NAB-PACLITAXEL (ABRAXANE) for breast cancer

Funded as an alternative treatment for metastatic breast cancer, only in patients who have documented taxane hypersensitivity

Funded as an alternative for the neo-adjuvant or adjuvant treatment of early stage breast cancer, only in patients who have documented taxane hypersensitivity (unlicensed use)

Blueteg registration is required before treatment may start

<table>
<thead>
<tr>
<th>Drugs/Dosage/Frequency</th>
<th>Metastatic setting, licensed dosing:</th>
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<tbody>
<tr>
<td></td>
<td>Nab-paclitaxel (Abraxane) 260mg/m² IV Day 1, every 3 weeks, for 6 cycles*</td>
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</table>

| Metastatic setting, unlicensed dosing: |
| Nab-paclitaxel (Abraxane) 125mg/m² IV Day 1, Day 8 and Day 15, every 4 weeks for 6 cycles* |

Unlicensed options, for neo-adjuvant or adjuvant use, as replacement for the paclitaxel or docetaxel component of the anthracycline-taxane regimen:

Nab-paclitaxel (Abraxane) 125mg/m² IV once weekly x 12 weeks* or
Nab-paclitaxel (Abraxane) 260mg/m² IV Day 1, every 2 weeks, for 4 cycles* with Primary G-CSF prophylaxis s/c once daily for 5 days, starting on Day 3

*If any cycles of docetaxel or paclitaxel were successfully administered before switching, remember to adjust the number of cycles of nab-paclitaxel required, accordingly

For use in combination with SC trastuzumab (Herceptin):
The first dose of s/c trastuzumab may be given on the same day as the 1st dose of nab-paclitaxel:
administer the s/c trastuzumab first, wait one hour, then initiate the nab-paclitaxel infusion.
For subsequent doses of s/c trastuzumab, there is no need for a specific time interval between the trastuzumab and starting the nab-paclitaxel.

Administration:
all nab-paclitaxel doses are infused over 30 minutes

Main Toxicities:
myelosuppression; alopecia; GI side effects; peripheral neuropathy; myalgia / arthralgia; rash; ovarian failure / infertility

Anti-emetics:
mildly emetogenic

Extravasation:
nab-paclitaxel is a vesicant

Regular Investigations:
FBC before each dose
U&Es every 2 or 3 weeks
LFTs 2- or 3-weekly dosing: before each dose
Weekly dosing: weekly if raised at baseline; otherwise 3-weekly
Comments: Hypersensitivity reactions to nab-paclitaxel are very rare. If a hypersensitivity reaction does occur, stop the infusion and initiate symptomatic treatment. The patient should not be re-challenged with nab-paclitaxel.

Dose Modifications

Haematological Toxicity: Note: Dose reduction and/or delay in early stage breast cancer can compromise outcome. If any delay due to neutropenia, consider addition of G-CSF with subsequent doses.

260mg/m² dose (2- or 3-weekly):
Neutrophils ≤ 1.5 x 10⁹/l or Platelets ≤ 100 x 10⁹/l
Delay next dose until counts above these limits.
If neut < 0.5 x 10⁹/l for a week or more, once recovered, reduce the dose to 220mg/m² for subsequent cycles.
If 2nd occurrence of neutrophils < 0.5 for a week or more, reduce nab-paclitaxel further to 180mg/m².

Weekly dosing:
Neutrophils ≤ 1.5 x 10⁹/l or Platelets ≤ 100 x 10⁹/l
Delay next dose until counts above these limits.
If neutrophils < 0.5 x 10⁹/l, once recovered, reduce the dose to 100mg/m² for subsequent cycles.
If 2nd occurrence of neutrophils < 0.5, reduce further¹ to 75mg/m².

Non-haematological Toxicities: For Grade 3 sensory neuropathy, withhold treatment until resolution to Grade 1 or 2, followed by a dose reduction for all subsequent doses.

Renal Impairment: No dose adjustment required if CrCl ≥ 30ml/min.
There are insufficient data to recommend dose modifications in patients with CrCl < 30ml/min.

Hepatic Impairment:

<table>
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<tr>
<th>LFTs</th>
<th>Nab-paclitaxel (Abraxane) dose</th>
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<tr>
<td>Bilirubin &gt; 1 to ≤ 1.5 x ULN and AST ≤ 10 x ULN</td>
<td>No dose adjustment required</td>
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<tr>
<td>Bilirubin &gt; 1.5 to ≤ 5 x ULN and AST ≤ 10 x ULN</td>
<td>Start with a 20% dose reduction. The reduced dose may be escalated to the dose for patients with normal hepatic function if the patient is tolerating the treatment for at least two cycles.</td>
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<tr>
<td>Bilirubin &gt; 5 x ULN or AST / ALT &gt; 10 x ULN</td>
<td>Insufficient data to recommend dose</td>
</tr>
</tbody>
</table>

References: Gradishar, W et al.; JCO 2005; 23 (31): 7794 – 7803 (metastatic, as licence)
Untch, M et al.; Lancet Oncol 2016; 17 (3): 345 - 356 (weekly x 12)
Martin, M; Breast Cancer Res 2015; 17 (1): 81 (nab-paclitaxel review in breast cancer)
¹No specific reference – agreed locally