Special considerations for chemotherapy: Organ dysfuntion or other medical statuses

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DECLARATION OF INTERESTS

I have no conflicts of interest to disclose

Why organ dysfunction matters

- Aging population → more CKD, CLD, cardiovascular disease
- More lines of systemic therapy and combination regimens
- Widespread use of nephrotoxic and hepatotoxic agents
- Need to balance efficacy, safety, and QoL

Objectives

Focused on gyn-oncology realities…

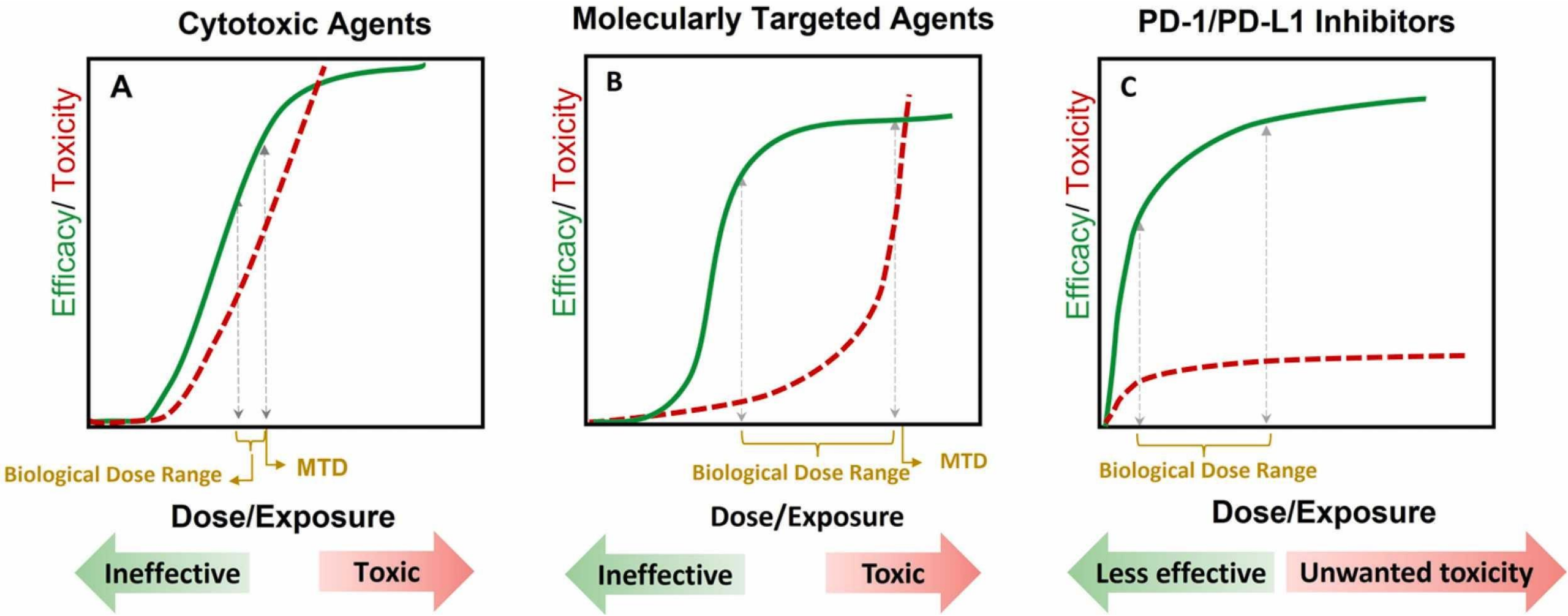
1. Renal: CKD, AKI, ESRD on intermittent hemodialysis

2. Hepatic: cholestasis, cirrhosis (Child-Pugh), tumor-related dysfunction

3. Cardiac: anthracyclines/anti-HER2, VEGF-TKI hypertension, QTc issues, ICI myocarditis

4. New agents: tisotumab vedotin & mirvetuximab-associated ocular toxicities

Exposure-Efficacy and Safety Relationships for CTAs, MTAs, PD/PD-L1 Inhibitors.



Critical Reviews in Oncology / Hematology 182 (2023) 103913

Drug Label Information; FDA vs. MFDS

NATIONAL LIBRARY OF MEDICINE | REPORT ADVERSE EVENTS | RECALLS

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Enter drug, NDC code, drug class, or Set ID

LABEL: ENHERTU

VIEW PACKAGE PHOTOS

SAFETY

- Boxed Warnings
- Report Adverse Ev
- FDA Safety Recalls
- Presence in Breast

ENHERTU- fam-trastuzumab deruxtecan-nxki injection, powder, lyophilized, for solution
Daiichi Sankyo Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ENHERTU safely and effectively. See full prescribing information for ENHERTU.

ENHERTU® (fam-trastuzumab deruxtecan-nxki) for injection, for intravenous use
Initial U.S. Approval: 2019

WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY

See full prescribing information for complete boxed warning.

- **Interstitial lung disease (ILD) and pneumonitis, including fatal cases, have been reported with ENHERTU. Monitor for and promptly investigate signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Permanently discontinue ENHERTU in all patients with Grade 2 or higher ILD/pneumonitis. Advise patients of the risk and to immediately report symptoms. (2.3, 5.1)**
- **Exposure to ENHERTU during pregnancy can cause embryo-fetal harm. Advise patients of these risks and the need for effective contraception. (5.4, 8.1, 8.3)**

RECENT MAJOR CHANGES

Indications and Usage (1.1)	12/2025
Indications and Usage (1.2)	01/2025
Dosage and Administration (2.1, 2.2, 2.3)	12/2025
Dosage and Administration (2.1, 2.2)	01/2025
Warnings and Precautions (5.1, 5.2, 5.3)	12/2025
Warnings and Precautions (5.1, 5.2, 5.3)	01/2025

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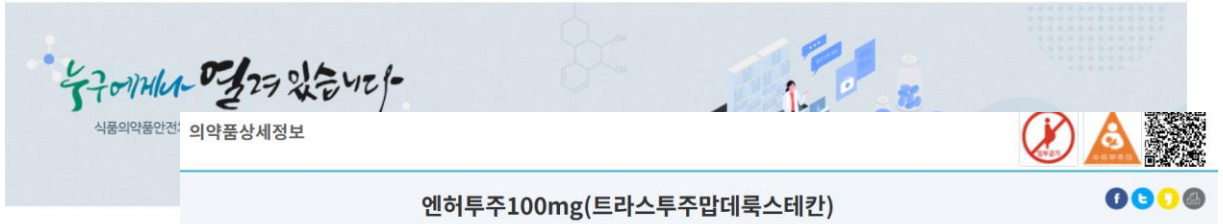
의약품안전나라 의약품통합정보시스템

전자민원/보고 | 의약품등 정보 | 고시/공고/알림 | 안전사용정보 | 공공데이터 정보 | 사용자별서비스

검색어로 메뉴·정보 검색



의약품상세정보

엔허투주100mg(트라스투주맙데룩스테칸)

DUR품목 검색

총 1 건

순번	
1	엔허투주100mg 룩스테칸)

기본정보

제품명	엔허투주100mg(트라스투주맙데룩스테칸)
성상	흰색 내지 미황색의 동결 건조물이 황색의 투명한 유리 바이알에 충전된 주사제로, 주사용수에 용해 후 투명하고 무색 내지 엷은 황색의 용액이다.
업체명	한국다이이찌산쿄(주)
위탁제조업체	Baxter Oncology GmbH, Boehringer Ingelheim Fremont, Inc., Daiichi Sankyo Chemical Pharma Co., Ltd. Onahama Plant, Daiichi Sankyo Chemical Pharma Co., Ltd., Tatebayashi Plant, Daiichi Sankyo Europe GmbH, FujiFilm Diosynth Biotechnologies Texas, LLC, Lonza AG
전문/일반	전문의약품
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허가심사유형	신약(유전자재조합의약품 및 세포배양의약품)

원료약품 및 분량

1바이알(616.97 밀리그램) 중-

순번	성분명	분량	단위	규격	성분정보	비교
1	트라스투주맙데룩스테칸	107	밀리그램	별규	트라스투주맙데룩스테칸(으)로서 100 밀리그램	(속주: CHO-S, 벡터: psDSLH-MAAL9001) 주사용수 5 mL로 용해시켜 조제 후 5 mL 중 트라스투주맙데룩스테칸 100 mg

첨가제 : L-히스티딘염산염일수화물,백당,L-히스티딘,폴리소르베이트80

Dose recommendations for anticancer drugs in patients with renal or hepatic impairment

Stefanie D Krens, Gerben Lassche, Frank G A Jansman, Ingrid M E D... Nielka P van Erp

Renal or hepatic impairment is a common comorbi... toxicity of previous anticancer treatments, or because... Because renal and hepatic function are among the m... might be altered for patients with cancer who have... Most anticancer drugs are dosed near their maximu... index. Consequently, selecting an adequate dose for ... challenging and definitive recommendations on dos... renal and hepatic impairment on the pharmacok... appropriate dose adjustments, information from ... combined to provide a practical set of recommenda... with hepatic and renal impairment.

THE LANCET Oncology

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CORRESPONDENCE · Volume 24, Issue 6, E229, June 2023 · Download Full Issue

Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update

Eline L Giraud [a] · Bas de Lijster [a] · Stefanie D Krens [a,c] · Ingrid M E Desar [b] · Emmy Boerrigter [a] · Nielka P van Erp [a]

Affiliations & Notes · Article Info · Linked Articles (1)

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Number of Anticancer Drug

160 in 2019 → 224 in 2023

Lancet Oncol 2019; 20: e200–07
Lancet Oncol 2023; 24: e229

THE LANCET
Oncology

To aid clinicians by providing dose recommendations for anticancer drugs in patients with varying degrees of renal or hepatic impairment.

Supplementary appendix

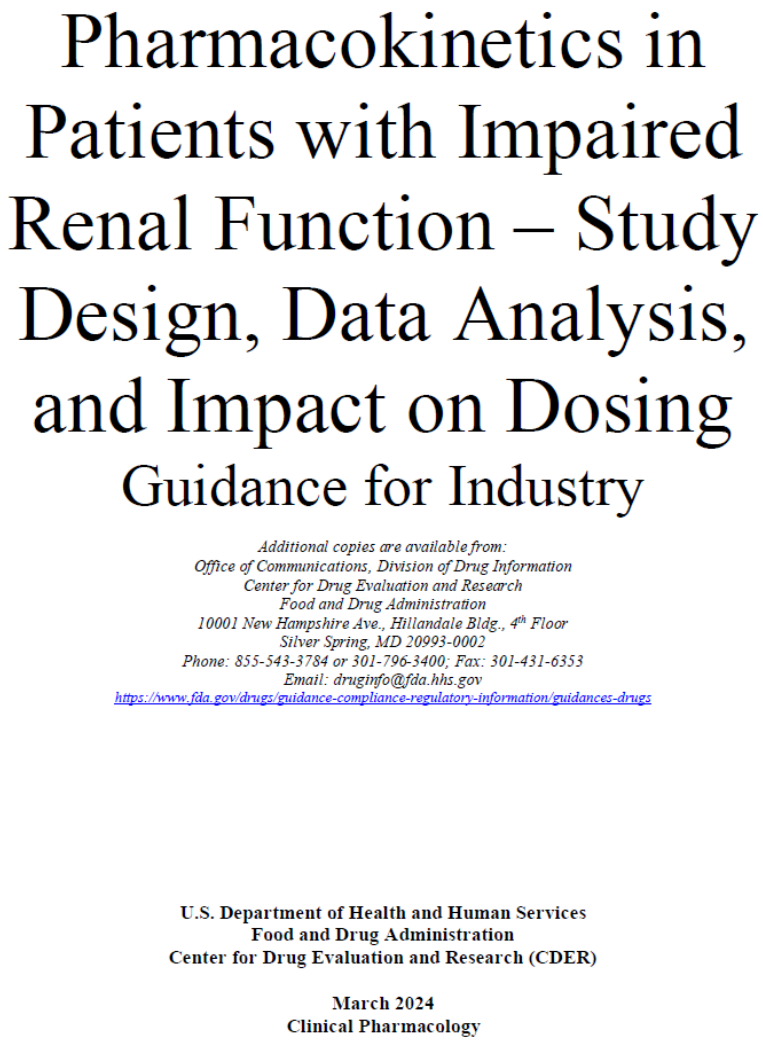
This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Giraud EL, de Lijster B, Krens SD, Desar IME, Boerrigter E, van Erp NP. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. *Lancet Oncol* 2023; 24: e229

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		minorly in feces (4%).	monitoring of renal function is advised in patients with renal impairment.	HD: dose reductions per indication according to the drug label			
114	Lenvatinib	Lenvatinib is metabolised in the liver. Lenvatinib and its metabolites are mainly excreted in feces (64%) and to a lesser extent in urine (24%), with approximately 2% as intactLenvatinib.	**EMA/FDA:** CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: Renal cell carcinoma (RCC): 10 mg QD; differentiated thyroid carcinoma (DTC): 14 mg QD; endometrial carcinoma (EC): 10 mg QD; hepatocellular carcinoma (HCC): not studied (EMA) HD: not studied (FDA), not recommended (EMA)	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: 50 % of the original dose (RCC and EC 10 mg QD, DTC: 14 mg QD) HD: 50% of the original dose may be considered	**EMA/FDA:** Child-Pugh A/B: no dose adjustment Child-Pugh C: RCC and EC 10 mg QD, DTC 14 mg QD, HCC not recommended (EMA) **Shumaker *et al.*** Child-Pugh A: $AUC_{0\text{-}inf}$ 1·2 (90% CI 0·8-1·8) Child-Pugh B: $AUC_{0\text{-}inf}$ 1·1 (90% CI 0·7-1·6) Child-Pugh C: $AUC_{0\text{-}inf}$ 1·8 (90% CI 1·2-2·7)	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: 50% of the original dose (RCC and EC 10 mg QD, DTC 14 mg QD)	Lenvima label[1] SPC Lenvima[2] SPC Kisplyx[2] Shumaker *et al.*[114]

Lancet Oncol 2019; 20: e200–07
Lancet Oncol 2023; 24: e229

PK in patients with renal impairment



Pharmacokinetics in Patients with Impaired Renal Function – Study Design, Data Analysis, and Impact on Dosing

Guidance for Industry

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

March 2024
Clinical Pharmacology

- This guidance assists sponsors in the design and analysis of studies that assess the influence of impaired renal function on the pharmacokinetics (PK) and/or pharmacodynamics (PD) of an investigational drug, provides recommendations on **how to determine the recommended dosage in patients with impaired renal function, and addresses how such information can inform the labeling.**

Renal impairment: classification & estimating renal function

Classifications of Renal Function

Group	Renal function (mL/min)
Normal	≥ 90 mL/min
Mild impairment	60 to <90
Moderate impairment	30 to <60
Severe/kidney failure (not receiving dialysis)	< 30

Cockcroft-Gault Formula for Estimating Creatinine Clearance

$$\text{CrCl (mL/min)} = \frac{(140\text{-age}) \times \text{Lean Body Weight (kg)}}{\text{Serum Creatinine (mg/dL)} \times 72} \quad (\times 0.85 \text{ if female})$$

eGFR units

- Clinical eGFR is often reported as mL/min/1.73 m².
- For dosing guidance, FDA recommends using eGFR in mL/min (patient-specific).
- Convert: eGFR(mL/min) = eGFR(mL/min/1.73m²) × (BSA/1.73).

Renal function assessment

Prefer **eGFR** (widely used in practice) over Cockcroft–Gault eCLcr for PK studies.
For dosing recommendations, use **eGFR in mL/min** rather than mL/min/1.73 m²;
convert using individual **BSA**.

Dosing of cytotoxic agents

Feature	Carboplatin	Most Other Cytotoxics (e.g., Paclitaxel, 5-FU)
Primary Dosing Metric	AUC (Total Exposure)	BSA (mg/m2)
Elimination	Primarily Renal (Glomerular)	Often Hepatic or Mixed
Dose Limiting Toxicity	Thrombocytopenia	Neutropenia, Mucositis, etc.
Individualization	Adjusted based on serum creatinine/GFR	Adjusted based on height and weight

The Calvert Formula for Carboplatin

$$\text{Dose (mg)} = \text{Target AUC} \times (\text{GFR} + 25)$$

- **Target AUC:** Usually ranges from 4 to 6, depending on the treatment plan and whether other drugs are being used.
- **GFR + 25:** This part of the equation accounts for the patient's renal clearance plus a constant (25) that represents non-renal clearance.

Clear relationship btw carboplatin exposure and GFR

GFR calculation

Feature	Cockcroft-Gault (CG)	BSA-Adjusted CKD-EPI (eGFR)
Status	Historical Standard	Current "Best Practice" Recommendation
Accuracy	Lower (especially at extremes of weight)	Higher (more precise across BMI ranges)
Lab Standards	Not designed for modern IDMS creatinine	Optimized for modern IDMS creatinine
Units	Directly in mL/min	Must be converted from 1.73m2

Many modern international guidelines, including the **ADDIKD** (Anticancer Drug Dosing in Kidney Dysfunction) consensus, now recommend moving toward **BSA-adjusted CKD-EPI** as the **preferred method** because it uses standardized creatinine assays (IDMS-traceable) that the CG formula was never designed for.

Dose adjustment for renal impairment

- Anticancer drugs with a wider therapeutic index, or with large inter-individual variability, might not directly need a dose adjustment.
- Monoclonal antibodies are subject to proteolytic catabolism and intracellular degradation after binding to their target, hence no need for dose adjustment is expected in case of renal or hepatic impairment
- Hypoalbuminaemia: less protein is available for drug binding as unbound drugs can exert efficacy but also drug toxicity.
- Renal impairment not only affect renal excretion of active compounds and metabolites, but can also influence drug absorption, distribution, or metabolism.

Renal dysfunction – classic cytotoxics

- **Carboplatin**

Primarily renally cleared

Reduce AUC or avoid if GFR is severely reduced; consider dialysis timing

- **Paclitaxel**

Mainly hepatic metabolism → usually no dose adjustment for isolated CKD

- **Ifosfamide, cisplatin**

Strongly nephrotoxic – prefer carboplatin in CKD, avoid if significant dysfunction

Practical tips

Re-check GFR before each cycle in unstable patients.

Adequate hydration.

Renal dysfunction – targeted and immune therapies

PARP inhibitors

Olaparib, niraparib: dose reduction in moderate renal impairment

Limited data in severe impairment or dialysis – use with caution

Anti-angiogenic therapy (e.g., bevacizumab)

Monitor for hypertension, proteinuria, thrombotic microangiopathy

ICIs

No formal dose adjustment for mild/moderate CKD in trials

However, ICI-associated AKI and interstitial nephritis can occur

Close collaboration with nephrology is essential!

Chemotherapy in Hemodialysis Patients

Always consult and work with patient's nephrology team and pharmacy.

Society of Gynecologic Oncology

Clinical Guide for Administering Chemotherapy in Hemodialysis Patients

Amanda Ramos, MD; Judith Smith, PharmD; Jaya Kala, MD; Tracilyn Hall, MD;
Melissa Hardesty, MD, MPH; and Jennifer MacDonald, PharmD

Important general guidelines for administering chemotherapy in dialysis patients: Always consult and work with patient's nephrology team and pharmacy. This guide is intended for patients on outpatient hemodialysis, not CRRT or peritoneal dialysis. Important considerations for every patient:

1. Is the proposed medication appropriate for a patient on hemodialysis?
2. Is a dose modification needed?
3. Does dialysis timing matter?

ESRD on hemodialysis

Dialyzability = drug + dialysis + patient

Drug: protein binding, molecular weight, volume of distribution, route of clearance

Dialysis: modality (IHD vs CRRT), membrane/pore size, flow rates

Patient: albumin level, residual kidney function, third spacing

Many anticancer drugs are highly protein bound → often not dialyzable; timing may still matter for metabolites

HD planning checklist

Confirm dialysis modality & schedule (this guide assumes outpatient intermittent HD)
Decide: “after HD” vs “non-HD day” vs “timing not important”
For dialyzable drugs or metabolites, specify timing window (e.g., start HD 6–12h after)
Co-manage with nephrology + pharmacy; reassess if residual function changes
Document a contingency plan for hypotension, access issues, missed sessions

Chemotherapy in Hemodialysis Patients

Cytotoxic Chemotherapy				
Medication	**Renal Excretion**	**Dose Modification Needed?**	**Dose Modification Recommendations**	**Timing of Hemodialysis (HD)**
5-FU	<10% eliminated by kidneys	No	• 5-FU may be used at its usual dosage in patients with ESRD on HD	• Administer the drug after HD sessions on HD days since the drug may be removed
Bleomycin	70% eliminated by kidneys	Yes	• In patients on hemodialysis, reduce to 50% of original dose	• Limited data for timing in relation to HD • Consider after HD session, work with nephrologist closely
Capecitabine	96% of active metabolites eliminated by the kidneys	No data in HD use, not recommended dose adjustment needed in renal insufficiency	No data in patients on HD or w/GFR <30 • CrCl less 30 mL/min contraindicated	Limited data for timing in relation to HD. Consider after HD session; work with nephrologist closely

Carboplatin	95% eliminated by kidneys	Yes	• Use Calvert formula to calculate appropriate dose:
			  • Dose (mg) = AUC x (GFR+25)
			  • Plug 0 into the Calvert equation for dialysis patients
				• Plan administration after an HD or on a non-dialysis day so that the following HD session occurs >24 hours after the dose

Cisplatin	90% eliminated through kidneys	Yes	• Initial doses of Cisplatin should be reduced by 50%; dose recommended is 25-50 mg/m^2 q3-6 weeks	• Plan administration after an HD session or on non-dialysis days
Cyclophosphamide (IV)	30-60% eliminated by the kidneys	Yes	• Mean cyclophosphamide clearance was seen to be lower in HD patients and exposure to drug is higher • May be necessary to reduce the dose of cyclophosphamide by 25-30% in HD patients, but studies are conflicting	• It is removed by dialysis, therefore it should be administered after HD sessions
Docetaxel	6% eliminated by the kidneys	Limited data, dose modification suggested	• Limited data, case report with plasma concentration similar between HD and non-HD patients • Not removed by dialysis; can be used with caution; consider starting treatment dose at 65 mg/m^2	• May be administered before or after dialysis sessions as it is not removed by HD
Doxil	Minimal renal excretion	May need dose reduction, but can start with full dose	• May need to reduce dose in CKD patients secondary to increased incidence of mucocutaneous and hematologic toxicities	• No data on timing of HD, work closely with nephrology team
Doxorubicin	Minimal renal excretion	No	• Does not typically need dose adjustment in HD patients; although AUC of doxorubicin may be higher in patients with renal insufficiency	• May be administered after or on a non-HD day
Etoposide	40% eliminated by kidneys	Yes	• Renal insufficiency: 15 50 mL/min – decrease dose by 25%; < 15 mL/min decrease dose by 50% • Consider 50% dose reduction (25-75mg/m^2/day) in HD	• Etoposide is not removed by dialysis; may administer before or after HD session

Chemotherapy in Hemodialysis Patients

Cytotoxic Chemotherapy				
Medication	**Renal Excretion**	**Dose Modification Needed?**	**Dose Modification Recommendations**	**Timing of Hemodialysis (HD)**
Gemcitabine	90% of the metabolites eliminated by kidneys	No	• In CrCl less than 30 mL/min: no dose adjustment required but increased risk for hematological toxicity	• Metabolized to dFdU which is shown to be removed by HD • Recommend starting HD sessions 6-12 hours after to minimize side effects of dFdU
Oxaliplatin	~50% eliminated by the kidneys	Minimal data, possible need for modified dose	• Lack of data results in inability to recommend Oxaliplatin in HD patient • If needed, for CrCl < 30 mL/min, reduce dose from 85 mg/m^2 to 65 mg/m^2; in HD-30% reduced dose	• Dialysis removal rate of Oxaliplatin is 80% • Administration of drug is best after HD or on non-HD days
Paclitaxel	Minimal renal excretion	No	• No dose adjustment needed • May also be given weekly	• Administer after or on non-HD session days; however may also consider on dialysis days as well; timing is ultimately not important
Topotecan	Some elimination by the kidneys	Unclear, conflicting studies	• Conflicting studies; may need to reduce dose 50-75% in HD patients; try to avoid in HD • In renal insufficiency; >40 mL/min, no change 39-20 mL/min, decrease dose by 30%; less than 20 mL/min, no data	• Cleared at a high rate by HD, consider administration following HD session or on a non-HD day
Vinorelbine	8% eliminated by the kidneys	Yes	• Limited data in HD cancer patients. One patient with toxicity that improved after reduced dose. Recommended to reduce the dose of Vinorelbine, initiate at 20 mg/m^2/ week IV	• Administer after or on non-HD days

Chemotherapy in Hemodialysis Patients

Monoclonal Antibody Therapies				
Medication	**Renal Excretion**	**Dose Modification Needed?**	**Dose Modification Recommendations**	**Timing of Hemodialysis (HD)**
Bevacizumab	Low renal excretion (proteolytic catabolism); may cause significant proteinuria	Likely no dose adjustment needed	• One case study assessing pharmacokinetics of bevacizumab in a patient receiving 5 mg/kg twice per month revealed equivalent concentrations of the drug compared to non-HD patients • Likely no dose adjustment needed, however use with caution because of limited data-only expert opinion; may consider dose reduction	• Not dialyzable; may be administered at any time in relation to HD session • Monitor for proteinuria
Lenvatinib	25% eliminated by kidneys	Yes for decreased creatinine clearance, no data for patients with ESRD on HD.	• Reduce dose by 50% for patients with CrCl 15-29 mL/min • Has not been approved for patients with ESRD as there is no data • Withhold or discontinue in patients with grade 3-4 renal impairment	• Consider not administering this medication to HD patients or working closely with nephrology • Not expected to be dialyzable because so highly protein bound • Monitor for proteinuria
Mirvetuximab sorvtansine	Metabolites (DM4 & DM4-sulfo-SpDB-lysine) detected in urine	Unknown	• No data; use with caution	• No data; use with caution
Tisotumab	6% eliminated by kidneys	Unknown	• No data available. Package insert describes no difference in exposure of tisotumab in patients with CrCl 30-90 versus patients with normal renal function. No data in patients with severe renal function (crCl <15)	• Consider not administering this medication to HD patients or working closely with nephrology
Trastuzumab	Low renal excretion (proteolytic catabolism)	Likely no dose adjustment needed in renal impairment	• Pharmacokinetic parameters similar between HD and non-HD patients • A lower GFR may be associated with increased risk of cardiotoxicity from Trastuzumab; seen in some patients but not all • Likely safe to administer in standard doses; discuss with nephrology. May need to follow LVEF for cardiotoxicity	• Limited data. Has a high molecular mass, therefore not dialyzable; may be administered at any time in relation to HD session

Chemotherapy in Hemodialysis Patients

Immune Checkpoint Inhibitors				
Medication	**Renal Excretion**	**Dose Modification Needed?**	**Dose Modification Recommendations**	**Timing of Hemodialysis (HD)**
Ipilimumab	Not eliminated by kidneys, cleared by proteolytic degradation (likely)	No	• Data is from case reports-patients can be successfully treated, usually given in combination with Nivolumab. • Patients may have higher risk of toxicity; however data is conflicting. • Monitor closely-particularly for anemia, need to be careful in patients with prior transplant/transplanted kidney (consider steroid use at initiation to prevent organ rejection; rejection may be more likely to occur with ICI use)	• Timing of dialysis: limited data, mAB likely not dialyzable due to size of molecule, timing of HD may not matter in these patients; consider after HD session
PD1 Inhibitors	Same as above	No	• Same as above	• Same as above

PARP Inhibitors				
Medication	**Renal Excretion**	**Dose Modification Needed?**	**Dose Modification Recommendations**	**Timing of Hemodialysis (HD)**
Niraparib	48% eliminated by kidneys	No data	• No data	• No data
Olaparib	42% eliminated by kidneys	Yes, consider 200 mg BID	• Due to the increased AUC (by 44%) and Cmax (maximal concentration, by 26%) in patients with moderate renal impairment (CC 30–50 ml/min); a dose adjustment (33% decrease of the daily dose) is recommended • No strong data in HD patients; some case reports with successful treatment on 200 mg BID	• Here may be lower drug concentrations on HD days, however in the case reports this did not impact outcomes; HD started after Olaparib administration
Rucaparib	45% eliminated by kidneys	No data	• No data	• No data

Hemodialysis: practical dosing & timing pearls

Selected examples from SGO hemodialysis guide

Drug	Dose modification (ESRD/HD)	Timing relative to HD
Carboplatin	Use Calvert: Dose = AUC × (GFR + 25). For dialysis, **plug GFR=0**.	Give after HD or on a non-HD day; next HD >24h after dose
Cisplatin	Start ~50% dose reduction (e.g., 25–50 mg/m² q3–6wk).	Give after HD session or on non-HD day
Etoposide	CrCl 15–50: ↓25%; CrCl <15: ↓50%. In HD, consider ~50% reduction; not dialyzable.	Before or after HD ok (not removed by HD)
Gemcitabine	No routine adjustment; higher hematologic risk when CrCl <30. Metabolite (dFdU) removed by HD.	**Start HD ~6–12h after dosing to reduce dFdU-related AEs**
Paclitaxel	No dose adjustment needed (minimal renal excretion).	Timing usually not important
Topotecan	**Avoid if possible in HD; may need 50–75% reduction**. If renal insufficiency: >40 no change; 20–39 ↓30%.	Cleared at high rate by HD → give after HD or on non-HD day

Renal dysfunction: targeted therapies & maintenance

PARP inhibitors (e.g., olaparib)

Moderate renal impairment (CrCl 30–50 mL/min):
AUC ↑ ~44% → recommend 33% daily dose reduction (e.g., 200 mg BID).

No strong data in HD; case reports describe use at 200 mg BID (HD started after dosing).

Anti-VEGF / TKI (e.g., lenvatinib & bevacizumab)

Lenvatinib: reduce dose ~50% when CrCl 15–29 mL/min; no approval-level data in ESRD/HD; monitor proteinuria.

Bevacizumab: not dialyzable; typically no dose adjustment but monitor for proteinuria and BP carefully.

ADCs in ESRD/HD (practical caution)

Tisotumab vedotin:
label suggests similar exposure for CrCl 30–90 vs normal; no data when CrCl <15 or in HD → consider avoiding or co-manage closely.

Mirvetuximab soravtansine:
metabolites detected in urine; no renal-impairment/HD data → use caution and monitor closely.

Hepatic impairment – assessment

- No single “hepatic eGFR” exists.
- Multiple hepatic impairment descriptions are presented in specific dose recommendations.

  - Child-Pugh score (Table1)
  - NCI Organ Dysfunction criteria (Table2)

Child-Pugh classification (A/B/C) includes:

- Bilirubin
- Albumin
- INR / prothrombin time
- Ascites
- Encephalopathy

	1 point	2 points	3 points
Total bilirubin (mg/dL)	<2	2–3	>3
Albumin (g/dL)	>3·5	2·8–3·5	<2·8
Prothrombin time (sec prolonged) or INR	<4 or <1·7	4–6 or 1·7–2·3	>6 or >2·3
Ascites	Absent	Slight	Moderate
Encephalopathy (grade)†	None	1 or 2	3 or 4

INR=international normalised ratio. *Child-Pugh classification is obtained by adding the score for each parameter. Grade A (mild)=5–6 points. Grade B (moderate)=7–9 points. Grade C (severe)=10–15 points. †Grade 0: normal consciousness, personality, neurological examination, and electroencephalogram. Grade 1: restless, sleep disturbed, irritable or agitated, tremor, and impaired handwriting, five cycles per s (cps) waves. Grade 2: lethargic, time-disoriented, inappropriate, asterixis, ataxia, slow triphasic waves. Grade 3: somnolent, stuporous, place-disoriented, hyperactive reflexes, rigidity, and slower waves. Grade 4: unarousable coma, no personality or behaviour, decerebrate, and slow 2–3 cps delta activity.

Table 1: **Child-Pugh score by clinical and lab criteria*[4,34]**

	Total bilirubin	Alanine aminotransferase or aspartate aminotransferase
Mild	B1: ≤ULN; B2: >1–1·5 x ULN	B1: >ULN; B2: Any
Moderate	>1·5–3 x ULN	Any
Severe	>3x ULN	Any

Group B (mild) is defined according to either of two criteria (B1 or B2). ULN=upper limit of normal.

Table 2: **Classification of hepatic impairment by the National Cancer Institute Organ Dysfunction Working Group[7]**

Hepatic impairment – assessment

FDA/EMA recommend Child-Pugh in studies; verify abnormalities reflect liver disease

Routine liver biochemistries are imperfect proxies for metabolic capacity (metastases, cholestasis, inflammation).

Reduced metabolism/biliary flow/protein binding → ↑ exposure for parent drugs; prodrugs may have ↓ active metabolite formation.

Clinical decision tips

- Cholestasis (bilirubin) often drives risk more than transaminases alone.
- Avoid “automatic” reductions without a rationale; tailor to intent (curative vs palliative).
- When evidence is sparse: start conservatively, monitor early, and escalate if tolerated.

Hepatic dysfunction: key agents in gyn oncology

Taxanes (paclitaxel/docetaxel):

- primarily hepatic metabolism & biliary excretion ⟶ adjust with hepatic impairment.
- Dose reduction based on bilirubin and transaminases

Anthracyclines:

- biliary excretion important ⟶ reduce when bilirubin is elevated.
- Both hepatically cleared and cardiotoxic; careful in combined liver–heart disease

Pegylated liposomal doxorubicin (PLD):

- dose reduction required for hepatic insufficiency.

Doxorubicin

- Dose reduction of ~50–70% in significant hepatic insufficiency (e.g., bilirubin > 1.5).
- consider baseline cardiac evaluation and cumulative dose limits.

Hepatic dysfunction: key agents in gyn oncology

Gemcitabine and others

- may still require adjustments depending on severity and regimen intent.

TKIs and ADCs

- Often have boxed warnings for hepatotoxicity; regular LFT monitoring

ICIs

- Immune-mediated hepatitis; treat with steroids and hold or discontinue drug
- Use available dose-modification tables from key reviews and guidelines

Cardiotoxicity

Who is “high risk”?

- Prior cardiovascular disease (HF, cardiomyopathy, MI, angina, arrhythmias)
- Elevated biomarkers (troponin, natriuretic peptide) at baseline
- Age > 65
- Hypertension, CKD/proteinuria, diabetes, hyperlipidemia
- Prior cardiotoxic therapy (anthracycline, trastuzumab, chest/mediastinal RT)
- Smoking history

Baseline evaluation

- History/physical (HF symptoms, angina, syncope)
- BP, ECG (QTc, rhythm)
- Echocardiogram (LVEF ± GLS) when indicated (anthracycline/anti-HER2/ICIs)
- Biomarkers (troponin/BNP) in selected high-risk patients
- Early cardiology co-management for high/very-high risk

Cardiotoxicity

- Lenvatinib + pembrolizumab (endometrial ca.)

→ HTN management is essential for continuation

- Bevacizumab-containing regimens

→ BP + proteinuria monitoring

- Some targeted agents/PARPi can affect QTc

→ review co-medications (antiemetics, antibiotics)

Cardiotoxicity: hypertension & QTc

Hypertension (VEGF inhibitors / TKIs)

- Adopt home BP monitoring for patients on therapies that cause/worsen HTN.
- Treat threshold: SBP ≥130 or DBP ≥80 if 10-yr CVD risk ≥10%; otherwise SBP ≥140 or DBP ≥90.
- **Hold** therapy threshold (typical): **SBP ≥180 or DBP ≥110.**
- First-line: ACE inhibitor or ARB (helpful with proteinuria).
- Second-line: dihydropyridine CCB; consider as first-line for VEGF-related HTN.
- Use combination therapy for SBP ≥160 and DBP ≥100.

QTc prolongation

- If **QTc >500 ms**: confirm, correct electrolytes, review drug-drug interactions. consider drug discontinuation/adjustment
- Normal QTc cutoff in females is ~470–480 ms
- Consider EKG monitoring for agents with known QTc risk and for symptomatic patients.

CTRCD (Cancer Therapy–Related Cardiac Dysfunction)

IC-OS definitions

- Asymptomatic moderate CTRCD: new LVEF 40–49% with ≥10% drop
  OR <10% drop + GLS decline (>15%) and/or biomarker rise.
- Severe CTRCD: new LVEF <40%.
- Symptoms (HF) drive urgency regardless of category.

Doxorubicin

- Cardiomyopathy risk increases with cumulative dose
  (e.g., ~3% at 450 mg/m²; ~7% at 550; ~15% at 600; ~40% at 700).
- Discontinue if LVEF decreases ≥10% to an absolute LVEF <50%.
- Consider echo/MUGA baseline and after cumulative ~300 mg/m².

Pegylated Liposomal Doxorubicin, PLD

- Less cardiotoxic

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Treatment Related Cardiotoxicity Review and Management

Common chemotherapy-related cardiovascular toxicities (IC-OS definitions)

Table 1

Cardiotoxicity	Definition	Common associated agents that may be used in gyn onc	Steps or Important Info for Providers
Cardiac dysfunction/ heart failure	Asymptomatic cardiac dysfunction or symptomatic HF, collectively termed cancer therapy-related cardiac dysfunction (CTRCD) to include: new CV symptoms, new abnormalities in cardiac function on CV imaging, and/or new increases in cardiac biomarkers	Anthracyclines alone or in combo with chest directed radiotherapy Doxorubicin (dose related - > 450 mg/m^2, dexrazoxane can be used as cardioprotectant as doses approach 300 mg/m^2) Trastuzumab Pertuzumab Trametinib Binimetinib Sunitinib Pazopanib Immune checkpoint inhibitors	1. Determine cardiac risk stratification (*see below and ESC guidelines Table 4*) 2. If moderate, high or very-high risk, refer to cardiology 3. See **Table 2** for monitoring recommendations 4. See **Table 3** for IC/OS cardiac dysfunction definitions 5. See **Table 4** for therapy recommendations if cardiac dysfunction develops
Myocarditis	Inflammatory disease of heart muscle cells (see Appendix B for more thorough definition)	Doxorubicin Fluorouracil Cyclophosphamide Chest directed radiation Immune checkpoint inhibitors	If toxicity develops, permanently discontinue therapy
Vascular toxicity	Induction or aggravation of vascular disease in the setting of cancer therapy, including coronary artery disease, thrombosis, abnormal vasoreactivity, stroke, Raynaud's.	Fluorouracil *Also noted in other cytotoxic medications including platinum drugs, gemcitabine, everolimus, bevacizumab*	If toxicity develops, permanently discontinue therapy

Table 1 (continued)

Cardiotoxicity	Definition	Common associated agents that may be used in gyn onc	Steps or Important Info for Providers
Hypertension	Increase in systolic and/or diastolic blood pressure (BP) after initiation of cancer therapy, without any other contributing changes.	Bevacizumab Everolimus Sunitinib Pazopanib Trametinib Binimetinib	Home BP monitoring should be adopted by all patients with cancer receiving therapy known to cause or worsen hypertension. 1. Treatment threshold for HTN before, during, and off therapy o SBP >=130 or DBP >=80, if CVD risk >=10% o SBP >=140 or DBP >=90, if CVD risk <10% 2. Threshold for holding therapy o SBP >=180 or DBP >= 110 3. ACE-I or ARB are the first-line antihypertensive drugs recommended for BP management in patient with cancer, and can be particularly helpful in those with proteinuria 4. Dihydropyridine CCB are recommended as second-line antihypertensive drugs for patients with cancer with uncontrolled BP. Consider as first line for those with VEGF related hypertension and African American patients 5. Combination therapy with ACE-I or ARB and dihydropyridine CCBB is recommended in patients with cancer with systolic BP >=160 and DBP >=100
Arrhythmias and QTc prolongation	QTc >500. Arrhythmias use general cardiology definitions.	Trametinib Pazaopanib Oxaliplatin Sunitinib Lenvatinib Rucaparib	Normal QTc cutoff in females is 470-480 ms If QTc prolongation noted: 1. Confirm QTc >500 ms before stopping therapy 2. Exclude electrolyte abnormalities (K, Mg, Ca) 3. Check potential drug-drug-interactions 4. Stop other QTc prolonging drugs

Agent-specific monitoring recommendations

Recommended or indicated, per ESC guidelines. Please refer to full guidelines for items that should or may be considered as part of monitoring. All patients scheduled for cardiotoxic therapies should undergo baseline clinical CV assessment and physical exam.

Table 2

Class	Baseline	Surveillance	After treatment
Anthracyclines	EKG ECHO **Troponin, BNP	**TTE Q2 cycles **cTn/NP each cycle	TTE 12 months post tx **TTE 3 months post tx **cTn/NP 3 and 12 months post tx
HER2-targeted therapies	EKG ECHO **Troponin, BNP	TTE every 3 months	TTE 12 months post tx **TTE 3 months post tx
Fluoropyrimidines	EKG +ECHO	If indicated based on symptoms	
VEGF inhibitors	EKG **ECHO	If indicated based on symptoms	
RAF and MEK inhibitors	EKG **ECHO	If indicated based on symptoms	
Immune checkpoint inhibitors	EKG **ECHO Troponin, BNP	**EKG Q6-12 months if >12 months therapy **cTN, NP Q6-12 months if >12 months therapy	

** Indicated if patient identified as being high or very-high risk for cardiac complications based on Table 4 of ESC guidelines

\+ If Prior CVD

IC-OS 2021 consensus definitions on cancer treatment-related cardiac dysfunction

Table 3

	Mild	Moderate	Severe	Very Severe
Asymptomatic (with or without additional biomarkers	LVEF >= 50% **AND** new relative decline in GLS by >15% from baseline **AND/OR** new rise in cardiac biomarkers	New LVEF reduction by >=10% to an LVEF of 40-49% **OR** New LVEF reduction by <10% to an LVEF of 40-49% **AND** new relative decline in GLS by >15% from baseline **AND/OR** new rise in cardiac biomarkers	New LVEF reduction to <40%	
Symptomatic (with LVEF and supportive diagnostic biomarkers)	Mild HF symptoms, no change in therapy	Need for outpatient intensification of diuretic and HF therapy	HF hospitalization	Requiring inotropic support, mechanical circulatory support or consideration for transplantation

* LVEF based on 2D echo

** Cardiac biomarkers include cardiac troponin I/T >99 percentile, BNP >= 35 pg/mL, NT-proBNP >= 125 pg/mL (or new significant rise from baseline)

Agent-specific management

Table 4

Class	Temporary interruption if:	Management includes:	Reinitiate if:	Discontinue if:
Anthracyclines	• Moderate symptomatic CTRCD • Moderate or severe asymptomatic CTRCD	• Multi-disciplinary approach including HF therapy (ACEI/ARB, beta-blocker, sodium-glucose co-transporter 2 inhibitor, mineralocorticoid receptor antagonist)	• Moderate symptomatic improves to baseline and monitor ECHO before each dose	• Severe symptomatic CTRCD
HER2-targeted therapies	• Moderate or severe symptomatic CTRCD • Severe asymptomatic CTRCD (LVEF,40%)	• Asymptomatic mild-moderate CTRCD patients: continue therapy, add cardio protectant (ACE/ARBi or beta-blocker), increasing monitoring intervals • Moderate or severe asymptomatic or symptomatic CTRCD: hold therapy, add cardio protectant	• LVEF returns to >40%, ideally back to > 50% • Resume with increased monitoring intervals (every 2 cycles for first 4 cycles after re-initiation)	• Cardiac function does not return to >40% • Multi-discplinary team decides it is unsafe given patient specific issues
Immune checkpoint inhibitors	• Suspected ICI-associated myocarditis	• Non-fulminant and fulminant ICI-associated myocarditis: methylprednisolone 500-1000 mg IV daily 3-5 days prior to considering PO steroid (1 mg/kg up to 80 mg/day)	• Case by case basis with heavy cardiology input if reinitiation is safe for patient	• Fulminant or non-fulminant ICI- associated myocarditis and the patient should be admitted to hospital and a level 2 or 3 bed with continuous ECG monitoring is required

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1. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS)
2. Defining cardiovascular toxicities of cancer therapies: an International Cardio-Oncology Society (IC-OS) consensus statement
3. Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline

Appendix A

Table 4
Heart Failure Association–International Cardio-Oncology Society baseline cardiovascular toxicity risk stratification

Baseline CV toxicity risk factors	Anthracycline chemotherapy	HER2-targeted therapies	VEGF inhibitors	BCR-ABL inhibitors	Multiple myeloma therapies	RAF and MEK inhibitors
Previous CVD						
HF/cardiomyopathy/CTRCD	VH	VH	VH	H	VH	VH
Severe VHD	H	H	–	–	–	H
MI or PCI or CABG	H	H	VH	–	–	H
Stable angina	H	H	VH	–	–	H
Arterial vascular disease	–	–	VH	VH	VH	–
Abnormal ankle-brachial pressure index	–	–	–	H	–	–
PH	–	–	–	H	–	–
Arterial thrombosis with TKI	–	–	–	VH	–	–
Venous thrombosis (DVT/PE)	–	–	H	M2	VH	–
Arrhythmia[a]	–	M2	M2	M2	M2	M1
QTc ≥ 480 ms	–	–	H	H	–	–
450 ≤ QTc < 480 ms (men); 460 ≤ QTc < 480 ms (women)	–	–	M2	M2	–	–
Prior PI CV toxicity	–	–	–	–	VH	–
Prior IMiD CV toxicity	–	–	–	–	H	–
Cardiac imaging						
LVEF < 50%	H	H	H	H	H	H
LVEF 50–54%	M2	M2	M2	–	M2	M2
LV hypertrophy	–	–	–	–	M1	–
Cardiac amyloidosis	–	–	–	–	VH	–

ADCs: ocular toxicity

Clinical pattern

- Ocular surface AEs are common with certain ADCs (rapidly dividing corneal/conjunctival cells).
- Median onset ~1.4 months (**tisotumab**) and ~1.5 months (**mirvetuximab**).
- Events include conjunctivitis, dry eye, keratitis/keratopathy, blurred vision; severe events are uncommon but clinically significant.

Prevention

- Baseline ophthalmic exam (visual acuity + slit lamp) and scheduled follow-ups
- Lubricating drops + steroid drops per agent-specific protocol
- Patient education: report new eye pain, photophobia, blurred vision promptly
- coordinate with ophthalmology

Recognize early, prevent systematically!

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Ocular Toxicities with ADCs Companion Card

Toxicities commonly involve ocular surface (robust blood supply, subpopulations of rapidly dividing cells, abundance/variety of cell surface receptors)

Tisotumab: Median onset time 1.4 months			Mirvetuximab: Median onset time 1.5 months		
	Grade 1-2	Grade 3		All grades	Grade 3/4
Any ocular AE	53%		Any ocular AE	52%	
Conjunctivitis	26%	0%	Blurred vision	41%	6%
Dry eye	23%	0%	Dry eye	25%	2%
Keratitis	11%	0%	Keratopathy	29%	9%
Ulcerative keratitis	0%	2%			

Recommended eye care

- Ophthalmic exams should consist of visual acuity and slit lamp exam
  - https://www.tivdakhcp.com/TivdakHCP_Eye_Care_Consult_Form.pdf
  - https://www.elaherehcp.com/pdf/ocular-assessment-form.pdf
- Avoid contact lenses
- Patients should monitor for symptoms: dry eyes, eye irritation, blurred vision, eye redness, light sensitivity, vision loss or impairment

Drug	Eye exam	Lubricating eye drops	Corticosteroid eye drops	Vasoconstrictor eye drops (0.2% brimonidine)	Cold packs
Tisotumab	Baseline and prior to each cycle	Daily and PRN for 30 days after infusion	Prednisolone 1%: 1 drop/eye TID D1-D3. First about 10 min prior to infusion	3 drops/eye immediately prior to infusion	Cover eyes x 60 min total (start prior to infusion + continue 20 min after infusion)
Mirvetuximab	Baseline and every other cycle x 8 cycles	At least QID (wait 10 min after steroid drop)	Dexamethasone 0.1%: D -1 to D4: 1 drop/eye 6x/day D5-D8: 1 drop/eye QID *Note: hold if cataracts develop and consider not using until symptoms develop to avoid issue with cataract*	Not recommended	Not recommended

Dose modifications

Tisotumab

Severity	Occurrence	Dose modification
Keratitis		
Superficial punctate keratitis (SPK)	Any	Monitor
Confluent superficial keratitis	First occurrence	Withhold until SPK or normal, then resume at next lower dose level
	Second occurrence	Permanently discontinue
Ulcerative keratitis or perforation	Any	Permanently discontinue
Conjunctival ulceration	First occurrence	Withhold until complete conjunctival re-epithelialization, then resume at next lower dose level
	Second occurrence	Permanently discontinue
Conjunctival or corneal scarring or symblepharon	Any	Permanently discontinue
Conjunctivitis and other ocular AEs		
Grade 1	Any	Monitor
Grade 2	First occurrence	Withhold until grade </= 1, then resume at same dose
	Second occurrence	Withhold until grade </= 1, then resume at next lower dose level. If no resolution to grade </= 1, then permanently discontinue
	Third occurrence	Permanently discontinue
Grade 3/4	Any	Permanently discontinue
Starting dose 2 mg/kg up to max 200mg 1st dose reduction: 1.3 mg/kg up to max 130mg 2nd dose reduction: 0.9mg/kg up to max 90mg		

Mirvetuximab

Keratitis/Keratopathy	
Nonconfluent superficial keratitis	Monitor
Confluent superficial keratitis, cornea epithelial defect, or 3-line or more loss in best correct visual accuity	Withhold until improved/resolved, resume at same dose or consider DR
Corneal ulcer or stromal opacity or best correct distance visual acuity 20/200 or worse	Withhold until improved/resolved then reduce by one dose level
Corneal perforation	Permanently discontinue
Uveitis	
Grade 1: rare cell in anterior chamber	Monitor
Grade 2: 1-2+ cell or for flare in anterior chamber	Withhold until grade </= 1, then resume at same dose
Grade 3: 3+ cell or flare in anterior chamber	Withhold until grade </= 1, then reduce by one dose level
Grade 4: Hypopyon	Permanently discontinue
Starting dose: 6 mg/kg 1st dose reduction: 5 mg/kg 2nd dose reduction: 4 mg/kg	

Risk of drug-induced interstitial lung disease

Drug	Indication	Incidence	Mortality	Management
Mirvetuximab soravtansine	Ovarian	10%*	0.1%*	Grade 2: Hold*Grade 3/4: Permanently discontinue*
Tisotumab vedotin	Cervical	0.9%*	0.2%*	Grade 2: Hold*Grade 3/4: Permanently discontinue*
Fam-trastuzumab deruxtecan	Solid Tumor	10.5%†	1.1%†	Grade 1: Hold*Grade 2/3/4: Permanently discontinue*
Pembrolizumab	Endometrial / Cervical	3.4%*	0.1%*	Grade 2: Hold*Grade 3/4: Permanently discontinue*
Dostarlimab	Endometrial	2.3%*	0.0%*	Grade 2: Hold*Grade 3/4: Permanently discontinue*
Durvalumab	Endometrial	2.4%*	0.1%*	Grade 2: Hold*Grade 3/4: Permanently discontinue*

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Risk factors for drug-related ILD

- Age≥65years
- Smoking history
- Baseline interstitial lung abnormalities Lung comorbidities: asthma, COPD, prior ILD, pulmonary fibrosis, and radiation pneumonitis
- Impaired renal function
- Higher drug dose
- Baseline oximetry readings <95%.
- Residency in Japan ?

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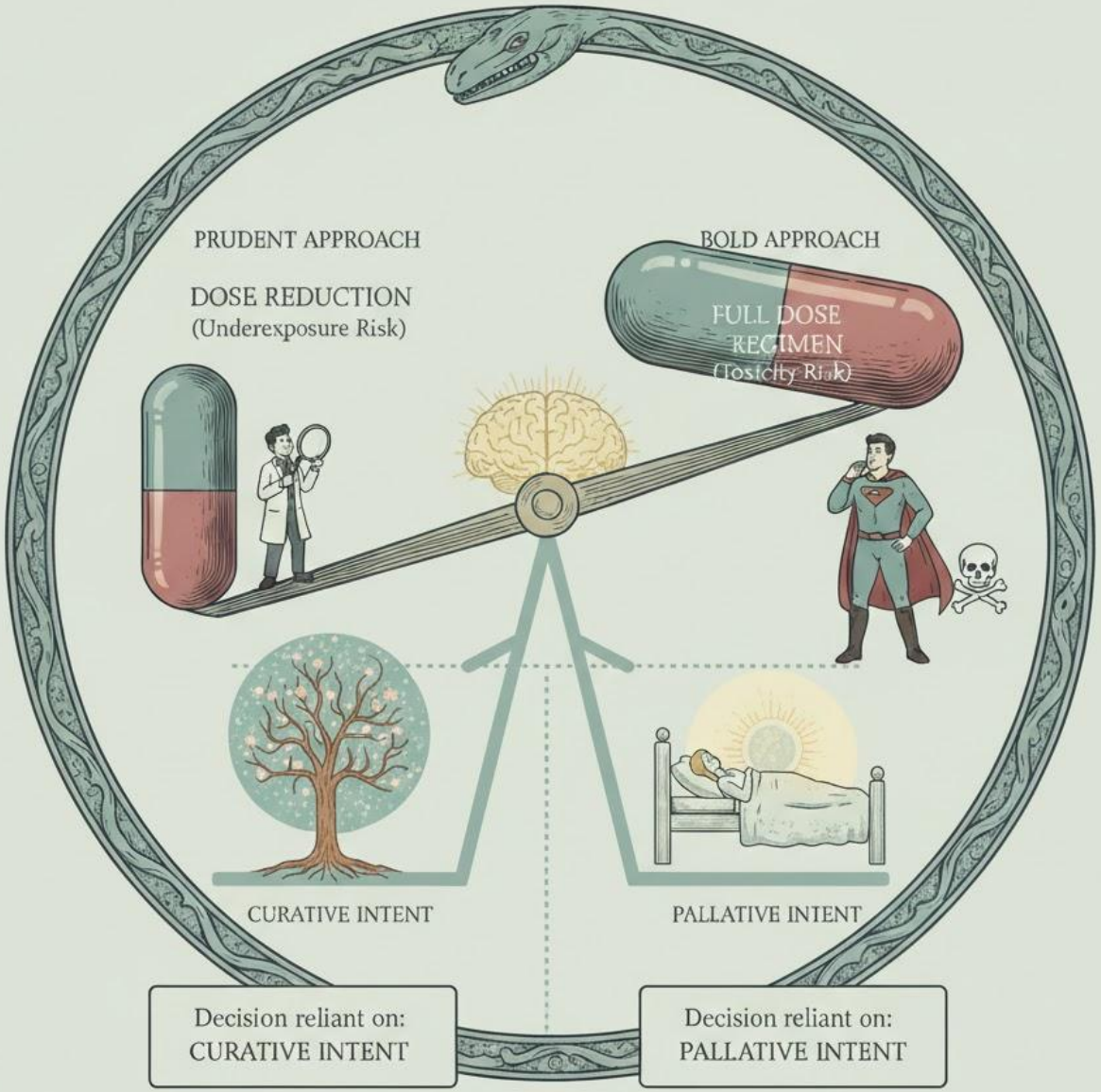
Take-home messages

- Always start from organ function and intent of treatment
- Use structured tools (eGFR, Child–Pugh, toxicity grading) + evidence-based dose recommendations
- Beware of modern therapy toxicities (ICI, TKI, PARPi, ADC)
- Organ dysfunctions, frailty, and dialysis require individualized decisions
- Multidisciplinary collaboration with nephrology, hepatology, cardiology is essential for safe and effective chemotherapy

THE DIFFICULT TRADE-OFF



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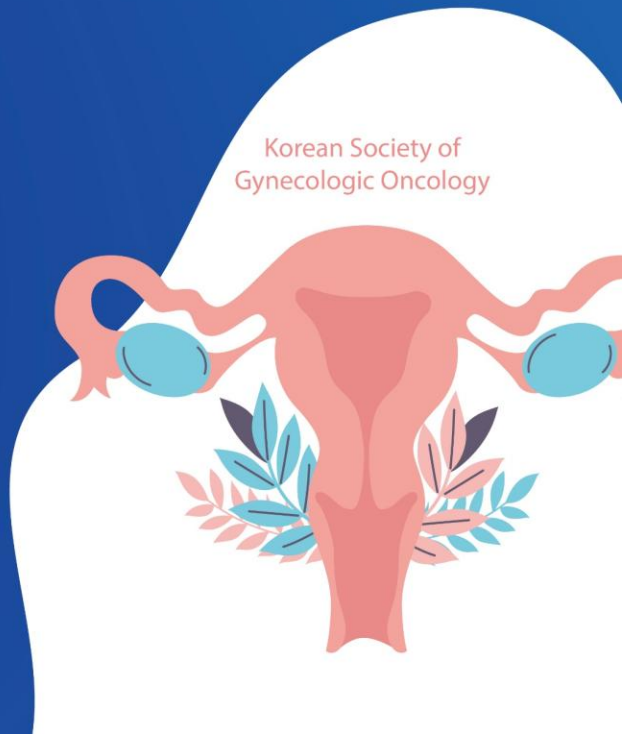
2026년 대한부인종양학회 제7회 동계학술대회 with Chemo-TIP Review

일자 2026년 1월 17일 (토)

장소 세종대학교 컨벤션센터

Thank you for your attention!

대한부인종양학회
Korean Society of Gynecologic Oncology



Hypersensitivity vs. infusion reactions

Common offenders in gyn-onc

- **Hypersensitivity to drug:** carboplatin, cisplatin, paclitaxel, docetaxel, etoposide, topotecan
- **Infusion-related reaction**(d/t formulation/diluent): paclitaxel (Cremophor), liposomal doxorubicin, rituximab
- Infusion reactions often resolve with slower rate + supportive care and do not automatically require desensitization

Operational safety

- Include hypersensitivity reaction rescue orders with every chemo order set.
- If continuing the same agent is necessary → use desensitization pathways, not “trial-and-error” spe ed changes.
- Plan 1:1 nursing and appropriate setting (ICU/inpatient/outpatient per protocol).

Premedication (baseline)

Steroid + H1 + H2 blockers ≥30 min prior to infusion (per protocol).

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Management of Chemotherapy Hypersensitivity Reactions and Desensitization

Most Common Offending Agents **This is not an all-inclusive list***

- **Hypersensitivity reaction to drug:** carboplatin, cisplatin, paclitaxel, docetaxel, etoposide, topotecan
- **Infusion related reaction (due to diluent/formulation):** paclitaxel (cremophor), liposomal doxorubicin, rituximab

SGO Education Committee Recommendations
1. To prevent reactions premedicate with each of the following: a corticosteroid, H_1 and H_2 blockers should be given **at least 30 minutes prior to infusion.**
2. Orders for **management of hypersensitivity reactions should be included with every chemotherapy order** so that a nurse may immediately proceed with immediate treatment interventions when needed.
3. All patients should receive at least a **H_1 antagonist** (i.e., diphenhydramine) and **H_2 antagonist** (i.e., famotidine) with corticosteroids (i.e., dexamethasone) for 24 hours prior to desensitization.
4. Chemotherapy desensitization should be done with one-to-one nurse staffing when done inpatient in ICU, inpatient on oncology floor, or in the outpatient setting.
5. Approach to desensitization is the 4- bag protocol with simple dilutions from original bag 1:1000 (0.1 mL), 1:100 (1 mL), 1:10 (10 mL) and 1:1 (original full dose bag) with each bag given over 1 hour with exception of paclitaxel that should be administered over 3 hours.

Management of Hypersensitivity Reactions

Drug Class	Medication	Indication
Supportive	Oxygen	• Relieves breathing difficulties
Hydration	Normal saline, IV	• Normalize blood pressure, especially in hypotensive patients
Corticosteroids	Hydrocortisone, 100mg IV Or Methylprednisolone 125 mg IV	• Used to treat/stop progression of hypersensitivity reactions. Modulates immune response and relieves inflammation
Non-selective adrenergic agonist	Epinephrine (1:1000) 0.2 to 0.5mL SQ or IM	• Used to treat/stop progression of hypersensitivity reactions; Increases blood • pressure; Relaxes smooth muscles in lungs; reduces wheezing and improves breathing; Increases heart rate; reduces hives and swelling around face and lips
H1 Blocker **H2 Blocker**	Diphenhydramine 25-50 mg IV Famotidine 20 mg IV	• Can be considered if has been more than 4 hours after last dose to relieve symptoms. It will not stop progression of reaction.

Acute management (safe re-start)

Management of hypersensitivity reactions

- Stop infusion; assess ABC; call for help
- Oxygen, IV fluids for hypotension
- IV corticosteroid (e.g., hydrocortisone 100 mg or methylpred 125 mg)
- IM/SC **epinephrine** for severe/life-threatening symptoms or if not improving quickly
- H1 blocker (diphenhydramine) + H2 blocker (famotidine) for symptom relief (do not rely on these alone to stop progression)

Infusion-reaction rate titration : Example (paclitaxel)

1. **Restart at 25% rate for 15 min**
2. If tolerated → 50% rate for 15 min
3. If tolerated → 75% rate for 15 min
4. If tolerated → resume full rate

If symptoms recur at any step: stop → allow res olution → resume at the previous tolerated rate, or stop and reassess.

Desensitization: SGO “4-bag” approach (operational summary)

Key recommendations

- Premedicate: steroid + H1 + H2 blockers; ensure rescue orders are pre-written.
- For desensitization, give H1/H2 + corticosteroid for 24 hours prior (per protocol).
- Use 1:1 nurse staffing (ICU/inpatient/outpatient depending on local pathway).

4-bag dilution scheme (from full-dose bag)

Bag 1 (1:1000) — 0.1 mL from Bag 4
Infuse 1 hour

Bag 2 (1:100) — 1 mL from Bag 4
Infuse 1 hour

Bag 3 (1:10) — 10 mL from Bag 4
Infuse 1 hour

Bag 4 (1:1) — Full dose (original)
Infuse 1 hour*

- Exception: Paclitaxel should be administered over 3 hours