LONDON CANCER ALLIANCE West and South

Skin Pathway Group – CHOP 21 +/- Rituximab for Primary Cutaneous Non-Hodgkin's Lymphoma

Indication:

CHOP 21:

- Mycosis Fungoides Stage IIb-IVb for good performance status patients with rapidly progressing disease, effaced lymph nodes, systemic metastases or debulking prior to reduced intensity stem cell transplant (RISCT).
- 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

CHOP 21 & Rituximab (CHOP-R):

- Primary Cutaneous diffuse large B cell Lymphoma, leg type
- Primary Cutaneous diffuse large B cell Lymphoma, other
- Primary cutaneous marginal zone B-cell Lymphoma with advanced systemic involvement
- Primary cutaneous follicle centre Lymphoma with advanced systemic involvement

Intrathecal Methotrexate prophylaxis is not routinely given
An alternative regimen to CHOP must be considered if lymphoma is detected in the cerebrospinal fluid by Lumbar Puncture. Discuss with Haemato-oncology.

Regimen details:

Cyclophosphamide	750mg/m^2	IV	Day 1
Doxorubicin	50mg/m^2	IV	Day 1
Vincristine	1.4mg/m^2 (max 2mg)	IV	Day 1
Prednisolone	100mg	Orally	Days 1 to 5
If indicated (see above):			
Rituximab	375mg/m^2	IV	Day 1

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

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Administration:	Rituximab	IV infusion in 500ml Sodium Chloride 0.9%. Administer Rituximab before CHOP
	Doxorubicin	Slow IV bolus injection via a fast-running Sodium Chloride 0.9% infusion
	Vincristine	IV infusion in 50ml Sodium Chloride 0.9% over 5 – 10 minutes
	Cyclophosphamide	IV infusion in 250ml Sodium Chloride 0.9% over 30 minutes or as an IV bolus
	Prednisolone	Orally, with or after food. Available as 5mg and 25mg tablets.

Frequency:

CHOP 21: every 21 days for 6 cycles

CHOP-R 21: every 21 days for 4 to 6 cycles

Pre-medication:

30 minutes prior to Rituximab:

Paracetamol	1000mg	orally
Chlorphenamine	10mg	IV
Prednisolone	100mg	orally (Day 1 of CHOP chemotherapy)

Anti- emetics:

High 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 (PPI) prophylaxis e.g. omeprazole 20mg od orally.
Mycosis fungoides and ATLL, antifungal, antiviral and PCP prophylaxis, doses as per local policy, with each cycle
GCSF per local policy and consider in all cases of CTCL.

Extravasation:

Vesicant
Vincristine and Doxorubicin should be administered with appropriate precautions to prevent extravasation.
If there is any possibility that extravasation has occurred, contact a senior member of the medical team and follow local protocol for dealing with cytotoxic extravasation

Regular investigations:

Prior to Cycle 1:

FBC	Day 1 (within 14 days)
Lymphocyte subsets	Day 1 (within 14 days)

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LFTs	Day 1 (within 14 days)
LDH	Day 1 (within 14 days)
U&Es	Day 1 (within 14 days)
Baseline Imaging	
Clinical Skin Scoring	

Prior to Cycle 2 onwards:

FBC	Day 1 (within 72 hours)
Lymphocyte subsets	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	Every cycle
Repeat Imaging	After cycle 4

Toxicities: Myelosuppression, nausea, vomiting, constipation, fatigue, alopecia, mucositis, taste alteration, gastrointestinal toxicity, increased appetite, urotoxicity, peripheral neuropathy**, hyperglycaemia, fluid retention, nail and skin changes, mood changes, cardiotoxicity, amenorrhoea

**Neurotoxicity – monitor for peripheral sensory loss, discuss with Consultant before administering further cycles.

DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≥1.0	**&**	≥ 100	100% dose
<1.0	**or**	< 100	Delay until neutrophils > 1.0 x 10^9/L and platelets > 100 x 10^9/L and dose reduce doxorubicin and cyclophosphamide by 20% for all further cycles.

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Non-haematological Toxicities

Renal Impairment

No dose modifications are required for vincristine, doxorubicin and rituximab.

Creatinine Clearance (ml/min)	Cyclophosphamide Dose
> 50	Give 100%
10 – 50	Give 75%

Hepatic Impairment

Bilirubin (µmol/l)	Doxorubicin Dose
20 – 50	Give 50%
51 – 85	Give 25%
> 85	Omit
AST/ALT (units)	**Doxorubicin Dose**
2 – 3 x normal	Give 55%

Vincristine: Elderly patients may be more susceptible to the neurotoxic effects of Vincristine
In the event of neurotoxicity, consider dose reduction of Vincristine as follows:

Bilirubin (µmol/l)		ALT / AST (unit/l)	Vincristine Dose
20 – 50	**or**	60-80	Give 50%
51 – 85	**&**	Normal	Give 50%
> 85	**&**	> 180	Omit

Dose modifications for other toxicities

Neurotoxicity symptoms	Vincristine Dose
Paresthesia (including tingling) but not interfering with function	Give 100%
Paresthesia interfering with function, but not interfering with ADL*	Give 75%
Paraesthesia interfering with ADL*	Omit Vincristine until toxicity resolved
Disabling	Omit Vincristine until toxicity resolved

*ADL= activities of daily living

Location of regimen delivery: Day case setting

Comments: Maximum cumulative lifetime dose Doxorubicin = 450mg/m^2

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A baseline MUGA scan or Echocardiogram should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy. MUGA scan or Echocardiogram should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum.

Drug interactions:

Cyclophosphamide and Doxorubicin:

- Clozapine : increased risk of agranulocytosis, avoid concomitant use
- Digoxin tablets : reduced absorption (resolved by giving the digoxin in liquid)
- Phenytoin : reduced absorption of the antiepileptic
- Warfarin : the anticoagulant effect is increased

Doxorubicin:

- Ciclosporin (high dose) increases Doxorubicin serum levels and myelotoxicity
- Concomitant use of other cardioactive compounds e.g. calcium channel blockers require monitoring of cardiac function throughout treatment
- Quinolones : antimicrobial effect of quinolones decreased

Cyclophosphamide:

- Amiodarone : increased risk of pulmonary fibrosis ; avoid combination if possible
- Grapefruit juice : decreased or delayed activation of Cyclophosphamide
- Avoid grapefruit juice for 48 hours before and on day of dose
- Indapamide : prolonged leucopenia is possible
- Itraconazole : might increase Cyclophosphamide side effects e.g.haemorrhagic cystitis, pigmentation of palms, nails and soles etc.

Vincristine:

- Fluconazole : if used, suspend 48 hours before and after Vincristine dose
- Itraconazole is contraindicated with Vincristine, causing an earlier onset and/or an increased severity of neuromuscular side-effects e.g. neuritic pain, sensory loss, paraesthesia, difficulty in walking etc.

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- Pyridoxine and isoniazid may increase the incidence of bone marrow depression
- Drugs acting on the peripheral nervous system can increase Vincristine neurotoxicity

References:

www.medicines.org.uk

Whittaker S et al. Joint British Association of Dermatologists and UK Cutaneous Lymphoma Group Guidelines for the management of primary cutaneous T cell lymphomas. Br J Derm 2003; 1;49;1095-1107

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