

IRINOTECAN PACLITAXEL OXALIPLATIN (IPO)

INDICATION (ICD10) C62

1. Treatment of relapsed germ-cell tumours. PS 0, 1, 2

REGIMEN

Day 1 Premedication: Atropine 250mcg subcutaneously 30 minutes prior to treatment
IRINOTECAN 200mg/m² in 250ml sodium chloride 0.9% (or licensed dose volume)
IV infusion over 60 minutes
Premedication 30 minutes prior to infusion:
Dexamethasone 8mg IV bolus
H₂ antagonist
Chlorphenamine 10mg IV bolus
PACLITAXEL 80mg/m² in 250ml** sodium chloride 0.9% IV infusion over 60 minutes
Day 2 OXALIPLATIN 200mg/m² in 500ml* glucose 5% IV infusion over 2 hours

Days 8 and 15

Premedication 30 minutes prior to infusion:
Dexamethasone 8mg IV bolus
H₂ antagonist
Chlorphenamine 10mg IV bolus
PACLITAXEL 80mg/m² in 250ml** sodium chloride 0.9% IV infusion over 60 minutes

*oxaliplatin doses 55mg to 200mg in 250ml glucose 5%

**paclitaxel doses 162mg to 600mg in 500ml sodium chloride 0.9%

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 4 cycles

ANTI-EMETICS

Moderately emetogenic days 1 and 2

Low emetogenic risk days 8 and 15

CONCURRENT MEDICATION REQUIRED

Irinotecan	Ensure premedication atropine given 30 minutes prior to treatment
Oxaliplatin	Flush with glucose 5% before and after infusion
Paclitaxel	Ensure premedication given before paclitaxel
GCSF	GCSF starting day 3 for 5 days

EXTRAVASATION AND TYPE OF LINE / FILTERS

Irinotecan - irritant

Oxaliplatin – exfoliant

Paclitaxel - vesicant

Administer paclitaxel via polyethylene lined administration set with ≤0.22micron filter

Consider central line

INVESTIGATIONS

Blood results required before SACT administration
 FBC, U&E and LFTs every cycle
 Neutrophils x $10^9/L$ ≥ 1.0
 Platelets x $10^9/L$ ≥ 100
 Serum creatinine
 Baseline weight and every cycle

MAIN TOXICITIES AND ADVERSE REACTIONS

Irinotecan	Acute cholinergic syndrome (including diarrhea and delayed diarrhoea, abdominal pain, hypotension, dizziness, malaise, increased salivation). Drink large volumes of fluid containing electrolytes and an appropriate antidiarrhoeal therapy - loperamide 4mg initially then 2mg every 2 hours, continuing for 12 hours after the last liquid stool (maximum of 48 hours in total).
Oxaliplatin	Peripheral sensory neuropathy and laryngeal spasm – avoid cold drinks and touching cold items
Paclitaxel	(2% risk of severe hypersensitivity) Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS (not exhaustive list check SPC/BNF/Stockleys)

Irinotecan	Aprepitant and fosaprepitant increases exposure to irinotecan. Carbamazepine decreases exposure to irinotecan, avoid. Enzalutamide, mitotane, phenobarbitone, phenytoin, primidone and rifampicin decreases exposure to irinotecan, avoid.
Paclitaxel	DOACs to be used with caution, need dose modifications or to be avoided eg apixaban. Clopidogrel interacts with paclitaxel, potentially increasing the concentration of paclitaxel. Paclitaxel is catalysed, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. inhibitors (e.g. erythromycin, fluoxetine, gemfibrozil) use with caution. inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, efavirenz, nevirapine) use with caution.

DOSE MODIFICATIONS

Non-haematological

Irinotecan

If patients suffer from severe diarrhoea, which required IV rehydration or neutropenic fever, consider reduction in subsequent cycles, discuss with SpR or Consultant.

Oxaliplatin

If patients develop acute laryngopharyngeal dysaesthesia infuse the next cycle over 4 hours.

If symptoms persist give 80% dose.

If persistent sensory symptoms occur, withdraw treatment

Paclitaxel

If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration

If grade ≥ 2 neuropathy, consider giving 75% dose

If grade >3 peripheral neuropathy is $>$ grade 3 omit further paclitaxel

Hepatic impairment

Paclitaxel

In the absence of Gilbert's syndrome:

Transaminase $<10\times\text{ULN}$ and bilirubin $\leq 1.25\times\text{ULN}$	no dose reduction
Transaminase $<10\times\text{ULN}$ and bilirubin 1.26-2xULN	give 77% of original dose
Transaminase $<10\times\text{ULN}$ and bilirubin 2.01-5xULN	give 51% of original dose
Transaminase $\geq 10\times\text{ULN}$ or bilirubin $>5\times\text{ULN}$	contraindicated

Irinotecan

Bilirubin 24-50micromol/L	give 50% dose
Bilirubin $>51\text{micromol/L}$	Clinical decision

Renal impairment

Oxaliplatin

CrCl $>30\text{ml/min}$	give 100% dose
CrCl $<30\text{ml/min}$	Dose reduce (consider 50% of original dose)

REFERENCES

1. Shamash J., Powles T., et al. A phase 2 study using a topoisomerase I-based approach in patients with multiply relapsed germ-cell tumours. Annals of Oncology 18; 925-930, 2007