Indication	First line treatment of patients with inoperable locally recurrent or metastatic squamous cell carcinoma of the anus (SCCA)
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days. Maximum of 6 cycles
Monitoring Parameters pre-treatment	• EDTA/DTPA should be used to measure GFR prior to cycle 1. C+G may be used to estimate CrCl if there is a delay in obtaining EDTA result, CrCl must be >/=30ml/min. • Monitor U+Es, and LFTs on Day 1, FBC on day 1, 8 and 15. If CrCl falls by >25% d/w consultant. • On day 1 proceed with treatment if ANC >/=1.5 and PLT >/=100, if ANC 1-1.4 or PLT 75-99 discuss with consultant, otherwise delay by 1 week. • On days 8 & 15 proceed with treatment if ANC >/=1.0 and PLT >/=75, otherwise omit dose. • **Hepatic impairment:** o Carboplatin: No dose adjustment required. o Paclitaxel: If bilirubin < 1.25 x ULN and transaminase < 10 x ULN, dose at full dose. Otherwise consider dose reduction, not recommended in severe hepatic impairment. • **Renal impairment:** o Carboplatin: stop if CrCl<30ml/min o Paclitaxel: no dose reduction necessary. • **Infusion-related reactions:** o **Paclitaxel:** Patients developing hypersensitivity reactions may be re-challenged with full dose paclitaxel following prophylactic medication (e.g. famotidine 40mg po given 4 hours prior to treatment plus hydrocortisone 100mg iv and chlorphenamine 10mg iv 30 minutes prior to treatment), then give paclitaxel over 3-6 hours (i.e. starting at over 6 hours and gradually increase rate if possible). If patients experience no hypersensitivity reactions after the first two doses of paclitaxel, remove pre-medication with dexamethasone, chlorphenamine (and H2 antagonist) from dose 3 onwards. o **Carboplatin:** Mild/moderate reactions (grade 1-2): If symptoms resolve after treatment with hydrocortisone and chlorphenamine, the infusion may be restarted at 50% rate for 30 mins, then, if no further reaction, increase to 100% rate. If symptoms do not resolve after treatment with hydrocortisone and chlorphenamine, do not restart the infusion. At consultant's discretion, patients may be re-challenged at a later date with additional prophylaxis. In the event of further reaction (grade 1-3), stop infusion and consider alternative treatment. Severe (grade 3): Do not restart infusion. Consider alternative treatment. Anaphylaxis (grade 4): Follow anaphylaxis protocol. Discontinue permanently and consider alternative treatment. • **Dose Modification:** Where dose reductions are required reduce as follows (unless for neuropathy – see below): o Paclitaxel 1st dose reduction 70mg/m², 2nd dose reduction 60mg/m². o Carboplatin 1st dose reduction AUC4, 2nd dose reduction AUC 3.

	○ Paclitaxel induced neuropathy: Dose reduce Paclitaxel by 20% in the event of >/= grade 2 neuropathy and consider delay until recovery to </= grade 1. ○ Consider omitting paclitaxel in event of recurrent grade >/= 3 neuropathy OR recurrent or persistent >/= grade 2 neuropathy following a dose reduction. ○ Dose reduction of carboplatin and paclitaxel should be considered if any other grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to </= grade 1. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ Paclitaxel: Caution should be exercised when administering paclitaxel concomitantly with medicines known to inhibit either CYP2C8 or CYP3A4 (e.g. ketoconazole, erythromycin, fluoxetine, clopidogrel, cimetidine, ritonavir and nelfinavir); toxicity may be increased. CYP2C8 or CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, efavirenz, nevirapine) may reduce efficacy. ○ Carboplatin: Caution with other nephrotoxic drugs.
References	KMCC protocol GYN-037 v1 InterAACT protocol v7 https://www.esmo.org/oncology-news/InterAACT-inoperable-locally-recurrent-metastatic-anal-cancer-Rao https://ascopubs.org/doi/10.1200/JCO.19.03266 SPC accessed online 04.01.21 BOPA Guidance on the use of H2 antagonists for the prevention and management of hypersensitivity v1 June 2020

NB For funding information, refer to CDF and NICE Drugs Funding List

Repeat every 28 days.

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1	**Give pre-meds 30 minutes prior to paclitaxel**				
	Dexamethasone	8mg (may be reduced to 4mg from cycle 1 day 8)	IV	Bolus	
	Chlorphenamine	10mg	IV	Slow bolus	Through the side of a fast running Sodium Chloride 0.9% intravenous infusion.
	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15 min	Sodium chloride 0.9% 50ml
	PACLITAXEL	**80mg/m²**	IV	1 hr	In 250ml Sodium Chloride 0.9% (non-PVC bag and non-PVC administration set) via in-line 0.22 microns filter. Flush with sodium chloride 0.9%
	CARBOPLATIN **Dose = (GFR + 25) x AUC**	**AUC 5 (maximum dose 750mg)**	IV	30 mins	Glucose 5% 500ml
Day 8	**Give pre-meds 30 minutes prior to paclitaxel**				
	Dexamethasone	8mg (may be reduced to 4mg from cycle 1 day 8)	IV	Bolus	
	Chlorphenamine	10mg	IV	Slow bolus	Through the side of a fast running Sodium Chloride 0.9% intravenous infusion.
	Metoclopramide	10mg	IV	Bolus	
	PACLITAXEL	**80mg/m²**	IV	1 hr	In 250ml Sodium Chloride 0.9% (non-PVC bag and non-PVC administration set) via in-line 0.22 microns filter. Flush with sodium chloride 0.9%
Day 15	**Give pre-meds 30 minutes prior to paclitaxel**				
	Dexamethasone	8mg (may be reduced to 4mg from cycle 1 day 8)	IV	Bolus	
	Chlorphenamine	10mg	IV	Slow bolus	Through the side of a fast running Sodium Chloride 0.9% intravenous infusion.
	Metoclopramide	10mg	IV	Bolus	
	PACLITAXEL	**80mg/m²**	IV	1 hr	In 250ml Sodium Chloride 0.9% (non-PVC bag and non-PVC administration set) via in-line 0.22 microns filter. Flush with sodium chloride 0.9%

TTO

TTO	Drug	Dose	Route	Directions
Day 1	Dexamethasone	See Directions	PO	After day 1 take 6mg OM for 3 days, then after day 8 take 4mg OM for 2 days and after day 15 take 4mg OM for 2 days.
	Metoclopramide	10mg	PO	After day 1, 8 & 15 take 10mg TDS for 3 days and then 10mg up to TDS PRN. (Maximum of 30mg per day). Do not take for more than 5 days continuously.