

BC Cancer Protocol Summary for MESNA Dosage Modification for Hematuria Secondary to Oxazaphosphorines (e.g. Ifosfamide and Cyclophosphamide)

Protocol Code

SCMESNA

Tumour Group

Supportive Care

Contact Physician

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TRANSIENT MICROSCOPIC HEMATURIA

No modification of the oxazaphosphorine or MESNA should be made for microscopic hematuria (defined as more than 50 RBC/hpf on the urinalysis report) that is transient (i.e. occurring on no more than two separate days during a cycle of chemotherapy). If urine dipstick is positive for hematuria, send urine sample for urinalysis for verification and accurate measurement of hematuria.

For significant (more than transient) hematuria occurring with protocols using more than 2500 mg/m²/day of ifosfamide, we recommend the protocol be changed as follows to ensure safe dosing of MESNA. Guidelines for MESNA dosing for protocols delivering more than 2500 mg/m²/day ifosfamide are quite arbitrary. It is felt that this switch will be safer for patients.

- SAAVIME3 should be switched to the 5 day protocol SAIME
- SAAI and SAAVI should be switched to the modification in this SCMESNA protocol with maximum 2500 mg/m²/day on Days 1 and 2 rather than 5000 mg/m²/day in one day. (see order sheet below)
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The specific inpatient preprinted orders must be selected:

- For SAAI, choose SCMESNA (SAAI) preprinted order
- For SAAVI, choose SCMESNA (SAAVI) preprinted order
- For SAAVIME3 and SAIME, choose SCMESNA (SAIME/SAAVIME3) preprinted order
- For SAVACM, choose SCMESNA (SAVACM) preprinted order
- For non-sarcoma protocols, choose SCMESNA (inpatient) preprinted order

PERSISTENT MICROSCOPIC HEMATURIA

This is defined as 3 or more episodes of microscopic hematuria (more than 50 RBC/hpf) occurring on 3 or more separate days during a cycle of chemotherapy.

1. Do not modify the total dose of oxazaphosphorine.
2. Increase total IV hydration to 4000 mL/m² over 24 hours: starting after oxazaphosphorine infusion is completed. Total IV hydration includes the chemotherapy infusion bag, mesna bag and hydration bag.
3. Use MESNA infusion: MESNA dose equal to 20% of oxazaphosphorine dose y-sited to oxazaphosphorine over time of infusion. Then MESNA dose equal to 80% of

oxazaphosphorine dose to run over 8 hours post oxazaphosphorine; this MESNA dose may be y-sited to additional hydration if ordered in (b)

4. For subsequent cycles, start at this level of the SCMESNA protocol, unless microscopic hematuria persists at the end of (c).
5. If MICROSCOPIC HEMATURIA is still present at the end of MESNA INFUSION in (c) on the last chemotherapy treatment day, see PERSISTENT GROSS HEMATURIA and start at section B. For subsequent cycles, start at same level (B) i.e. FIRST EPISODE OF PERSISTENT GROSS HEMATURIA

GROSS HEMATURIA

All patients should be evaluated by urine culture and consideration given to cystoscopy. If a cause other than hemorrhagic cystitis is discovered, then treatment need not be altered.

A. SINGLE EPISODE OF GROSS HEMATURIA lasting less than 24 hours and reducing to microscopic hematuria during or after the cycle:

1. Do not modify the total dose of oxazaphosphorine.
2. Increase total IV hydration to 4000 mL/m² over 24 hours: starting after oxazaphosphorine infusion is completed. Total IV hydration includes the chemotherapy infusion bag, mesna bag and hydration bag.
3. Use MESNA infusion: MESNA dose equal to 20% of oxazaphosphorine dose y-sited to oxazaphosphorine over time of infusion. Then MESNA dose equal to 10% of oxazaphosphorine dose every hour to complete 24 hours of treatment day. (e.g., 30 to 60 minutes for etoposide or DOXOrubicin plus 2 hours of oxazaphosphorine infusion followed by 21 hours of MESNA infusion); this MESNA dose may be y-sited to additional hydration if ordered in (b).
4. For subsequent cycles, start at this level (A) i.e. SINGLE EPISODE OF GROSS HEMATURIA.

B. FIRST EPISODE OF PERSISTENT GROSS HEMATURIA that persists more than 24 hours during or after a cycle of chemotherapy

1. Stop oxazaphosphorine if during cycle and increase hydration and MESNA as per (c). Clinician to decide whether to continue the rest of the chemotherapy.
2. Do not re-start oxazaphosphorine; wait until next cycle is due.
3. Hydration and MESNA:
 - Increase total IV hydration to 4000 mL/m² over 24 hours: starting after oxazaphosphorine infusion is completed. Total IV hydration includes the chemotherapy infusion bag, mesna bag and hydration bag.
 - Use MESNA infusion: MESNA dose equal to 20% of oxazaphosphorine dose (y-sited to oxazaphosphorine – if ordered – over time of infusion)
 - Then MESNA dose equal to 10% of oxazaphosphorine dose every hour to complete 24 hours of treatment day. (eg., 30 to 60 minutes for etoposide or DOXOrubicin plus 2 hours of oxazaphosphorine infusion followed by 21 hours of MESNA infusion); this MESNA dose may be y-sited to additional hydration if ordered
4. Start next cycle only when persistent gross hematuria has abated to at most microscopic.

5. For subsequent cycles, start at this level (B) i.e. FIRST EPISODE OF PERSISTENT GROSS HEMATURIA

C. SECOND EPISODE OF PERSISTENT GROSS HEMATURIA OR PERSISTENT MICROSCOPIC HEMATURIA DESPITE MESNA INFUSION

1. Stop oxazaphosphorine if during cycle and increase hydration and MESNA as per (c). Clinician to decide whether to continue the rest of the chemotherapy.
2. Do not re-start oxazaphosphorine; wait until next cycle is due.
3. Hydration and MESNA:
 - Increase total IV hydration to 4000 mL/m² over 24 hours: starting after oxazaphosphorine infusion is completed. Total IV hydration includes the chemotherapy infusion bag, mesna bag and hydration bag.
 - Use DOUBLE DOSE MESNA infusion: MESNA dose equal to 40% of oxazaphosphorine dose (y-sited to oxazaphosphorine - if ordered - over time of infusion).
 - Then MESNA dose equal to 20% of oxazaphosphorine dose every hour to complete 24 hours of treatment day. This MESNA dose may be y-sited to additional hydration if ordered.
 - After last day of oxazaphosphorine infusion, continue MESNA infusion at same rate for another 48 hours.
4. Start next cycle only when persistent gross hematuria has abated to at most microscopic.
5. For subsequent cycles, start at this level (C) i.e. SECOND EPISODE OF PERSISTENT GROSS HEMATURIA.

PERSISTENT HEMATURIA IN FACE OF DOUBLE DOSE PROLONGED MESNA INFUSION
is cause to discontinue oxazaphosphorine treatment.

Call Dr. Christine Simmons at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References

1. Children's Oncology Group AEWS0031 trial of chemotherapy intensification through interval compression in Ewing sarcoma and related tumors - a phase III Intergroup Study (pg 29-30).