LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Oral Vinorelbine 3 weekly cycle in Advanced Breast Cancer

Indication:	Second line or subsequent treatment of advanced breast cancer where anthracyclines have failed or are unsuitable. In combination with chemotherapy
Regimen details:	In combination chemotherapy: Vinorelbine 60mg/m^2 PO Day 1 & 8 After 3rd dose * 80mg/m^2 PO (*See dose escalation guidance under dose modification section) Total dose should not exceed 120mg for 60mg/m^2 or 160mg at 80mg/m^2
Administration:	Vinorelbine is available as 20mg, 30mg and 80mg soft capsules. Capsules to be swallowed with water without chewing or sucking the capsule. It is recommended that vinorelbine is taken with food. Oral vinorelbine 80mg/m^2 corresponds to IV vinorelbine 30mg/m^2 Oral vinorelbine 60mg/m^2 corresponds to IV vinorelbine 25mg/m^2
Frequency:	Day 1 & 8, every 21 days Objectively assess response after 3 cycles. If responding, continue to a total of 6 cycles. Occasionally treatment may be continued beyond 6 cycles after consultant review.
Pre-medication:	Not routinely required
Anti- emetics:	Mild/ Moderate emetogenicity Follow local anti-emetic policy
Supportive medication:	Not routinely required
Extravasation:	Not applicable

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Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Isabel Munoz	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Lisa Yuen	Date prepared: November 2014 Review Date: November 2016

Regular investigations:

Prior to Cycle 1:

FBC	Day 1 (within 14 days)
LFTs	Day 1 (within 14 days)
U&Es	Day 1 (within 14 days)

Prior to Day 8 (all cycles):

FBC	Day 8 (within 48 hours)

Prior to Day 1 (all cycles):

FBC	Day 1 (within 48-72 hours)
LFTs	Day 1 (within 48-72 hours)
U&Es	Day 1 (within 48-72 hours)

Clinical toxicity assessments (including neuropathy & local toxicity)

Toxicities: Myelosuppression, ovarian failure/infertility, peripheral neuropathy and neuropathy induced constipation, alopecia (usually mild), GI symptoms,

DOSE MODIFICATIONS

Haematological Toxicity

Day 1:

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Day 1 Dose
> 1.5	&	> 100	100% dose
< 1.5	&	< 100	Delay day 1 until recovered to above these levels then resume treatment. For second delay, consider 75% dose.

Day 8:

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Day 8 Dose
> 1.5	&	> 100	100% dose
1.0 – 1.49	or	75 - 99	75% dose
< 1.0	&	< 75	Omit day 8 and consider dose reduction for next cycle

If significant myelotoxicity, or more than 2 delays, consider giving as a 4-weekly schedule on day 1 and day 15

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Dose escalation	**Dose modification**
Neutrophil count during 1st three administrations of 60mg/m^2	
> 1.0	Increase to 80mg/m^2 at 4th dose
≥ 0.5 and < 1.0 (1st episode)	Increase to 80mg/m^2 at 4th dose
≥ 0.5 and < 1.0 (2nd episode)	**Continue 60mg/m^2 – do not escalate**
< 0.5	**Continue 60mg/m^2 – do not escalate**
Dose de-escalation	
Neutrophil count from 4th dose onwards	
> 1.0	Continue 80mg/m^2
≥ 0.5 and < 1.0 (1st episode)	Continue 80mg/m^2
≥ 0.5 and < 1.0 (2nd episode)	Delay treatment until recovery, then reduce to 60mg/m^2
< 0.5	Delay treatment until recovery, then reduce to 60mg/m^2 It is possible to re-escalate the dose after further 3 administrations with lower dose if well tolerated.

Non-haematological Toxicities

Renal Impairment

Dose adjustment not required if CrCl ≥ 30ml/min.
If CrCl < 30ml.min, discuss with Consultant.

Hepatic Impairment

If hepatic insufficiency is due to metastatic involvement, the liver function may recover in response to treatment. Therefore, for patients with massive liver metastases, i.e. > 75% of liver volume replaced by tumour, it is empirically suggested to reduce the dose of vinorelbine to 85% and monitor closely haematological toxicity.

If hepatic insufficiency is due to other reasons, use the table below:

Bilirubin		**AST / ALT**	**Dose**
< 1.5 x ULN	&	< 5 x ULN	100%
1.5 to 3 x ULN	&	< 5 x ULN	Postpone and reassess in 1 week, consider vinorelbine 50% dose. If toxicity persists for more than 3 weeks, discontinue treatment.

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> 3 x ULN			Omit
		> 5 x ULN	Clinical decision, consider 33% dose reduction

Dose modifications for other toxicities as appropriate

	Vinorelbine dose
Grade 1 or 2 neurotoxicity	100% dose
Grade 3 or 5 neurotoxicity	Omit
Grade 3 mucositis	Give 75% dose
Grade 4 mucositis	Omit
Grade 3 or 4 constipation	Omit
Any other grade 3 toxicities	Give 75% dose
Any other grade 4 toxicities	Omit

Location of regimen delivery: Vinorelbine to be supplied to the patient for oral self-administration. Ensure that the patient has an information pack and the treatment plan.
Suitable for home delivery

Comments: None

Drug interactions: Aprepitant – increased vinorelbine plasma levels
Itraconazole – increased risk of neurotoxicity.
Omeprazole and fluoxetine may inhibit vinorelbine metabolism
Posazonazole and voriconazole- increased vinorelbine plasma levels

The following table gives the dose required for appropriate ranges of body surface area (BSA)

BSA (m^2)	**60mg/m^2 Dose (mg)**	**80mg/m^2 Dose (mg)**
0.95 to 1.04	60	80
1.05 to 1.14	70	90
1.15 to 1.24	70	100
1.25 to 1.34	80	100
1.35 to 1.44	80	110
1.45 to 1.54	90	120
1.55 to 1.64	100	130
1.65 to 1.74	100	140
1.75 to 1.84	110	140
1.85 to 1.94	110	150

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≥ 1.95	120	160

Even for patients with BSA ≥ 2m^2 the total dose should never exceed 160mg

References:

SELCN network protocols (PO Vinorelbine), accessed May 09
SWSHCN Protocols. Vinorelbine. Revised Jan 09
NWLCN Breast Cancer protocols Oct 2012
www.medicines.org.uk Pierre Fabre 08.2011
UCLH- Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009
UCLH- Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009
LCA Breast Cancer Clinical Guidelines October 2013

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