



Solid Tumor Pharmacotherapy Pearls

Amy Ly Indorf, PharmD, BCOP
Clinical Oncology Pharmacist
October 7, 2025

A decorative graphic on the right side of the slide consisting of several overlapping, rounded shapes in dark blue, teal, purple, and yellow. The teal shape is the largest and most prominent, with a purple circle overlapping it. A dark blue shape is at the top, and a yellow shape is at the bottom.

UW Medicine

Land Acknowledgement

Fred Hutchinson Cancer Center acknowledges the Coast Salish peoples of this land, the land which touches the shared waters of all tribes and bands within the Duwamish, Puyallup, Suquamish, Tulalip and Muckleshoot nations.



Patient Case 1

Taxane Dermatologic Toxicities

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy and radiation receiving adjuvant docetaxel and cyclophosphamide.

Which of the following are dermatologic adverse effects associated with this regimen?

- a. Alopecia
- b. Paronychia and onycholysis
- c. Macular and papular eruptions
- d. Palmar-plantar erythrodysesthesia
- e. All of the above

Taxane Dermatologic Toxicities

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy and radiation receiving adjuvant docetaxel and cyclophosphamide.

Which of the following are dermatologic adverse effects associated with this regimen?

- a. Alopecia
- b. Paronychia and onycholysis
- c. Macular and papular eruptions
- d. Palmar-plantar erythrodysesthesia
- e. **All of the above**

Taxane Dermatologic Toxicities - Alopecia

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy and radiation receiving adjuvant docetaxel and cyclophosphamide.

Which of the following statements are true regarding alopecia?

- a. Minoxidil may help in prevention of hair loss once cytotoxic chemotherapy is initiated
- b. Randomized clinical trials show 90% of patients developing grade 1 alopecia with scalp cooling versus 0% without scalp cooling
- c. Guidelines do not recommend considering scalp cooling to reduce chemotherapy-induced alopecia
- d. Scalp cooling trials show greater efficacy with taxane-based regimens and lower efficacy when anthracyclines are combined with taxane or cyclophosphamide

Taxane Dermatologic Toxicities - Alopecia

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy and radiation receiving adjuvant docetaxel and cyclophosphamide.

Which of the following statements are true regarding alopecia?

- a. Minoxidil may help in prevention of hair loss once cytotoxic chemotherapy is initiated
- b. Randomized clinical trials show 90% of patients developing grade 1 alopecia with scalp cooling versus 0% without scalp cooling
- c. Guidelines do not recommend considering scalp cooling to reduce chemotherapy-induced alopecia
- d. **Scalp cooling trials show greater efficacy with taxane-based regimens and lower efficacy when anthracyclines are combined with taxane or cyclophosphamide**

Taxane Dermatologic Toxicities - Alopecia

Depends on hair thickness and texture, and studies do not address this and enroll a low% of Black and/or non-White patients

TABLE 1. Suggestions for Black Patients With Tightly Curled Hair Undergoing Scalp Cooling

Hair Type	Preferable Hairstyles	Other Considerations
Natural hair with no chemical straightener or relaxer	Thermally straighten hair before treatment and apply hair grease to the hair only (not scalp) to keep the hair in partially straight form before lightly dampening the entire scalp with cold water. Small single twists or braids of natural hair without extensions are permissible.	Minimize curl reversion by avoiding excessive wetting of the hair and focus water on scalp as much as possible. Cornrows with and without extensions should be avoided as well as dreadlocks because of the potential for large portions of unexposed scalp under the braids.
Chemically straightened (eg, keratin, Japanese straightener) or relaxed hair	Treat hair before scalp cooling per manufacturer’s recommendations. It is permissible to wet hair before treatment. Small twists or braids without extensions are acceptable.	If the hair is only partially relaxed (eg, texturized), consider recommendations for natural hair.
Considerations for all patients (natural or chemically straightened hair)	During treatment, avoid all forms of extensions that use synthetic hair, including braids, twists, cornrows, weaves, lacefront wigs, and crochet braids.	

Taxane Dermatologic Toxicities – Nail toxicities

Onycholysis: 43.7% with paclitaxel, 32.9% with docetaxel

- Severe onycholysis almost exclusively occurs with taxanes
- Dose-related and cumulative dose related
- More common with once weekly regimen

Management

- Hold for grade 3 or higher and resume when severity is grade 1
- Consider frozen gloves and socks for taxane based therapies
- Consider topical povidone iodine 2% BID for paronychia
- Consider topical antibiotics and/or steroids for paronychia
 - Topical clobetasol solution
 - Topical clindamycin or ketoconazole
- Consider antibiotics covering *S. aureus* and gram positive bugs for onycholysis

Taxane Dermatologic Toxicities – Cutaneous Changes

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy and radiation receiving adjuvant docetaxel and cyclophosphamide.

Which of the following statements are true regarding cutaneous toxicities with taxanes? (Choose all that apply)

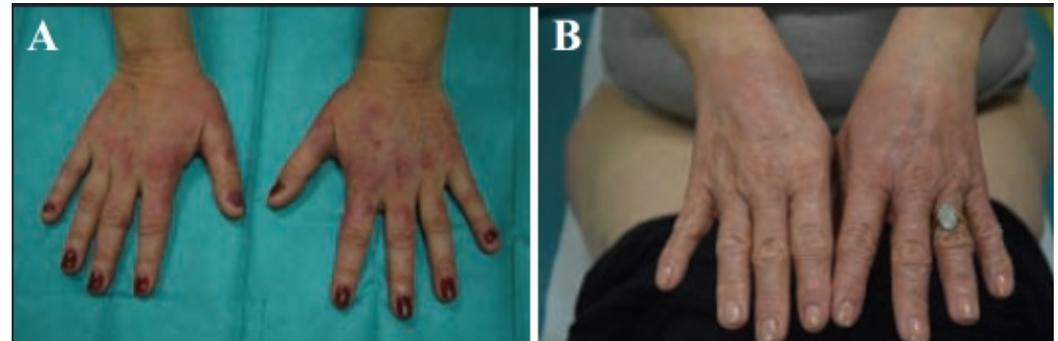
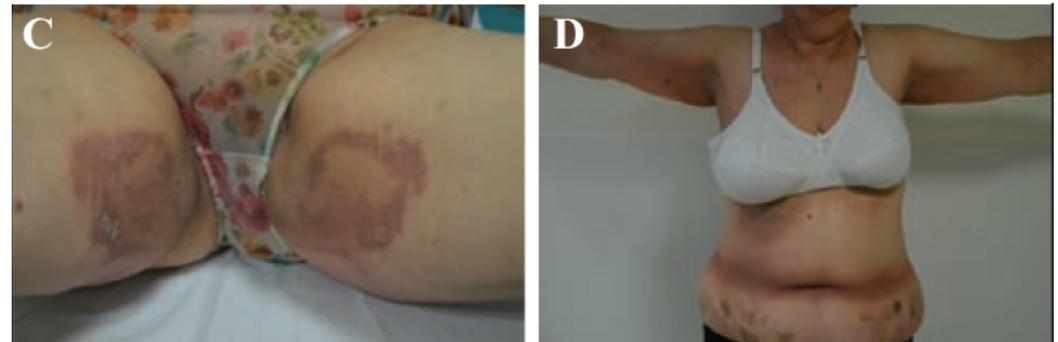
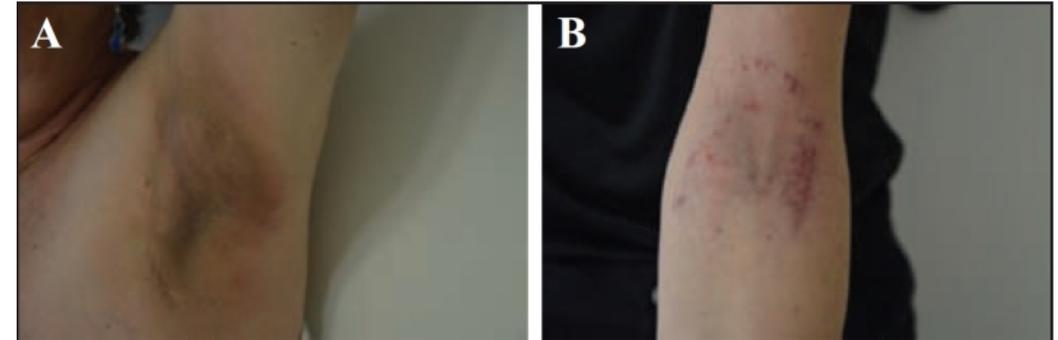
- a. Macular and papular eruptions tend to occur in flexural areas or intertriginous zones
- b. Folliculitis may occur but is not dose-limiting
- c. Palmar plantar erythrodysesthesia (hand foot syndrome) is more common docetaxel and distinctly presents on the dorsal surface
- d. There is a higher incidence of hand-foot syndrome with taxanes compared to 5-fluorouracil based therapies.

Taxane Dermatologic Toxicities – Cutaneous Changes

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy and radiation receiving adjuvant docetaxel and cyclophosphamide.

Which of the following are true regarding cutaneous toxicities with taxanes? (Choose all that apply)

- a. **Macular and papular eruptions tend to occur in flexural areas or intertriginous zones**
- b. **Folliculitis may occur but is not dose-limiting**
- c. **Palmar plantar erythrodysesthesia (hand foot syndrome) is more common docetaxel and distinctly presents on the dorsal surface**
- d. There is a higher incidence of hand-foot syndrome with taxanes compared to 5-fluorouracil based therapies.



Patient Case 2

Laboratory abnormalities with CDK 4/6 Inhibitors

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy, radiation, and adjuvant docetaxel and cyclophosphamide x4 cycles. She will be receiving adjuvant CDK 4/6 inhibitor and endocrine therapy with ribociclib and letrozole.

Ten days after initiation, her AST is 75 (2xULN) and her ALT is 195 (5.9xULN). Her Tbili is WNL. What is our next course of action?

- a. This is Grade 1 (>ULN to 3xULN) elevation, no changes necessary
- b. This is Grade 1 AST elevation and Grade 3 ALT elevation, no changes necessary.
- c. This is Grade 2 (3-5xULN), hold ribociclib until recovery to baseline and restart at the same dose
- d. This is Grade 3 (5-20xULN), hold ribociclib until recovery to baseline and resume at the next lower dose level

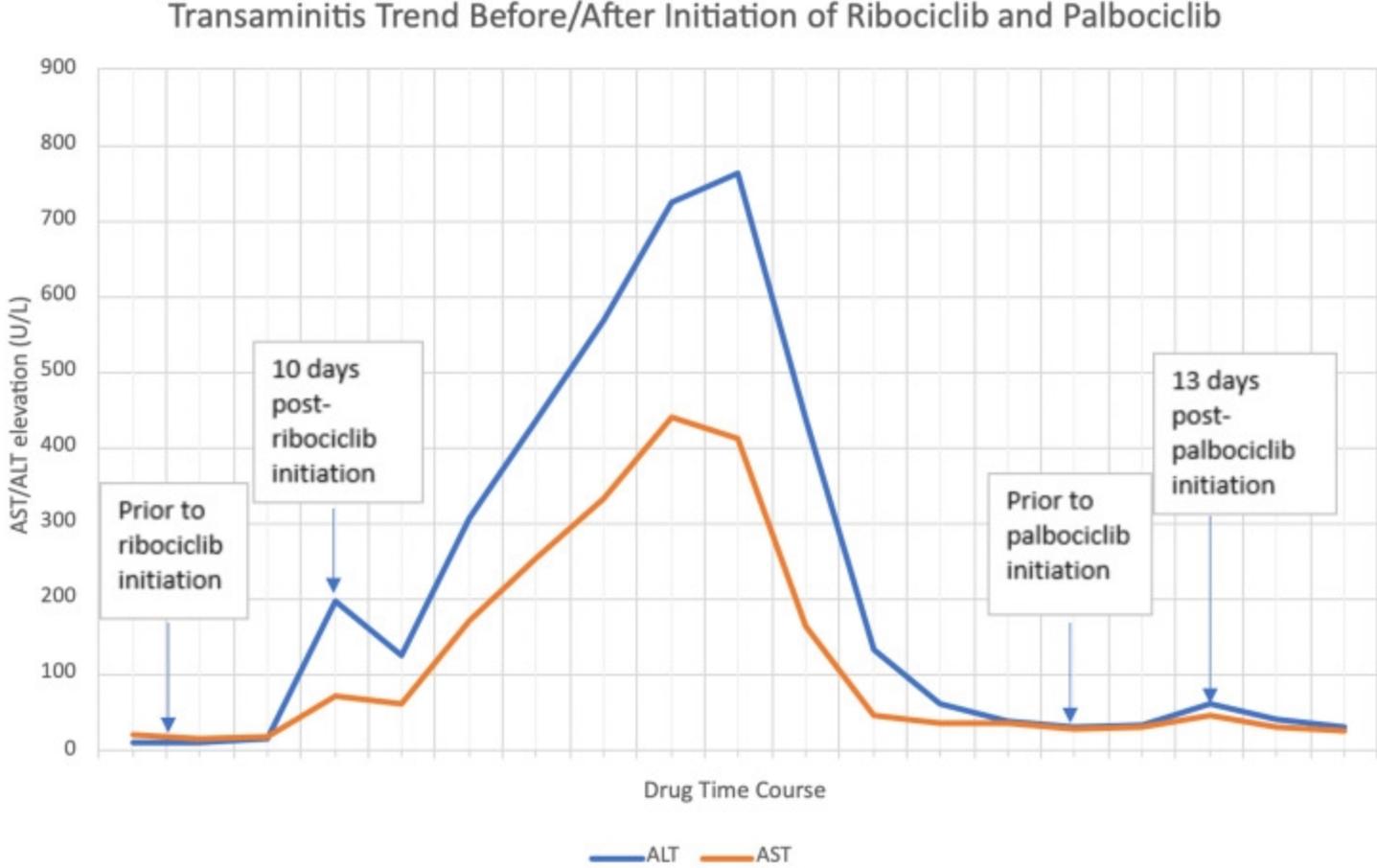
Laboratory abnormalities with CDK 4/6 Inhibitors

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy, radiation, and adjuvant docetaxel and cyclophosphamide x4 cycles. She will be receiving adjuvant CDK 4/6 inhibitor and endocrine therapy with ribociclib and letrozole.

Ten days after initiation, her AST is 75 (2xULN) and her ALT is 195 (5.9xULN). Her Tbili is WNL. What is our next course of action?

- a. This is Grade 1 (>ULN to 3xULN) elevation, no changes necessary
- b. This is Grade 1 AST elevation and Grade 3 ALT elevation, no changes necessary.
- c. This is Grade 2 (3-5xULN), hold ribociclib until recovery to baseline and restart at the same dose
- d. **This is Grade 3 (5-20xULN), hold ribociclib until recovery to baseline and resume at the next lower dose level**

LFT abnormalities



Laboratory abnormalities with CDK 4/6 Inhibitors

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy, radiation, and adjuvant docetaxel and cyclophosphamide x4 cycles. She started ribociclib and letrozole and discontinued due to hepatotoxicity. She started abemaciclib with letrozole.

Two weeks after initiation, labs show a SCr of 1.1mg/dl. Her baseline SCr is 0.8mg/dl. She denies diarrhea, fever, signs or symptoms of UTI or other infections. She is drinking 8-12 cups of water a day. Which of the following statement best represents management of serum creatinine increase?

- a. Abemaciclib is known to increase SCr, continue abemaciclib
- b. As all other causes of AKI have been ruled out, hold drug and draw a cystatin C. Resume when cystatin C results show normal GFR
- c. As all other causes of AKI have been ruled out, draw a cystatin C and continue abemaciclib.
- d. Abemaciclib is renally cleared, hold the medication until recovery to baseline

Laboratory abnormalities with CDK 4/6 Inhibitors

54 year old woman with ER+, PR-, HER2 1+ invasive ductal carcinoma with 2 positive lymph nodes s/p lumpectomy, radiation, and adjuvant docetaxel and cyclophosphamide x4 cycles. She started ribociclib and letrozole and discontinued due to hepatotoxicity. She started abemaciclib with letrozole.

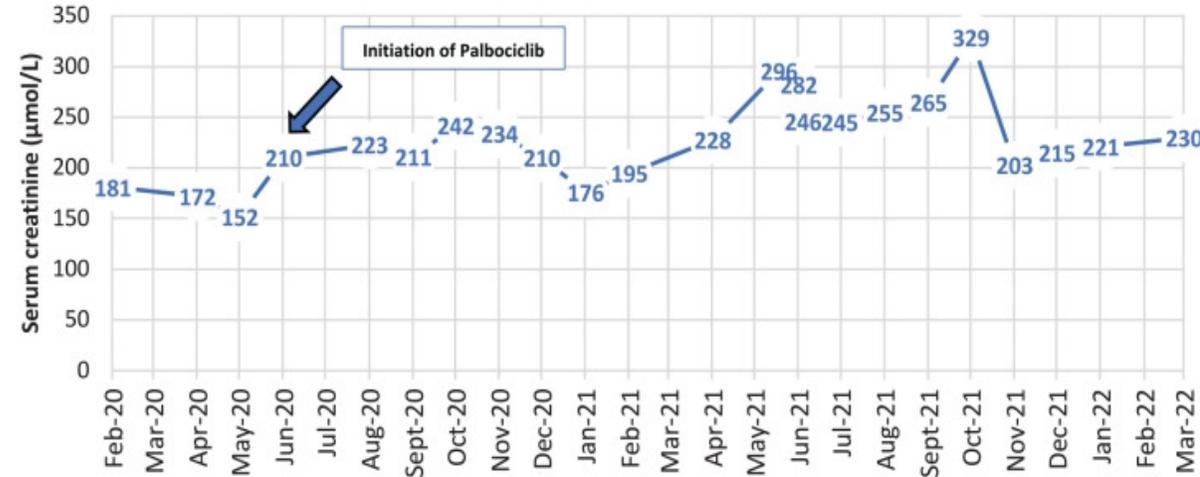
Two weeks after initiation, labs show a SCr of 1.1mg/dl. Her baseline SCr is 0.8mg/dl. She denies diarrhea, fever, signs or symptoms of UTI or other infections. She is drinking 8-12 cups of water a day. Which of the following statement best represents management of serum creatinine increase?

- a. Abemaciclib is known to increase SCr, continue abemaciclib
- b. As all other causes of AKI have been ruled out, hold drug and draw a cystatin C. Resume when cystatin C results show normal GFR
- c. As all other causes of AKI have been ruled out, draw a cystatin C and continue abemaciclib.**
- d. Abemaciclib is renally cleared, hold the medication until recovery to baseline

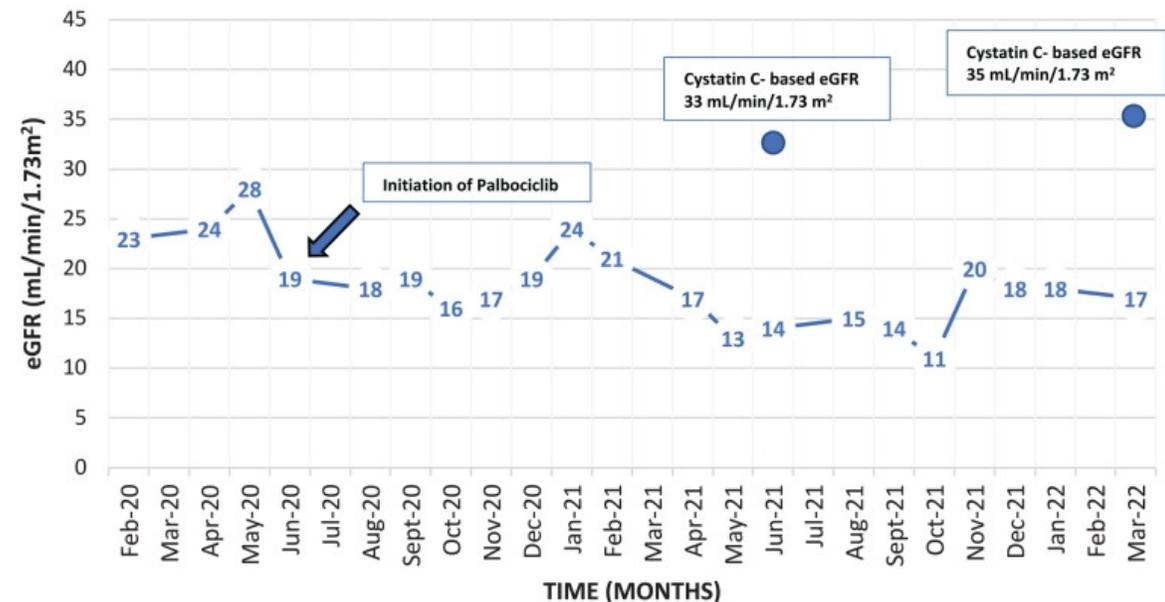
Inhibition of Renal Tubular Secretion

- Inhibition of renal transporters such as OCT-2, MATE1, MATE2-K
- False elevation of *serum* creatinine
- GFR unaffected
- Consider measuring cystatin C to estimate GFR

CHANGES IN SERUM CREATININE OVER TIME



ESTIMATED GLOMERULAR FILTRATION RATE OVER TIME



Renal transporter inhibitors

- Targeted agents that cause asymptomatic rise in SCr through inhibition of active tubular secretion
 - CDK 4/6 inhibitors: palbociclib, ribociclib, abemaciclib
 - PARP inhibitors: Olaparib, rucaparib, niraparib
 - ALK inhibitors: crizotinib, alectinib, ceritinib
 - BCR-ABL inhibitors: imatinib
 - EGFR inhibitors: gefitinib
 - VEGFR inhibitors: pazopanib, sunitinib, sorafenib
 - HER2 inhibitors: tucatinib
 - MET inhibitors: capmatinib
 - ROS-1: talectrectinib

Patient Case 3

Overlapping Adverse Effects: mAbs + ICIs

BB is a 79 year old man with a new diagnosis of right upper tract urothelial carcinoma with metastases to the L acetabulum. He will be initiating therapy with enfortumab vedotin and pembrolizumab along with zoledronic acid to reduce the risk for bone fractures.

Two weeks after initiation, patient's non-fasting blood glucose was 268mg/dl. His last random blood glucose was 87mg/dl with no history of diabetes or hyperglycemia. Which statement best represents the next course of action?

- a. Hold pembrolizumab and enfortumab vedotin
- b. Continue pembrolizumab and hold enfortumab vedotin
- c. Hold pembrolizumab and continue enfortumab vedotin
- d. Continue both pembrolizumab and enfortumab vedotin

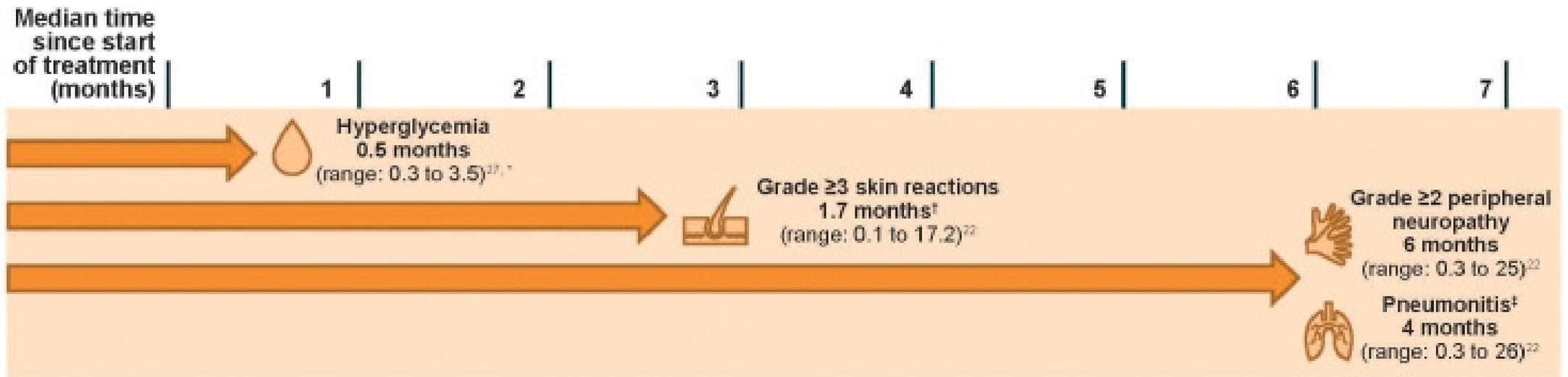
Overlapping Adverse Effects: mAbs + ICIs

BB is a 79 year old man with a new diagnosis of right upper tract urothelial carcinoma with metastases to the L acetabulum. He will be initiating therapy with enfortumab vedotin and pembrolizumab along with zoledronic acid to reduce the risk for bone fractures.

Two weeks after initiation, patient's non-fasting blood glucose was 268mg/dl. His last random blood glucose was 87mg/dl with no history of diabetes or hyperglycemia. Which statement best represents the next course of action?

- a. Hold pembrolizumab and enfortumab vedotin
- b. Continue pembrolizumab and hold enfortumab vedotin**
- c. Hold pembrolizumab and continue enfortumab vedotin
- d. Continue both pembrolizumab and enfortumab vedotin

Timeline of Overlapping Adverse Effects



Overlapping Adverse Effects

Enfortumab vedotin

- Hyperglycemia
- Peripheral neuropathy
- Ocular disorders

Combination

- Skin reactions
- Pneumonitis

Pembrolizumab

- Other IRAE

Management of Overlapping Adverse Effects

Grade 1

- Monitor
- Symptom management

Grade 2

- Symptom management with close monitoring and consider escalating supportive care
- Consider holding likely offending agent (EV for hyperglycemia, peripheral neuropathy)
- Consider specialist consult
- Hold both agents for severe adverse effects (pneumonitis)

Grade 3

- Hold both agents, reintroduce one agent at a time with symptom resolution
- Consider dose reduction for EV
- Ensure appropriate supportive care for steroid tapers >1 month
- Consider specialist consult

Antibody-drug Conjugates – Ocular Toxicities

	AE	Baseline eye exam	Regular eye exam	Steroid eye drops	Vasoconstrictor eye drops	Lubricating eye drops	Cooling eyedrops	Avoid packs to eyes	FDA REMS
Trastuzumab emtansine	Blurred vision, conjunctivitis, dry eye, lacrimation								
Belantamab mafodotin	Severe vision loss, corneal ulcer, blurred vision, dry eyes	x				x		x	x
Enfortumab vedotin	Keratitis, blurred vision, dry eye								
Tisotumab vedotin	Severe vision loss, corneal ulceration	x	x	x	x	x	x	x	
Mirvetuximab soravtansine	Visual impairment, keratopathy, dry eye, photophobia, eye pain, uveitis	x	x	x		x		x	
Telisotuzumab vedotin	Blurred vision, visual impairment, keratitis, dry eye								
Datopotamab deruxtecan	Dry eye, keratitis, blepharitis, blurred vision, lacrimation, conjunctivitis	x				x		x	

Patient Case 4

Overlapping Adverse Effects – Chemo and TKIs

SR is a 55 year old man with adenocarcinoma of the sigmoid colon with metastases to the liver. The molecular profile reveals an ERBB2 copy number gain, MSS, and TMB 5.3 mutations/mb. He has received FOLFOX with bevacizumab, CapeOx, and FOLFIRI in the past. He last received FOLFIRI 2 months ago with progression on this regimen. He has residual debilitating neuropathy from oxaliplatin. SR will be starting tucatinib + trastuzumab.

SR reports feeling nervous about the adverse effect profile of the capecitabine he received in the past and the tucatinib, based on the patient education handouts he has read. Which of the following are reported overlapping adverse effects of capecitabine and tucatinib?

- a. Cardiotoxicity
- b. Hand-foot syndrome
- c. Diarrhea
- d. Transaminitis
- e. All of the above

Overlapping Adverse Effects – Chemo and TKIs

SR is a 55 year old man with adenocarcinoma of the sigmoid colon with metastases to the liver. The molecular profile reveals an ERBB2 copy number gain, MSS, and TMB 5.3 mutations/mb. He has received FOLFOX with bevacizumab, CapeOx, and FOLFIRI in the past. He last received FOLFIRI 2 months ago with progression on this regimen. He has residual debilitating neuropathy from oxaliplatin. SR will be starting tucatinib + trastuzumab.

SR reports feeling nervous about the adverse effect profile of the capecitabine he received in the past and the tucatinib, based on the patient education handouts he has read. Which of the following are reported overlapping adverse effects of capecitabine and tucatinib?

- a. Cardiotoxicity
- b. Hand-foot syndrome
- c. Diarrhea
- d. Transaminitis
- e. **All of the above**

Hand-foot Syndrome

Druga	Incidence of HFS	Incidence of severe HFS
Capecitabine	50-60%	10-17%
Cytarabine	14-33%	-
Docetaxel	6-37%	0-4%
Doxorubicin	22-26%	-
5FU CIV	35%	7%
Pegylated liposomal doxorubicin	40-50%	20%
Sorafenib	48%	17%
Sunitinib	34%	30%



Overlapping Adverse Effects – Chemo and TKIs

What preventative measures do you routinely recommended for prevention of hand-foot syndrome?

- a. None
- b. Topical urea
- c. Oral celecoxib
- d. Topical diclofenac
- e. Emollient creams

Hand-foot Syndrome

- 5FU: accumulation and breakdown of the chemotherapy in hands and feet
- PLD: hydrophilic liposomes cause drug accumulation in the eccrine ducts
- Symptoms: redness or hyperpigmentation, discomfort, swelling, tingling in palms and soles

Urea-based creams

- Randomized, phase III trial of patients with GI or breast cancer on capecitabine, n=152
- Mapisal cream TID (antioxidant) vs urea 10% cream TID for 6 weeks
- Use of urea cream decreased all grade HFS (22.4% vs 39.5%, OR 2.37, p=0.02) compared to mapisal cream
- Time to any-grade HFS longer with the urea group, p=0.03
- Time to grade >2 HFS no different between groups
- No control only group
- Commercially available over-the-counter (OTC) at 5-40%

Diclofenac

- Single site phase III randomized, placebo controlled, double-blind trial in breast and GI cancer patients on capecitabine (monotherapy or combo), n=264
- Topical diclofenac 1g to each hand BID vs placebo for 12 weeks or development of HFS
- Incidence of grade 2-3 HFS 3.8% vs 15% favoring diclofenac group, p=0.003
- Grade 1-3 HFS 6.1% vs 18.1% favoring diclofenac
- Less capecitabine dose reductions with diclofenac 3.8% vs 13.5%
- Available OTC

Cardiotoxicity

Fluoropyrimidines

- Angina
- Ischemia-related ECG changes
- Takotsubo syndrome
- Coronary vasospasm
- Myocardial infarction
- Baseline ECHO recommended for patients with history of CV disease

HER2 targeting agents

- Left ventricular dysfunction
- Baseline ECHO recommended in all patients

Patient Case 5

Overlapping Adverse Effects: TKIs and ICIs

AW is a 60 year old man newly diagnosed with metastatic clear cell renal cell carcinoma. He underwent a partial nephrectomy of the right kidney 2 years ago. He presents one year ago with a palpable mass on the abdomen and biopsy pathology was consistent with papillary renal cell carcinoma. He is starting therapy with lenvatinib and pembrolizumab.

Three weeks after starting lenvatinib and pembrolizumab, the patient reports 6 stools in the past 24 hours despite taking loperamide 4mg four times a day. This is increased from a baseline of 1 bowel movement daily. He is eating and hydrating adequately. Denies fever or blood in stool, labs WNL. What adjustment would you make to his regimen?

- a. Hold pembrolizumab and lenvatinib
- b. Hold lenvatinib
- c. Hold pembrolizumab
- d. Continue both agents

Overlapping Adverse Effects: TKIs and ICIs

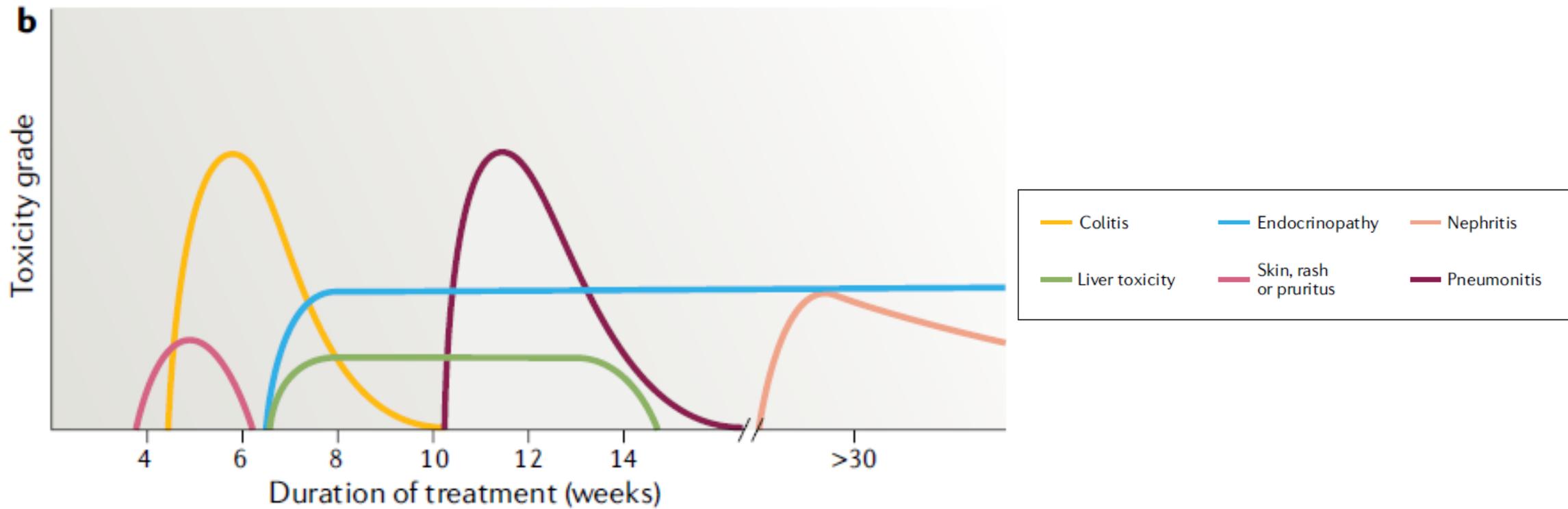
AW is a 60 year old man newly diagnosed with metastatic clear cell renal cell carcinoma. He underwent a partial nephrectomy of the right kidney 2 years ago. He presents one year ago with a palpable mass on the abdomen and biopsy pathology was consistent with papillary renal cell carcinoma. He is starting therapy with lenvatinib and pembrolizumab.

Three weeks after starting lenvatinib and pembrolizumab, the patient reports 6 stools in the past 24 hours despite taking loperamide 4mg four times a day. This is increased from a baseline of 1 bowel movement daily. He is eating and hydrating adequately. Denies fever or blood in stool, labs WNL. What adjustment would you make to his regimen?

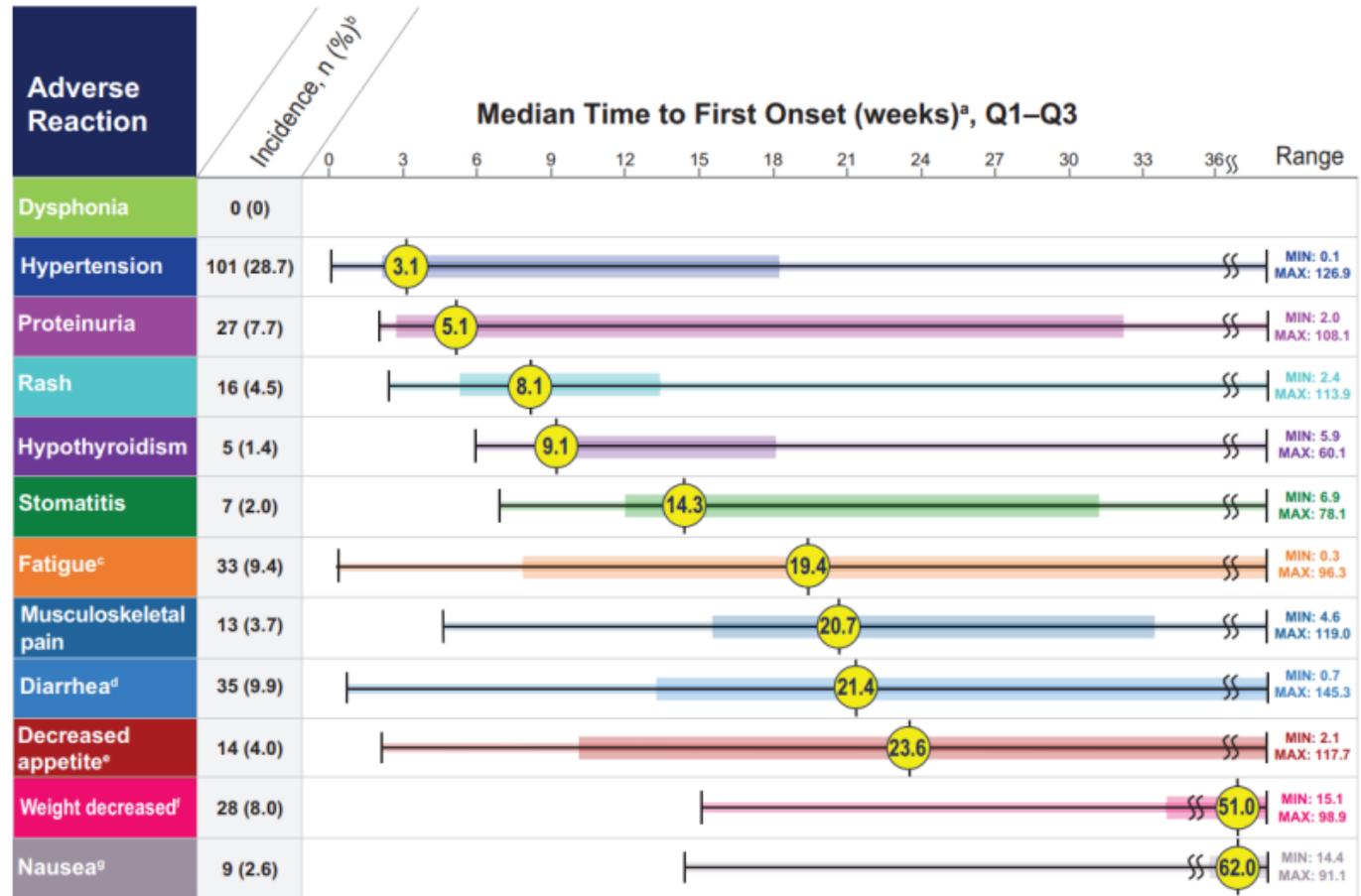
- a. **Hold pembrolizumab and lenvatinib**
- b. **Hold lenvatinib**
- c. Hold pembrolizumab
- d. Continue both agents

Single Agent Pembrolizumab

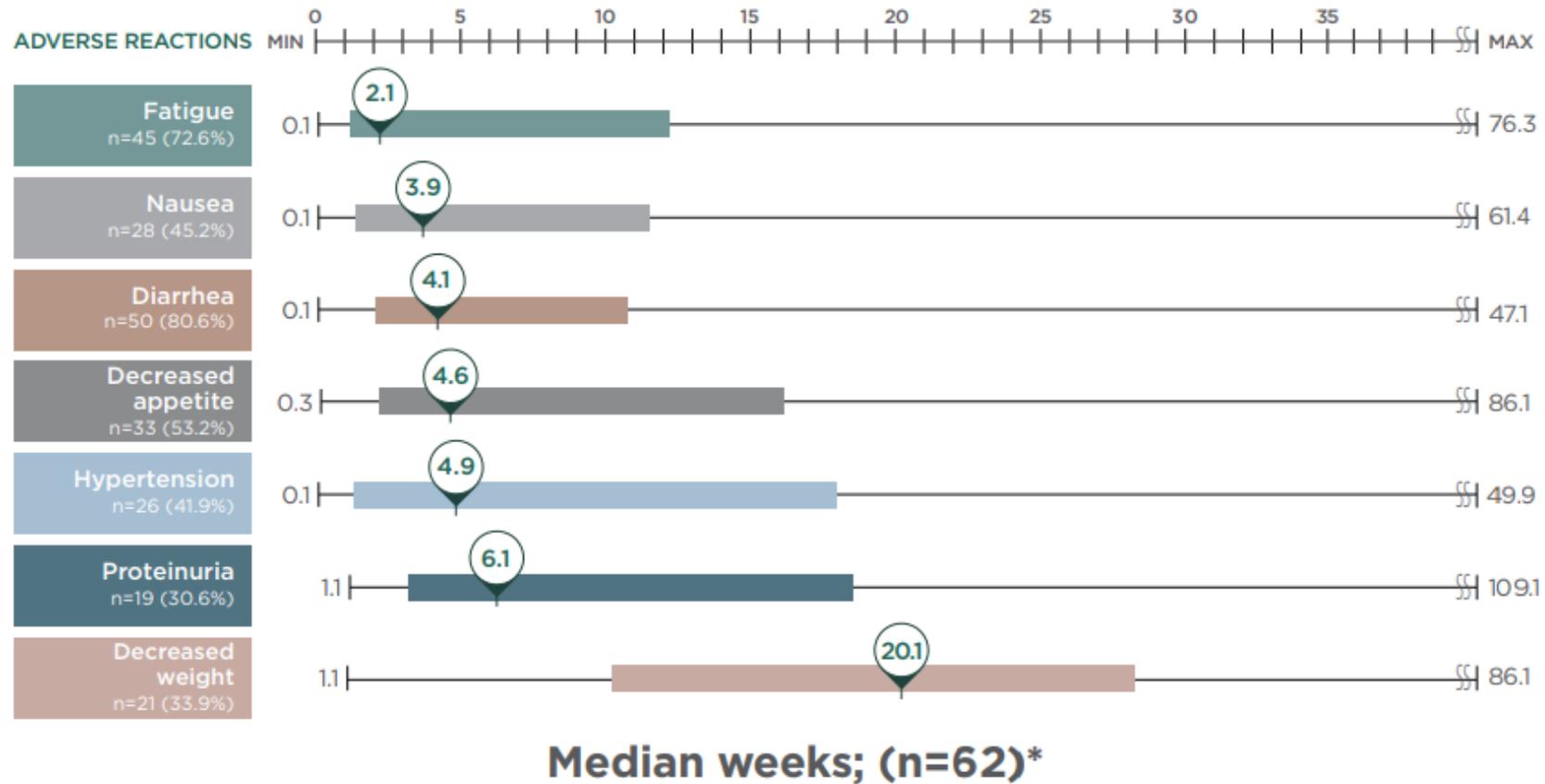
Onset of select IRAEs with PD-1/PD-L1 Inhibitor



Oral TKI and ICI: Lenvatinib + Pembrolizumab



Single Agent Lenvatinib



Skin Reactions

HFSR with multikinase inhibitors

- Focal, well-demarcated hyperkeratosis
- Sites prone to trauma/friction
- 10% urea based cream TID

IRAE rash with ICI

- Maculopapular
- Pruritic
- Topical and PO steroids



Patient Case 6

Supportive Care with EGFR Inhibitors

BT is a 62 year old women with metastatic EGFR L858R adenocarcinoma of the right lung with metastases to the ribs, sacrum, and brain. She was on osimertinib for the past 8 months. She develop osimertinib related pneumonitis and stopped osimertinib. Her most recent imaging shows a new concern for leptomenigeal disease. She will be starting amivantamab and lazertinib.

What supportive care should be recommended for BT (select all that apply)?

- a. Apixaban 2.5mg BID for four months
- b. Enoxaparin 1mg/kg daily for four months
- c. Oral doxycycline 100mg BID
- d. Topical emollient creams and limiting sun exposure

Supportive Care with EGFR Inhibitors

BT is a 62 year old women with metastatic EGFR L858R adenocarcinoma of the right lung with metastases to the ribs, sacrum, and brain. She was on osimertinib for the past 8 months. She develop osimertinib related pneumonitis and stopped osimertinib. Her most recent imaging shows a new concern for leptomenigeal disease. She will be starting amivantamab and lazertinib.

What supportive care should be recommended for BT (select all that apply)?

- a. Apixaban 2.5mg BID for four months**
- b. Enoxaparin 1mg/kg daily for four months
- c. Oral doxycycline 100mg BID**
- d. Topical emollient creams and limiting sun exposure**

Dermatologic Toxicities – Acneiform Rash Prevention

- Wash with lukewarm water
- Use perfume –free moisturizing creams and lotions
- Use sunscreen SPF ≥ 25 and wear sun protective clothing
- Consider oral antibiotic prophylaxis with doxycycline 100-200mg/day or minocycline 100mg/day for 6-8 weeks

- Avoid:
 - Blow drying hair
 - Shaving
 - Skin manipulations
 - Direct sun exposure
 - Contacts with solvents, cleaning agents, detergents, etc

Dermatologic Toxicities – Acneiform Rash

Severity	Intervention
Grade 1-2 (10-30% BSA, limiting instrumental ADLs)	<ul style="list-style-type: none"> • Continue drug at current dose • Oral antibiotic for at least 6 weeks and topical low/moderate steroid • Reassess in two weeks
Grade ≥ 3 (>30% BSA, limiting self-care ADLs, associated with local superinfection)	<ul style="list-style-type: none"> • Interrupt until Grade 0-1 • Continue or initiate oral antibiotic and topical low/moderate steroid • Continue or initiate systemic steroids (prednisone 0.5-1mg/kg for 7 days) • Consider isotretinoin at low doses (20-30mg/day) • Reassess in two weeks

- Most common with EGFR inhibitors and agents that affects EGFR pathway
 - IV: cetuximab, pertuzumab, panitumumab
 - Oral: afatinib, gefitinib, osimertinib, erlotinib, dacomitinib, neratinib, sunvozertinib
 - IV/Oral: amivantamab + lazertinib



Patient Case 7

Combination chemotherapy: Cisplatin + paclitaxel + bevacizumab + pembrolizumab

ML is a 60 year old woman with adenocarcinoma of the cervix extending to the uterus and upper vagina with abutment of the rectosigmoid junction. Her PET scan showed avid right external iliac nodal metastasis as well as hypermetabolic nodules in the lung. She initiated cisplatin + paclitaxel + bevacizumab + pembrolizumab.

ML tolerates Cycle 1 of chemotherapy well. She presents for Cycle 2 and receives pembrolizumab, bevacizumab, and paclitaxel. Right as her infusion of cisplatin starts, she has low back pain, flushing, and itching. It resolved with diphenhydramine. Which of the following statements best represents hypersensitivity reactions with this regimen?

- a. This is likely a paclitaxel reaction. Continue premedications and consider increasing diphenhydramine dose or a rate titration with next infusion.
- b. This is likely a cisplatin reaction. Reactions to platinum compounds are most common with cisplatin in the 1st or 2nd infusion.
- c. As she's received pembrolizumab, bevacizumab, and paclitaxel, it could be either of the three agents. Rate titrate all three agents for subsequent infusions.
- d. This is likely a cisplatin reaction. She will require cisplatin desensitization for future cycles.

Combination chemotherapy: Cisplatin + paclitaxel + bevacizumab + pembrolizumab

ML tolerates Cycle 1 of chemotherapy well. She presents for Cycle 2 and receives pembrolizumab, bevacizumab, and paclitaxel. Right as her infusion of cisplatin starts, she has low back pain, flushing, and itching. It resolved with diphenhydramine. Which of the following statements best represents hypersensitivity reactions with this regimen?

- a. **This is likely a paclitaxel reaction. Continue premedications and consider increasing diphenhydramine dose or a rate titration with next infusion.**
- b. This is likely a cisplatin reaction. Reactions to platinum compounds are most common with cisplatin in the 1st or 2nd infusion.
- c. As she's received pembrolizumab, bevacizumab, and paclitaxel, it could be either of the three agents. Rate titrate all three agents for subsequent infusions.
- d. This is likely a cisplatin reaction. She will require cisplatin desensitization for future cycles.

-Paclitaxel reactions are most likely to occur during the first or second infusion and are due to the cremaphor diluent.
-Taxane hypersensitivity reactions can be managed with slowing the rate of infusion and additional premedications.
-Of the platinum compounds, reactions are most common with carboplatin and this is most common during cycles 6 – 8 of carboplatin. These can be managed with desensitization with future cycles.
-Infusion reactions are rare with pembrolizumab and bevacizumab.

Combination chemotherapy: Cisplatin + paclitaxel + bevacizumab + pembrolizumab

ML is a 60 year old woman with adenocarcinoma of the cervix extending to the uterus and upper vagina with abutment of the rectosigmoid junction. Her PET scan showed avid right external iliac nodal metastasis as well as hypermetabolic nodules in the lung. She initiated cisplatin + paclitaxel + bevacizumab + pembrolizumab.

ML arrives for Cycle 3 of this regimen. Her blood pressure in clinic is 165/90 and she does not know what her home blood pressure is. She is not on any anti-hypertensives. Her BP prior to starting chemotherapy was 130s/80s.

Which of the following is an appropriate strategy to manage bevacizumab induced hypertension?

- a. Start amlodipine 10mg daily. Hold bevacizumab infusion today
- b. Start lisinopril 20mg. Hold bevacizumab infusion today.
- c. Continue bevacizumab infusion, start amlodipine 5-10mg daily.
- d. Continue bevacizumab infusion, have patient start monitoring home blood pressure.

Combination chemotherapy: Cisplatin + paclitaxel + bevacizumab + pembrolizumab

ML is a 60 year old woman with adenocarcinoma of the cervix extending to the uterus and upper vagina with abutment of the rectosigmoid junction. Her PET scan showed avid right external iliac nodal metastasis as well as hypermetabolic nodules in the lung. She initiated cisplatin + paclitaxel + bevacizumab + pembrolizumab.

ML arrives for Cycle 3 of this regimen. Her blood pressure in clinic is 165/90 and she does not know what her home blood pressure is. She is not on any anti-hypertensives. Her BP prior to starting chemotherapy was 130s/80s.

Which of the following is an appropriate strategy to manage bevacizumab induced hypertension?

- a. Start amlodipine 5mg daily. Hold bevacizumab infusion today**
- b. Start lisinopril 10mg. Hold bevacizumab infusion today.**
- c. Continue bevacizumab infusion, start amlodipine 5mg daily.**
- d. Continue bevacizumab infusion, have patient start monitoring home blood pressure.**

All of the above can be options. Consider:

- Availability of at-home blood pressure monitoring
- Concomitant nephrotoxicity with cisplatin
- Concerns with medication adherence
- Disease control

Combination chemotherapy: Cisplatin + paclitaxel + bevacizumab + pembrolizumab

ML is a 60 year old woman with adenocarcinoma of the cervix extending to the uterus and upper vagina with abutment of the rectosigmoid junction. Her PET scan showed avid right external iliac nodal metastasis as well as hypermetabolic nodules in the lung. She initiated cisplatin + paclitaxel + bevacizumab + pembrolizumab.

Which of the following are guideline-based recommendations for treatment or prevention of chemotherapy induced peripheral neuropathy? (Select all that apply)

- a. There are no pharmacologic agents recommended for the prevention of CIPN
- b. Duloxetine may be recommended for treatment of CIPN, starting at 30mg daily for a week, then 60mg daily.
- c. Cryotherapy to the hands and feet may be considered to decrease the risk for neuropathy
- d. Vitamin B12, glutamine, and folic acid may be used to decrease the risk for neuropathy.

Combination chemotherapy: Cisplatin + paclitaxel + bevacizumab + pembrolizumab

ML is a 60 year old woman with adenocarcinoma of the cervix extending to the uterus and upper vagina with abutment of the rectosigmoid junction. Her PET scan showed avid right external iliac nodal metastasis as well as hypermetabolic nodules in the lung. She initiated cisplatin + paclitaxel + bevacizumab + pembrolizumab.

Which of the following are guideline-based recommendations for treatment or prevention of chemotherapy induced peripheral neuropathy? (Select all that apply)

- a. **There are no pharmacologic agents recommended for the prevention of CIPN**
- b. **Duloxetine may be recommended for treatment of CIPN, starting at 30mg daily for a week, then 60mg daily.**
- c. **Cryotherapy to the hands and feet may be considered to decrease the risk for neuropathy**
- d. Vitamin B12, glutamine, and folic acid may be used to decrease the risk for neuropathy.

- Cumulative dose effect with platinums and taxanes
- Primary sensory neuropathy with stocking-glove distribution with taxanes (primarily paclitaxel) and platinums (primarily oxaliplatin and cisplatin).
- Paclitaxel neuropathy tends to improve over months after cessation of therapy
- Oxaliplatin neuropathy tends to worsen over 2-3 months after cessation of therapy, then improves.

Patient Case 8

Trastuzumab deruxtecan

AK is a 66 year old woman with Stage IIIC2 high grade uterine carcinoma. She has received neoadjuvant carboplatin + paclitaxel one year ago, followed by debulking surgery with pathology revealing p53 overexpression, HER2 1+ by IHC, FOLR1 30% by IHC (negative), and MSS and TMB-L. She started pembrolizumab + levnatinib with progression after 7 cycles. She is now starting trastuzumab deruxtecan.

After 4 cycles, AK reports new shortness of breath and cough. Imaging reveals pneumonitis. Which of the following statements best represents management of trastuzumab deruxtecan related ILD?

- a. Hold trastuzumab deruxtecan, initiate prednisone 1mg/kg until symptom resolution, then taper. Rechallenge with trastuzumab deruxtecan is contraindicated.
- b. Continue trastuzumab deruxtecan, initiate prednisone 1mg/kg until symptom resolution, then taper. Rechallenge with trastuzumab deruxtecan is contraindicated.
- c. Hold trastuzumab deruxtecan, initiate prednisone 1mg/kg until symptom resolution, then taper. Consider rechallenge with shared, multidisciplinary decision making.
- d. Continue trastuzumab deruxtecan, initiate prednisone 1mg/kg until symptom resolution, then taper. Rechallenge with trastuzumab deruxtecan is contraindicated.

Trastuzumab deruxtecan

AK is a 66 year old woman with Stage IIIC2 high grade uterine carcinoma. She has received neoadjuvant carboplatin + paclitaxel one year ago, followed by debulking surgery with pathology revealing p53 overexpression, HER2 1+ by IHC, FOLR1 30% by IHC (negative), and MSS and TMB-L. She started pembrolizumab + levnatinib with progression after 7 cycles. She is now starting trastuzumab deruxtecan.

After 4 cycles, AK reports new shortness of breath and cough. Imaging reveals pneumonitis. Which of the following statements best represents management of trastuzumab deruxtecan related ILD?

- a. **Hold trastuzumab deruxtecan, initiate prednisone 1mg/kg or higher until symptom resolution, then taper. Rechallenge with trastuzumab deruxtecan is contraindicated.**
- b. Continue trastuzumab deruxtecan, initiate prednisone 0.5mg/kg or higher until symptom resolution, then taper. Rechallenge with trastuzumab deruxtecan is contraindicated.
- c. **Hold trastuzumab deruxtecan, initiate prednisone 1mg/kg or higher until symptom resolution, then taper. Consider rechallenge with shared, multidisciplinary decision making.**
- d. Continue trastuzumab deruxtecan, initiate prednisone 0.5mg/kg or higher until symptom resolution, then taper. Rechallenge with trastuzumab deruxtecan is contraindicated.

Trastuzumab deruxtecan Interstitial Lung Disease

- ILD in 12% of patients with breast cancer and NSCLC, median onset 5.5 months
- ILD in 10% of patients with gastric cancer, median onset 2.8 months
- Higher incidence of ILD in patients with renal dysfunction
- Package insert recommends permanent discontinuation for grade 2 or higher ILD

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4
Pneumonitis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; medical intervention indicated; limiting instrumental ADL	Severe symptoms; limiting self care ADL; oxygen indicated	Life-threatening respiratory compromise; urgent intervention indicated (e.g., tracheotomy or intubation)
Definition: A disorder characterized by inflammation focally or diffusely affecting the lung parenchyma. Navigational Note: -				

Cardiotoxicity

Trastuzumab

- Baseline, every 3 months during treatment,
- May reduced to every 4-6 months if asymptomatic*

Pertuzumab

- Baseline, every 3 months during treatment in the metastatic setting
- Baseline, every 6 months in the neoadjuvant setting

Margetuximab

- Baseline, every 3 months during treatment

Trastuzumab emtansine

- Baseline, every 3 months during treatment

Trastuzumab deruxtecan

- Baseline, at regular intervals during treatment and as clinically indicated

Tucatinib, lapatinib, neratinib, zongertinib

- No recommendations for tucatinib or neratinib
- Baseline and during treatment for lapatinib, zongertinib

Patient Case 9

Datopotamab deruxtecan

AK is a 66 year old woman with metastatic EGFR mutated NSCLC who has received osimertinib and platinum based chemotherapy in the past. She will be starting datopotamab deruxtecan.

Which of the following statements best represents prophylaxis strategies for the management of adverse effects with dato-Dxd?

- a. Use preservative free lubricating eyedrops four times a day and avoid contact lenses while on treatment.
- b. Antihistamine, acetaminophen, and ondansetron prior to infusion.
- c. Use dexamethasone mouthwash four times a day when starting treatment and hold ice chips or ice water in the mouth during infusion
- d. All of the above

Datopotamab deruxtecan

AK is a 66 year old woman with metastatic EGFR mutated NSCLC who has received osimertinib and platinum based chemotherapy in the past. She will be starting datopotamab deruxtecan.

Which of the following statements best represents prophylaxis strategies for the management of adverse effects with dato-Dxd?

- a. Use preservative free lubricating eyedrops four times a day and avoid contact lenses while on treatment.
- b. Antihistamine, acetaminophen, and ondansetron prior to infusion.
- c. Use dexamethasone mouthwash four times a day when starting treatment and hold ice chips or ice water in the mouth during infusion
- d. All of the above**

Mucositis/Stomatitis Prophylaxis

- Generally not well distinguished
 - Mucositis = due to chemo or radiation (5FU, methotrexate, etoposide)
 - Stomatitis = due to targeted and immunotherapy agents (mTORi, EGFRi, multikinase inhibitors)
- Patients with mucositis have 2x risk for infection, 4x risk of death, and is associated with financial toxicity
- SWISH Trial: phase II, single-arm prevention trial
 - Enrolled postmenopausal women with hormone receptor positive, HER2 negative breast cancer on everolimus and exemestane, n=92
 - Treatment: 10ml dexamethasone 0.5mg/ml solution to swish for 2 min and spit, four times daily for 8 weeks
 - Results: compared to historical cohort in BOLERO-2 trial
 - Incidence of grade >2 stomatitis was 2% with dex vs 33% historically

Mucositis/Stomatitis Prophylaxis

- Baseline oral exam, dentist exam and treatment as needed for high risk patients
- Non-pharmacologic prevention: brush with soft toothbrush, floss, rinse with bland solutions
- Pharmacologic prevention with certain agents: dexamethasone rinse 0.5mg/5ml s/s QID

Subtype	Treatment suggestions
Limited and easily accessed ulcers	Topical steroids, topical NSAIDs, adhesive bases if needed
Widespread or difficult to access ulcers	Topical steroids
Highly symptomatic, recurrent, or esophageal ulcers	Systemic steroids 1mg/kg x1 week, taper over second week

- When using mouth rinses:





Thank you

UW Medicine