Gemcitabine in Cutaneous T-cell Lymphoma

Indication: Primary Cutaneous T cell Lymphoma and its variants:
- Mycosis Fungoides Stage IIb to IVb
- Sezary Syndrome
- Primary Cutaneous Peripheral T cell Lymphoma NOS
- Adult T cell Leukaemia/Lymphoma (HTLV1) (in combination with AZT and interferon)
- Subcutaneous panniculitis-like T cell Lymphoma (gamma/delta variant)
- Primary cutaneous Peripheral T cell Lymphoma, unspecified
- Primary cutaneous aggressive epidermotropic CD8 T cell lymphoma
- Cutaneous Gamma Delta Lymphoma

Regimen details: Gemcitabine 1000mg/m² IV D1, D8, D15 q28 days

Dose can be increased to 1200 mg/m² in patients who have not received previous chemotherapy

Concomitant Bexarotene:

In some patients with Mycosis Fungoides, Bexarotene is initiated at the same time as Gemcitabine or continued in attempt to prolong the duration of response to chemotherapy. For details of doses, monitoring and ongoing treatment with Bexarotene, see separate protocol for Bexarotene

Administration: Gemcitabine in 250 - 500ml Sodium Chloride 0.9% IV infusion over 30 min (depending on contract for Dose banding product)

Frequency: Every 28 days, for a total of 4 to 6 cycles

Extravasation: Gemcitabine: Non-vesicant

Anti- emetics: Low emetogenic. Follow local Anti-emetic Policy

Supportive medication: Allopurinol 300mg od orally (100mg if renal impairment) for prevention of tumour lysis syndrome for first cycle only.
Proton Pump Inhibitor prophylaxis e.g. omeprazole 20mg od orally

Prophylaxis

Because of T-cell immune suppression and the high risk of skin infection and opportunistic infection, patients who have received prior chemotherapy should be given with each cycle antifungal, antiviral and pneumocystis pneumonia prophylaxis:

Co-trimoxazole (Septrin) 960mg od Mon Wed Fri
Aciclovir 400mg bd daily continuous
Fluconazole 50mg od continuous
Regular investigations:  
FBC  D1, D8, D15  
Differential Lymphocytes  D1  
LFTs  D1  
U&E s  D1  
LDH  D1  
Clinical Skin Scoring and Imaging  Every 2 cycles

Comments:  
Haemolytic anaemia – Gemcitabine  
Gemcitabine should be discontinued at the first signs of any evidence of micro-angiopathic haemolytic anaemia, such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevation of serum bilirubin, serum creatinine, blood urea nitrogen, or LDH, which may indicate development of haemolytic uraemic syndrome. Renal failure may not be reversible, even with discontinuation of therapy, and dialysis may be required

DOSE MODIFICATIONS

Haematological Toxicity

<table>
<thead>
<tr>
<th>Neutrophils</th>
<th>Platelets</th>
<th>Gemcitabine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.0 x 10⁹/L</td>
<td>&gt; 100 x 10⁹/L</td>
<td>Give full dose</td>
</tr>
<tr>
<td>0.5 – 1.0 x 10⁹/L</td>
<td>50 - 100 x 10⁹/L</td>
<td>Give 75% dose or delay, based on clinical assessment</td>
</tr>
<tr>
<td>&lt; 0.5 x 10⁹/L</td>
<td>&lt; 50 x 10⁹/L</td>
<td>Delay for 1 week / Omit</td>
</tr>
</tbody>
</table>

If Day 8 or 15 are omitted due to haematological toxicity, the next cycle can be continued at the planned time at 75% dose on D1 if the Neutrophils are > 1.0 x 10⁹/L and the Platelets are > 100 x 10⁹/L

Renal Impairment:  
Gemcitabine should be used with caution in patients with impaired renal function:

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Gemcitabine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 30</td>
<td>Give 100%</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Consider dose reduction. Discuss with Consultant</td>
</tr>
</tbody>
</table>

Hepatic Impairment  
Gemcitabine: Use with caution in the presence of hepatic dysfunction  
Administration of Gemcitabine in patients with liver metastatases or a pre-existing medical history of hepatitis, alcoholism, or liver cirrhosis may lead to exacerbation of the underlying hepatic insufficiency

If bilirubin > 27 µmol/L, initiate treatment with Gemcitabine 800mg/m²  
BUT  
If Bilirubin > 30µmol/L or ALT/ALP > 3 X ULN (> 5 x ULN if liver metastasises are present), treatment should be deferred unless approved by Consultant. These patients are at high risk of potentially fatal sepsis

Bilirubin: 27 µmol/L
DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE

NON – HAEMATOLOGICAL TOXICITY

- Grade 1 or 2 toxicity: No dose reduction of Gemcitabine, unless this toxicity significantly affects the patient’s quality of life. Discuss with Consultant

- Grade 3 or 4 toxicity: Restart Gemcitabine at 50% dose. This is a permanent dose reduction

- Recurrent Grade 3 or 4 toxicity despite dose reduction: Discontinue treatment

- Dose reductions should not be performed for alopecia or nausea and/or vomiting that are not treated with aggressive anti-emetic support

Toxicities:  Myelosuppression; nausea; vomiting; mucositis; proteinuria and haematuria; flu-like syndrome; elevation of transaminases; peripheral oedema; dyspnoea; allergic skin rash often associated with pruritus; alopecia (mild)

Drug interactions:  Gemcitabine

  - Gemcitabine is radiosensitizer
  - Warfarin: increased anticoagulant effect of warfarin

References:

- www.medicines.org.uk
  Micromedex review. Gemcitabine
  Gemcitabine. Cancerbackup. February 2009
  NLNC- Dosage Adjustment for Cytotoxics in Renal Impairment. November 2003
  NLNC- Dosage Adjustment for Cytotoxics in Hepatic Impairment. November 2003
  GSTT guidelines for treating nausea and vomiting in adult patients. September 2007
  Stockley’s Drug Interactions. Interactions search: Gemcitabine. Feb’ 09
  CTCAE v3.0. August 2006