LONDON CANCER ALLIANCE West and South

Skin Pathway Group – 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 Gemcitabine in not licensed for this indications, and therefore use should be in line with individual Trust governance process
Regimen details:	Gemcitabine 1000mg/m^2 IV Day 1, Day 8, Day 15 Dose can be increased to 1200mg/m^2 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 over 30 min
Frequency:	Every 28 days, for a total of 4 to 6 cycles
Pre-medication:	Not routinely required

Version: 1.0 Supersedes: all other versions	Approved by LCA Skin Pathway Chemotherapy Lead: Mark Harries
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Ravi Shaunak	Approved by LCA Medicines & Chemotherapy Steering Group Chair:
Second check by: Sanna Eestila	Date prepared: January 2015 Review Date: January 2017

Anti- emetics: Low emetogenicity
Follow Local Anti-emetic Policy

Supportive medication: Allopurinol 300mg od orally (100mg if renal impairment, CrCl < 20ml/min) 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

Extravasation: Non-vesicant

Regular investigation:

Prior to Cycle 1:

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

Prior to Cycle 2 onwards:

FBC	Day 1 (within 72 hours)
Differential Lymphocytes	Day 1 (within 72 hours)
LFTs	Day 1 (within 72 hours)
LDH	Day 1 (within 72 hours)
U&Es	Day 1 (within 72 hours)
Clinical Skin Scoring and Imaging	Every 2 cycles

Prior to Day 8 and Day 15 doses (all cycles)

FBC	Day 8 and Day 15 (within 72 hours)

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)

DOSE MODIFICATIONS

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Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Gemcitabine Dose
> 1.0	**&**	> 100	Give full dose
0.5 – 1.0	**or**	50 - 100	Give 75% dose or delay, based on clinical assessment
< 0.5	**or**	< 50	Delay for 1 week / Omit

Non-haematological Toxicities

Renal Impairment

CreatinineClearance (ml/min)	Gemcitabine Dose
> 30	Give 100%
< 30	Consider dose reduction. Discuss with Consultant

Hepatic Impairment

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.

Hepatic dysfunction	Gemcitabine dose
If bilirubin > 27 µmol/L	Initiate treatment with Gemcitabine 800mg/m^2
Bilirubin > 30µmol/L or ALT/ALP > 3 X ULN (> 5 x ULN if liver metastatses are present)	Treatment should be deferred unless approved by Consultant. These patients are at high risk of potentially fatal sepsis

DOSE MODIFICATIONS FOR OTHER TOXICITIES

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

Location of regimen Day case setting

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delivery:

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
Drug interactions:	Gemcitabine is radiosensitizer Warfarin : increased anticoagulant effect of warfarin
References:	www.medicines.org.uk Marchi E et al. Phase II study.Cancer 2005;104(11):2437-41 Zinzani PL et al. J Clin Oncol. 2000;18(13):2603-6 Gemcitabine. Cancerbackup. February 2009

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