DOXORUBICIN +/- OLARATUMAB

For adults with with advanced soft tissue sarcoma which are not amenable to curative treatment with surgery or radiotherapy

Blueteq registration is required before treatment may start with olaratumab

Drug/Dosage:	Doxorubicin	75 mg/m^2	IV	Day 1
	+/-			
	Olaratumab	15mg/kg	IV	Day 1 and Day 8

Administration: Pre-medication for olaratumab:

Chlorphenamine 10mg IV	30 – 60 minutes before all doses of olaratumab
Dexamethasone 8mg IV	30 – 60 minutes before olaratumab on days 1 and 8 of cycle 1 only (plus see below for patients who experience an infusion-related reaction)

Olaratumab diluted in 250ml sodium chloride 0.9% and infused over a minimum of 60 minutes (dose ≤ 1500mg over 60 minutes; dose > 1500mg over 90 minutes)
then
Doxorubicin via a fast-running infusion of sodium chloride 0.9%

Infusion-related reaction to olaratumab	Management
Grade 1 - 2	Stop the olaratumab infusion and manage symptomatically. Once the symptoms have resolved, restart at a 50% decreased infusion rate. Monitor patient for worsening of condition. For all subsequent infusions; • premedication with chlorphenamine 10mg IV, paracetamol 1000mg po and dexamethasone should be given • infuse over 2 hours
Grade 3 - 4	Immediately and permanently discontinue olaratumab

Frequency: Doxorubicin administered every 3 weeks for 6 cycles
Olaratumab to continue on days 1 and 8 of a 3 week cycle, until disease progression or unacceptable toxicity

Main Toxicities: myelosuppression; alopecia; mucositis; cardiomyopathy (see Comments); ovarian failure/infertility
olaratumab side-effects include infusion-related reactions, neutropenia and musculoskeletal pain

Anti-emetics: doxorubicin: highly emetogenic
olaratumab: mildly emetogenic

Extravasation: doxorubicin is a vesicant

Reason for Update: olaratumab available	Approved by Consultant: Dr A Neal
Version: 1	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: all doxorubicin-only versions	Date: 27.9.17
Prepared by: S Taylor	Checked by: C Tucker

Regular Investigations:	FBC	Day 1 and Day 8
	LFTs	Day 1
	U&Es	Day 1
	MUGA scan	see Comments
	CT scan	after cycle 3

Comments: Offer scalp cooling with doxorubicin

Maximum cumulative dose of doxorubicin = 450 - 550mg/m^2

A baseline MUGA scan should be performed where the patient is considered at risk of having significantly impaired cardiac contractility. If ejection fraction is less than 50%, an alternative regimen should be given. MUGA scan should be repeated if there is suspicion of cardiac toxicity at any point during treatment.

Dose Modifications

Haematological Toxicity:

Day 1 of doxorubicin + olaratumab:

Neutrophils < 1.5 x 10^9/l	Delay treatment for 1 week
or	Repeat FBC. If within normal parameters, resume with full
Platelets < 100 x 10^9/l	dose doxorubicin and olaratumab as below:

All olaratumab doses:

Neutropenic fever / infection	Delay olaratumab until neutrophils ≥ 1.0 x 10^9/l.
or	Then resume olaratumab at reduced dose of 12 mg/kg.
Neutrophils < 0.5 x 10^9/l for more than 1 week	If recurrence despite dose reduction, reduce dose further to 10mg/kg.

Non-haematological Toxicities: For any serious Grade ≥ 3 non-haematological toxicity deemed related to olaratumab, the dose of olaratumab should be withheld until toxicity is ≤ Grade 1 or has returned to pre-treatment baseline.
For subsequent infusions, the dose should be reduced to 12 mg/kg for serious Grade 3 toxicities and to 10 mg/kg for Grade 4 toxicities.
If a Grade 3 toxicity recurs despite the dose reduction, the dose should be reduced further to 10 mg/kg.
In case of recurrence of a Grade 4 toxicity, treatment with olaratumab should be permanently discontinued.

Hepatic Impairment:

Bilirubin (µmol/l)	Doxorubicin Dose
20 – 50	Give 50%
51 – 85	Give 25%
> 85	Omit

There are no data for olaratumab in patients with severe hepatic impairment.

Renal Impairment: There are no data for olaratumab in patients with CrCl < 30 ml/min.

References: Tap, W et al; Lancet 2016; 388 (10043): 488 - 497

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