NAB-PACLITAXEL (ABRAXANE) & GEMCITABINE

First line treatment of metastatic adenocarcinoma of the pancreas,
only if other combination therapies are unsuitable and they would otherwise have gemcitabine monotherapy

Blueteq registration is required before treatment may start

Drugs/Dosage:	Nab-paclitaxel (Abraxane)	125mg/m^2	IV	Day 1, Day 8 and Day 15
	Gemcitabine	1000mg/m^2	IV	Day 1, Day 8 and Day 15

Administration: Nab-paclitaxel (Abraxane) infused over 30 minutes
then
Gemcitabine in 250 ml 0.9% sodium chloride infused over 30 minutes

Frequency: Nab-paclitaxel (Abraxane) and gemcitabine both administered on Day 1, Day 8 and Day 15 of a 28 day cycle (i.e. 1 cycle = weekly for 3 weeks, then 1 week off)
Repeat until unacceptable toxicity or disease progression.

Main Toxicities: myelosuppression; rash; flu-like syndrome; alopecia; GI side effects; peripheral oedema; raised transaminases; peripheral neuropathy; myalgia/arthralgia; pneumonitis; ovarian failure/infertility

Anti-emetics: moderately emetogenic

Extravasation: nab-paclitaxel is a vesicant

Regular Investigations:	FBC	Day 1, Day 8 and Day 15 of each cycle
	U&Es	Day 1 of each cycle
	LFTs	Day 1 of each cycle
	CA 19-9	4 weekly

Comments: Hypersensitivity reactions to nab-paclitaxel are very rare. If a hypersensitivity reaction does occur, stop the infusion and initiate symptomatic treatment. The patient should not be re-challenged with nab-paclitaxel.

Dose Modifications: Dose level reductions:

Dose Level	Abraxane Dose (mg/m^2)	Gemcitabine Dose (mg/m^2)
Full dose	125	1000
1st dose level reduction	100	800
2nd dose level reduction	75	600
If additional reduction required	Discontinue treatment	Discontinue treatment

NOTE:

- No dose escalations should be made after a dose reduction.
- If both Day 8 and Day 15 doses are omitted from a cycle, start the next cycle at the next lower dose level.

Reason for Update: re-instated following +ve NICE FAD; extra info about dose reductions added	Approved by Consultant: Dr S Cummins
Version: 2	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 1	Date: 23.8.17
Prepared by: S Taylor	Checked by: C Tucker

Haematological Toxicity:

Day of Cycle	Neutrophils (x10^9/l)		Platelets (x 10^9/l)	Nab-paclitaxel and Gemcitabine Doses
Day 1	< 1.5	or	< 100	Delay doses until recovery
Day 8	≥ 0.5 but < 1.0	or	≥ 50 but < 75	Proceed, but reduce doses by 1 level
	< 0.5	or	< 50	Omit doses (do **not** delay)
Day 15	**If Day 8 doses were given without modification:**			
	≥ 0.5 but < 1.0	or	≥ 50 but < 75	Reduce doses by 1 dose level from Day 8 doses
	< 0.5	or	< 50	Omit doses (do **not** delay)
Day 15	**If Day 8 doses were reduced:**			
	≥ 1.0	and	≥ 75	Treat with same doses as Day 8
	≥ 0.5 but < 1.0	or	≥ 50 but < 75	Reduce doses by 1 dose level from Day 8 doses
	< 0.5	or	< 50	Omit doses (do **not** delay)
Day 15	**If Day 8 doses were omitted:**			
	≥ 1.0	and	≥ 75	Reduce doses by 1 dose level from Day 1 doses
	≥ 0.5 but < 1.0	or	≥ 50 but < 75	Reduce doses by 2 dose levels from Day 1 doses
	< 0.5	or	< 50	Omit doses (do **not** delay)

Non-haematological Toxicities:

Adverse Drug Reaction	Abraxane Dose	Gemcitabine Dose
Febrile neutropenia Grade 3 or 4	Withhold doses of both drugs until fever resolves and neutrophils ≥ 1.5; resume at next lower dose level	
Peripheral neuropathy Grade 3 or 4	Withhold dose until improves to ≤ Grade 1; resume at next lower dose level	Treat with same dose
Cutaneous toxicity Grade 2 or 3	Reduce to next lower dose level for both drugs; discontinue treatment if ADR persists	
Grade 3 mucositis or Grade 3 diarrhoea	Withhold doses of both drugs until improves to ≤ Grade 1; resume at next lower dose level	

Renal Impairment: If CrCl < 30ml/min, consider gemcitabine dose reduction – clinical decision
Nab-paclitaxel has not been studied in renal impairment and insufficient data are currently available to recommend dose modifications in patients with renal impairment.

Hepatic Impairment: If bilirubin > 27 µmol/L, initiate treatment with gemcitabine 800mg/m^2.
Nab-paclitaxel should not be used if bilirubin > 5 x ULN or AST / ALT > 10 x ULN.
A dose reduction of nab-paclitaxel in patients with bilirubin > 2 ULN must be considered since paclitaxel clearance is decreased in patients with high bilirubin levels.
Insufficient data are currently available to recommend specific dose modifications in patients with mild to moderate hepatic impairment.

References: Von Hoff, D et al ; NEJM 2013 ; 369 : 1691 - 1703

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