

DESMOID TUMOR

IMATINIB MESYLATE

Imatinib

400 mg BID

PO

Ongoing

Imatinib mesylate doses should be taken with food. Imatinib is available as 100 mg capsules, 100 mg tablets, and 400 mg tablets.

Reference: [Heinrich MC, et al. / Clin Oncol 2006;24:1195 - 203.](#)

NOTES:

EWING'S SARCOMA AND PNET

ALTERNATING VDC (VINCRIStINE – DOXORUBICIN – CYCLOPHOSPHAMIDE) AND IFOSFAMIDE – ETOPOSIDE (IE) [POG 9354]

Courses of chemotherapy were administered every 3 weeks for a total of 17 courses. See schema on next page.

VAC

| | | | |
|------------------|---|--------|---|
| Vincristine | 1.5 mg/m ² * | IV | Day 1 |
| Doxorubicin | 75 mg/m ² | CIVI** | Days 1 and 2 |
| Cyclophosphamide | 1200 mg/m ² | IV | Day 1 |
| Mesna | Doses specified in protocol pertain to children i.e., 360 mg/m ² every 3 hours starting pre-cyclophosphamide and for 3 additional doses. In adults less frequent dosing of mesna can be administered; typically use in a dose of 20% of the cyclophosphamide dose before each dose of cyclophosphamide and then repeat 4 hours and 8 hours later (total dose of mesna is 60% of the cyclophosphamide dose) | | |
| Filgrastim | 5 mcg/kg | SQ | Daily starting 24–36 hours after completion of chemotherapy (exception vincristine) |

*Maximum dose 2 mg; **Administer as a continuous infusion over 48 hours.

DOSE MODIFICATIONS: If cardiac irradiation of greater than 2000 cGy has occurred or is anticipated, omit doxorubicin at week 27. The maximum dose of doxorubicin is 300 mg/m² for patients undergoing cardiac irradiation.

Repeat cycle every 21 days; alternating with the regimen listed below:

IFOSFAMIDE – ETOPOSIDE

| | | | |
|------------|---|----|---|
| Ifosfamide | 1800 mg/m ² /day | IV | Days 1 – 5 |
| Mesna | Doses specified in protocol pertain to children i.e., 360 mg/m ² every 3 hours starting pre-cyclophosphamide and for 3 additional doses. In adults less frequent dosing of mesna can be administered; typically use in a dose of 20% of the cyclophosphamide dose before each dose of cyclophosphamide and then repeat 4 hours and 8 hours later (total dose of mesna is 60% of the ifosfamide dose) | | |
| Etoposide | 100 mg/m ² /day | IV | Days 1 – 5 |
| Filgrastim | 5 mcg/kg | SQ | Daily starting 24–36 hours after completion of chemotherapy (exception vincristine) |

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ALTERNATING VDC (VINCRIStINE – DOXORUBICIN – CYCLOPHOSPHAMIDE) AND IFOSFAMIDE – ETOPOSIDE (IE) [POG 9354] – CONTINUED

REGIMEN A:

| | | | | | | | | | | | | | | | | | |
|------|---|---|---|---|----|----|----|----|----|-----|----|----|----|----|----|----|----|
| WEEK | 0 | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 | 27* | 30 | 33 | 36 | 39 | 42 | 45 | 48 |
| K | | | | | | | | | | * | | | | | | | |
| | V | I | V | I | V | I | I | V | I | V | I | V | I | V | I | V | V |
| | D | E | D | E | D | E | E | D | E | D | E | | E | | E | | |
| | C | | C | | C | | | C | | C | | C | | C | | C | C |

Local Control

↑Delayed surgery if planned

Reference: Pediatric Oncology Group (POG) Protocol 9354.

CYCLOPHOSPHAMIDE – TOPOTECAN

Cyclophosphamide 250 mg/m²/day IV* Days 1 – 5

Followed immediately by

Topotecan 0.75 mg/m²/day IV* Days 1 – 5
 Filgrastim 5 mcg/kg/day SQ Day 6 until ANC recovery to 1.5 x 10⁹/L or greater

*Administered over 30 minutes. Patients were hydrated with 500 mL of fluid orally or intravenously 2 – 4 hours prior to cyclophosphamide dosing. Following the cyclophosphamide infusion – hydration was continued at a rate of 3000 mL/m²/day.

NOTE: This regimen was evaluated in patients aged 21 years or younger with relapsed or refractory solid tumors including Ewing’s sarcoma, osteosarcoma, or rhabdomyosarcoma.

Repeat cycle every 21 days until progression or unacceptable toxicity.

Reference: [Saylor RL, et al. J Clin Oncol 2001;19:3463 – 9.](#)

KAPOSI'S SARCOMA

ABV (DOXORUBICIN – BLEOMYCIN – VINCRISTINE)

| | | | |
|-------------|-------------------------|----|-------|
| Doxorubicin | 20 mg/m ² | IV | Day 1 |
| Bleomycin | 10 units/m ² | IV | Day 1 |
| Vincristine | 1 mg | IV | Day 1 |

Repeat cycle every 14 days to a maximum of 6 cycles.

Reference: [Northfelt DW, et al. *J Clin Oncol* 1998;16:2445 – 51.](#)

ETOPOSIDE

| | | | |
|-----------|--------------------------|----|------------|
| Etoposide | 25 mg/m ² BID | PO | Days 1 – 7 |
|-----------|--------------------------|----|------------|

Repeat cycle every 14 days.

NOTE: Used the parenteral solution of etoposide and diluted the dose in orange or lemon juice.

Reference: [Schwartzmann G, et al. *J Clin Oncol* 1997;15:2118 – 24.](#)

LIPOSOMAL DAUNORUBICIN

| | | | |
|------------------------|----------------------|-----|-------|
| Liposomal daunorubicin | 40 mg/m ² | IV* | Day 1 |
|------------------------|----------------------|-----|-------|

*Administer over 30 – 60 minutes.

Repeat cycle every 14 days to CR + 2 cycles, toxicity or disease progression.

Reference: [Gill PS, et al. *J Clin Oncol* 1996;14:2353 – 64.](#)

LIPOSOMAL DOXORUBICIN

| | | | |
|-----------------------|----------------------|-----|-------|
| Liposomal doxorubicin | 20 mg/m ² | IV* | Day 1 |
|-----------------------|----------------------|-----|-------|

*Administer over 30 minutes.

Repeat cycle every 14 – 21 days to a maximum of 6 cycles.

References: [Northfelt DW, et al. *J Clin Oncol* 1998;16:2445 – 51](#); [Stewart S, et al. *J Clin Oncol* 1998;16:683 – 91.](#)

PACLITAXEL

| | | | |
|-------------|-----------------------|-----|-------|
| Paclitaxel‡ | 135 mg/m ² | IV* | Day 1 |
|-------------|-----------------------|-----|-------|

‡Routine premedication administered; *Administer over 3 hours.

NOTE: Dose escalated to a maximum of 175 mg/m² on subsequent cycles if tolerated.

Repeat cycle every 21 days.

Reference: [Welles L, et al. *J Clin Oncol* 1998;16:1112 – 21.](#)

PACLITAXEL

Paclitaxel‡

100 mg/m²

IV*

Day 1

‡Routine premedication administered; *Administer over 3 hours.

Repeat cycle every 14 days.

Reference: [Gill PS, et al. *J Clin Oncol* 1999;17:1876 – 83.](#)

LEIOMYOSARCOMA

CISPLATIN – IFOSFAMIDE

| | | | |
|------------|-----------------------------|------|------------|
| Cisplatin | 20 mg/m ² /day | IV | Days 1 – 4 |
| Ifosfamide | 1500 mg/m ² /day | IV | Days 1 – 4 |
| Mesna | 1500 mg/m ² /day | CIVI | Days 1 – 4 |

Repeat cycle every 21 days up to 8 cycles of therapy.

NOTE: Due to unacceptable toxicity the original regimen was reduced by 20% (i.e., the original was 5 days of therapy, and is now 4 days of therapy). Reduce ifosfamide dose further to 1200 mg/m²/day if prior pelvic radiation. The combination of cisplatin and ifosfamide led to a slight improvement in progression free survival but with added toxicity compared to ifosfamide alone. If using ifosfamide monotherapy, use ifosfamide 1500 mg/m²/day for 5 days (with mesna).

Reference: [Sutton G, et al. *Gynecol Oncol* 2000;79:147 – 53.](#)

GEMCITABINE – DOCETAXEL

PATIENTS WHO HAD NOT PREVIOUSLY RECEIVED RADIATION THERAPY:

| | | | |
|-------------|-----------------------|-----|--------------|
| Gemcitabine | 900 mg/m ² | IV* | Days 1 and 8 |
|-------------|-----------------------|-----|--------------|

Followed immediately by

| | | | |
|------------|--|------|-------------|
| Docetaxel‡ | 100 mg/m ² | IV** | Day 8 |
| G-CSF | 150 micrograms/m ² /day*** SQ | | Days 9 – 15 |

‡Routine premedication administered; *Administer over 90 minutes; **Administer over 1 hour;

***Doses rounded to 300 or 480 micrograms.

PATIENTS WHO HAD RECEIVED PRIOR RADIATION THERAPY:

| | | | |
|-------------|-----------------------|-----|--------------|
| Gemcitabine | 675 mg/m ² | IV* | Days 1 and 8 |
|-------------|-----------------------|-----|--------------|

Followed immediately by

| | | | |
|------------|--|------|-------------|
| Docetaxel‡ | 75 mg/m ² | IV** | Day 8 |
| G-CSF | 150 micrograms/m ² /day*** SQ | | Days 9 – 15 |

‡Routine premedication administered; *Administer over 90 minutes; **Administer over 1 hour;

***Doses rounded to 300 or 480 micrograms.

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

Reference: [Hensley ML, et al. *J Clin Oncol* 2002;20:2824 – 31.](#)

OSTEOSARCOMA

CYCLOPHOSPHAMIDE – TOPOTECAN

| | | | |
|------------------|----------------------------|-----|------------|
| Cyclophosphamide | 250 mg/m ² /day | IV* | Days 1 – 5 |
|------------------|----------------------------|-----|------------|

Followed immediately by

| | | | |
|------------|-----------------------------|-----|---|
| Topotecan | 0.75 mg/m ² /day | IV* | Days 1 – 5 |
| Filgrastim | 5 mcg/kg/day | SQ | Day 6 until ANC recovery to 1.5 x 10 ⁹ /L or greater |

*Administered over 30 minutes. Patients were hydrated with 500 mL of fluid orally or intravenously 2 – 4 hours prior to cyclophosphamide dosing. Following the cyclophosphamide infusion, hydration was continued at a rate of 3000 mL/m²/day.

NOTE: This regimen was evaluated in patients aged 21 years or younger with relapsed or refractory solid tumors including Ewing's sarcoma, osteosarcoma or rhabdomyosarcoma.

Repeat cycle every 21 days until progression or unacceptable toxicity.

Reference: [Saylor RL, et al. J Clin Oncol 2001;19:3463 – 9.](#)

DOXORUBICIN – CISPLATIN

| | | | |
|-------------|---------------------------|-------|------------|
| Doxorubicin | 25 mg/m ² /day | IV* | Days 1 – 3 |
| Cisplatin | 100 mg/m ² | CIV** | Day 1 |

*Administer over 4 hours; **Administer as a continuous 24-hour infusion.

Repeat cycle every 21 days.

NOTE: ¹Plan composed of 3 cycles of neoadjuvant chemotherapy, followed by surgery and then followed by 3 cycles of adjuvant chemotherapy (starting 2 weeks post-operatively).

References: ¹[Souhami RL, et al. Lancet 1997;350:911 – 7;](#) ²[Lewis IJ, et al. J Natl Cancer Inst 2007;99:112 – 8.](#)

DOXORUBICIN/CISPLATIN/HIGH-DOSE METHOTREXATE (HDMTX)

PRE-OPERATIVE THERAPY/INDUCTION:

| | | | |
|-------------|---------------------------|-------|---------------------------|
| Doxorubicin | 25 mg/m ² /day | CIVI* | Days 1–3 of weeks 0 and 5 |
|-------------|---------------------------|-------|---------------------------|

Concurrent with

| | | | |
|-----------|-----------------------|------|------------------------|
| Cisplatin | 120 mg/m ² | IV** | Day 1 of weeks 0 and 5 |
|-----------|-----------------------|------|------------------------|

| | | | |
|--------------|-----------------------|-------|---|
| Methotrexate | 12 g/m ² # | IV*** | Day 1 of weeks 3, 4, 8 and 9 |
| Leucovorin | 10 mg | IV | Begin 24 hours after initiation of HDMTX. Patients MUST receive leucovorin rescue with this regimen. Dosing and schedules for leucovorin not otherwise outlined in manuscript. See leucovorin dosing recommendations in the miscellaneous section of this handbook. |

*Administered as a 72 hour continuous infusion; **Administer over 4 hours; Routine prehydration required; ***Administered as a 4 hour infusion; Prehydrate and alkalinize the urine to a pH of greater than 7; To maintain dose intensity of doxorubicin, the protocol specified that if there was a delay of one week between each pair of high dose methotrexate the second dose of high dose methotrexate could be eliminated; #Dose of methotrexate capped at 20 grams.

DEFINITIVE SURGERY IS TO BE PERFORMED AT WEEK 10–11.

ADJUVANT CHEMOTHERAPY TO BE STARTED AT WEEK 12, OR WHEN SURGEON DETERMINES WOUND HEALING TO BE ADEQUATE

| | | | |
|-------------|---------------------------|-------|-------------------------------------|
| Doxorubicin | 25 mg/m ² /day | CIVI* | Days 1–3 of weeks 12, 17, 22 and 27 |
|-------------|---------------------------|-------|-------------------------------------|

Concurrent with

| | | | |
|-----------|-----------------------|------|-------------------------------|
| Cisplatin | 120 mg/m ² | IV** | Day 1 of weeks 12 and 17 only |
|-----------|-----------------------|------|-------------------------------|

| | | | |
|--------------|-----------------------|-------|---|
| Methotrexate | 12 g/m ² # | IV*** | Day 1 of weeks 15, 16, 20, 21, 25, 26, 30 and 31 |
| Leucovorin | 10 mg | IV | Begin 24 hours after initiation of HDMTX. Patients MUST receive leucovorin rescue with this regimen. Dosing and schedules for leucovorin not otherwise outlined in manuscript. See leucovorin dosing recommendations in the miscellaneous section of this handbook. |

*Administered as a 72 hour continuous infusion; **Administer over 4 hours; Routine prehydration required; ***Administered as a 4 hour infusion; Prehydrate and alkalinize the urine to a pH of greater than 7; To maintain dose intensity of doxorubicin, the protocol specified that if there was a delay of one week between each pair of high dose methotrexate the second dose of high dose methotrexate could be eliminated; #Dose of methotrexate capped at 20 grams.

Reference: [Meyers P, et al. J Clin Oncol 2005;23:2004 – 111.](#)

IFOSFAMIDE – ETOPOSIDE

| | | | |
|-----------|----------------------------|-----|------------|
| Etoposide | 100 mg/m ² /day | IV* | Days 1 – 5 |
|-----------|----------------------------|-----|------------|

Followed by

| | | | |
|------------|--------------------------------|------|------------|
| Ifosfamide | 1800 mg/m ² /day | IV* | Days 1 – 5 |
| Mesna | 360 mg/m ² /day | IV** | Days 1 – 5 |
| Mesna | 2520 mg/m ² /day*** | IV | Days 1 – 5 |

*Administered over 1 hour; **Mesna 360 mg/m² mixed together with the ifosfamide in the same infusion bag over 1 hour; ***In the publication, mesna is scheduled to be administered as a separate 3 hour infusion times one, followed by boluses every 3 hours for 6 doses. For ease of administration place the equivalent of 7 doses of mesna into an infusion bag and run as a continuous infusion, therefore saving nursing time.

Repeat cycle every 21 days for 12 total cycles.

NOTE: Evaluate for surgery or radiation after 4 cycles.

Reference: [Miser JS, et al. J Clin Oncol 1987;5:1191 – 8.](#)

UF OSTEOSARCOMA REGIMEN

NEO-ADJUVANT (PREOPERATIVE)

WEEK 1 AND WEEK 3

| | | | |
|-------------|-----------------------------|-------|------------|
| Ifosfamide | 2500 mg/m ² /day | CIVI* | Days 1 – 3 |
| Mesna | 2500 mg/m ² /day | CIVI* | Days 1 – 4 |
| Doxorubicin | 20 mg/m ² /day | IV | Days 1 – 3 |

*Administer as a continuous infusion over 24 hours.

WEEK 5 AND WEEK 7

| | | | |
|-------------|---------------------------|----|------------|
| Cisplatin | 30 mg/m ² /day | IV | Days 1 – 3 |
| Doxorubicin | 20 mg/m ² /day | IV | Days 1 – 3 |

With filgrastim or sargramostim support Days 4 – 13 during each of 4 cycles.

NOTE: No chemotherapy administered on weeks 2, 4, 6, and 8. Definitive surgery on week 10 – 11 with adjuvant treatment starting 1 week post-operatively.

ADJUVANT

ADJUVANT GOOD RESPONSE ARM: IF 90% OR GREATER TUMOR NECROSIS THEN GIVE THE FOLLOWING

| | | | |
|-------------|-----------------------------|------|----------------------------------|
| Ifosfamide | 2000 mg/m ² /day | CIVI | Days 1 – 3, weeks 1 and 4 |
| Mesna | 2000 mg/m ² /day | CIVI | Days 1 – 4, weeks 1 and 4 |
| Doxorubicin | 15 mg/m ² /day | IV | Days 1 – 3, weeks 1, 4, 7 and 10 |
| Cisplatin | 20 mg/m ² /d | IV | Days 1 – 3, weeks 7 and 10 |

With filgrastim or sargramostim support on Days 4 – 13 during each of 4 cycles.

ADJUVANT POOR RESPONSE ARM: IF LESS THAN 90% TUMOR NECROSIS THEN GIVE THE FOLLOWING

| | | | |
|--------------|-----------------------------|------|------------------------------------|
| Methotrexate | 3750 mg/m ² | IV* | Day 1 of week 1, 7, 13, and 19 |
| Leucovorin** | 50 mg Q6H | IV | See below |
| Ifosfamide | 2000 mg/m ² /day | CIVI | Days 1 – 3, weeks 4 and 10 |
| Mesna | 2000 mg/m ² /day | CIVI | Days 1 – 4, weeks 4 and 10 |
| Etoposide | 100 mg/m ² /day | CIVI | Days 1 – 3, weeks 4, 10, 16 and 22 |
| Cisplatin | 20 mg/m ² /day | IV | Days 1 – 3, weeks 16 and 22 |

*Administer over 6 hours; **Start 24 hours after the initiation of methotrexate. Administer Q6H for 10 doses (may adjust according to nomogram or 24 and 48 hours MTX levels) on weeks 1, 7, 13 and 19.

With filgrastim or sargramostim support on Days 4 – 13 during each of 8 cycles.

Reference: [Patel SJ, et al. Am J Clin Oncol 2002;25:489 – 95.](#)

RHABDOMYOSARCOMA

CYCLOPHOSPHAMIDE – TOPOTECAN

| | | | |
|------------------|----------------------------|-----|------------|
| Cyclophosphamide | 250 mg/m ² /day | IV* | Days 1 – 5 |
|------------------|----------------------------|-----|------------|

Followed immediately by

| | | | |
|------------|-----------------------------|-----|---|
| Topotecan | 0.75 mg/m ² /day | IV* | Days 1 – 5 |
| Filgrastim | 5 mcg/kg/day | SQ | Day 6 until ANC recovery to 1.5 x 10 ⁹ /L or greater |

*Administered over 30 minutes. Patients were hydrated with 500 mL of fluid orally or intravenously 2 – 4 hours prior to cyclophosphamide dosing. Following the cyclophosphamide infusion – hydration was continued at a rate of 3000 mL/m²/day.

NOTE: This regimen was evaluated in patients aged 21 years or younger with relapsed or refractory solid tumors including Ewing’s sarcoma, osteosarcoma or rhabdomyosarcoma.

Repeat cycle every 21 days until progression or unacceptable toxicity.

Reference: [Saylor RL, et al. J Clin Oncol 2001;19:3463 – 9.](#)

VAC (VINCRIStINE – DACTINOMYCIN – CYCLOPHOSPHAMIDE)

INDUCTION WEEK 0 – 16

| | | | |
|------------------|---|----|---|
| Vincristine | 1.5 mg/m ² * | IV | Weekly, during weeks 0 – 8; 9 – 12 and 16 |
| Dactinomycin | 0.015 mg/kg/day** | IV | Days 1 – 5 weeks 0, 3, 6 and 16 |
| Cyclophosphamide | 2200 mg/m ² | IV | Day 1 weeks 0, 3, 6, 9, 12 and 16 |
| Mesna | Dose not specified in regimen; typically use in a dose of 20% of the cyclophosphamide dose before each dose of cyclophosphamide and then repeat 4 hours and 8 hours later (total dose of mesna is 60% of the cyclophosphamide dose) | | |

*Maximum dose 2 mg; **Maximum daily dose 0.5 mg.

Vincristine administered Q week from week 0 – 8; Dactinomycin and cyclophosphamide Q3weeks from week 0 – 8, then reevaluate the patient. Starting week 9 patient to undergo radiation therapy. During this time (weeks 9 – 14) do not administer dactinomycin. Resume vincristine weekly from week 9 through week 12. Resume cyclophosphamide every 3 weeks from week 9 through week 12. No chemotherapy week 13 – 15. Resume VAC week 16. Then evaluate the patient again. Resume therapy week 20 = CONTINUATION.

CONTINUATION THERAPY WEEK 20 – 28

| | | | |
|------------------|------------------------------|----|-----------------------------|
| Vincristine | 1.5 mg/m ² * | IV | Weekly during weeks 20 – 25 |
| Dactinomycin | 0.015 mg/kg/day** | IV | Days 1–5, weeks 20 and 23 |
| Cyclophosphamide | 2200 mg/m ² | IV | Day 1, weeks 20 and 23 |
| Mesna | See induction for directions | | |

NOTE: No chemotherapy weeks 26 – 28.

CONTINUED ON NEXT PAGE.....

VAC (VINCRIStINE – DACTINOMYCIN-D – CYCLOPHOSPHAMIDE) – CONTINUED

CONTINUATION THERAPY WEEK 29 – 46

| | | | |
|------------------|------------------------------|----|---|
| Vincristine | 1.5mg/m ^{2*} | IV | Weekly during weeks 29 – 34 and 38 – 43 |
| Dactinomycin | 0.015mg/kg/day** | IV | Day 1, weeks 29, 32, 38 and 41 |
| Cyclophosphamide | 2200 mg/m ² | IV | Day 1, weeks 29, 32, 38 and 41 |
| Mesna | See induction for directions | | |

*Maximum dose 2 mg; **Maximum daily dose 0.5 mg.

NOTE: No chemotherapy during Weeks 35 – 37.

Treatment schema per protocol:

| Regimen | INDUCTION: Treatment Week 0-16 | | | | | | | | | | | | | | CONTINUATION: Treatment Week 20-28 | | | | | | | | | | | | | | |
|---|--------------------------------|---|---|---|---|---|----|---|---|----|--------------------|----|----|----|------------------------------------|----|----|----|----|----|----|----|----|----|----|----|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | | | |
| VAC | V | V | V | V | V | V | V | V | V | E | V | V | V | V | - | - | - | V | E | V | V | V | V | V | V | V | - | - | - |
| | A | | | A | | | | A | | V | C | | | C | | | A | V | A | | | A | | | | | | | |
| | C | | | C | | | | C | | A | Radiation Therapy* | | | | | | C | V | C | | | C | | | | | | | |
| | | | | | | | | | | A | | | | | | | | A | | | | | | | | | | | |
| VAI | V | V | V | V | V | V | V | V | V | L | V | V | V | V | - | - | - | V | L | V | V | V | V | V | V | V | - | - | - |
| | A | | | A | | | | A | | U | I | | | I | | | A | U | A | | | A | | | | | | | |
| | I | | | I | | | | I | | A | Radiation Therapy* | | | | | | I | A | I | | | I | | | | | | | |
| | | | | | | | | | | T | | | | | | | | T | | | | | | | | | | | |
| VIE | V | V | V | V | V | V | V | V | V | I | V | V | V | V | - | - | - | V | I | V | V | V | V | V | V | V | - | - | - |
| | I | | | I | | | | I | | O | I | | | I | | | I | O | I | | | I | | | | | | | |
| | E | | | E | | | | E | | N | Radiation Therapy* | | | | | | E | N | E | | | E | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| CONTINUATION: Treatment Week 29-46 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Regimens 40, 41, 42, 43, 45, 46, 47 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 2 | 3 | 3 | 3 | 3 | 3 | // | 3 | 3 | 4 | 4 | 4 | 4 | // | 4 | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | |
| | 9 | 0 | 1 | 2 | 3 | 4 | | 8 | 9 | 0 | 1 | 2 | 3 | | 6 | | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | | | | |
| | V | V | V | V | V | V | | V | V | V | V | V | V | - | E | | V | V | V | V | V | V | V | V | V | V | V | E | |
| | A | | | A | | | | A | | | | | | | V | | A | | | | A | | | | | | | V | |
| | C | | | C | | | | C | | | | | | | A | | C | | | | C | | | | | | | A | |
| | | | | | | | | | | | | | | | L | | | | | | | | | | | | | L | |
| VA | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | // | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | // | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | |
| | - | V | V | V | V | V | V | V | V | E | - | V | V | V | V | V | V | V | E | - | V | V | V | V | V | V | V | V | E |
| | A | | | | | | | | | A | V | A | | | A | | | A | V | A | | | | A | | | | A | V |
| | | | | | | | | | | L | | | | | | | | | L | | | | | | | | | | L |

Reference: [Crist WM, et al. J Clin Oncol 2001;19:3091 – 102.](#)

ADULT SOFT TISSUE SARCOMA

AI (DOXORUBICIN – IFOSFAMIDE)

| | | | |
|-------------|------------------------------|--------|--------------|
| Doxorubicin | 30 mg/m ² /day | IV | Days 1 and 2 |
| Ifosfamide | 3750 mg/m ² /day | IV* | Days 1 and 2 |
| Mesna | 2250 mg/m ² / day | CIVI** | Days 1 and 2 |

*Administer over 4 hours. Accompanied by deliberate IV hydration (300 mL/hour) beginning 3 hours before each treatment cycle and for 3 total days (at 100 mL/hour); **Administer immediately preceding Ifosfamide dose and continue for 8 hours after Ifosfamide administration.

Repeat cycle every 21 days.

Reference: [Edmonson JH, et al. *J Clin Oncol* 1993;11:1269 – 75.](#)

CAD (CYCLOPHOSPHAMIDE – DOXORUBICIN – DACARBAZINE)

| | | | |
|------------------|----------------------------|----|--------------|
| Cyclophosphamide | 500 mg/m ² | IV | Day 1 |
| Doxorubicin | 60 mg/m ² | IV | Day 2 |
| Dacarbazine | 400 mg/m ² /day | IV | Days 1 and 2 |

Doxorubicin discontinued after achieving a total dose of 450 mg/m²; Cyclophosphamide and doxorubicin were continued for a total duration of 1 year. Radiation was added (if applicable) between cycles number 3 and 4 (with 4th course not administered until radiation complete and toxicity resolved).

Repeat cycle every 21 days. Start approximately 3 weeks post-operatively.

Reference: [Antman KH, et al. *Cancer* 1983;51:396 – 401.](#)

CYVADIC (CYCLOPHOSPHAMIDE – VINCRIStINE – DOXORUBICIN – DACARBAZINE)

| | | | |
|------------------|----------------------------|-----|------------|
| Cyclophosphamide | 500 mg/m ² | IV | Day 1 |
| Vincristine | 1.5 mg/m ² | IV* | Day 1 |
| Doxorubicin | 50 mg/m ² | IV | Day 1 |
| Dacarbazine | 400 mg/m ² /day | IV | Days 1 – 3 |

*Maximum vincristine dose is 2 mg.

Repeat cycle every 28 days to a maximum of 8 cycles. Start chemotherapy no later than 13 weeks after the surgery. Radiation (if indicated) completed prior to chemotherapy.

Reference: [Bramwell V, et al. *J Clin Oncol* 1994;12:1137 – 49.](#)

DOXORUBICIN

| | | | |
|-------------|----------------------|-----|-------|
| Doxorubicin | 75 mg/m ² | IV* | Day 1 |
|-------------|----------------------|-----|-------|

*Administer as IV bolus.

DOSE MODIFICATION: Treatment was delayed by 1 week for incomplete count recovery prior to the next cycle. Febrile neutropenia requiring hospitalization or antibiotics resulted in subsequent dose reductions of 20%. Treatment was discontinued if the LVEF decreased to less than 45%.

Repeat cycle every 21 days to a maximum of 6 cycles, until disease progression, or unacceptable toxicity.

Reference: [Lorigan P, et al. J Clin Oncol 2007;25:3144 – 50.](#)

GEMCITABINE – DOCETAXEL

| | | | |
|-----------------------------|-----------------------|------|-----------------------------------|
| Gemcitabine | 900 mg/m ² | IV* | Days 1 and 8 |
| Docetaxel‡ | 100 mg/m ² | IV** | Day 8 |
| Filgrastim or pegfilgrastim | | SQ | Starting day 9 until ANC recovery |

‡Routine premedication administered; *Administer over 90 minutes (fixed dose rate of 10 mg/m²/minute); **Administer over 60 minutes.

DOSE MODIFICATIONS: Up to two 25% dose reductions were permitted in subsequent cycles of therapy for patients experiencing febrile neutropenia, ≥ grade 2 neuropathy, ≥ grade 3 LFT abnormalities, or other grade 3 or 4 nonhematologic toxicity. Patients with prior pelvic irradiation started therapy with 25% dose reductions.

Repeat cycle every 21 days.

Reference: [Maki RG, et al. J Clin Oncol 2007;25:2755 – 63.](#)

IE (IFOSFAMIDE – ETOPOSIDE)

| | | | |
|-----------|----------------------------|-----|------------|
| Etoposide | 100 mg/m ² /day | IV* | Days 1 – 5 |
|-----------|----------------------------|-----|------------|

Followed by

| | | | |
|------------|------------------------------|------|------------|
| Ifosfamide | 1800 mg/m ² /day | IV** | Days 1 – 5 |
| Mesna | 360mg/m ² /day | IV** | Days 1 – 5 |
| Mesna | 2520 mg/m ² /day# | IV | Days 1 – 5 |

*Administer over 1 hour; **Mesna 360mg/m² mixed together with the ifosfamide in the same infusion bag over 1 hour; #In the publication, mesna is scheduled to be administered as a separate 3 hour infusion times 1, followed by boluses every 3 hours for 6 doses. For ease of administration put the equivalent of 7 doses of mesna into an infusion bag and run as a continuous infusion, therefore saving nursing time.

Repeat cycle every 21 days for a total of 12 cycles.

NOTE: Evaluate the patient for surgery or radiation after 4 cycles.

Reference: [Miser JS, et al. J Clin Oncol 1987;5:1191 – 8.](#)

IE (IFOSFAMIDE – ETOPOSIDE)

| | | | |
|------------|--|------|------------|
| Ifosfamide | 2500 mg/m ² /day | IV* | Days 1 – 3 |
| Etoposide | 100 mg/m ² /day | IV** | Days 1 – 3 |
| Mesna | 20% of ifosfamide dose prior to and 4, 8 and 12 hours after ifosfamide administration. | | |

*Administer over 2 hours; **Administer over 1 hour.

Repeat cycle every 28 days.

Reference: [Edmonson JH, et al. *J Natl Cancer Inst* 1989;81:863 – 6.](#)

MAID (MESNA – DOXORUBICIN – IFOSFAMIDE – DACARBAZINE)

| | | | |
|-------------|------------------------------|------|------------|
| Mesna | 2000 mg/m ² /day* | CIVI | Days 1 – 4 |
| Doxorubicin | 15 mg/m ² /day | CIVI | Days 1 – 4 |
| Ifosfamide | 2000 mg/m ² /day* | CIVI | Days 1 – 3 |
| Dacarbazine | 250 mg/m ² /day | CIVI | Days 1 – 4 |

Repeat cycle every 21 days until progression or a cumulative anthracycline dose of 450 mg/m².

*NOTE: The doses of ifosfamide and mesna were reduced to those listed above secondary to myelosuppression.

References: [Antman K, et al. *Cancer* 1998;82:1288 – 95;](#) [Antman K, et al. *J Clin Oncol* 1993;11:1276–85.](#)

MISCELLANEOUS SARCOMAS

ANGIOSARCOMA

PACLITAXEL

| | | | |
|-------------|----------------------|----|-------------------|
| Paclitaxel‡ | 80 mg/m ² | IV | Days 1, 8, and 15 |
|-------------|----------------------|----|-------------------|

‡Routine premedication administered.

Repeat cycle every 28 days until disease progression or unacceptable toxicity.

Reference: [Penel, N, et al. *J Clin Oncol* 2007;25 \(18S\). Abstract 10002.](#)

UTERINE CARCINOSARCOMA

IFOSFAMIDE - PACLITAXEL

| | | | |
|-------------|------------------------------|--------|---|
| 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/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.

Reference: [Homesley HD, et al. *J Clin Oncol* 2007;25:526 - 31.](#)