Nab-Paclitaxel (Abraxane) and Gemcitabine for Pancreatic Adenocarcinoma

NHS Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Drug	Dose	Route	Diluent & Rate
1	Sodium Chloride 0.9%	500ml	Infusion	Fast Running
	Dexamethasone	8mg	Oral	
	Ondansetron	8mg	Oral /Slow bolus/15 min infusion	
	Chlorphenamine	10mg	Intravenous	Slow bolus via saline drip
	Ranitidine	50mg	Intravenous	Slow bolus via saline drip
	Nab-Paclitaxel (Abraxane®)	**125mg/m^2**	**Intravenous**	IV over 30 minutes
	Gemcitabine	**1000mg/m^2**	**Intravenous**	250ml 0.9% NaCl over 30minutes
8	*Pre-meds as per day one above*			
	Nab-Paclitaxel (Abraxane®)	**125mg/m^2**	**Intravenous**	IV over 30 minutes
	Gemcitabine	**1000mg/m^2**	**Intravenous**	250ml 0.9% NaCl over 30minutes
15	*Pre-meds as per day one above*			
	Nab-Paclitaxel (Abraxane®)	**125mg/m^2**	**Intravenous**	IV over 30 minutes
	Gemcitabine	**1000mg/m^2**	**Intravenous**	250ml 0.9% NaCl over 30minutes

- Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.

CYCLE LENGTH AND NUMBER OF DAYS

Treatment given on day 1, 8 and 15 of a 28-day cycle for six cycles or until disease progression

APPROVED INDICATIONS

Paclitaxel as albumin-bound nanoparticles (nab-paclitaxel) with gemcitabine is recommended as an option for untreated metastatic adenocarcinoma of the pancreas in adults, only if other combination chemotherapies are unsuitable (e.g. FOLFIRINOX) and they would otherwise have gemcitabine monotherapy.

EXCLUSION CRITERIA

Pregnancy or lactation
severe hepatic dysfunction contraindicating nab-paclitaxel

PREMEDICATION

As above

RECOMMENDED TAKE HOME MEDICATION

Dexamethasone 4mg twice daily for 1 to 3 days
Metoclopramide 10mg three times daily as required
Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details

INVESTIGATIONS / MONITORING REQUIRED

Prior to each cycle - FBC, U&Es, LFTs
Prior to day 8 & 15, FBC
Assessment of cardiac function, e.g. ECHO/MUGA scan pre- treatment and alternative cycles if significant cardiac history, or previous anthracycline therapy.

ASSESSMENT OF RESPONSE

Metastatic: Tumour size and patient symptomatic response

REVIEW BY CLINICIAN

To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

NURSE / PHARMACIST LED REVIEW

On cycles where not seen by clinician.

PREPARATION NOTES

- Nab-paclitaxel must only be prepared in an approved pharmacy aseptic preparation facility according to the following protocol:
- Using a sterile syringe, 20 ml of sodium chloride 0.9% solution for infusion should slowly be injected into a vial of nab-paclitaxel over a minimum of 1 minute. The solution should be directed onto the inside wall of the vial. The solution should not be injected directly onto the powder as this will result in foaming.
- Once the addition is complete, the vial should be allowed to stand for a minimum of 5 minutes to ensure proper wetting of the solid. Then, the vial should gently and slowly be swirled and/or inverted for at least 2 minutes until complete resuspension of any powder occurs. The generation of foam must be avoided. If foaming or clumping occurs, the solution must stand for at least 15 minutes until foam subsides.
- The reconstituted suspension should be milky and homogenous without visible precipitates. If precipitates or settling are visible, the vial should be gently inverted again to ensure complete resuspension prior to use. Some settling of the reconstituted suspension may occur. Complete re-suspension should be ensured by mild agitation before use.
- Calculate the exact total dosing volume of 5 mg/ml suspension required for the patient and inject the appropriate amount of reconstituted Abraxane into an empty, sterile, PVC or non-PVC type intravenous bag. The use of specialized DEHP-free solution containers or administration sets is not necessary to prepare or administer Abraxane infusions.

ADMINISTRATION NOTES

- The use of medical devices containing silicone oil as a lubricant (i.e. syringes and IV bags) to reconstitute and administer Abraxane may result in the formation of proteinaceous strands. Administer Abraxane using an infusion set incorporating a 15 µm filter to avoid administration of these strands.
- The incidence of hypersensitivity is much lower than other taxanes, however If hypersensitivity occurs, product should be discontinued immediately, symptomatic treatment should be initiated, and that patient should not be re-challenged with paclitaxel.
- Nab-paclitaxel is metabolized by CYP2C8 and CYP3A4; caution should be exercised when administering with drugs which are CYP2C8 or CYP3A4 inducers or inhibitors, e.g. amiodarone, ciclosporin, grapefruit juice, verapamil, etc.
- Gemcitabine is a radiation sensitiser and should therefore be used in caution with radiotherapy.
- Abraxane is an albumin-bound nanoparticle formulation of paclitaxel, which may have substantially different pharmacological properties compared to other formulations of paclitaxel**.** Abraxane should not be substituted for or with other paclitaxel formulations.

EXTRAVASATION *See NCA/ Local Policy*

Nab-Paclitaxel causes pain and tissue necrosis if extravasated, therefore extreme care must be taken when infusion pumps are used to control rate of administration. The injection site must be regularly monitored during infusion.

TOXICITIES

- Myelosuppression, particularly, thrombocytopenia, anaemia & neutropenia
- Nausea and vomiting
- Haematuria
- Dizziness during infusion
- Oedema/peripheral oedema
- Alopecia
- Flu like symptoms
- Rarely pulmonary effects e.g. ARDS Lethargy
- Peripheral neuropathy
- Arthralgia or Myalgia
- Back pain on administration
- Cardiac toxicity has been reported rarely while patients receive nab-Paclitaxel.

DOSE MODIFICATION / TREATMENT DELAYS

Dose 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 dose reduction required	Discontinue treatment	Discontinue treatment

FBC on day of treatment

Cycle Day	ANC count		Platelet count	Abraxane Dose	Gemcitabine Dose
Day 1	< 1.5	OR	< 100	Delay doses until recovery	
Day 8	≥ 0.5 but < 1.0	OR	≥ 50 but < 75	Reduce doses 1 dose level	
	< 0.5	OR	< 50	Withhold doses	
Day 15: IF Day 8 doses were given without modification:					
Day 15	≥ 0.5 but < 1.0	OR	≥ 50 but < 75	Reduce doses 1 dose level from Day 8 doses	
	< 0.5	OR	< 50	Withhold doses	
Day 15: IF Day 8 doses were reduced:					
Day 15	≥ 1.0	AND	≥ 75	Treat with same doses as Day 8	
	≥ 0.5 but < 1.0	OR	≥ 50 but < 75	Reduce doses 1 dose level from Day 8 doses	
	< 0.5	OR	< 50	Withhold doses	
Day 15: IF Day 8 doses were withheld:					
Day 15	≥ 1.0	AND	≥ 75	Reduce doses 1 dose level from Day 1 doses	
	≥ 0.5 but < 1.0	OR	≥ 50 but < 75	Reduce doses 2 dose levels from Day 1 doses	
	< 0.5	OR	< 50	Withhold doses	

Adverse Drug Reaction (ADR)	Abraxane Dose	Gemcitabine Dose
Febrile Neutropenia: Grade 3 or 4	Withhold doses until fever resolves and ANC ≥ 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; discontinue treatment if ADR persists	
GI Toxicity: Grade 3 mucositis or diarrhoea	Withhold doses until improves to ≤ Grade 1; resume at next lower dose level	

- If Hb < 10 & patient symptomatic may need blood transfusion but may proceed with chemotherapy as planned if performance status (PS) stable.
- If pre-treatment U&E's & LFT's abnormal, delay treatment one week and discuss with Oncologist as may need dose reduction,
- If PS deteriorates to 3 or 4 and on assessment patient is more symptomatic withhold treatment and discuss with Oncologist
- Gemcitabine should be used with caution in patients with renal or hepatic impairment
- Patients with pre-existing renal impairment should be monitored closely for haemolytic uremic syndrome

TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit

REFERENCES:

1. Celgene Ltd. Summary of Product Characteristics – Abraxane. https://www.medicines.org.uk/emc/product/6438/smpc . Last updated 14/02/2018, accessed 14/02/2018.
2. Von Hoff DD et al. Increased Survival in Pancreatic Cancer with nab-Paclitaxel plus Gemcitabine N Engl J Med 2013;369:1691-703

Document Control

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Summary of Changes	1.1	Protocol reviewed and reissued, Antiemetic advice updated	
	1.2	Updated against Chemocare protocol, updated with NICE approval & filter advice.	