ENDOMETRIAL CANCER

**CARBOPLATIN**
Carboplatin  270 - 360 mg/m²  IV  Day 1

*Dose reduced to 270 mg/m² in those who received prior pelvic radiation. Otherwise, starting dose was 360 mg/m² with dose escalation by 30 mg/m² per cycle to maximum of 450 mg/m² pending hematologic tolerance.

Repeat cycle every 28 days until intolerance or disease progression.


**CARBOPLATIN – PACLITAXEL**
Paclitaxel‡  175 mg/m²  IV  Day 1

Followed by

Carboplatin  AUC 6 – 7**  IV#  Day 1

‡Routine premedication used; *Administer over 3 hours; **AUC calculated using the Calvert formula; #Administer over 30 minutes.

Repeat cycle every 28 days to a maximum of 6 cycles.


**CISPLATIN**
Cisplatin  50 mg/m²  IV  Day 1

*Administer with routine pre- and post- hydration.

Repeat cycle every 21 days.


**DOXORUBICIN**
Doxorubicin  60 mg/m²  IV  Day 1

NOTE: Patients older than 65 years and/or those completing external radiation therapy before entering the study initiated doxorubicin at 45 mg/m² and were to be escalated to 60 mg/m² on the 2nd cycle, provided they experienced no toxicity worse than Grade 1.

DOSE MODIFICATION: Dose modified for elevated bilirubin. For bilirubin 1.1 – 3 mg/dL doxorubicin started at a dose of 30 mg/m² and increased to 45 mg/m² and 60 mg/m² provided no toxicity worse than Grade 1 occurs.

Repeat cycle every 21 days until unacceptable toxicity/disease progression/cumulative dose of 500 mg/m².

DOXORUBICIN - CISPLATIN

Doxorubicin  45 - 60 mg/m²  IV¹,²  Day 1
Cisplatin    50 mg/m²  IV³  Day 1

*Routine pre- and post-hydration required.

NOTE: ¹The maximum dose of doxorubicin was 420 mg/m², therefore only cisplatin was administered during the eighth cycle; ²Patients older than 65 years and/or those completing external radiation therapy before entering the study initiated doxorubicin at 45 mg/m² and were to be escalated to 60 mg/m² on the second cycle, provided there was no toxicity worse than Grade 1.

DOSE MODIFICATION:  ²Dose modified for elevated bilirubin. For bilirubin 1.1 – 3 mg/dL doxorubicin started at a dose of 30 mg/m² and increased to 45 mg/m² and 60 mg/m² provided no toxicity worse than Grade 1 occurs.

Repeat cycle every 21 days until unacceptable toxicity/disease progression/cumulative dose of 500 mg/m² of doxorubicin.


IFOSFAMIDE – PACLITAXEL (UTERINE CARCINOSARCOMA)

Ifosfamide  1600 mg/m²/day* IV  Days 1 – 3
Mesna      2000 mg/m²/day  CIVI**  Days 1 – 3
Paclitaxel‡  135 mg/m²  IV***  Day 1
Filgrastim  5 mcg/kg/day  SQ  Day 4 until ANC greater than 2 x 10⁹/L

‡Routine premedication administered; ¹Ifosfamide dose was reduced to 1200 mg/m²/dose for patients who had received prior radiation therapy; **Mesna started 15 minutes prior to ifosfamide daily and then continued as a 12-hour infusion daily; ***Administered over 3 hours.

Repeat cycle every 21 days until disease progression or unacceptable toxicity to a maximum of 8 cycles.

DOSE MODIFICATIONS: Depending on toxicity, ifosfamide was to be reduced in 0.4 g/m² decrements and paclitaxel was to be reduced to 100 mg/m². If hematologic toxicity was grade ≤1, ifosfamide was to be escalated to a maximum of 2000 mg/m² and paclitaxel was to be escalated to a maximum of 200 mg/m². No subsequent chemotherapy was to be administered until the absolute neutrophil count was ≥1.5 x 10⁹/L and platelets were ≥100 x 10⁹/L. If therapy was delayed for myelosuppression, weekly recounts were obtained. For nonhematologic toxicity, doses were to be reduced by one level for microscopic hematuria. The dose was held until serum albumin ≥3 g/dL. If grade 2 ifosfamide-related neurologic symptoms (such as confusion) developed, ifosfamide was to be reduced one dose level. Study therapy was discontinued for the following reasons: treatment delay lasting 6 weeks or more due to myelosuppression; persistent low (< 3 g/dL) serum albumin unresolved after 6 weeks; recurring grade 2 ifosfamide-induced neurologic symptoms despite dose reduction; development of grade 3 or 4 neurotoxicity; and disease progression.

MEDROXYPROGESTERONE ACETATE
Medroxyprogesterone acetate 200 mg/day PO Daily


PACLITAXEL
Paclitaxel‡ 175 - 200 mg/ m² IV** Day 1

‡Administer routine premedication; *Patients with prior pelvic radiation received a dose of 175 mg/ m²; **Administer over 3 hours.

Repeat cycle every 21 days.


PACLITAXEL – CISPLATIN
Paclitaxel‡ 175 mg/ m² IV Day 1

Followed by

Cisplatin 75 mg/ m² IV** Day 1
G- CSF 5 mcg/kg/day SQ Day 5 until ANC recovery

‡Administer routine premedication; *Administer over 3 hours; **Administer over 2 hours with routine pre- and post- hydration.

DOSE MODIFICATION: Cisplatin withheld for a serum creatinine greater than 2 mg/dL.

Repeat cycle every 21 days to a maximum of 6 cycles.


TAP (DOXORUBICIN – CISPLATIN – PACLITAXEL)
Doxorubicin 45 mg/ m² IV Day 1

Followed immediately by

Cisplatin 50 mg/ m² IV* Day 1
Paclitaxel‡ 160 mg/ m² IV** Day 2
Filgrastim 5 mcg/kg/day SQ Days 3 to 12

‡Administer routine premedication; *Administer over 1 hour with adequate pre- and post- hydration; **Administer over 3 hours.

NOTE: Dosing weight was capped at 2 m², i.e. any patient with a BSA greater than 2 m² was given a maximum dose of mg/ m² multiplied by 2 m².

Repeat cycle every 21 days to a maximum of 7 cycles.

**TOPOTECAN**
Topotecan 0.8 - 1 mg/m²/day IV* Days 1 - 5

*Administer over 30 minutes.

NOTE: Protocol was amended after toxicity analysis to a reduced starting dose of 1mg/m²/day (0.8 mg/m²/day for patients with prior pelvic radiation), to exclude patients with a performance status of more than 1, and to allow the use of hematopoietic growth factors for patients who developed hematologic toxicity after the first cycle.

Repeat cycle every 21 days until toxicity or disease progression.