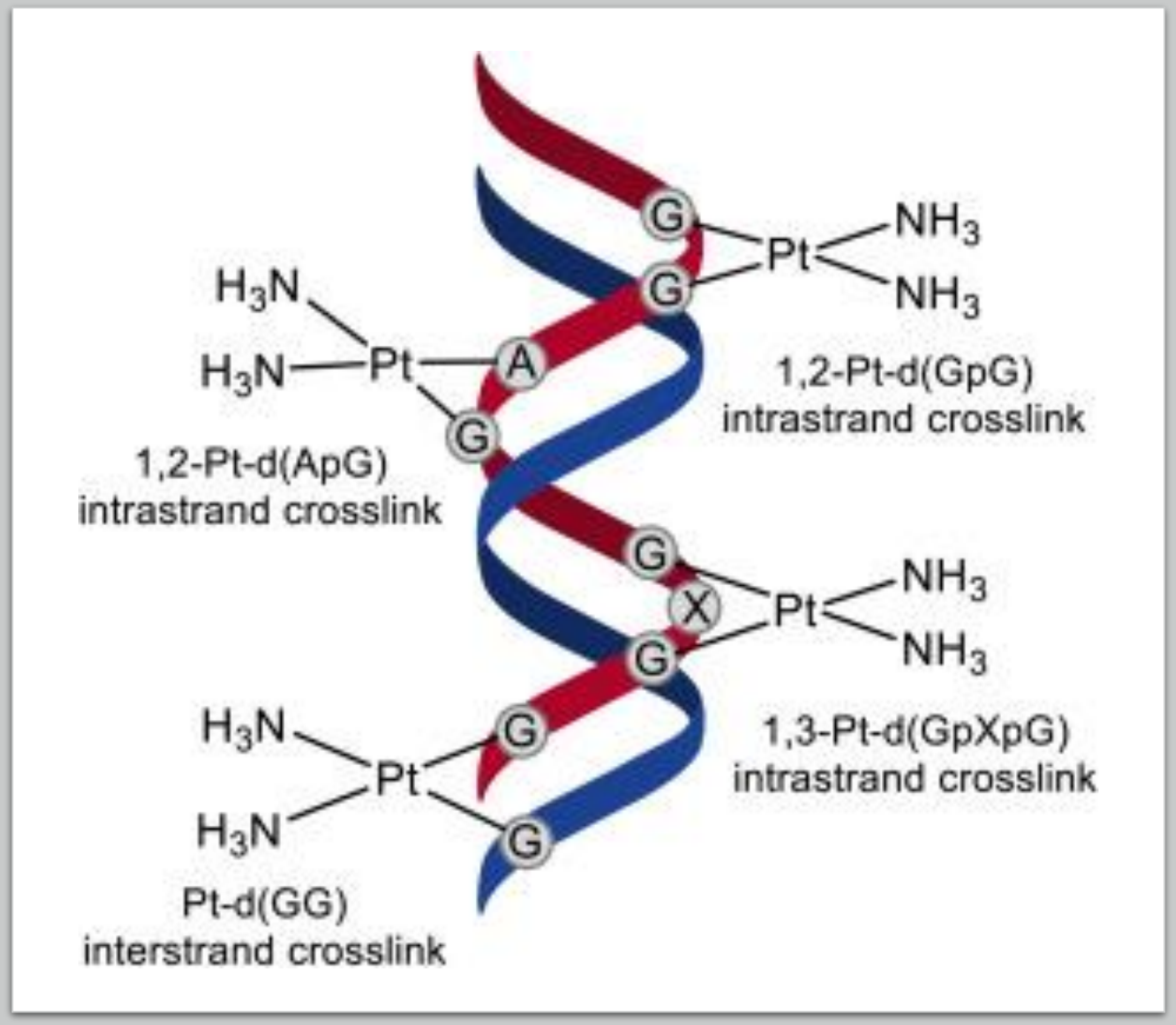
(a) Alkylation occuring during G_0 (resting) phase of cell cycle

(b) Strand breaks occuring when DNA replicates during S phase of cell cycle

Weinberg RA. The Biology of Cancer, 2nd ed. 2014. New York: Garland Science

Platinum Analogs

- Alkylating agent
- Intrastrand and interstrand DNA cross-links



Wang Z, et al. Reference Module in Chemistry, Molecular Sciences and Chemical Engineering. 2018.

Chemotherapy

Non-Cell Cycle Specific

- Alkylating agents
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- Hypomethylators
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Cell Cycle Specific

- Antimetabolites
- Microtubule inhibitors
- Topoisomerase inhibitors
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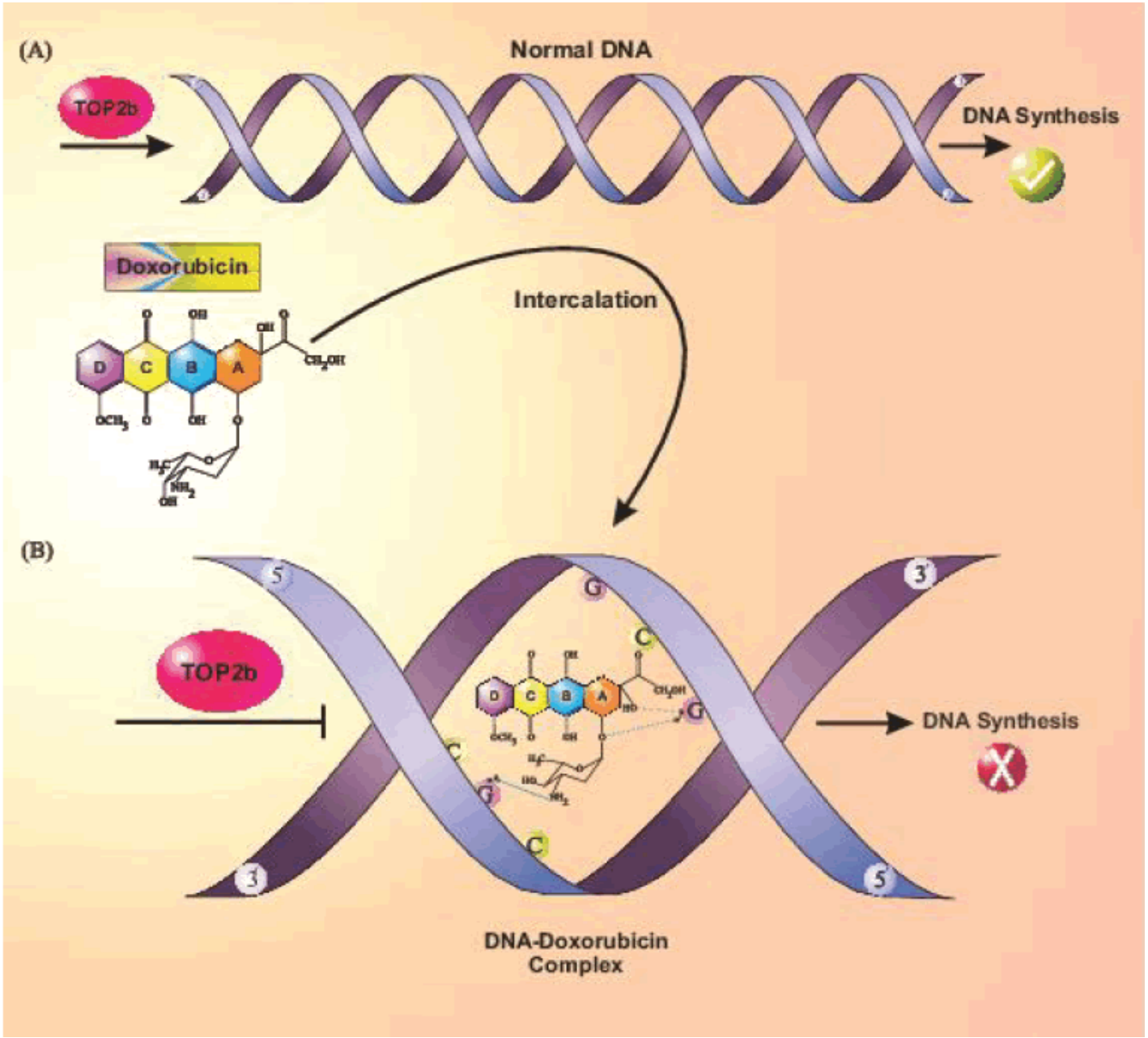
Anthracyclines

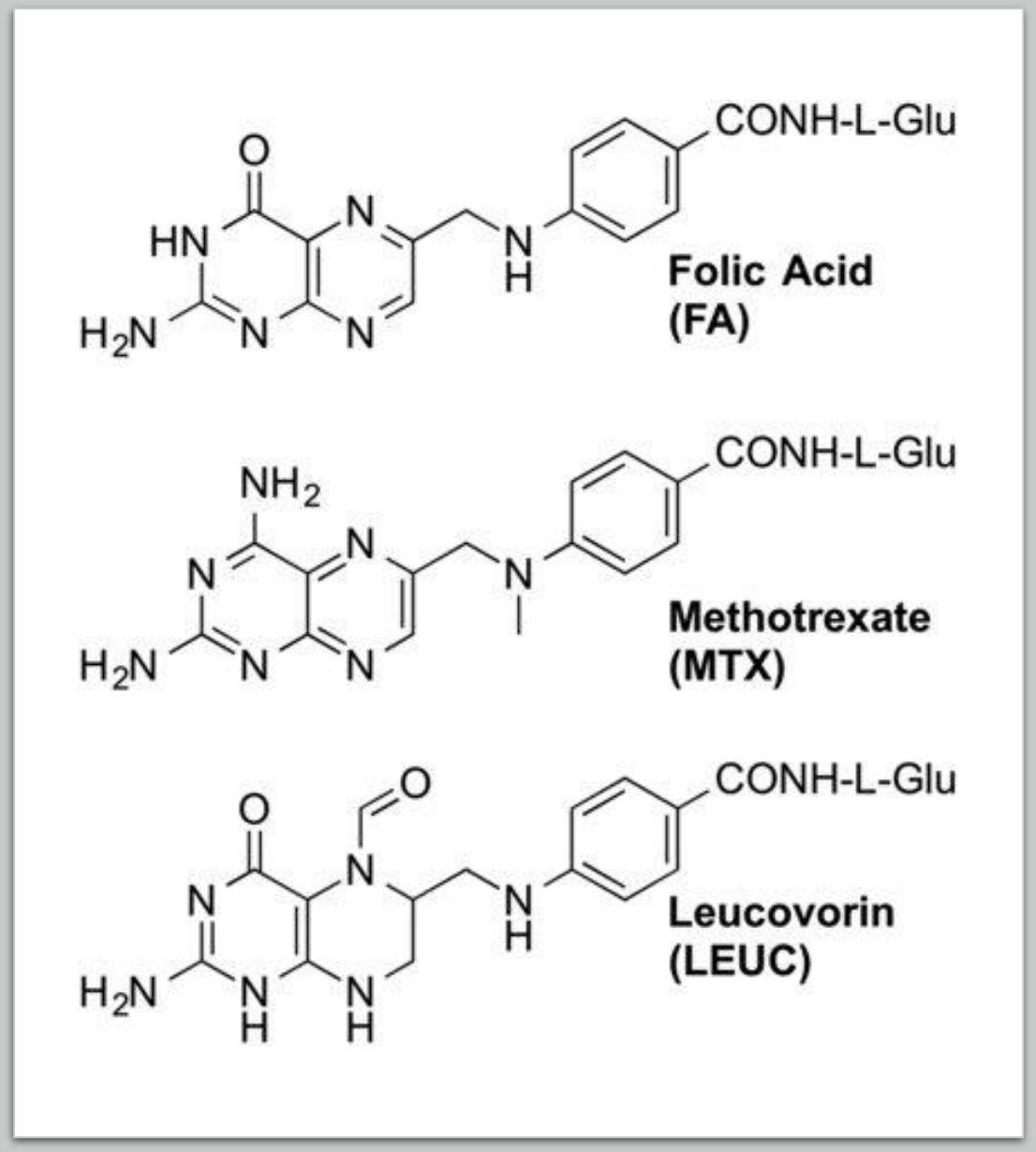
- Anticancer antibiotic
- Intercalate DNA base pairs
- Inhibits topoisomerase I and II
- Free radical formation



Mobaraki M, et al. Indian J Pharmaceutical Sciences 2017. 79(3): 335-344

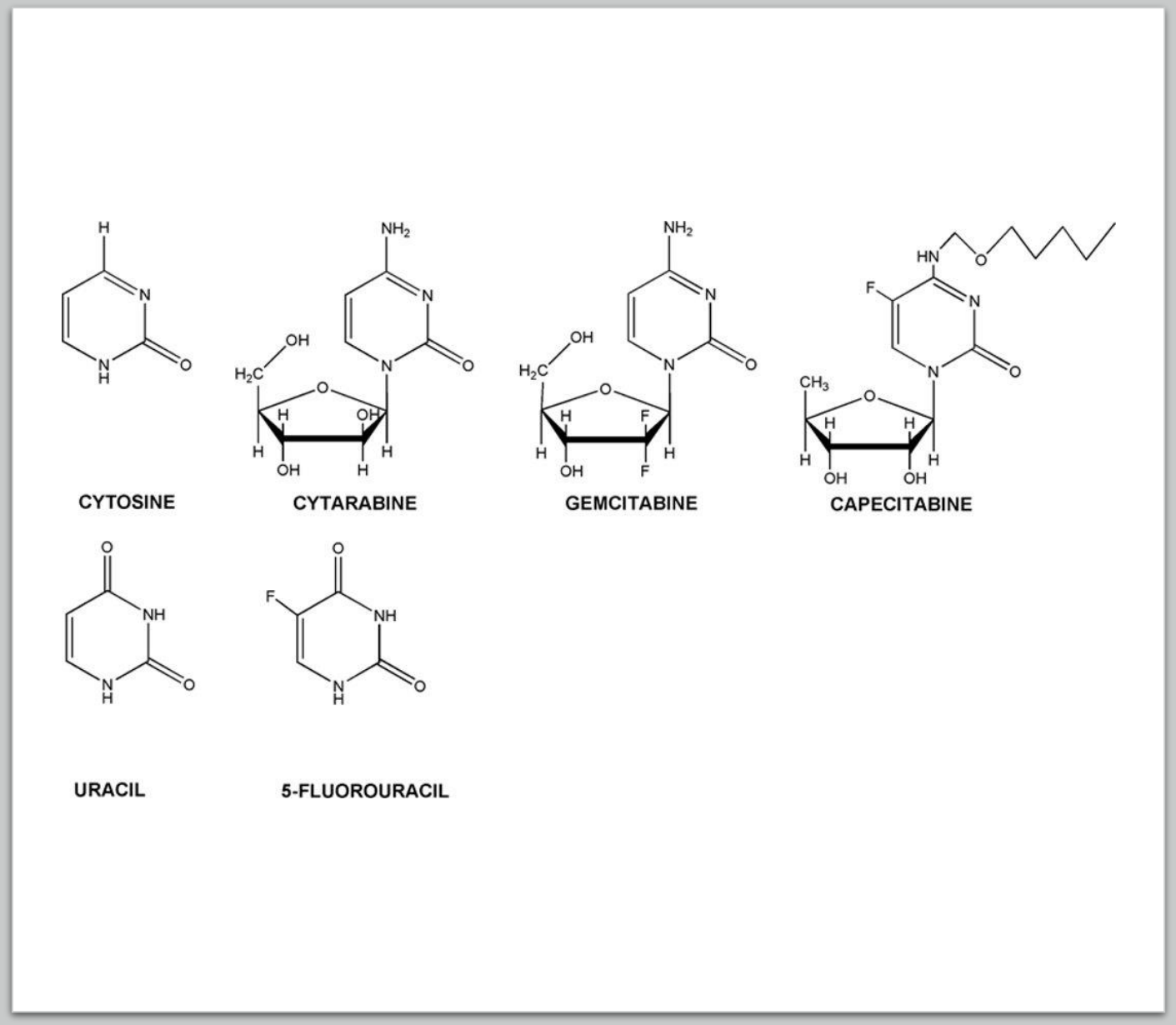
Antimetabolites

- Analogs of naturally occurring nucleotides
- Antifolate agents



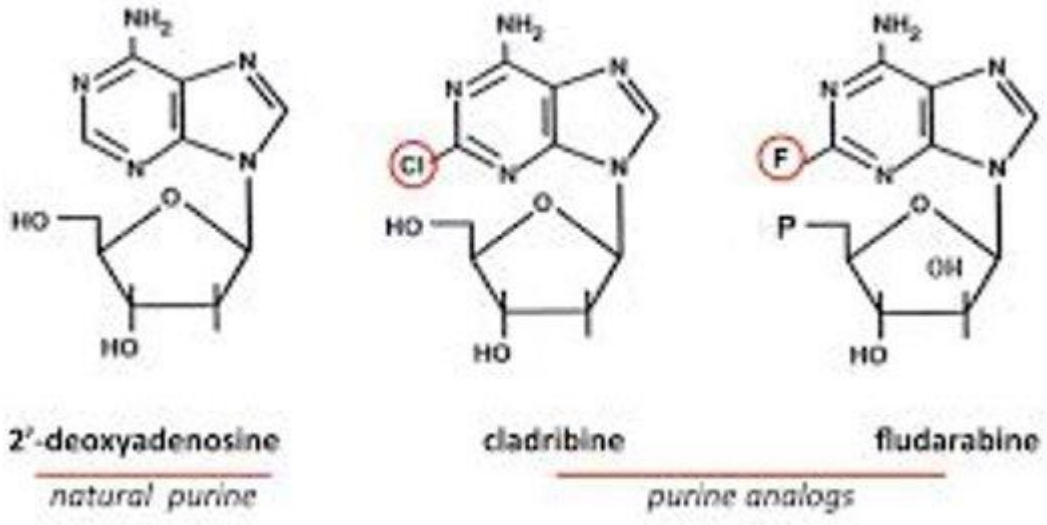
Antimetabolites

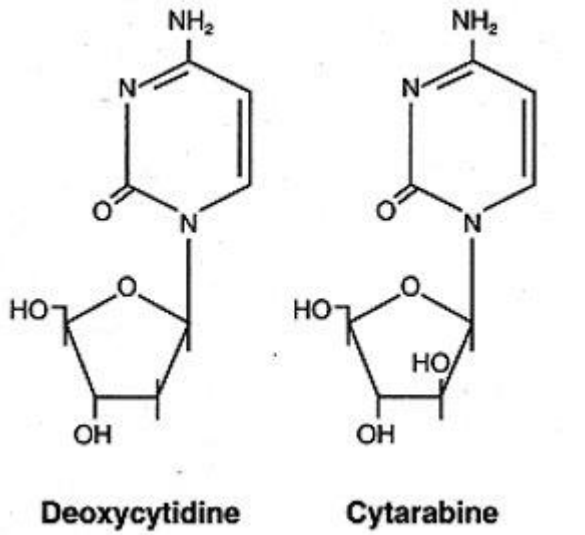
- Analogs of naturally occurring nucleotides
- Pyrimidine Analogs

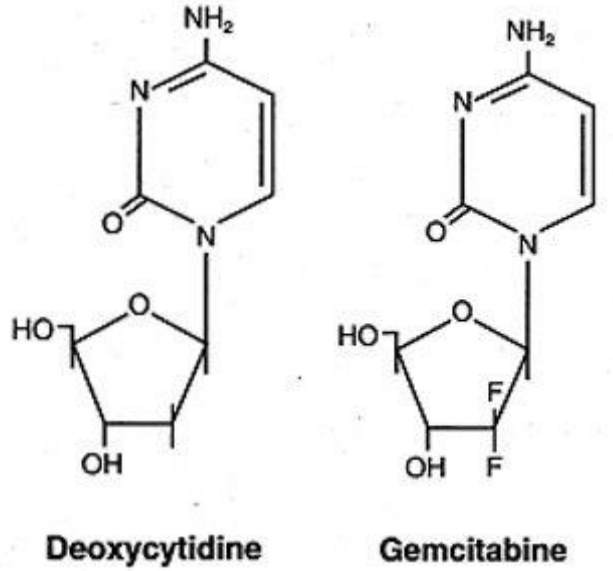


Antimetabolites

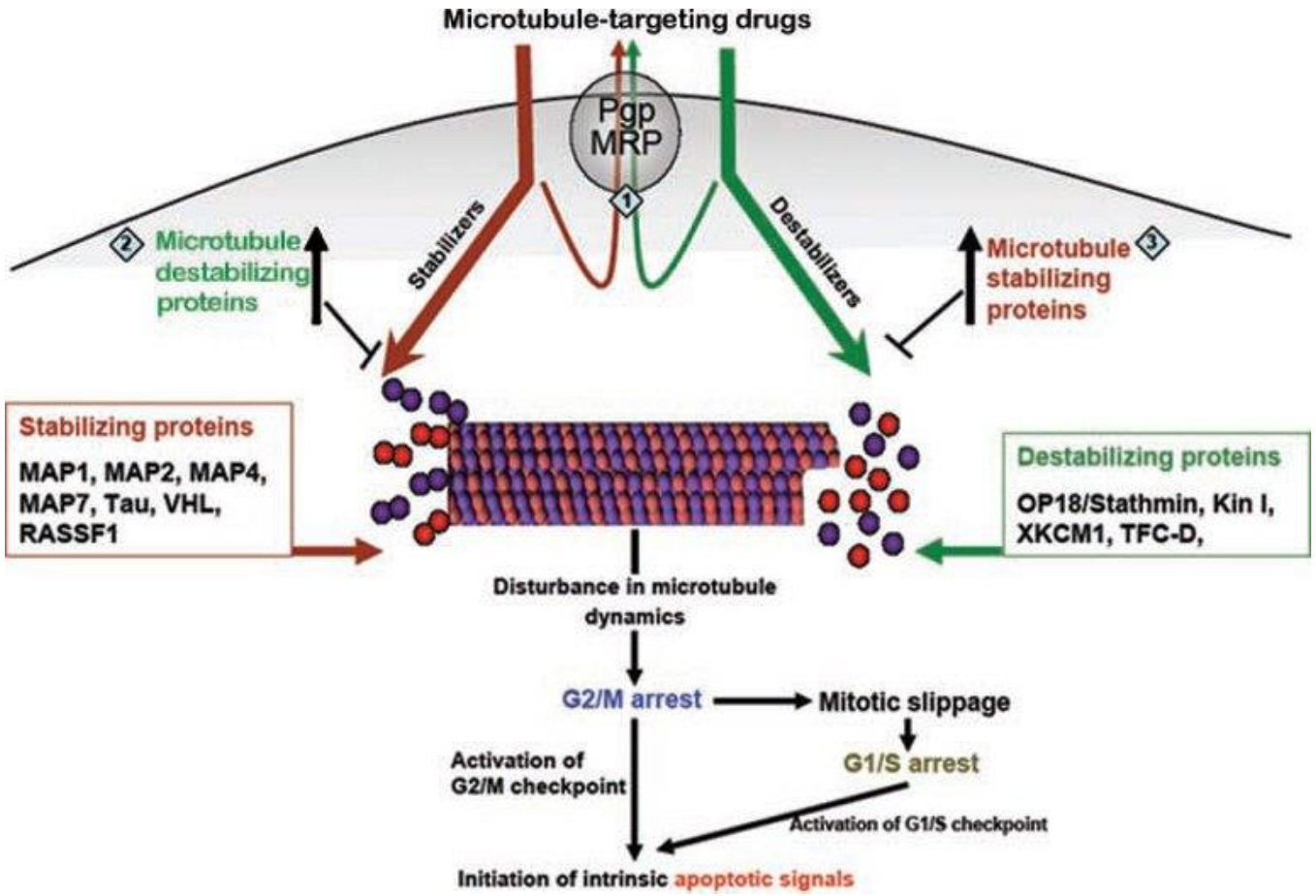
- Analogs of naturally occurring nucleotides
- Purine Analogs







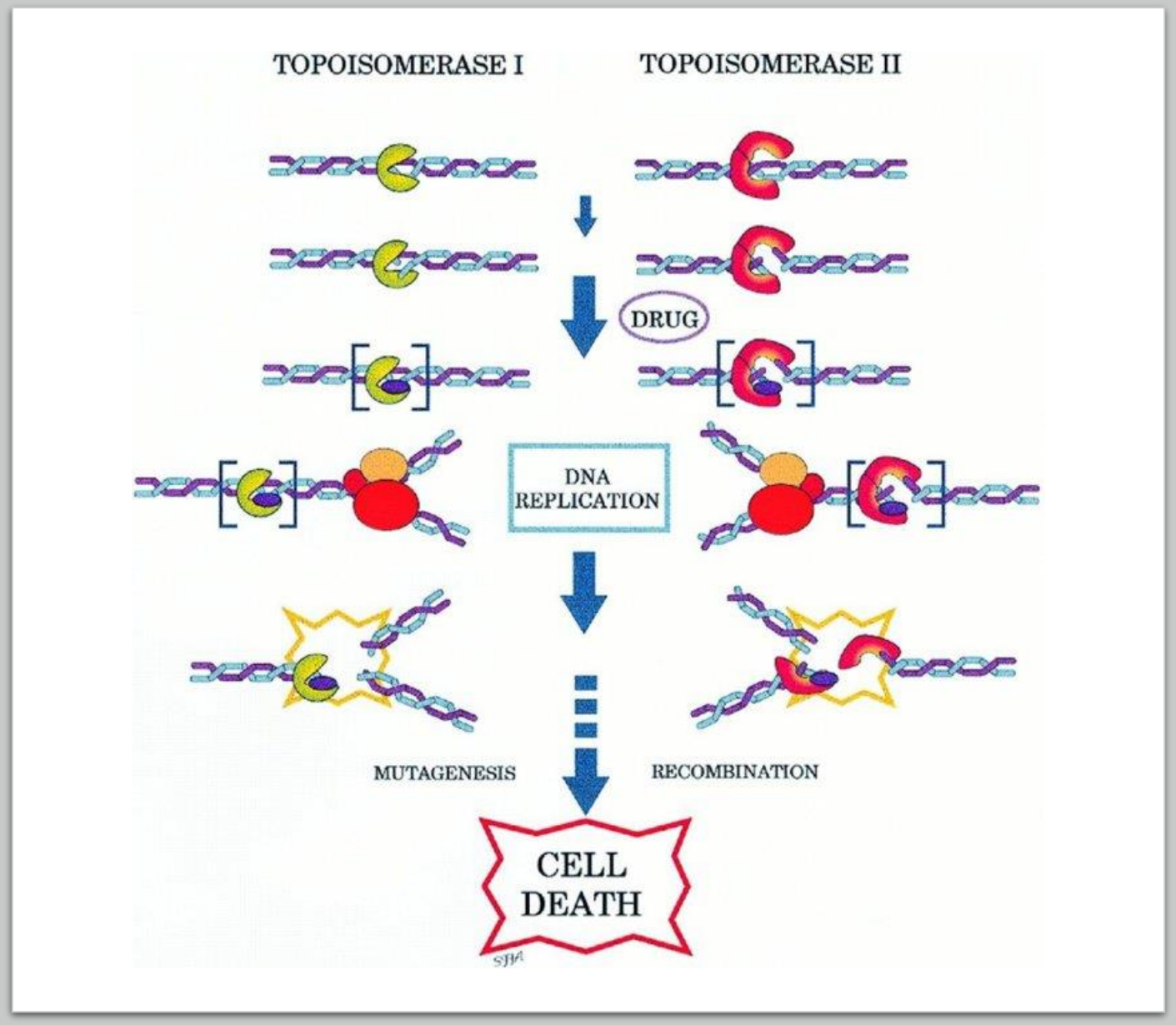
Microtubule Inhibitors



Clin Cancer Res 2007;13: 2849-54.

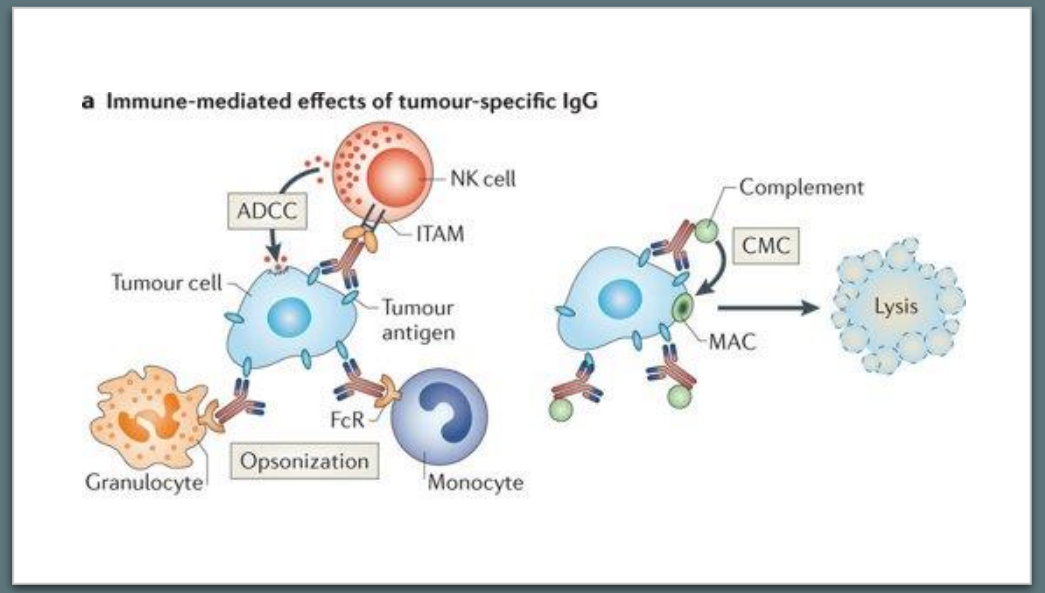
Topoisomerase Inhibitor

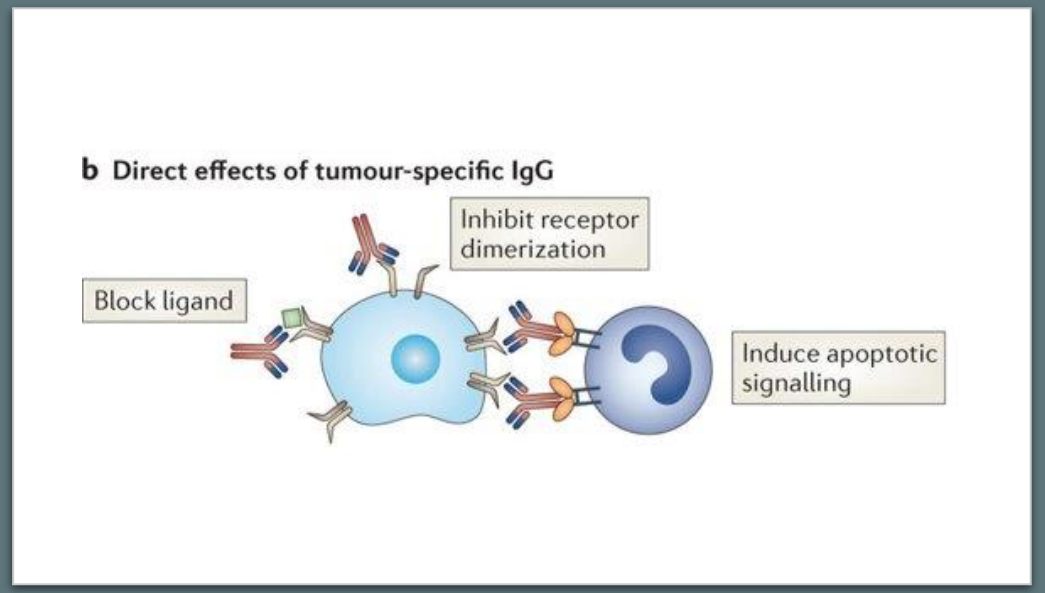
- Topoisomerase I inhibitors stabilize the topo-DNA complex and prevents re-ligation of the cleaved DNA strand leading to single strand breaks
- Topoisomerase II inhibitors stabilize the topo-DNA complex and prevents re-ligation of DNA strands leading to double strand breaks



Monoclonal Antibody (mAb) Overview

- Mechanism of action
- Engineered antibody binds target transmembrane protein
- Direct effects on malignant/target cells to disrupt cell signaling and growth
- Blocks binding of a ligand or inhibits dimerization of a receptor
- Mediate antibody-dependent cellular cytotoxicity
- Mediate complement mediated cytotoxicity
- Enhance responsiveness to chemotherapy or radiation





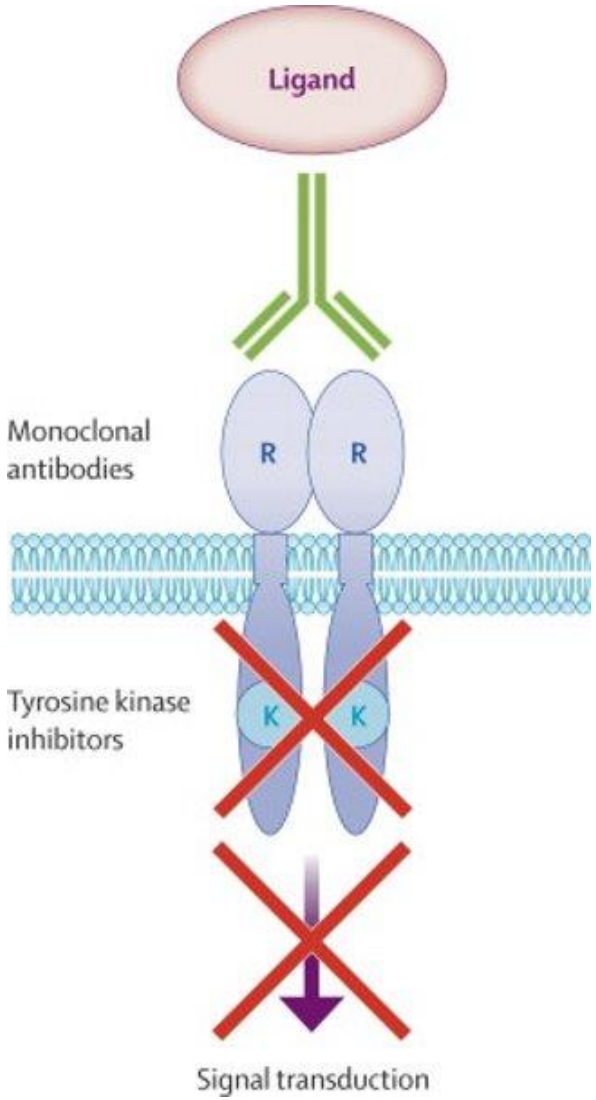
Nature Reviews Cancer. 2015. 15;361-370.

Monoclonal Antibody (mAb) Overview

- Most do not require dose adjustments (or not studied) for renal or hepatic impairment
- Many mAbs carry a **Black Box Warning** for infusion reactions
- Premedications: H1 blocker, H2 blocker, corticosteroid, acetaminophen
  - Varies by agent
  - 1st infusion vs. all infusions
- Monitoring period post-infusion suggested for some agents
- Management of infusion reactions:
  - Stop infusion
  - Medication management includes agents above if not given initially, additional steroid (hydrocortisone), meperidine for rigors, oxygen, epinephrine, etc.
  - Grade 1-2: resume at 50% of previous rate after symptom resolution

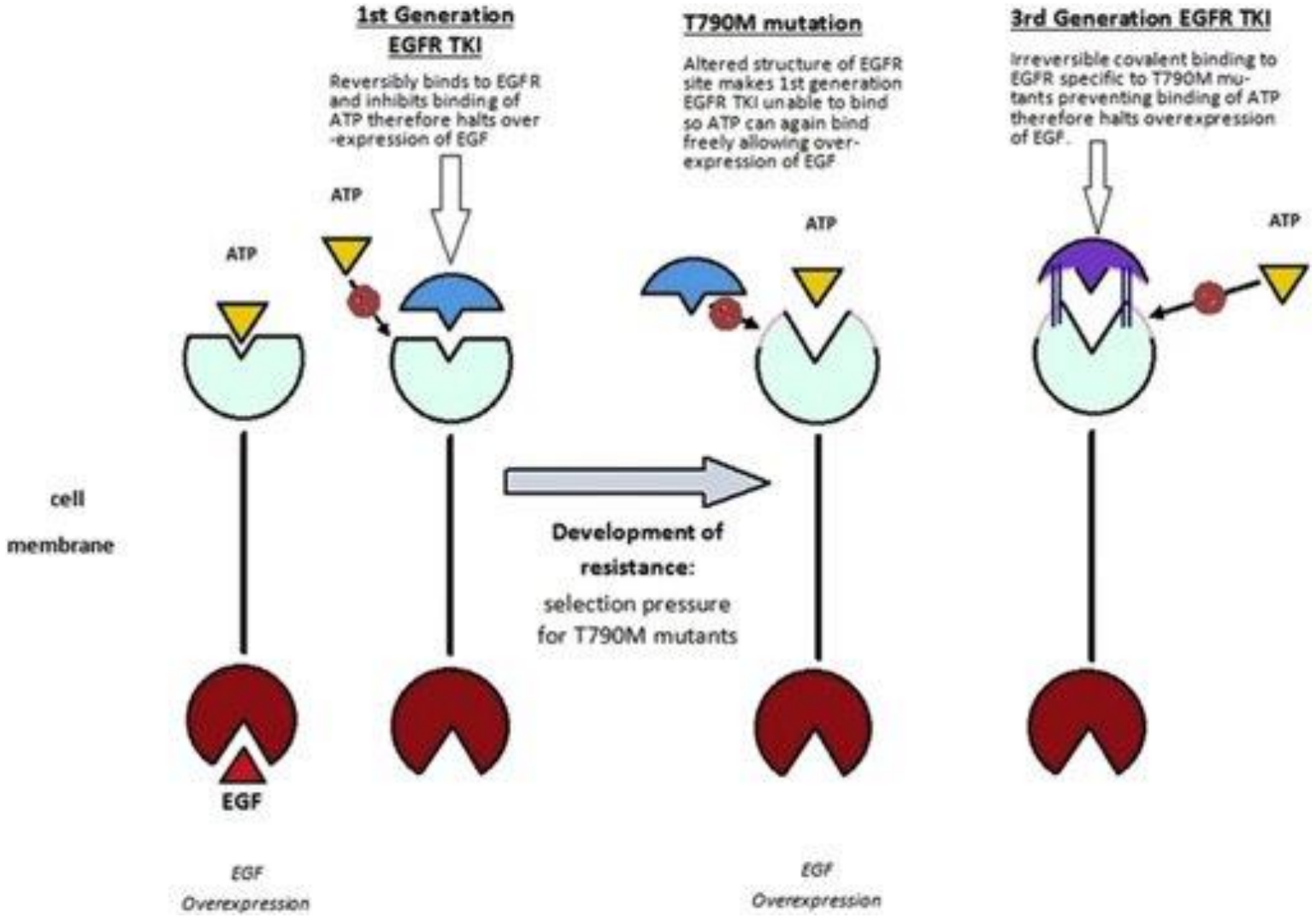
Tyrosine Kinase Inhibitors (TKI) Overview

- Mechanism:
  - Inhibition of tyrosine kinase enzyme results in blockade of multiple cell signal transduction pathways
  - Affects cell proliferation, survival, and invasion
- Must consider timing of administration in relation to food
- Must consider patient compliance
  - Multiple tablets per doses
  - Multiple doses per day
  - Ability to take tablets
- Must consider drug-drug interactions (DDIs) that require specific dose adjustment



Lancet Oncol. 2007. 8(8):738-743.

TKI Binding



Batholomew C, et al. Resp Med Case Reports 2017; 20:137-140

TKIs and QTc prolongation

- FDA considers any drug that prolongs the QTc by 5msec to be a QTc prolonging agent
  - QTc varies by up to 60 msec in the same patient throughout the day
- Some TKIs have specific dose adjustments/parameters for QTc: Nilotinib
  - Dose dependent effect
  - Obtain baseline EKG, 7 days after any dose change, and periodically
  - Contraindicated in hypokalemia, hypomagnesemia, or long QT syndrome
  - Correct electrolyte imbalances prior to initiation

Yap YG, et al. Heart. 2003. 89:1363-1372.

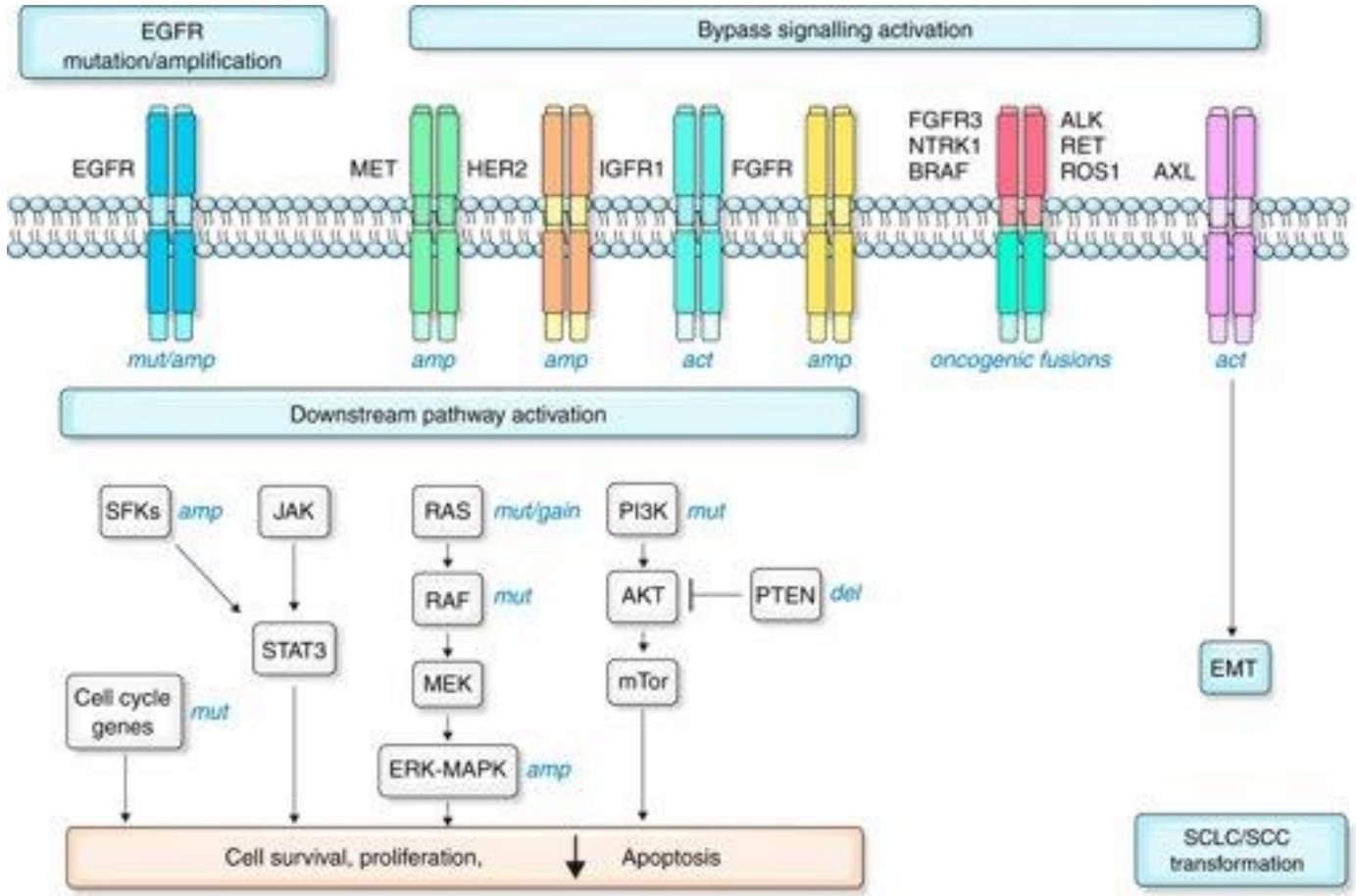
TKIs as CYP P450 substrates

- Food to avoid: grapefruit juice, pomegranate juice, starfruit, Seville oranges
- Smoking is a CYP1A2 inducer
- Most common interaction is through CYP3A4

Strong 3A4 inhibitors	Strong 3A4 inducers
Voriconazole, ritonavir, posaconazole,ketoconazole, itraconazole,clarithromycin, diltiazem, idelalisib	Rifampin, carbamazepine, enz alutamide, phenytoin, St. John's wort

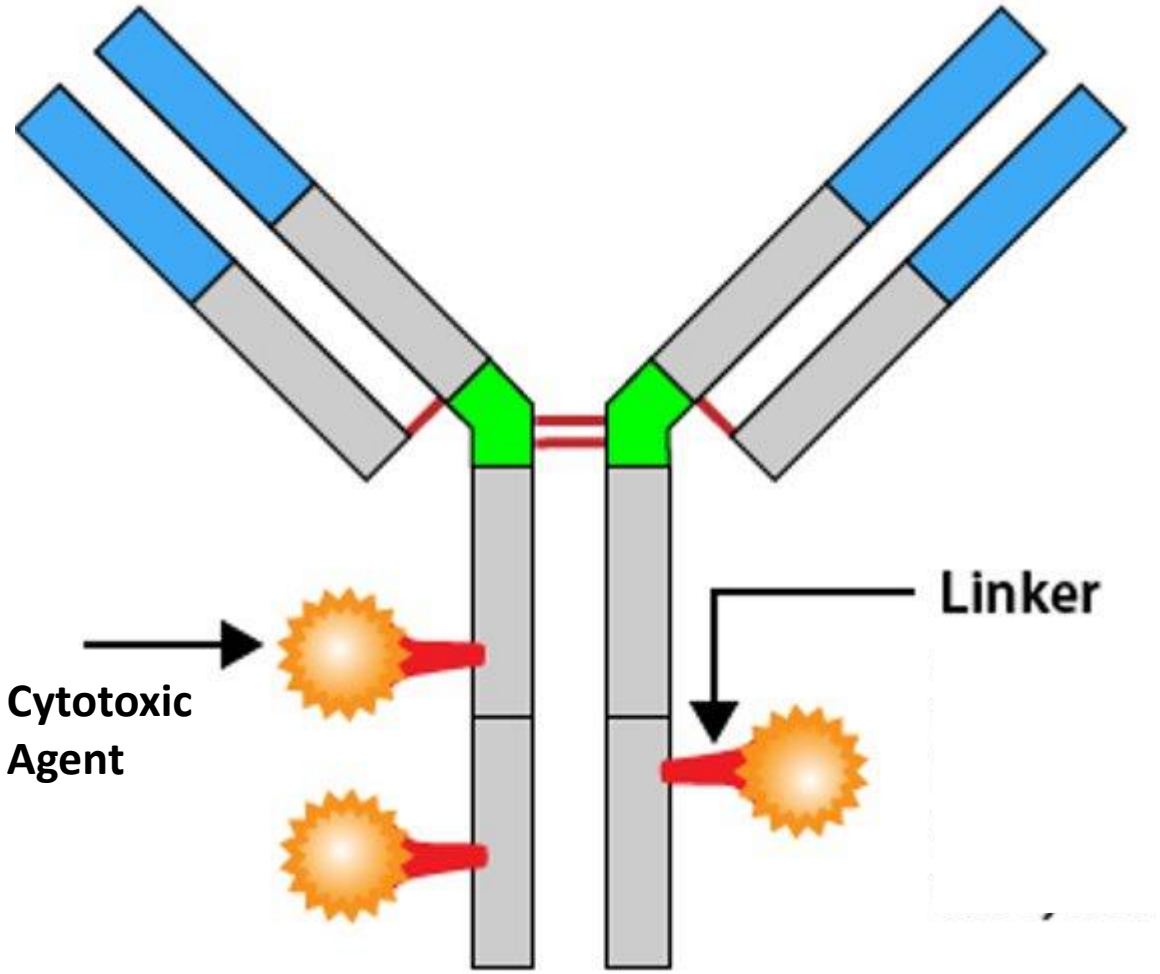



TKI Resistance Mechanisms



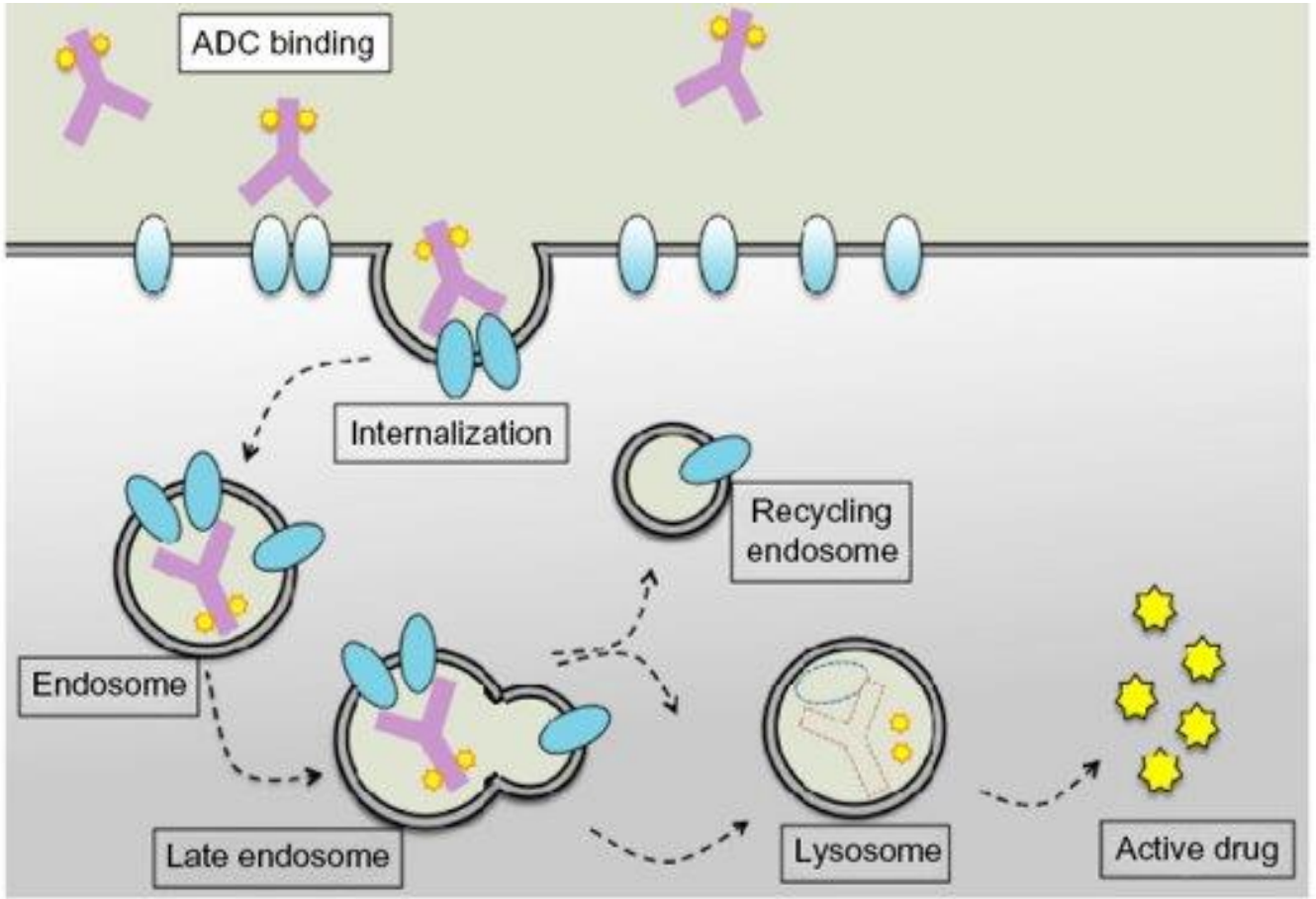
British Journal of Cancer 2019. 121,L725–737

Antibody-Drug Conjugates (ADCs)



Cytotoxic Agent	Side effect profile
Vedotin, mafodotin – auristatin	Neuropathy
Ozogamicin – calicheamicin	Hepatotoxicity
Emtansine – maytansinoid	Neuropathy
Immunotoxin – Pseudomonas exotoxin, diphtheria toxin	Capillary leak syndrome
Deruxtecan, govitecan	Neutropenia, diarrhea

Mechanism of ADCs



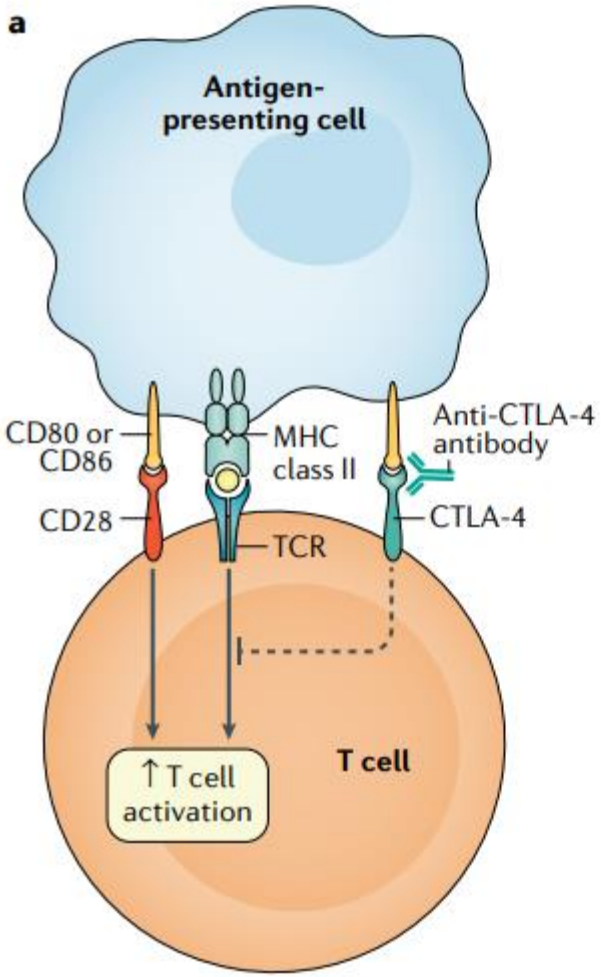
Scotti C, et al. Antibody Technology Journal 2015. 5:1-13

Antibody-drug conjugates

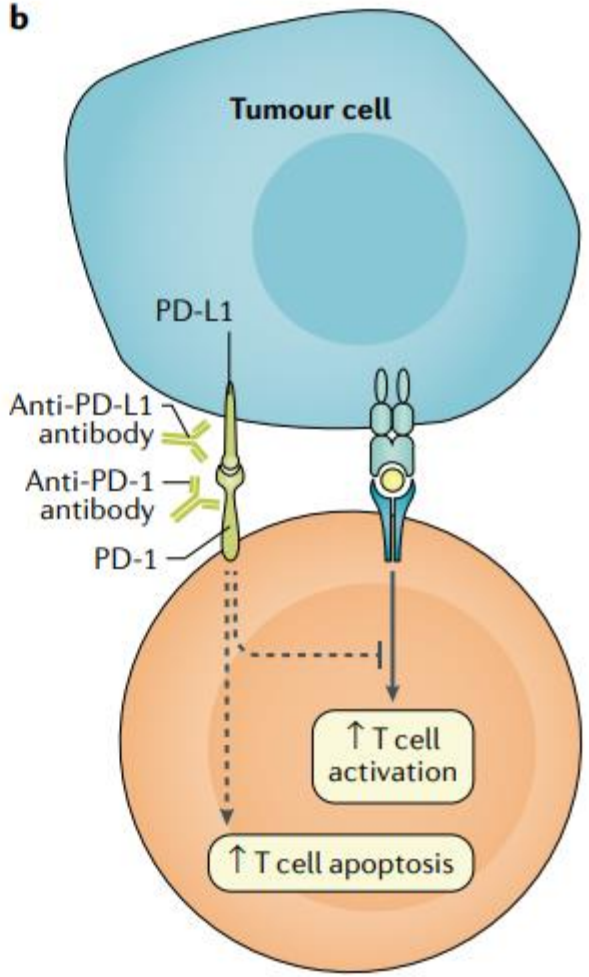
- No dose loading with antibody-drug conjugates
- Most require premedication regimens
- Knowing the cytotoxic agent can predict side effect profile

Immunotherapy

- Immune checkpoint therapy
- Bispecific antibodies
- Vaccine therapy
- Talimogene laherparepvec
- CarT cell therapy
  - Sipuleucel-T



CTLA-4 inhibitors



PD-1 PD-L1 inhibitors

Ramos-Casals M, et al. Nat Rev Dise Primers 2020. 6(1):38

Biosimilars

- Per FDA, the biosimilar product is:
  - Expected to produce the same clinical result as the reference product
  - Switching between products does not increase safety risks or decrease effectiveness
- Interchangeability depends on your health system
- Insurance coverage of the drug varies by insurance company

Current Oncology Biosimilars

Originator product	Biosimilar
Filgrastim (Neupogen)	Filgrastim-sndz (Zarxio) Filgrastim-aafi (Nivestym) **Filgrastim-ayow (Releuko)** Tbo-filgrastim (Granix) is not a biosimilar
Pegfilgrastim (Neulasta)	Pegfilgrastim-jmdb (Fulphila) Pegfilgrastim-cbqv (Udenyca) Pegfilgrastim-bmez (Ziextenzo) Pegfilgrastim-apgf (Nyvepria)
Trastuzumab (Herceptin)	Trastuzumab-dkst (Ogivri) Trastuzumab-pkrb (Herzuma) Trastuzumab-dttb (Ontruzant) Trastuzumab-qyyp (Trazimera) Trastuzumab-anns (Kanjinti)
Rituximab (Rituxan)	Rituximab-abbs (Truxima) Rituximab-pvvr (Ruxience) Rituximab-arrx (Riabni)
Bevacizumab (Avastin)	Bevacizumab-awwb (Mvasi) Bevacizumab-bvzr (Zirabev) **Bevacizumab-maly (Alymsys)**

Order of Administration

- Administer the agent with the highest concern for extravasation first
- Administer biologic agents first
- Administer taxanes before platinums

Morales ASR, et al. J Oncol Pharm Pract 2020. 26(4): 933-942

Patient Case

- MS is a 45 year old female with cervical cancer
- She is starting treatment with cisplatin + paclitaxel + pembrolizumab + bevacizumab
- At her prechemotherapy visit, she has a few questions:
  - Are all these agents necessary? What is the rationale behind combining these agents?
  - Which one will be given first?
  - Why am I getting biosimilar for bevacizumab? Will it work the same?

New Formulations

- Drug with different formulations must undergo FDA approval for the specific formulation
- Hyaluronidase reversibly opens up interstitial space in SubQ tissue to deliver volumes >2.3ml
- Currently approved drugs with new formulations:
  - Rituximab hyaluronidase (Rituxan Hycela)
  - Trastuzumab hyaluronidase (Herceptin Hylecta)
  - Daratumumab hyaluronidase (Darzalex Faspro)
  - Pertuzumab, trastuzumab, hyaluronidase (Phesgo)

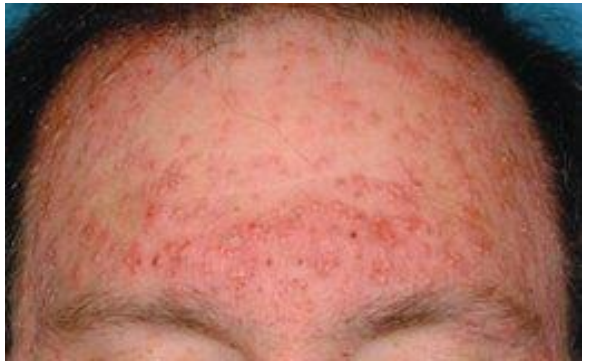
Common Toxicities and Management

Common Toxicities and Management

Skin Toxicities

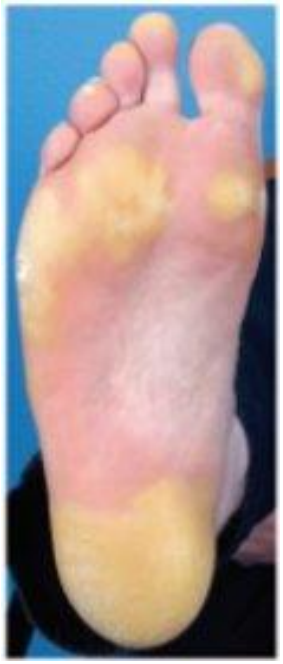
EGFR Dermatologic Toxicity Management

- Rash correlated with drug response
  - Dose reductions only for severe reactions
- Develops within first 2 weeks of treatment
- Limit sun exposure, use sunscreen
- Moisturize
- Topical or systemic antibiotics
- May use topical corticosteroids, sparingly



Am Fam Physician 2008;77:311-19

VEGF Dermatologic Toxicity

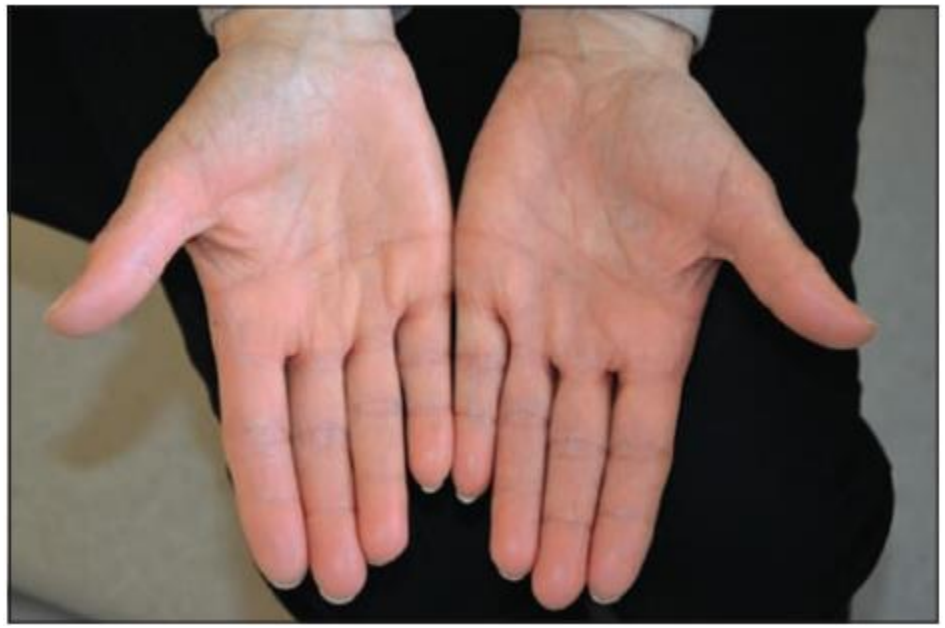


Hand-foot skin reaction

Hair discoloration

Hand-Foot Syndrome

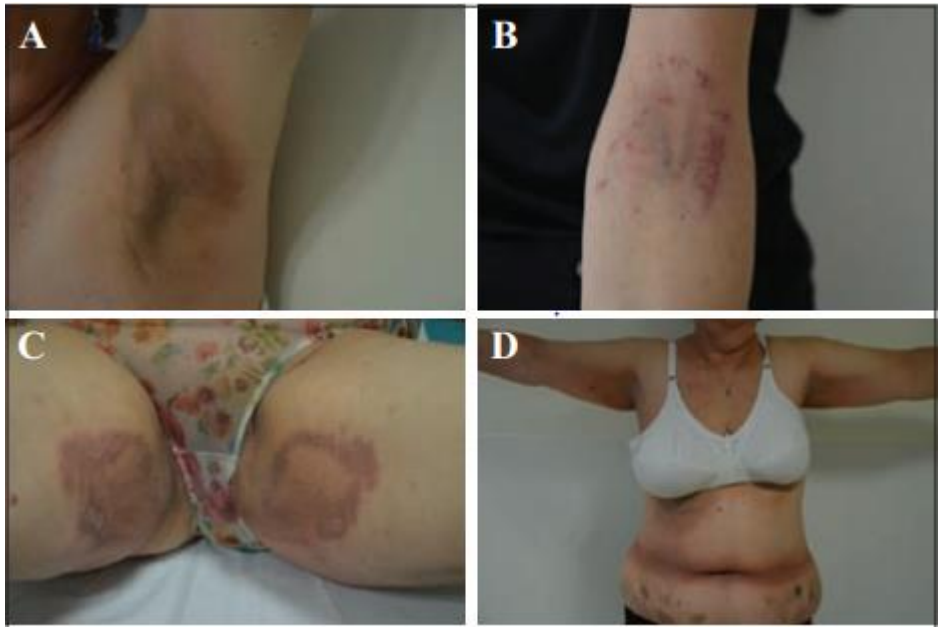
- Common agents that cause HFS:
  - Capecitabine
  - Liposomal doxorubicin
  - Everolimus
  - Multikinase inhibitors
- Microtrauma



Macedo LT, et al. Support Care Cancer. 2014. 22;1585-93

Taxane Skin Reactions

- Macular and popular eruption
- Warm sites prone to trauma



Sibaud V, et al. Eur J Dermatol. 2016. 26;427-43

Taxane Skin Reactions

Severity (CTCAE v.4)	Intervention
Grade 0	Gentle skin care instructions given
Grade 1	Continue drug at current dose and monitor for change in severity
	Topical low/moderate-strength steroid to affected areas bid[1] AND If infection is suspected, apply topical antibiotic or anti-fungal agent
	Reassess after 2 weeks (either by healthcare professional or patient self-report); if reactions worsen proceed to next step
Grade 2	Continue drug at current dose and monitor for change in severity; obtain bacterial/viral/fungal cultures if infection is suspected; continue treatment of skin reaction with the following:
	Topical moderate-strength steroid to affected areas bid[1] AND If infection is suspected, apply topical antibiotic or anti-fungal agent
	Reassess after 2 weeks (either by healthcare professional or patient self-report); if reactions worsen or do not improve proceed to next step
Grade 3	Interrupt treatment until severity decreases to Grade 0-1; obtain bacterial/viral/fungal cultures if infection is suspected; and continue treatment of skin reaction with the following:
	Topical moderate-strength steroid to affected areas bid[1] AND If infection is suspected, apply topical antibiotic or anti-fungal agent
	Reassess after 2 weeks; if reactions worsen or do not improve, consider dose interruption or discontinuation per protocol and switch to another antineoplastic agent[2]

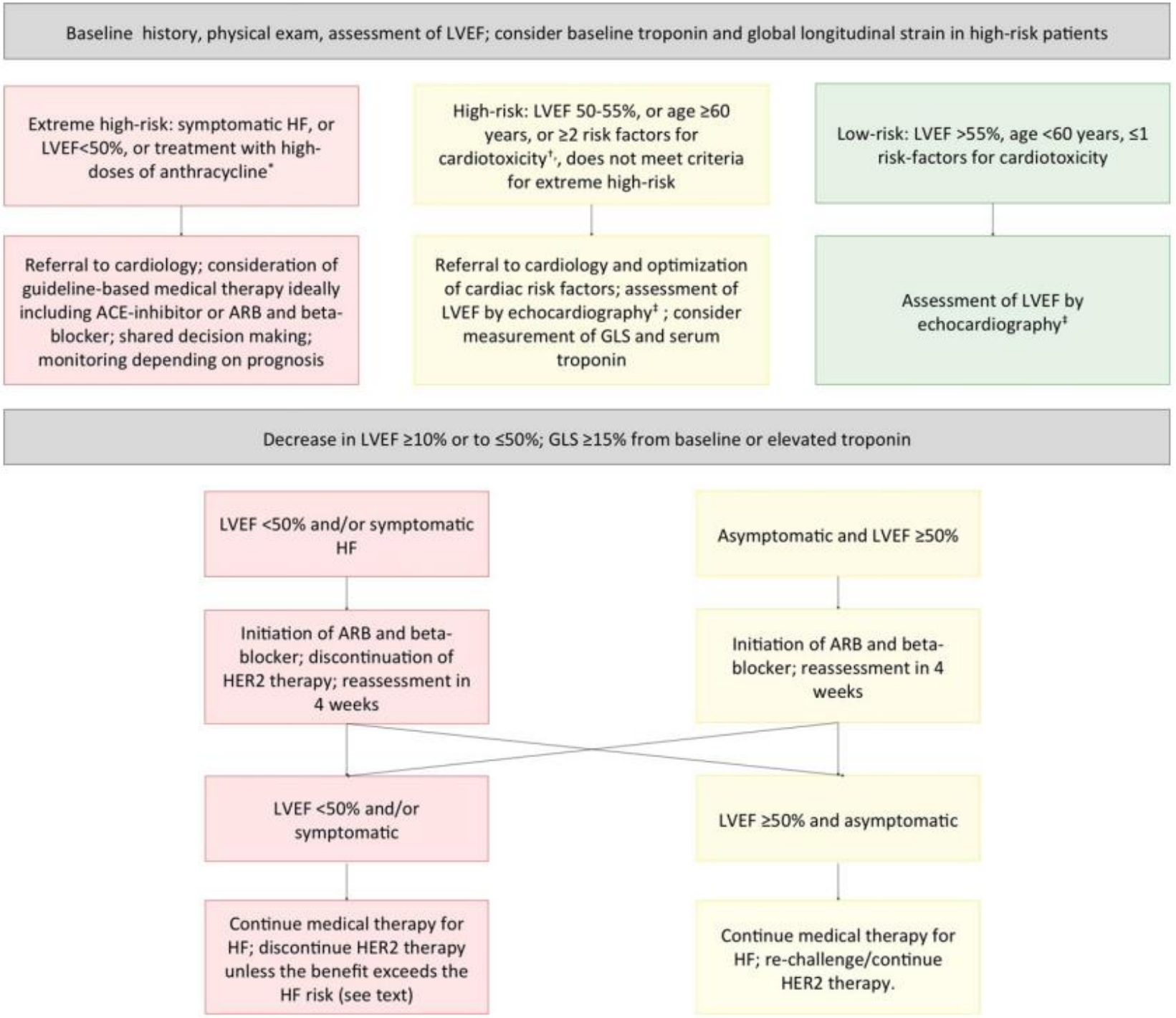
Sibaud V, et al. Eur J Dermatol. 2016. 26;427-43

Common Toxicities and Management

Cardiotoxicity

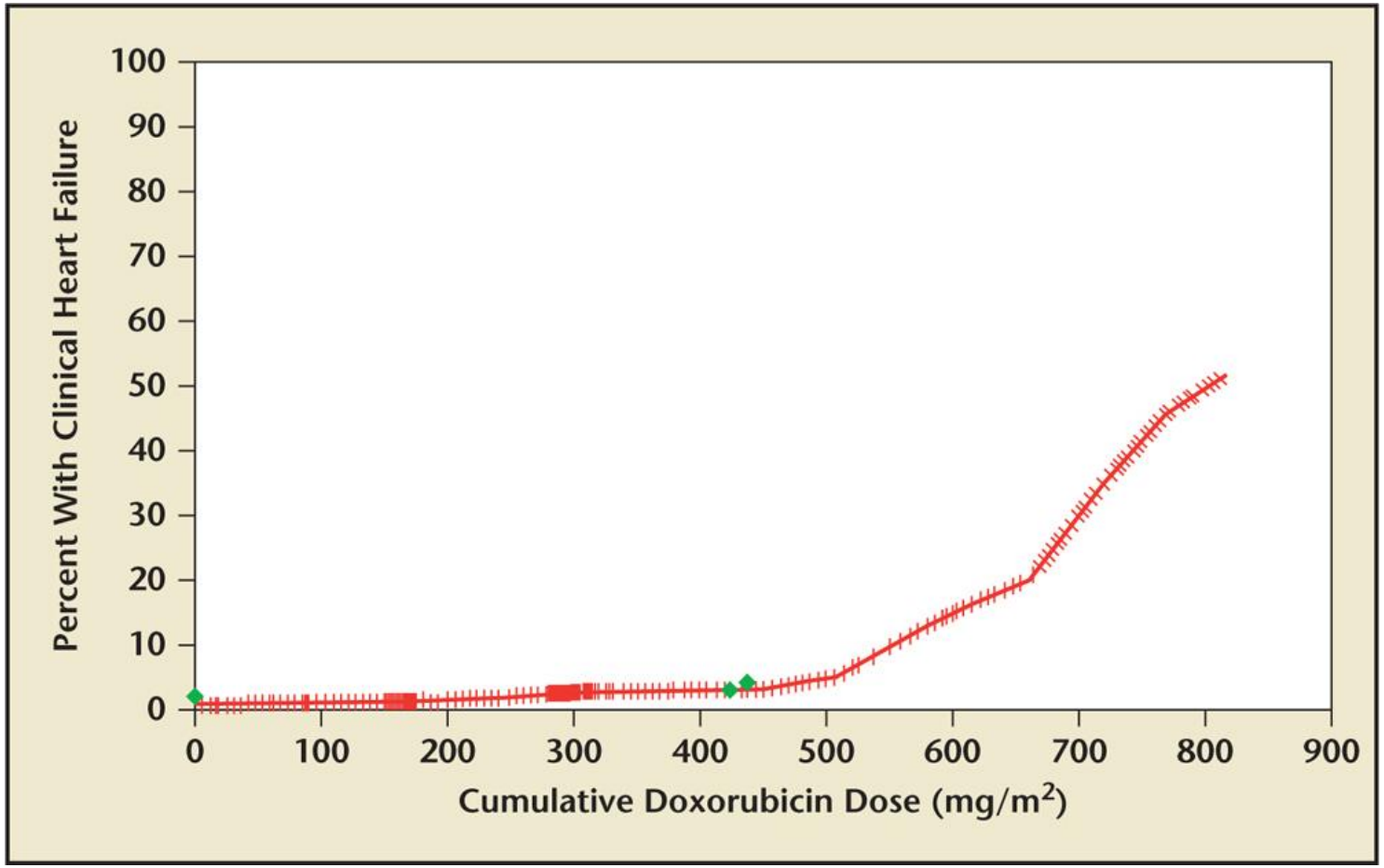
HER2 Therapy Related Cardiotoxicity

- Generally reversible
- Monitoring every 3 months while on therapy
- Increase risk when combined with anthracyclines



Florido R, et al. J Am Heart Assoc. 2017. 6;e006915.

Anthracycline Cardiotoxicity



Muppidi R, et al. Reviews in Cardiovascular Medicine 2015. 16(4):225-234

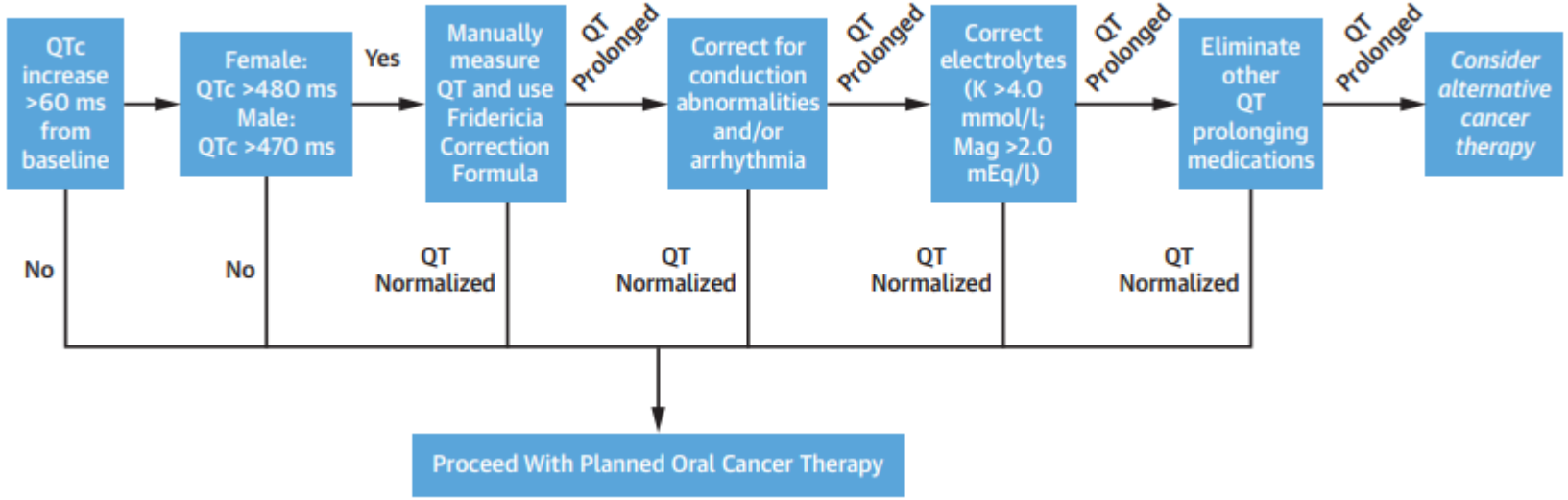
5FU/Capecitabine Coronary Vasospasm

- More common with continuous infusion 5FU and capecitabine
- Effects endothelial nitric oxide synthase leading to coronary spasm and vasoconstriction
- Presentation: chest pain/angina, ECG changes
- Management:
  - Calcium channel blockers or nitroglycerin for immediate symptom management
  - Consider verapamil/nifedipine or nitrates

Chong JH, et al. Interv Cardiol 2019. 14(2):89-94
Yuan C, et al. Cardio-Oncology 2019; 5(13): 1-7

Cardiotoxicity of Chemotherapy Agents

- QTc prolongation



Rau V, et al. JACC 2021. 77;2693-716

Cardiotoxicity of Chemotherapy Agents

- Hypertension
- VEGF-targeting agents

Before bevacizumab therapy				
Clinic BP (mmHg) ABPM/HBPM[a] (mmHg)	<160/100 <150/95		≥160/100 ≥150/95	
Bevacizumab administration	Start		Delay	
Antihypertensive treatment	• Not required in antihypertensive-naive patients • No change to existing treatment required by the oncology team in patients receiving antihypertensive drugs		• Arrange ABPM/HBPM and review at next clinic • If BP remains ≥150/95 mmHg, follow treatment algorithm (Fig. 2) and reassess at next clinic	
During bevacizumab therapy				
Clinic BP (mmHg) ABPM/HBPM[a] (mmHg)	<160/100 <150/95	≥160/100 or an increase of ≥20 systolic or 10 diastolic ≥150/95	≥180/110 n/a	Hypertensive crisis n/a
Bevacizumab administration	Continue/re-start	Omit dose	Omit dose	Discontinue
Antihypertensive treatment	*In antihypertensive-naive patients*			• Emergency admission for in-patient care
	• Not required	• Reassess clinic BP or ABPM/HBPM[b] and review at next clinic • If clinic BP remains ≥160/100 and/or ABPM/HBPM ≥150/95 mmHg, follow treatment algorithm (Fig. 2) and reassess at next clinic	• Start amlodipine 5 mg daily and reassess clinic BP or ABPM/HBPM after at least 2 weeks • Follow treatment algorithm (Fig. 2) until BP <160/100 mmHg[b]	
	In patients already receiving antihypertensive drugs for pre-existing hypertension			
	• No change to existing treatment required by the oncology team	• Reassess clinic BP or ABPM/HBPM[b] and review at next clinic • If clinic BP remains ≥160/100 and/or ABPM/HBPM ≥150/95 mmHg, step up treatment in accordance with NICE guidelines[50] and reassess at next clinic	• Step up treatment in accordance with NICE guidelines[50] and reassess clinic BP or ABPM/HBPM after at least 2 weeks • Follow NICE guidelines until BP <160/100 mmHg[b]	
Referral to clinician with special interest in hypertension	• Not required	• Not required	• Consider referral if BP not <160/100 mmHg on ≥3 drugs or multiple drug intolerances	• Emergency admission

Rau V, et al. JACC 2021. 77;2693-716

Common Toxicities and Management

Peripheral Neuropathy

Chemotherapy Induced Peripheral Neuropathy

Cryotherapy	• Frozen gloves and booties • Conflicting data, ongoing studies
Pharmacotherapy for Treatment	• Duloxetine • Gabapentin, venlafaxine, pregabalin
Treatment Changes	• Dose reduction, dose holds • Changing therapy
Prevention	• No data to support pharmacologic interventions for prevention

Cryotherapy - Hanai A. J Natl Cancer Inst. 2018. 111;djx178
General Algorithm. 2019. Pain Medicine. Bates et al.
ASCO Guidelines 2020 - Loprinzi CL. J Clin Oncol. 2020

Patient Case

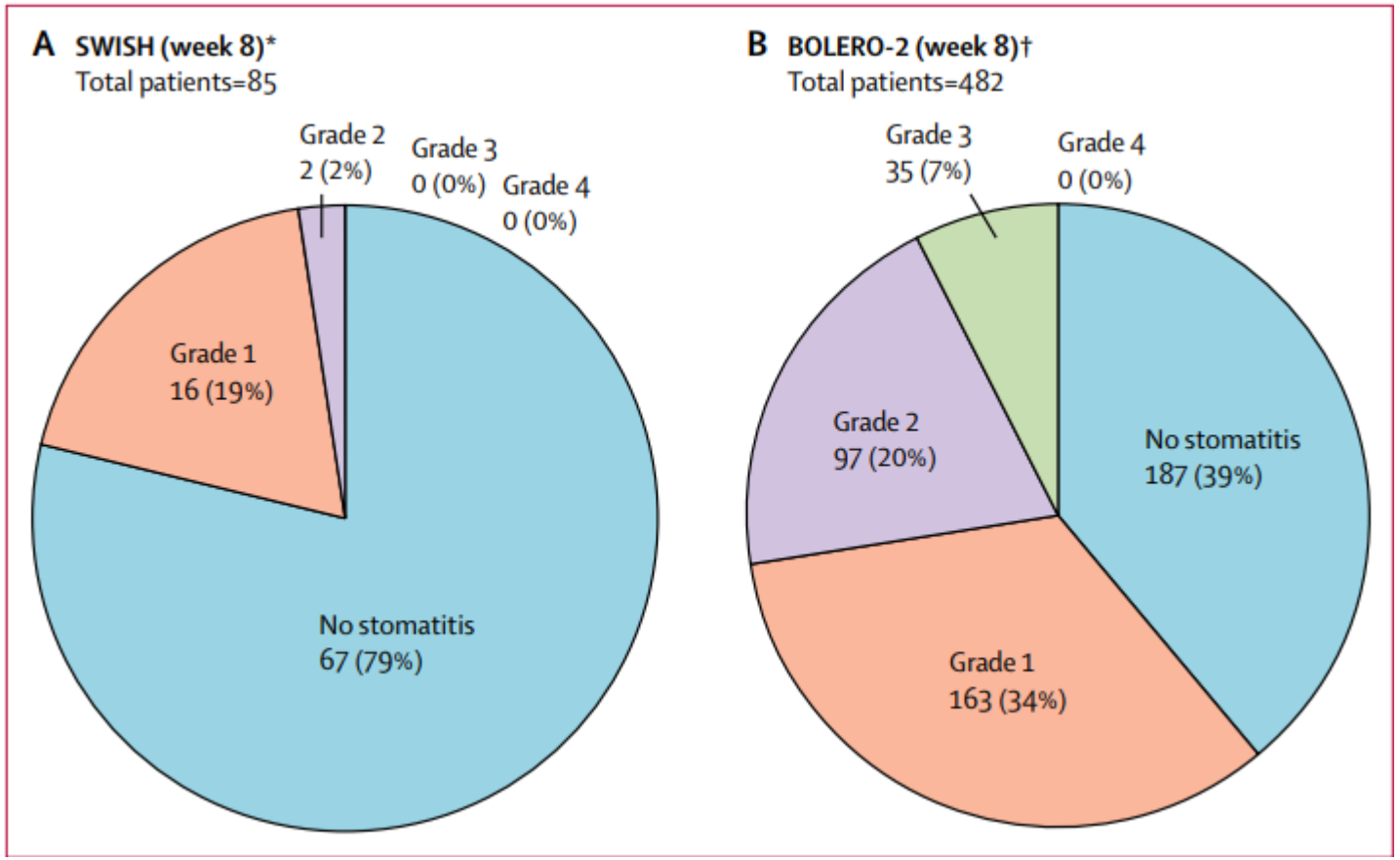
- MS is a 45 year old female with cervical cancer
- She is starting treatment with cisplatin + paclitaxel + pembrolizumab + bevacizumab
- At her prechemotherapy visit prior to cycle 2, she reports tingling and numbness in her fingers and toes.
  - What agent could this be related to?
  - What treatment options are available to her?

Common Toxicities and Management

GI Toxicity

Mucositis

- Supportive care
  - Brush and floss twice daily
  - Baking soda/salt water rinses
  - Good dental hygiene
  - Avoiding irritants
- Everolimus: SWISH trial



Rugo H, et al. Lancet Oncol 2017. 18:654-662

Chemotherapy Induced Nausea

IN CLINIC	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date:							
Aprepitant (Cinvanti)	X						
Palonosetron (Aloxi)	X						
Dexamethasone	X						
AT HOME	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Dexamethasone		Twice daily	Twice daily	Twice daily			
Ondansetron (Zofran)				As needed	As needed		
Prochlorperazine (Compazine)	As needed	As needed	As needed	As needed	As needed		

Chemotherapy Induced Nausea

- Refractory CINV
- Olanzapine
- Prochlorperazine
- Metoclopramide
- Layering antiemetics

	RECEPTOR ANTAGONISM							
	D_2	H_1	Ach_M	$5HT_2$	$5HT_3$	$5HT_4$	CB_{1+2}	NK_1
Metoclopramide	+++				+	++		
Domperidone	++++					+		
Haloperidol	++++	+						
Methotrimeprazine	++++	+++	++	+++				
CPZ	++++	++	+					
Olanzapine	++	+	+	+++	++			
Prochlorperazine	++	+						
Dimenhydrinate	+	++++	++					
Ondansetron					++++			
Granisetron					++++			
Scopolamine	+	+	++++					
Aprepitant								+++

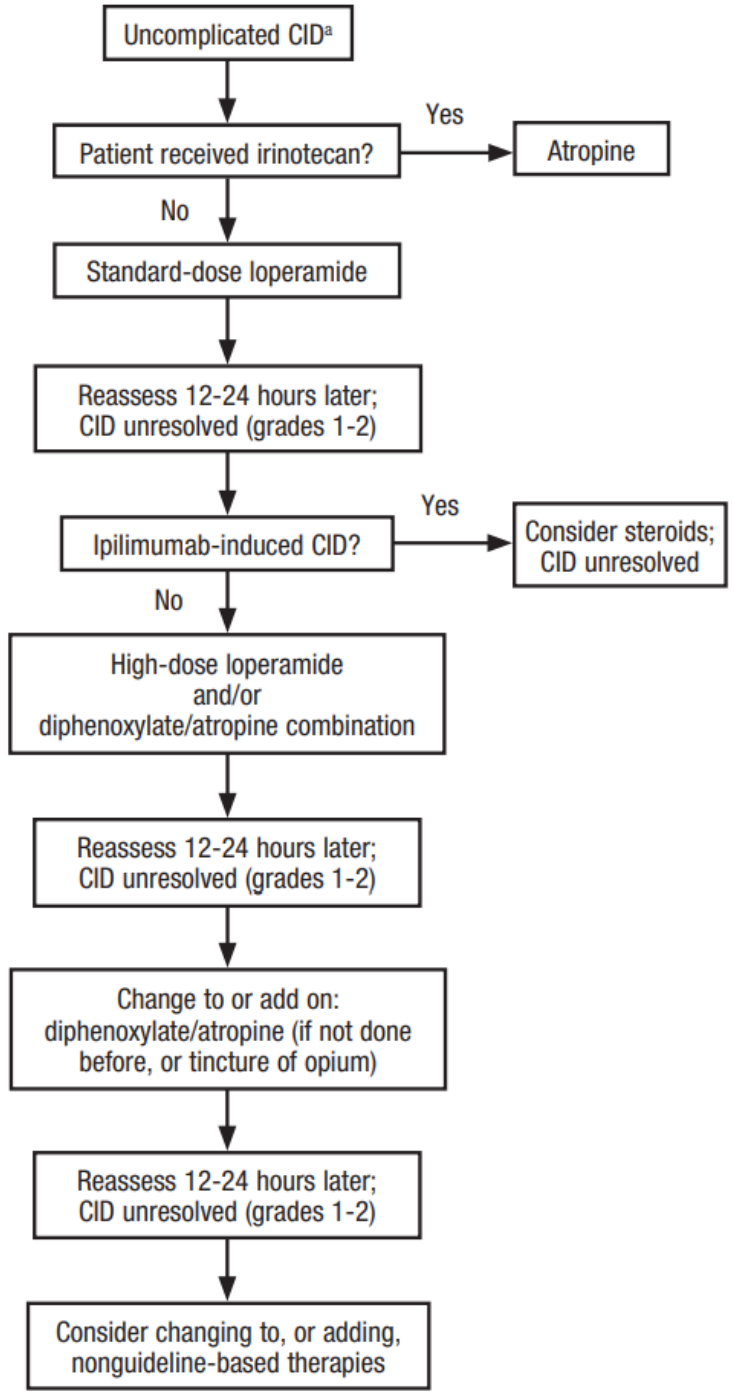
Chemotherapy Induced Constipation and Diarrhea

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of >=7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by an increase in frequency and/or loose or watery bowel movements. **Navigational Note:** -					
Constipation	Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema	Persistent symptoms with regular use of laxatives or enemas; limiting instrumental ADL	Obstipation with manual evacuation indicated; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by irregular and infrequent or difficult evacuation of the bowels. **Navigational Note:** -					

NCI CTCAE v5.0. 2017

Chemotherapy Induced Diarrhea

- Irinotecan induced diarrhea
- IRAE diarrhea
- EGFR related diarrhea
- Layering loperamide and lomotil
- Refractory: tincture of opium, octreotide



Koselke E, et al. J Hematol Oncol Pharm 2012. 2(4):143-151

Chemotherapy Induced Constipation

- Causes: anti-emetics, chemotherapy adverse effect, opioids, disease
  - Vincristine, temozolomide

Drug therapy	Mechanism of action	Onset of action
Psyllium, methylcellulose	Bulk-forming – stimulates peristalsis, reduce GI transit time	Up to 72h
Miralax, lactulose, magnesium hydroxide, glycerin	Osmotic – retains water in gut lumen	24-72h
Senna, bisacodyl	Stimulative – increase peristalsis resulting in reduced net absorption of water from lumen	Senna: 6-24h Bisacodyl: 6-12h (PO), <1h (suppository
Mineral oil	Lubricant – coat feces and rectum for easier passage	6-8h (PO), <15min (rectal)
Bisacodyl, glycerin suppositories	Rectal – avoid with neutropenic or thrombocytopenic patients	

Koselke E, et al. J Hematol Oncol Pharm 2012. 2(4):143-151

Patient Case

- MS is a 45 year old female with cervical cancer
- She is starting treatment with cisplatin + paclitaxel + pembrolizumab + bevacizumab
- At her subsequent prechemotherapy visit, she has a few questions:
  - I have constipation starting a couple days after chemotherapy. What is this due to? How can I prevent it?

Common Toxicities and Management

Hematologic Toxicity

Hematologic Toxicity

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophil count decreased	<LLN - 1500/mm3; <LLN - 1.5 x 10e9 /L	<1500 - 1000/mm3; <1.5 - 1.0 x 10e9 /L	<1000 - 500/mm3; <1.0 - 0.5 x 10e9 /L	<500/mm3; <0.5 x 10e9 /L	-
Definition: A finding based on laboratory test results that indicate a decrease in number of neutrophils in a blood specimen. **Navigational Note:** -					
Platelet count decreased	<LLN - 75,000/mm3; <LLN - 75.0 x 10e9 /L	<75,000 - 50,000/mm3; <75.0 - 50.0 x 10e9 /L	<50,000 - 25,000/mm3; <50.0 - 25.0 x 10e9 /L	<25,000/mm3; <25.0 x 10e9 /L	-
Definition: A finding based on laboratory test results that indicate a decrease in number of platelets in a blood specimen. **Navigational Note:** -					
Anemia	Hemoglobin (Hgb) <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L	Hgb <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80g/L	Hgb <8.0 g/dL; <4.9 mmol/L; <80 g/L; transfusion indicated	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by a reduction in the amount of hemoglobin in 100 ml of blood. Signs and symptoms of anemia may include pallor of the skin and mucous membranes, shortness of breath, palpitations of the heart, soft systolic murmurs, lethargy, and fatigability. **Navigational Note:** -					

- Treatment holds
- Dose reductions
- Granulocyte colony stimulating factor (GCSF?)

Common Toxicities and Management

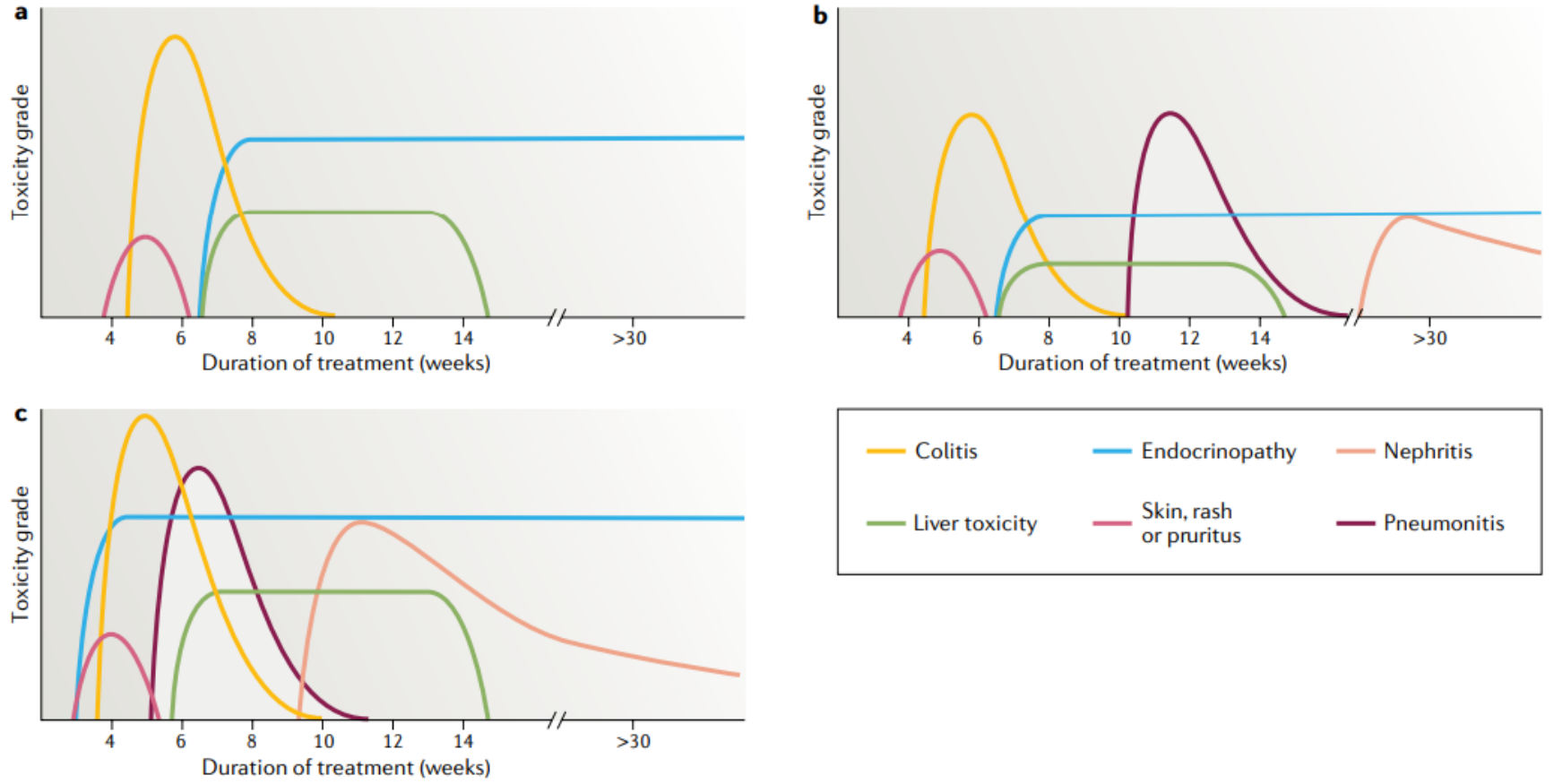
Immune Related Adverse Events

Time Course of Common IRAEs

A: Ipilimumab

B: anti-PD-1 or anti-PD-L1

C: Ipilimumab + anti-PD-1



Martins F, et al. Nature Reviews. 2019. 16; 563-78

Patient Case

- MS is a 45 year old female with cervical cancer
- She is starting treatment with cisplatin + paclitaxel + pembrolizumab + bevacizumab
- At her prechemotherapy visit prior to cycle 3, she reports having 6 stools a day for the past day.
  - What agent could this be related to?

Questions?

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