PEMBROLIZUMAB (Keytruda) CISPLATIN (40) with concurrent RT

INDICATION (ICD10) C53

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (PEMB36)

1. Pembrolizumab in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy) for untreated locally advanced (FIGO 2018 stage 3A-C or stage 4A) cervical cancer pembrolizumab will be given in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy). PS 0 or 1.

REGIMEN (pembrolizumab before chemotherapy)

Cycle 1

Day 1	**PEMBROLIZUMAB**	790mg	subcutaneous*	(4.8ml) over 2 minutes
Days 1, 8, 15, 22 and 29	Prehydration			
	CISPLATIN	40mg/m^{2*}	IV infusion	#ml sodium chloride 0.9% over 60 minutes
	Post hydration			

Cycle 2 to 24 months

Day 1	**PEMBROLIZUMAB**	790mg	subcutaneous*	(4.8ml) over 2 minutes

Cisplatin should be given as early as possible in the week as cisplatin potentiates the radiotherapy
*Gynae patients cap dose at maximum 70mg

CYCLE FREQUENCY AND NUMBER OF CYCLES

Gynae – every 42 days until disease progression a maximum of 24 months

ADMINISTRATION

Pembrolizumab SC - withdraw the required volume using a transfer needle (18-21G recommended). To avoid needle clogging, change the needle to a 25-30G, 13 mm hypodermic injection needle immediately prior to SC injection.
Do not administer other medicinal products for injection at the same site as the pembrolizumab.

ANTI-EMETICS

Moderate emetic risk days 1, 8, 15, 22 and 29 cycle 1 only

CONCURRENT MEDICATION REQUIRED

Cisplatin	Ensure adequate pre and post hydration. If urine output is <100ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cisplatin – exfoliant

Filter not required
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E including Mg^{++} (>0.4) and LFTs Neutrophils x 10^9/L ≥1.0 provided patient is well Platelets ≥100x10^9/L	baseline and days 8, 15, 22 and 29 cycle 1 then every cycle
Ideally EDTA GFR should be used GFR assessed using EDTA result (BMI <19 or >30 or calculated creatinine clearance at the Consultant's discretion	baseline and every cycle
Serum creatinine	baseline and every cycle
Thyroid function	baseline and every cycle
Random cortisol	baseline and every cycle (or as specified in Trust guideline)
Random glucose	baseline and every cycle
HbA1c	Baseline then every 3 months
Virology	before cycle 1 if not previously checked
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Pembrolizumab	Immune related toxicities - pneumonitis, colitis or hepatitis etc Pembrolizumab SC skin reactions at site of administration route

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Cisplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Cisplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

DOSE MODIFICATIONS

Non-haematological

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Pembrolizumab
Immune-related adverse reactions - refer to Acute Oncology Initial Management guidelines
If the drug-related toxicity does not resolve to grade 0-1 within 12 weeks after onset of toxicity, discontinuation is recommended.

Hepatic impairment

Cisplatin
No need for dose adjustment is expected

Pembrolizumab
No need for dose adjustment is expected

Renal impairment

Cisplatin

CrCl >60ml/min	give 100% dose
CrCl 50-59ml/min	give 75% dose
CrCl 40-49ml/min	give 50% dose (curative intent) not recommended (palliative intent)
CrCl <40ml/min	not recommended

Pembrolizumab

No need for dose adjustment is expected

REFERENCES

1. CDF list

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Every cycle
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E, calcium, magnesium & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
Imaging assessment	X					At cycle 6, Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle