

Lung Pathway Group – Oral Vinorelbine in Non-Small Cell Lung Cancer (NSCLC)

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| Indication: | Advanced or metastatic NSCLC for patients unsuitable for platinum based treatment regimen, performance status 2 or significant co-morbidities. Eligible for patients able to tolerate and comply with oral dosage forms. |
| Regimen details: | Vinorelbine 60mg/m ² PO Day 1 and Day 8 (first cycle) *Vinorelbine 80mg/m ² PO Day 1 and Day 8 (second cycle onwards) * See dose escalation guidance under 'Dose modifications' |
| Administration: | Vinorelbine available as 20mg, 30mg and 80mg soft capsules. Capsules to be swallowed whole with water without chewing or sucking. Capsules are recommended to be taken with food. |
| Frequency: | Day 1 and Day 8, every 21 days, for 4 to 6 cycles |
| Pre-medication: | Not routinely required |
| Anti- emetics: | Day 1: Low emetogenicity Day 8: Low emetogenicity Follow local anti-emetic policy |
| Supportive medication: | Mouthcare as per local policy |
| Extravasation: | Not applicable |

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| Version: 1.0 Supersedes: all other versions | Approved by LCA Lung Pathway Chemotherapy Lead: Rohit Lal |
| Reason for Update: LCA Protocol Development | Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl |
| Prepared by: Lisa Yuen | Approved by LCA Medicines & Chemotherapy Steering Group Chair: |
| Second check by: Laura Cameron | Date prepared: April 2015 Review Date: April 2017 |
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| 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) |
| | CT scan | Baseline |
| | Prior to Day 8 (all cycles): | |
| | FBC | Day 8 (within 72 hours) |
| | Prior to Day 1 (all cycles): | |
| | FBC | Day 1 (within 72 hours) |
| | LFTs | Day 1 (within 72 hours) |
| | U&Es | Day 1 (within 72 hours) |
| | Imaging | After 3 cycles |

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

DOSE MODIFICATIONS

Haematological Toxicity

Prior to day 1 and day 8

| Neutrophils (x 10 ⁹ /L) | | Platelets (x 10 ⁹ /L) | Vinorelbine Dose |
|---------------------------------------|--------------|-------------------------------------|--|
| ≥ 1.5 | & | ≥ 100 | 100% dose |
| < 1.0 | or | < 100 | Delay day 1 for 1 week. Repeat FBC, if recovered to above these levels, give 100% dose. |

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

Vinorelbine Dose escalation after 1st cycle

If the first cycle is well tolerated, it is recommended to increase the dose of vinorelbine to 80mg/m² at cycle 2 in the following settings:

Adjuvant/ induction setting, and when vinorelbine is used as a single agent.

When relevant, dose escalation should take place at cycle 2 only if:

- no grade 4 neutropenia (<0.5 x 10⁹/L) at day 8.
- no febrile neutropenia

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Vinorelbine Dose de - escalation from 2nd cycle onwards

If grade 4 neutropenia ($<0.5 \times 10^9/L$) occurs during cycles with 80mg/m² dose, delay treatment until recovered, then reduce to 60mg/m².

It is possible to re-escalate the dose after further 3 administrations with lower dose if well tolerated. Follow monitoring in following cycles as detailed above.

Non-haematological Toxicities

Renal Impairment Dosage adjustment not required

Hepatic Impairment

If hepatic insufficiency is due to metastatic involvement, 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 that the dose of vinorelbine be reduced by 1/3rd and haematological toxicity monitored.

If hepatic insufficiency is due to other reasons, the table below should be used:

| Bilirubin | ALT / AST | Vinorelbine Dose |
|------------------|------------------|---|
| < 1.5 x ULN | < 5 x ULN | Give 100% dose |
| 1.5 – 3 x ULN | 5 – 20 x ULN | Delay day 1 for 1 week/omit day 8, and reassess*. Consider dose reduction to 25-50% dose. |
| > 3 x ULN | > 20 x ULN | Discontinue |

*If liver toxicity persists for more than 3 weeks, discontinue treatment

Dose modifications for other toxicities as appropriate

Neurotoxicity

| Neurotoxicity | Vinorelbine Dose |
|----------------------|-------------------------|
| Grade 2 | Give 100% dose |
| Grade 3 or 4 | Discontinue |

Other toxicities

| | Vinorelbine Dose |
|---|---------------------------|
| Grade 3 mucositis | Give 75% of previous dose |
| Grade 4 mucositis | Give 50% of previous dose |
| Any grade 3 toxicities (except mucositis) | Give 75% of previous dose |
| Any grade 4 toxicities (except mucositis) | Omit |
| Grade 3 or 4 constipation | Omit |

Location of regimen delivery: Outpatient setting

Comments: Adequate contraceptive methods should be used during therapy and for 3 months after completing treatment

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Drug interactions: Itraconazole - increased risk of neurotoxicity
Posaconazole, voriconazole - increased vinorelbine plasma levels

References: www.medicines.org.uk

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