Systemic Anti Cancer Treatment Protocol

Vinorelbine
Advanced Breast Cancer

PROTOCOL REF: MPHAVINOBR
(Version No: 1.0)

Approved for use:

As an option for second or subsequent line treatment for locally advanced/ metastatic breast cancer

Dosage:

Oral regimen

Drug	Dosage	Route	Frequency
Vinorelbine	60mg/m² Can be increased to 80mg/m^2 from the 3rd administration onwards if tolerated* **Maximum dose 160mg weekly**	Oral	Days 1 and 8 of 21 day cycle Until disease progression or unacceptable toxicity

If unsuitable for dose escalation to 80mg/m^2 consider increasing frequency to include day 15 if treatment tolerated well and patient has good performance status.

Consider using the oral route first line. In case of swallowing difficulties or persistent nausea and vomiting, switch to the IV route.

Oral dose	Equivalent IV dose
80mg/m^2	30mg/m^2
60mg/m^2	25mg/m^2

Intravenous regimen

Drug	Dosage	Route	Frequency
Vinorelbine	25mg/m² Can be increased to 30mg/m² from the 3rd administration onwards if tolerated*.	IV	Days 1 and 8 of 21 day cycle Until disease progression or unacceptable toxicity

***Dose Escalation**

ANC during the first 3 administrations of 60 mg/m²/week	ANC > 1.0 x 10^9/L	0.5 ≤ ANC < 1.0 x 10^9/L 1 episode	0.5 ≤ ANC < 1.0 x 10^9/L 2 episodes	ANC < 0.5 x 10^9/L
Recommended oral dose starting with the 4th administration (mg/m²)	80 mg/m²	80 mg/m²	60 mg/m²	60 mg/m²

Dose Modification

ANC beyond the 4th administration of 80 mg/m²/week	ANC > 1.0 x 10^9/L	0.5 ≤ ANC < 1.0 x 10^9/L 1 episode	0.5 ≤ ANC < 1.0 x 10^9/L 2 episodes	ANC < 0.5 x 10^9/L
Recommended oral dose starting with the next administration (mg/m²)	80 mg/m²		60 mg/m²	

Supportive treatments:

Dexamethasone 4mg orally twice daily for 3 days for oral vinorelbine

Domperidone 10mg tablets orally three times a day as required

Extravasation risk:

Vinorelbine (IV): vesicant

Refer to the network guidance for the prevention and management of extravasation.

Drug Interactions

Concomitant use with live attenuated vaccines, phenytoin and itraconazole is not recommended; please refer to the SmPC for full details on the nature of the interaction.

Vinca-alkaloids are known as substrates for P-glycoprotein, and in the absence of specific study, caution should be exercised when combining vinorelbine with strong modulators (cyclosporine, digoxin, diltiazem, verapamil, simvastatin etc.) of this membrane transporter.

Caution is strongly recommended when vinorelbine is used in combination with strong inducers (rifampicin, carbamazepine, phenobarbital, phenytoin etc.) or inhibitors (clarithromycin, fluconazole, erythromycin, nefazodone, itraconazole, ketoconazole, HIV protease inhibitors etc.) of the CYP 3A4 isoenzyme.

Administration:

Oral regimen

Day	Drug	Dose	Route	Diluent and rate
1	Ondansetron	16mg	Oral	30 minutes prior to vinorelbine
	Dexamethasone	8mg	Oral	30 minutes prior to vinorelbine
	Vinorelbine	**60 mg/m^2 or 80mg/m^2**	**Oral**	
8	Ondansetron	16mg	Oral	30 minutes prior to vinorelbine
	Dexamethasone	8mg	Oral	30 minutes prior to vinorelbine
	Vinorelbine	**60mg/m^2 or 80mg/m²**	**Oral**	

- Due to sorbitol content, patients with rare hereditary problems with fructose intolerance should not take the capsules.
- The liquid content within the capsules is irritant and therefore contact with skin, mucosa or eyes should be strictly avoided. If accidental contact occurs the affected area should be rinsed immediately with water or preferably normal saline

solution. Damaged/broken capsules should not be swallowed and instead disposed of appropriately and pharmacy informed.

- The capsules should be swallowed whole with water, not chewing or sucked. If this occurs, rinse mouth out with water or preferably a normal saline solution.
- In the case of vomiting within a few hours after drug intake, do not re-administer.
- Vinorelbine soft capsule is associated with a higher incidence of nausea/vomiting than the intravenous formulation. Primary prophylaxis with anti-emetics and administration of the capsules with some food is recommended as this has also been shown to reduce the incidence of nausea and vomiting.
- Patients receiving concomitant morphine or opioid analgesics: laxatives and careful monitoring of bowel mobility are recommended. Prescription of laxatives may be appropriate in patients with prior history of constipation.

Intravenous regimen

Day	Drug	Dose	Route	Diluent and rate
1	**Vinorelbine**	**25 mg/m^2 or 30mg/m^2**	**IV**	50mL Sodium Chloride 0.9% over 10 minutes
8	**Vinorelbine**	**25mg/m^2 or 30mg/m^2**	**IV**	50mL Sodium Chloride 0.9% over 10 minutes

Administration should always be followed by a 250ml sodium chloride 0.9% infusion to flush the vein.

Main Toxicities:

Haematological	Neutropenia, anaemia, thrombocytopenia,
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, mucositis
Nervous system	Peripheral neuropathy
Hepatobiliary	Elevation of liver transaminases, alkaline phosphatase and bilirubin.

Skin and subcutaneous tissue disorders	Alopecia Allergic reaction
General disorders and administration site conditions	Fatigue, insomnia, visual disorders, dyspnoea Infertility, early menopause With intravenous preparation care during administration is crucial as extravasation can lead to signficant skin damage

Investigations:

	Pre	C1	C1D8	C2D1	C2D8 dose increase recommended	Ongoing
Medical Assessment	X			X	X	Every cycle
Nursing Assessment		X	X	X	X	Every treatment
FBC	X		X	X	X	Every treatment
U&E & LFT	X		X	X	X	Every treatment
Informed Consent	X					
CT scan	X					Every 8 to 12 weeks as clinically indicated
PS recorded	X	X	X	X	X	Every treatment
Toxicities documented	X		X	X	X	Every treatment
Weight recorded	X	X	X	X	X	Every treatment

Dose Modifications:

Haematological Toxicity:

Proceed on day 1 if-

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if-

Plt ≤ 99 x 10^9/L	ANC ≤ 0.9 x 10^9/L

Proceed on day 8 if-

Plt ≥ 75 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Omit on day 8 if-

Plt ≤ 74 x 10^9/L	ANC ≤ 0.9 x 10^9/L

On day 8 of the cycle if blood results do not meet the above levels the patient will miss that dose and proceed to the next cycle.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non-haematological Toxicity

Renal Impairment:

No dose adjustment is necessary.

Hepatic Impairment

AST/ALT > 5 x ULN or bilirubin > 2 x ULN- reduce dose by a third.

In breast cancer patients, clearance is not altered in presence of moderate liver metastases (i.e. <75% of liver volume replaced by the tumour). In these patients there is no pharmacokinetic rationale for reducing doses. In patients with massive liver metastases (i.e. >75% of liver volume replaced by the tumour), it is suggested that the dose is reduced by 1/3 and the haematological toxicity closely followed.

References:

NICE guideline 'Advanced Breast Cancer: Diagnosis and Treatment' (CG81)- accessed 14th of June 2018.

SmPC Navelbine 20mg soft capsule and 10mg/mL concentrate for infusion - accessed 19th June 2018

The North London Cancer Network (2009) 'Dosage Adjustment for Cytotoxics in Hepatic Impairment'.