Systemic Anti-Cancer Therapy Protocol

Abraxane® and Gemcitabine

Repeated every 28 days until disease progression

PROTOCOL REF: HPBABG
(Version No: 3.0)

Approved for use in

- First line treatment of metastatic adenocarcinoma of pancreas (locally advanced are ineligible)
- Patients with PS 0-1 who are not suitable candidates for FOLFIRINOX chemotherapy
- Patients who have not received any previous systemic chemotherapy for pancreatic cancer unless given as a radiosensitiser in the adjuvant setting and completed at least 6 months previously

Patients registered in England require registration with NHS England via Blueteq.

Patients registered in Wales do not require Blueteq registration.

Dosage

Drug	Dose	Route	Frequency
Abraxane® (Albumin bound Paclitaxel)	125mg/m^2	IV	Day 1, 8 and 15 of 28 day cycle
Gemcitabine	1000mg/m^2	IV	Day 1, 8 and 15 of 28 day cycle

Supportive Treatments:

Dexamethasone 4mg BD for 3 days

Domperidone 10mg TDS prn

Thromboprophylaxis:

In line with recent NICE recommendations, patients with pancreatic cancer receiving chemotherapy should receive thromboprophylaxis with a LMWH unless contra-indicated. Contra-indications include high bleeding-risk. The decision regarding thromboprophylaxis as part of chemotherapy has to be clearly documented by the consultant.

- Dalteparin 5000 IU by subcutaneous injection once daily

Extravasation risk

Abraxane (Albumin bound Paclitaxel)

VESICANT – can cause pain and tissue necrosis, treat as for paclitaxel

Gemcitabine

NEUTRAL – use heat and compression, consider hyaluronidase

Refer to Clatterbridge Policy 'Prevention and Management of Extravasation Injuries' for further guidance.

Administration

Abraxane contains paclitaxel formulated as albumin-bound nanoparticles and the reconstituted suspension should be milky but without visible particulates. Some settling of the suspension may occur on storage, complete re-suspension should be ensured prior to administration by gentle agitation of the infusion bag (DO NOT SHAKE)

Day	Drug	Dose	Route	Diluent and rate
1	**Ondansetron** 30mins before chemotherapy	**16mg**	**PO**	
	Dexamethasone 30mins before chemotherapy	**8mg**	**PO**	
	Abraxane® (Albumin bound Paclitaxel)	**125mg/m^2**	**IV**	Administer over 30 minutes Lines containing 15 micron filters can be used
	Gemcitabine	**1000mg/m^2**	**IV**	250ml sodium chloride 0.9% over 30 minutes

8	**Ondansetron** 30mins before chemotherapy	**16mg**	**PO**	
	Dexamethasone 30mins before chemotherapy	**8mg**	**PO**	
	Abraxane® (Albumin bound Paclitaxel)	**125mg/m^2**	**IV**	Administer over 30 minutes Lines containing 15 micron filters can be used
	Gemcitabine	**1000mg/m^2**	**IV**	250ml sodium chloride 0.9% over 30 minutes
15	**Ondansetron** 30mins before chemotherapy	**16mg**	**PO**	
	Dexamethasone 30mins before chemotherapy	**8mg**	**PO**	
	Abraxane® (Albumin bound Paclitaxel)	**125mg/m^2**	**IV**	Administer over 30 minutes Lines containing 15 micron filters can be used
	Gemcitabine	**1000mg/m^2**	**IV**	250ml sodium chloride 0.9% over 30 minutes

A "go-ahead" SACT assessment is required 24-48 hours prior to the treatment date in order for pharmacy to prepare the treatment.

Main Toxicities

Abraxane
Neutropenia, thrombocytopenia, anaemia, neuropathy, alopecia, arthralgia. Raised liver transaminases (AST/ALT) and alkaline phosphatase, hypokalaemia
Gemcitabine
Nausea, vomiting, neutropenia, thrombocytopenia, anaemia, proteinuria and haematuria, alopecia, myalgia. Raised liver transaminases (AST/ALT) and alkaline phosphatase

Investigations and treatment plan:

	Pre	C1 D1	C1 D8	C1 D15	C2 D1	C2 D8	C2 D15	Ongoing
Clinical Assessment	X	X			X			For palliative, alternate cycles.
SACT Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	X	X	Repeat if clinically indicated
Random blood glucose	X	X			X			Every cycle
CA19.9	X	X			X			Every cycle
CT scan	X							Every 12 weeks
Informed Consent	X							
Blood pressure*	X							Repeat if clinically indicated
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle
Height recorded	X							

Dose Modifications and Toxicity Management

Dose reduction schedule	Abraxane® (Albumin bound Paclitaxel)	Gemcitabine
1st dose reduction	100mg/m^2	800mg/m^2
2nd dose reduction	75mg/m^2	600mg/m^2
Requirement for further dose reduction	Discontinue treatment	Discontinue treatment

Haematological Toxicity

Cycle day	Neutrophil count x10^9/L		Platelet count x10^9/L	Abraxane® (Albumin bound Paclitaxel)	Gemcitabine
Day 1	<1.5	OR	<100	Delay doses until recovery	
Day 8	≥0.5 but <1	OR	≥50 but <75	Reduce doses by 1 dose level	
Day 8	<0.5	OR	<50	Withhold doses	
Day 15: If Day 8 doses were given without modifications:					
Day 15	≥0.5 but <1	OR	≥50 but <75	Reduce doses by one dose level from day 8 doses	
	<0.5	OR	<50	Withhold doses	
Day 15: If Day 8 doses were reduced:					
Day 15	≥1	AND	≥75	Treat with the same doses as day 8	
	≥0.5 but <1	OR	≥50 but <75	Reduce doses by one dose level from day 8	
	≥0.5	OR	≥50	Withhold doses	
Day 15: If Day 8 doses were withheld:					
Day 15	≥1	AND	≥75	Reduce doses by one dose level from day 1	
	≥0.5 but <1	OR	≥50 but <75	Reduce doses by **two** dose levels from day 1 doses	
	<0.5	OR	<50	Withhold doses	

Hepatic impairment

Abraxane®
Hepatic metabolism and biliary clearance is the principal mechanism for elimination. If bilirubin < 1.25 x upper limit of normal and transaminase < 10 x upper limit of normal, refer to oncologist for clinical decision on treatment. If bilirubin >2 x upper limit of normal a dose reduction should be considered.
Gemcitabine
AST elevations do not seem to cause dose limiting toxicities. If bilirubin > 27 µmol/L, initiate treatment with dose of 800 mg/m^2.

Renal impairment

Abraxane®
The effects of renal dysfunction on the elimination of Abraxane have not been formally investigated for patients with renal impairment refer to oncologist for clinical decision on treatment.
Gemcitabine
CrCl > 30ml/min – standard dosing CrCl < 30ml/min – consider dose reduction – clinical decision.

References:

1. Abraxane 5 mg/ml powder for suspension for infusion. Summary of Product Characteristics. Celgene Ltd, Uxbridge 11/01/08. Available from https://www.medicines.org.uk/emc last updated 13/02/14.

2. Gemcitabine 2 g Powder for Solution for Infusion. Summary of Product Characteristics. Accord Healthcare Ltd Middlesex 13/07/11. Available from https://www.medicines.org.uk/emc last updated 10/02/12.

3. Dosage Adjustment for Cytotoxics in Renal and Hepatic Impairment. University College London Hospital NHS Foundation Trust January 2009.

4. NICE guideline NG89. Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism (August 2019)