Gemcitabine & Docetaxel (Sarcoma)

Indication

Third- or fourth-line treatment of patients with advanced soft tissue sarcoma who have failed, or are unsuitable for/intolerant to, treatment with anthracycline or ifosfamide.

Second- or third-line treatment for osteosarcoma

Performance status 0-2.

ICD-10 codes

Codes prefixed with C49.

Regimen details

Day	Drug	Dose	Route
1 and 8	Gemcitabine	675mg/m^2	IV infusion
8	Docetaxel	75mg/m^2	IV infusion

Cycle frequency

21 days

Number of cycles

Up to 6 cycles

Administration

Gemcitabine is administered as an IV infusion in 250ml sodium chloride 0.9% over 90 minutes. On day 8, gemcitabine is administered first, followed by docetaxel.

Docetaxel is administered as an IV infusion in 250mL or 500mL (concentration dependent) PVC free sodium chloride 0.9% over 60 minutes.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions.

Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of docetaxel and therefore facilities for the treatment of hypotension and bronchospasm must be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve re-started at a slower infusion rate. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate therapy.

Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel.

Pre-medication

Dexamethasone 8 mg BD (morning and lunchtime) for 3 days starting 24 hours prior to **docetaxel** chemotherapy.
Note: Patients must receive 3 doses of dexamethasone prior to docetaxel. In the case where 3 doses have not been taken, dexamethasone 16-20mg IV should be administered 30-60 minutes prior to chemotherapy and the remaining 3 oral doses should be taken as normal

Emetogenicity

Day 1 has low emetogenic potential
Day 8 has moderate emetogenic potential

Additional supportive medication

Antiemetics as per local guideline
Filgrastim once daily for 7 days, starting on day 9
PPI whilst on dexamethasone, and additionally if required
Loperamide as required
Benzydamine mouthwash as required

Extravasation

Gemcitabine is neutral (Group 1)
Docetaxel is an exfoliant (Group 4)

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	96 hours pre day 1 and 24 hours pre day 8
U+E (including creatinine)	7 days
LFT	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit day 1
Neutrophils	≥1.0 x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine clearance	≥30 ml/min
Bilirubin	≤1.5 x ULN
ALT/AST	≤1.5 x ULN
Alkaline phosphatase (ALP)	≤2.5 x ULN (unless due to bone metastases only)

Dose modifications

Dose modifications should be made as per the following table:

Dose level	Gemcitabine	Docetaxel
1st dose reduction	80% dose	80% dose
2nd dose reduction	66% dose	66% dose
3rd dose reduction	Stop treatment	Stop treatment

- **Haematological toxicity**

If neutrophils <1.0 x 10^9/L and/or platelets <100 x 10^9/L, delay 1 week or until recovery.

If occurring at day 8, patients should ideally be delayed a week and if toxicity has resolved sufficiently by day 15, the gemcitabine and docetaxel can be administered but at the next dose reduction level as outlined above. If capacity does not allow for treatment delay, omit day 8 and reduce to next dose level for future cycles.

If recurrent episodes, or any episode of febrile neutropenia, consider dose reduction to 80% dose of gemcitabine and docetaxel. If further episodes despite dose reduction, dose can be reduced to 66% dose for subsequent cycles.

- **Renal impairment**

Gemcitabine: If creatinine clearance <30ml/min consider dose reduction (discuss with prescriber/consultant).

Docetaxel: no need for dose adjustment is expected in renal impairment

- **Hepatic impairment**

Bilirubin		AST/ALT		ALP*	Gemcitabine dose	Docetaxel dose
≤ 1.5 x ULN	and	≤ 1.5 x ULN	and	≤ 2.5 x ULN	100%	100%
	and	> 1.5 – 3 x ULN	or	> 2.5 – 5 x ULN	100%	80%
> 1.5 x ULN	or	> 3 x ULN	or	> 5 x ULN	Consider omitting dose - discuss with prescriber/consultant	

* unless due to bone metastases only.

- **Other toxicities**

Toxicity	Grade	Dose adjustment
Neuropathy	1	Continue full dose
	2	Omit until ≤ grade 1 then restart at next dose reduction level
	3/4	Discontinue

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Pneumonitis
Hepatotoxicity
Myelosuppression
Infusion related reactions/anaphylaxis
Peripheral neuropathy

- **Frequently occurring side effects**

Diarrhoea, constipation
Fatigue
Nausea and vomiting
Dyspnoea
Stomatitis and mucositis
Arthralgia and myalgia
Alopecia
Elevated liver enzymes
Rash/nail changes
Oedema
Flu-like symptoms

Significant drug interactions – for full details consult product literature/ reference texts

CYP3A4 Enzyme inducers/inhibitors: in vitro studies suggest that CYP3A inhibitors (such as ketoconazole, ritonavir, clarithromycin and erythromycin) may raise docetaxel levels, whereas CYP3A inducers (such as rifampicin and barbiturates) may reduce docetaxel levels.
Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin or DOAC during treatment. If the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Additional comments

Nil

References

- Seddon B et al. Gemcitabine and docetaxel versus doxorubicin as first-line treatment in previously untreated advanced unresectable or metastatic soft-tissue sarcomas (GeDDiS): a randomised controlled phase 3 trial. Lancet Oncology Oct 2017; 18(10):1397-1410.
- Summary of Product Characteristics – Docetaxel (Accord) accessed 20th January 2022 via www.medicines.org.uk
- Summary of Product Characteristics – Gemcitabine (Accord) accessed 20th January 2022 via www.medicines.org.uk

Written/reviewed by: Dr T Spencer (Consultant Clinical Oncologist, UHBW NHS Trust), Dr G Ayre (Consultant Clinical Oncologist, UHBW NHS Trust), D A Dangoor (Consultant Medical Oncologist, UHBW NHS Trust)

Checked by: Kate Gregory (Lead Pharmacist for SACT protocols, SWAG Cancer Alliance)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)

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