ENDOMETRIAL CANCER

CARBOPLATIN

Carboplatin	270 - 360 mg/m2*	IV	Day 1

*Dose reduced to 270 mg/m^2 in those who received prior pelvic radiation. Otherwise, starting dose was 360 mg/m^2 with dose escalation by 30 mg/m^2 per cycle to maximum of 450 mg/m^2 pending hematologic tolerance.

Repeat cycle every 28 days until intolerance or disease progression.

Reference: Burke TW, et al. *Gynecol Oncol* 1993;51:397 - 400.

CARBOPLATIN – PACLITAXEL

Paclitaxel‡	175 mg/m^2	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.

Reference: Hoskins PJ, et al. *J Clin Oncol* 2001;19:4048 – 53.

CISPLATIN

Cisplatin	50 mg/m^2	IV*	Day 1

*Administer with routine pre- and post-hydration.

Repeat cycle every 21 days.

Reference: Thigpen JT, et al. *Gynecol Oncol* 1989;33:68 - 70.

DOXORUBICIN

Doxorubicin	60 mg/m^2	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/m^2 and were to be escalated to 60 mg/m^2 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/m^2 and increased to 45 mg/m^2 and 60 mg/m^2 provided no toxicity worse than Grade 1 occurs.

Repeat cycle every 21 days until unacceptable toxicity/disease progression/cumulative dose of 500 mg/m^2.

Reference: Thigpen JT, et al. *J Clin Oncol* 2004;22:3902 - 8.

DOXORUBICIN - CISPLATIN

Doxorubicin	45 - 60 mg/m^2	IV[1,2]	Day 1
Cisplatin	50 mg/m^2	IV*	Day 1

*Routine pre- and post-hydration required.

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

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

Repeat cycle every 21 days until unacceptable toxicity/disease progression/cumulative dose of 500 mg/m^2 of doxorubicin.

References: [1]Randall ME, et al. *J Clin Oncol* 2006;24:36 – 44; [2]Thigpen JT, et al. *J Clin Oncol* 2004;22:3902 - 8.

IFOSFAMIDE – PACLITAXEL (UTERINE CARCINOSARCOMA)

Ifosfamide	1600 mg/m^2/day*	IV	Days 1 – 3
Mesna	2000 mg/m^2/day	CIVI**	Days 1 – 3
Paclitaxel‡	135 mg/m^2	IV***	Day 1
Filgrastim	5 mcg/kg/day	SQ	Day 4 until ANC greater than 2 x 10^9/L

‡Routine premedication administered; *Ifosfamide dose was reduced to 1200 mg/m^2/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/m^2 decrements and paclitaxel was to be reduced to 100 mg/m^2. If hematologic toxicity was grade ≤1, ifosfamide was to be escalated to a maximum of 2000 mg/m^2 and paclitaxel was to be escalated to a maximum of 200 mg/m^2. No subsequent chemotherapy was to be administered until the absolute neutrophil count was ≥1.5 x 10^9/L and platelets were ≥100 x 10^9/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.

Reference: Homesley HD, et al. *J Clin Oncol* 2007;25:526 – 31.

MEDROXYPROGESTERONE ACETATE

Medroxyprogesterone acetate	200 mg/day	PO	Daily

Reference: Thigpen TJ, et al. *J Clin Oncol* 1999;17:1736 – 44.

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.

Reference: Lincoln S, et al. *Gynecol Oncol* 2003;88:277 - 81.

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.

Reference: Dimopoulos MA, et al. *Gynecol Oncol* 2000;78:52 – 7.

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.

Reference: Fleming GF, et al. *J Clin Oncol* 2004;22:2159 – 66.

TOPOTECAN

Topotecan	0.8 - 1 mg/m^2/day IV*	Days 1 - 5

*Administer over 30 minutes.

NOTE: Protocol was amended after toxicity analysis to a reduced starting dose of 1mg/m^2/day (0.8 mg/m^2/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.

Reference: Wadler S, et al. *J Clin Oncol* 2003;21:2110 – 4.