Dacarbazine
Metastatic Malignant Melanoma

**Background:** Dacarbazine is the standard 1\textsuperscript{st} line treatment for patients with malignant metastatic melanoma.

**Patient Group:**

<table>
<thead>
<tr>
<th>Metastatic malignant melanoma</th>
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<tbody>
<tr>
<td>Life expectancy &gt; 12 weeks</td>
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<tr>
<td>ECOG PS 0-2</td>
</tr>
</tbody>
</table>

**Pre-treatment Assessment:**

- Weight, FBC, U&E, LDH, LFTs and Creatinine clearance
- CT Scan and tumour measurements

**Treatment Threshold**

\[
\begin{align*}
\text{WBC} & \geq 3.0 \times 10^9 / \text{L} \\
\text{ANC} & \geq 1.5 \times 10^9 / \text{L} \\
\text{Platelets} & \geq 100 \times 10^9 / \text{L} \\
\text{Cr Cl} & > 60 \text{mL/min}
\end{align*}
\]

**Regimen Details:**

**Day 1**

Dacarbazine $850 \text{mg/m}^2$ \text{IV} in 250mL sodium chloride 0.9% infused over 30 minutes.

The infusion and administration set should be protected from light.

Repeated every 21 days for 6 cycles
Administration:
- It is recommended to test the patency of the vein first with a 10mL flush of sodium chloride 0.9%. The line should also be flushed with 10 - 50mL sodium chloride after the infusion.
- Care should be taken to avoid extravasation as dacarbazine can cause tissue damage and severe pain.
- **Vein Irritation**: Dacarbazine often causes pain during administration that usually responds to slowing the infusion rate.
- **The infusion should be protected from light during administration.**

**Pre-Meds:** 30 minutes prior to chemotherapy
Dexamethasone 8mg IV bolus over 3-5 minutes
Ondansetron 8mg IV bolus over 3-5 minutes

**Anti-emetics:** Very highly emetic – may require aprepitant.

**Additional Medication:** None

**Monitoring and Assessment:**
Clinical Assessment- medical review prior to each cycle
FBC – prior to each cycle
U&E, LFT (including LDH) creatinine clearance (calculated) – prior to each cycle
Tumour measurements and CT scan after 2\textsuperscript{nd} and 4\textsuperscript{th} cycle or as clinically indicated.

**Dose Modifications:**

*Haematological toxicity*

Neutrophils  $< 1.0 \times 10^9/L$ delay by 1 week
Platelets  $< 100 \times 10^9/L$ delay by 1 week

Repeat FBC and resume treatment at 100% dose if within normal parameters. Consider 20% dose reduction if there is more than one week’s delay due to myelosuppression or if myelosuppression recurs. G-CSF support is not indicated.
Renal Impairment

<table>
<thead>
<tr>
<th>Clearance (mL/min)</th>
<th>Dacarbazine (% of previous)</th>
</tr>
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<tbody>
<tr>
<td>&gt;60</td>
<td>100%</td>
</tr>
<tr>
<td>45-60</td>
<td>80%</td>
</tr>
<tr>
<td>30-45</td>
<td>75%</td>
</tr>
<tr>
<td>&lt;30</td>
<td>70%</td>
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</table>

Hepatic Impairment

Activated and metabolised in the liver. Dacarbazine can be hepatotoxic. No dose modifications are recommended for mild to moderate hepatic impairment, but dose reduction may be considered if the patient also has renal impairment.

Rarely liver necrosis due to occlusion of intrahepatic veins (veno-occlusive disease of the liver) has been observed after administration of dacarbazine. In general the syndrome occurred during the second cycle of therapy. Symptoms included fever, eosinophilia, abdominal pain, enlarged liver, jaundice and shock which worsened rapidly over a few hours or days. As fatal outcome has been described special care has to be taken of frequently monitoring of liver size, function and blood counts (especially eosinophils). In single cases of suspected veno-occlusive disease early therapy with high-dose corticosteroids (for example hydrocortisone 300 mg/day) with or without fibrinolytic agents like heparin or tissue plasminogen activator was successful.

Pharmaceutical Care:

- Dacarbazine is a moderate immunosuppressive agent.
- Hepatotoxic drugs and alcohol should be avoided during chemotherapy
- Dacarbazine may influence the ability to drive or operate machines because of its central nervous side effects or because of nausea and vomiting.
- Dacarbazine solution is chemically incompatible with heparin, and hydrocortisone.
- Dacarbazine infusion must be protected from light.
- Dacarbazine is a major substrate of cytochrome P450 CYP1A2 and CYP 2E1. CYP1A2 and CYP2E1 inhibitors may increase the levels/
effects of dacarbazine. CYP1A2 inducers may decrease the levels/effects of dacarbazine.

**Most Common Toxicities:**
- Neutropenia
- Anaemia
- Thrombocytopenia
- Nausea and vomiting (may be severe)
- Anorexia
- Diarrhoea
- Headache, confusion
- Alopecia
- Phlebitis
- ↑LFTs
- Flu-like symptoms

References:

1. SPC Dacarbazine powder for Infusion. Medac GmbH. [accessed 5th June 2013]

