Regimen Monograph

A - Regimen Name

CISPVINO(W) Regimen

CISplatin-Vinorelbine

Disease Site	Lung - Non-Small Cell
Intent	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	Postoperative adjuvant treatment for patients with completely resected stage II or stage IIIA non-small cell lung cancer.

back to top

B - Drug Regimen

CISplatin	50 mg /m²	IV	Days 1 and 8
vinorelbine	25 mg /m²	IV	Days 1, 8, 15, 22

back to top

C - Cycle Frequency

REPEAT EVERY 28 DAYS

For a usual total of 4 cycles unless disease progression or unacceptable toxicity occurs

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate (D1, 8)
Minimal (D15, 22)

Febrile Neutropenia Risk: Moderate

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

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

back to top

E - Dose Modifications

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

Dosage with toxicity

Hematologic Toxicities

	Dosage for subsequent cycle	
Worst Toxicity / Counts in the Previous Cycle	**Cisplatin (% previous dose)**	**Vinorelbine (% previous dose)**
Febrile neutropenia, Thrombocytopenic bleeding, ANC < 0.5 for ≥ 5 to 7 days and/or Grade 4 thrombocytopenia	75%*	75%*
≥ Grade 2 ototoxicity	Discontinue	No change
Grade 2 peripheral neuropathy	75%	Discontinue
Grade 3 peripheral neuropathy	Discontinue	Discontinue
Grade 3 organ / non-hematologic toxicity	75%*	75%*
Grade 4 organ / non-hematologic toxicity	Discontinue	Discontinue

* Do not retreat until non-hematologic/ organ toxicity ≤ grade 2, platelets ≥ 100 x 10^9/L and ANC ≥ 1.5 x 10^9/L

Dose on day 8, 15, 22 of cycle

Toxicity on Day 8, 15 and 22 of cycle					
Non–hematologic (related organ)		**Hematologic**			**Day 8 (or 15, 22) Vinorelbine (% day 1 dose)**
		ANC (x 10^9/L)		**Platelets (x 10^9/L)**	
≤ grade 2	and	≥ 1.5	and	≥ 100	100%
≤ grade 2	and	1-1.49	and/or	75-99	50%
Grade 3 or 4 related organ	or	< 1	or	< 75	Omit

Hepatic Impairment

Total bilirubin	Cisplatin (% previous dose)	Vinorelbine (% previous dose)
< 2 x ULN	No change	100%
2-4 x ULN		25-50%
> 4 x ULN		Discontinue
Consider dose reduction of vinorelbine for moderate- severe elevations of transaminases		

Renal Impairment

Creatinine Clearance (mL/min)	Cisplatin (% previous dose)	Vinorelbine (% previous dose)
>60	100%	No change
>40-60	50%	
<40	OMIT	

Dosage in the Elderly

- Vinorelbine: No dosage adjustments are required for increased age
- CISplatin: Geriatric patients may be at higher risk of developing nephrotoxicity, ototoxicity/neurotoxicity or hematologic adverse effects with cisplatin.

back to top

F - Adverse Effects

Refer to vinorelbine, 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) • Nausea and vomiting • Nephrotoxicity • Neurotoxicity (including ototoxicity; may be severe) • Fatigue • Electrolyte imbalances • ↑ LFTs • Anorexia	• Hypersensitivity • Hemolytic uremic syndrome • Arterial thromboembolism • Venous thromboembolism • Pneumonitis • SIADH • Secondary malignancy • Radiation recall reaction • Seizure

• Mucositis • Diarrhea • Fever • Tumour pain • Alopecia	

back to top

G - Interactions

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

back to top

H - Drug Administration and Special Precautions

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

back to top

I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- CBC; baseline and before each cycle. Interim counts should be done in first cycle and repeated if dose modifications necessary.
- Renal function tests (including electrolytes and magnesium) and urinalysis; baseline and before each cycle
- Liver function tests; baseline and before each cycle
- Clinical toxicity (including nausea, neuropathy, ototoxicity, local toxicity); at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Audiogram; baseline and as clinically indicated

back to top

J - Administrative Information

Approximate Patient Visit	4 hours
Pharmacy Workload (average time per visit)	28.326 minutes
Nursing Workload (average time per visit)	41.667 minutes

back to top

K - References

Cisplatin and vinorelbine drug monographs, Cancer Care Ontario.

Arriagada R, Bergman B, Dunant A, Le Chevalier T, Pignon JP, Vansteenkiste J; International Adjuvant Lung Cancer Trial Collaborative Group.. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. N Engl J Med. 2004 Jan 22;350(4):351-60.

Kris MG, Gaspar LE, Chaft JE, et al. Adjuvant Systemic Therapy and Adjuvant Radiation Therapy for Stage I to IIIA Completely Resected Non-Small-Cell Lung Cancers: American Society of Clinical Oncology/Cancer Care Ontario Clinical Practice Guideline Update. J Clin Oncol 2017;35(25):2960-74.

Kreuter M, Vansteenkiste J, Fischer JR, et al. Three-Year Follow-Up of a Randomized Phase II Trial on Refinement of Early-Stage NSCLC Adjuvant Chemotherapy with Cisplatin and Pemetrexed versus Cisplatin and Vinorelbine (the TREAT Study). J Thorac Oncol 2016;11(1):85-93.

Winton T, Livington D, Johnson D et al. Vinorelbine plus cisplatin as compared with oberservation in resected non small cell lung cancer. NEJM 2005; 352: 2589-97.

PEBC Advice Documents or Guidelines

- Adjuvant Systemic and Radiation Therapy for Stage I to IIIA Completely Resected Non–Small-Cell Lung Cancers: ASCO-CCO Clinical Practice Guideline Update

June 2021 removed vinorelbine NDFP funding info

back to top

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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back to top