Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

CISPGEMC Regimen

Gemcitabine-CISplatin

Disease Site

Genitourinary - Bladder / Urothelial

Intent

Neoadjuvant
Adjuvant

Regimen Category

Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses

- Neoadjuvant treatment of transitional cell carcinoma of the bladder*
- Adjuvant treatment of deep muscle-invasive transitional cell carcinoma of the bladder*

(*based on retrospective analyses suggesting similar outcomes to those reported for MVAC)

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B - Drug Regimen

Standard schedule:

gemcitabine	1000 mg /m²	IV	Days 1, 8 and 15
CISplatin	70 mg /m²	IV	Day 1

Alternative Schedule:

gemcitabine	1000-1250 mg /m²	IV	Days 1 and 8
CISplatin	70 mg /m²	IV	Day 1

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C - Cycle Frequency

Standard Schedule: REPEAT EVERY 28 DAYS

Alternative Schedule: REPEAT EVERY 21 DAYS

Neoadjuvant / Adjuvant: For 3 to 4 cycles unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: High (D1)
Low (D8, 15)

Febrile Neutropenia Risk: Moderate

Other Supportive Care:

Standard regimens for Cisplatin premedication and hydration should be followed. Refer to institutional guidelines.

Also refer to CCO Antiemetic Recommendations.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Dose on Day 1 of Cycle:

Worst Toxicity in Previous Cycle			Gemcitabine	Cisplatin
Non-Hematologic (related organ)		**Hematologic**	**% Full Dose***	**% Full Dose***
Grade 3	or	Febrile neutropenia, thrombocytopenic bleeding	75%	75%
Grade 4			Consider discontinuing, or ↓ to 75%	Consider discontinuing, or ↓ to 75%
Day 8 or 15 holds in > 1 cycle			75%	100%
• Pneumonitis • Hemolytic Uremic Syndrome (HUS) • Stevens-Johnson syndrome (SJS) • Toxic epidermal necrolysis (TEN) • Capillary Leak Syndrome (CLS)			Discontinue	Discontinue

* Do not restart until ANC ≥ 1500x 10^6/L, platelets ≥ 100,000 x 10^6/L and non-hematologic toxicity ≤ grade 2.

Dose on Day 8 and 15 (if applicable) of Cycle:

Toxicity on Day 8 or 15 of cycle					
Non-hematologic (related organ)		**Hematologic**			**Gemcitabine (% Full Dose)**
		AGC (x 10^6/L)		**Platelets (x 10^6/L)**	
≤ grade 2	and	> 1000	and	> 100,000	100%

≤ grade 2	and	500-1000	or	50,000-100,000	Consider Omit*, or ↓ to 75%
Grade 3 or 4	or	< 500	or	< 50,000	Omit*, ↓ to 75% at restart (if applicable) for non-hematologic toxicity
Pneumonitis, HUS, SJS, TEN, CLS		-		-	Discontinue

*If day 15 is omitted, may use q21 day cycle.

Hepatic Impairment

Bilirubin		AST/ALT	Gemcitabine (% previous dose)	Cisplatin (% previous dose)
1-2 x ULN	and/ or	<2 x ULN	100%	100%
2-4 x ULN		2-5 x ULN	Caution	100%
> 4 x ULN		> 5 x ULN	Caution, consider ↓	Caution, consider↓

Renal Impairment

Creatinine Clearance (mL/min)	Gemcitabine (% previous dose)	Cisplatin (% previous dose)
> 60	100%	100%
>45-60	Caution	75%
30-45	Caution	50%
< 30	Consider discontinuing or ↓	Discontinue

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F - Adverse Effects

Refer to gemcitabine, CISplatin drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Myelosuppression ± infection, bleeding (may be severe) • Fatigue, flu-like symptoms, musculoskeletal pain • Edema • Nausea and vomiting • Elevated LFTs (may be severe) • Neurotoxicity and ototoxicity (may be severe) • Nephrotoxicity (may be severe), proteinuria • Electrolyte abnormalities • Diarrhea • Anorexia • Rash (may be severe)	• Hemolytic uremic syndrome, vasculitis • Hemolysis • Pneumonitis, ARDS • Capillary leak syndrome • Arrhythmia • Cardiotoxicity • Arterial thromboembolism • Venous thromboembolism • Secondary malignancy • Seizures • PRES • Hypersensitivity

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G - Interactions

Refer to gemcitabine, CISplatin drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to gemcitabine, CISplatin drug monograph(s) for additional details

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; baseline and before each cycle
- Electrolytes, including magnesium, sodium, potassium, phosphate and calcium; baseline and regular
- Liver function tests; baseline and regular
- Renal function tests; baseline and regular
- Audiogram; baseline as clinically indicated
- Clinical toxicity assessment (infection, bleeding, flu-like symptoms, lethargy, dyspnea, rash, nausea/vomiting and other GI effects, neurotoxicity, ototoxicity); at each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

INR for patient receiving warfarin; Baseline and as clinically indicated

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J - Administrative Information

Approximate Patient Visit	Day 1: 4 to 5 hours; Gemcitabine only day: 0.75 hour
Pharmacy Workload (average time per visit)	31.387 minutes
Nursing Workload (average time per visit)	40.000 minutes

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K - References

Cisplatin, gemcitabine drug monographs, Cancer Care Ontario.

Advanced Bladder Cancer (ABC) Meta-analysis Collaboration. Neoadjuvant chemotherapy in invasive bladder cancer: update of a systematic review and meta-analysis of individual patient data advanced bladder cancer (ABC) meta-analysis collaboration. Eur Urol 2005;48(2):202-5.

Booth CM, Siemens DR, Li G, et al. Perioperative chemotherapy for muscle-invasive bladder cancer: A population-based outcomes study. Cancer 2014;120(11):1630-8.

Fléchon A, Fizazi K, Gourgou-Bourgade S, et al. Gemcitabine and cisplatin after radical cystectomy for bladder cancer in an adjuvant setting: feasibility study from the Genito-Urinary Group of the French Federation of Cancer Centers. Anticancer Drugs 2006;17(6):705-8.

Herchenhorn D, Dienstmann R, Peixoto FA, et al. Phase II trial of neoadjuvant gemcitabine and cisplatin in patients with resectable bladder carcinoma. Int Braz J Urol 2007;33(5):630-8.

Yeshchina O, Badalato GM, Wosnitzer MS, et al. Relative efficacy of perioperative gemcitabine and cisplatin versus methotrexate, vinblastine, adriamycin, and cisplatin in the management of locally advanced urothelial carcinoma of the bladder. Urology 2012 Feb;79(2):384-90.

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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