Wayne State University
DMC The Detroit Medical Center

BARBARA ANN KARMANOS CANCER INSTITUTE

Bone Marrow Transplantation (10WN) Pearls

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1. AMINOGLYCOSIDES AND VANCOMYCIN:

"Ground" rules:

- All BMT vancomycin/aminoglycosides orders are all considered an *automatic* consult
- Try to consolidate timing of levels to reduce the frequency of central venous line manipulations in an immunosuppressed patient.
- IVDT draws blood levels for adult 10WN patients. Order levels as "IVDT to draw".
- IVDT does not draw blood from pediatric patients. Order Vancomycin levels for RN to draw.

❖ Vancomycin (in febrile neutropenic patients):

- In order to reduce the frequency of central venous line manipulations,
  Vancomycin 1-1.5g IVPB Q12H (instead of q8h dosing) is recommended.

- **Pediatric patients:**

  10-15** mg/kg IVPB q6h

  ********Initial dose for CNS infection; otherwise, use 40 mg/kg/d*

  For children < 10-year-old: peak (25-40 mg/dl) and trough (5-15 mg/dl) levels are desirable. This would reduce guesswork when initial dosing yields a non-detectable trough secondary to brisk vancomycin clearance

- Acceptable trough=5-15 mg/dl

- Pre-dose level (trough) are drawn before the 4th dose (if a prolong treatment course is entertained); however, it may deferred or delayed for the following reasons:
  1. To avoid weekend follow-up
  2. If patient discharge is planned within 48-72 hours

❖ Aminoglycosides

- Institutional guidelines are in order.

- **Pediatric patients:**

  Initial dose: ***2-2.5 mg/kg IVPB q8h***

  Desired pediatric levels are identical to adult levels (for the same infection site), obtained when the conventional aminoglycoside dosing is used.

2. ANTIBIOTICS/ANTIVIRALS/ANTI-FUNGALS

❖ **Cefepime**

Febrile neutropenia (adult dose): ***2 g IVPB q8h***

Pediatric dose: ***50 mg/kg q8h (max. dose 2g IVPB q8h)***

❖ **GI decontamination:**

Norfloxacin 400 mg po q12h
(pediatrics may use Cirpofloxaxin 20-30 mg/kg/d solution)
Fluconazole 100 mg po qd

❖ **Itraconazole**

Pediatric dose for fungal prophylaxis: ***2.5 mg/kg q12h(oral solution)***
(note: IV pediatric dose for prophylaxis has not been studied)

❖ **IVIG:**

- **Hypogammaglobulinemia:**

400-500 mg/kg IV qweek (if IgG serum levels < 400 mg/dl)
use IBW (or AdjBW if need be)
Round to the nearest 10-g vial

- Palivizumab (Synagis®):

Although it is FDA-approved for **IM** administration, it can also be given **IV as:**

15 mg/kg IV x 1 (may repeat in 7-10 days) *for RSV infection*

Preparation:

1) Reconstitute 100 mg vial with 5 ml of sterile water for injection to give a final concentration of 20 mg/ml.
2) Withdraw the reconstituted solution into a syringe using a 0.22 microns filter
3) Administer the product @ 1-2 ml/min (20-40 mg/min) through an **in-line 0.22 micron filter**. For larger patients, infuse over 30 minutes.
4) Flush IV line with a small volume of D5W (NS not compatible)

- RSV-IVIG (Respigam®)

1500 mg/kg IV x 1 (may repeat in 7 days) *for RSV infection*

Time After Start of Infusion	**Rate of Infusion (mL/kg of Body Mass per Hour)**
0 - 15 minutes	1.5 mL/kg/hr (75 mg Ig/kg/hr)
15 minutes to end of infusion	3.6 mL/kg/hr (180 mg Ig/kg/hr)

Note: fluid overload with adult doses (vial concentration is only 50 mg/ml)

❖ **Metronidazole:**

Avoid in patients receiving carmustine (BCNU) infusion. Do not administer 24 hours before or within 48 hours from the initiation of infusion.

"Carmustine infusion contains Ethanol and, when combined with metronidazole, it may precipitate an "Antabuse" effect."

❖ **Nebulized liposomal amphotericin (Abelcet®)**

- Draw up ABLCET® 50 mg (10 ml) using a *filter* needle. Then, send the complete preparation in amber-colored syringes (or regular syringes protected from light)

- The preparation will be administered via a nebulizer (Hudson RCI Up-Draft, Model # 1724) and aerosolized with compressed air at a flow rate of 7 to 8 Litres per minute and **inhaled over at least 10 to 15 minutes** (until finished). At all times, protect the preparation from light.

- **Schedule:** 50 mg (10 ml) once every day x 4 days, then once per week x 7 weeks (Lung transplant data). Use 50 mg q12h if the patient is intubated.

- **Stability:** no data; therefore: SHAKE GENTLY BEFORE USE; ADMINISTER AS SOON AS POSSIBLE; PROTECT FROM LIGHT.

❖ **Acyclovir**

	Intravenous	Oral
Prophylactic dose	**Adult:** 5 mg/kg q12h	**Adult:** 200 mg q8h 800 mg q12h (for VZV prophylaxis)
	Pediatric: 250 mg/m^2 q8h	**Pediatric:** 10 mg/kg q6h
Treatment dose	**Adult:** 5 mg/kg q8h *(HSV except encephalitis)* 10 mg/kg q8h *(HSV encephalitis and VZV)*	**Adult:** 400 mg q8h *(HSV except encephalitis)* Valacyclovir 1 g q8h *(HSV encephalitis and VZV)*
	Pediatric: 250 mg/m^2 q8h *(HSV except encephalitis)* 500 mg/m^2 q8h *(HSV encephalitis and VZV)*	**Pediatric:** 10 mg/kg q6h **HSV encephalitis and VZV:** 20 mg/kg 4 times daily (**max:** 800 mg q6h)

❖ **Cidofovir (Topical)**

Cidofovir **1%** gel **(1 application bid)** can be prepared for resistant-HSV mucocutaneous lesions at the following pharmacies:

Heyden Pharmacy/Detroit (Phone: 313-533-8200)
Pharmalogics/Southfield (Phone: 248-552-0070)
Riverside Pharmacy/Trenton (Phone: 734-676-3784)

❖ **Ribavirin**

2 g inhalation q8h *for RSV infection*
(in pediatric and adult patients)

❖ **Valganciclovir**

900 mg **oral** valganciclovir = 5 mg/kg **IV**

Karmanos BMT CMV prophylaxis protocol:
Valganciclovir 900 mg po twice a week
Give with meals, preferred in A.M

3. ANTICOAGULATION

- The Detroit Medical Center nomogram is in order when considering unfractionated heparin

❖ ***Enoxaparin 40-mg SC*** once daily is used in the following scenarios:

- The substitution for full anticoagulation in patients receiving DVT treatment with platelets <50K. The threshold for change from full-dose anticoagulation to 40 mg SC qd should be at a platelet count of ~80-100K
- Irrespective of the indication, ***discontinue*** when platelets <20K.

(*Annals of Pharmacotherapy* 2002; 36: 1478-79; *Pharmacotherapy* 2003; 23 (10): 1341; abstr. #88)

*** Giving Low-dose Low-Molecular-Heparin therapy should only be undertaken when the risk of thrombotic event is deemed higher than the risk of bleeding***

❖ **Anti-thrombin III (AT-III)**

$$\textit{AT-III bolus} = \frac{(120^{*}\text{-patient's level})}{1.4} \times \textit{actual body weight (in Kg)}$$

* Often, higher targets AT-III level are chosen, usually in the range of 140-180%.
AT-III is used for the treatment of VOD. **Round to the nearest vial size**.

❖ **Factor VII:**

90 mcg/kg q3h x 3-4 doses (x 2-3 days); may stop or maintain at q6h as dictated by the clinical scenario

❖ **Bleeding**
GI bleed

Octreotide: 50 mcg IVPB bolus x 1, then start infusion 25-50 mcg/hour

Note: 500 mcg SC/IV q8h x 7 days for GVHD-induced diarrhea
100 ml in D5W/NS over 15-20 minutes
Onset: 6 days (median, range 1-12)

Adverse event: if given >7 days: ileus, hyperglycemia, and risk of cholecystitis

Pantoprazole:
Pediatric doses:
IV: 0.8 mg-1.6 mg/kg/d
PO: 0.5-1 mg/kg/d
(Pantoprazole solution can be compounded (Am J Health-Syst Pharm 2003; 60: 1324-9; however, owing to better palatability, lansoprazole solu-tab is still preferred.)

Menstrual bleed

- **Conjugated estrogens** 25 mg IVPB q6-12 hours until resolution of bleeding episode
- **Medroxyprogesterone (Provera®)** 10-20 mg orally to ***prevent*** menstrual bleeding (maintain until platelets > 50K)

4. CENTRAL VENOUS CATHETERS

- Acidic precipitate: 0.1 Hydrochloric acid
(e.g., TPN, calcium phosphate)

Preparation: inject 3 ml of 0.1 N HCL (up to 1 ml in infants between 1 and 3 Kg)

- Alkaline precipitate: Sodium bicarbonate 1 mEq/mL
(e.g., phenytoin, tobramycin)

Preparation: instill 5-ml (~5 mEq) of 8.4% syringes at 30-minute interval x **2**

- Lipid or protein deposition: 70% Ethanol or 0.1N sodium hydroxide

Preparation: inject 3 ml of 70% ethanol (maximum 0.55ml/kg)

5. DIURETICS

❖ **Furosemide IV push**
Avoid in Cispatin-containing protocols as it may increase the risk of ototoxicity

❖ **Amiloride**
Used to control Amphotericin B-induced hypokalemia (lipid formulations or conventional)

Dose: **5 mg po qd-q12h;** may escalate **to 10 mg q12h** (higher incidence of hyperkalemia with the latter regimen)

➢ ***Non-formulary*** at the Detroit Medical Center

➢ ***Avoid*** stopping amiloride when amphotericin B is completed since hypokalemia may persist for few weeks following the discontinuation of amphotericin B

6. IMMUNOSUPPRESSANTS

❖ **Sirolimus:**
Treatment of GVHD: ***4 mg/m^2/d x 14 days***
(*Transplantation* 2001; 12: 1924)
Prevention of GVHD: ***12 mg po on D-3, then 4 mg po qd thereafter***

(*Blood 2003*; 102: 1601-1605)

Target "trough" levels: **3-12 ng/ml (whole blood)**

Drug-interactions: cyclopsorin needs to be given 4 hours before sirolimus. Tacrolimus can be co-administered with sirolimus

AEs in BMT: hyperlipidemia, thrombocytopenia, leucopenia, and impaired wound healing

"Doses in BMT are different from solid organ transplantation doses"

- **Cyclosporin**

  Target "trough" levels: 200-400 ng/ml
  (Non-myeloablative and aplastic anemia protocols may call for 400-600 ng/ml)

- **Tacrolimus:**

  Target "trough" levels: 5-15 ng/ml (may target up to 20 ng/ml)

- **Methotrexate:**

  Target "trough" levels: undectecble (<0.02)

- **TNF-blockers:**

  Infliximab (Remicade®): *10 mg/kg/week IVPB*

  "Doses in BMT are different from the auto-immune disease doses"

  Etanercept (Enbrel®): *25 mg SC 2-3 times/week*

- **Dexamethasone:**

  Used as a topical relief for oral GVHD. It is prescribed as:

  5 ml (dexamethasone solution 0.5mg/5 ml) swish and spit qid, followed by nystatin 5 ml swish and swallow qid. Write for alcohol-free solution manufactured by Roxane®

- **IL-2 soluble receptor antagonist:**

  Daclizumab: 1mg/kg IVPB on days 1,4,8,15,22

  Basiliximab: 20 mg IVPB D1 and D2, then 20 mg/weekly thereafter ***(prefer < 4 weeks)***

- **Denileukin diftitox (Ontak®)**

  9 mcg/kg IVPB on days 1, 3, 5,15,17,19.

  Monitor albumin and possible infusion-related reactions

- **Budesonide oral**

  Dose: 3 mg po tid

  - Local treatment of GI GVHD
  - Non-formulary at the DMC

Bone Marrow Transplant. 1999; 24(11):1185-9***: median dose***= 193 mg (54-725 mg)

❖ **Anti-Thymocyte Globulin (horse ATG)**

Test dose:
Use an intradermal injection of 0.1 ml of 1:1000 dilution (of ATG) in normal saline for a total dose of 5 mcg horse IgG. A contra-lateral Na Cl control is recommended. Observe every 15-20 minutes over first hour after injection. A local reaction of 10 mm or greater with a wheal or erythema, or both, with or without pseudopod formation and itching or marked local swelling should be considered a positive test. **Dispense in TB syringe**.

7. LUMBAR PUNCTURE HEADACHE

Pharmacological treatment:

Caffeine sodium benzoate 500 mg IVPB in 1L of D5W over 1 hour x 1
May repeat X 1 **(4 HOURS** after the first dose**)**

8. TPN

On 10 WN, the lipids are universally given separate from the TPN (and not 3:1). This practice is in keeping with CHM recommendations in regards to ***pediatric*** TPN. Lipids are usually given over 20 hours.

9. N-Acetyl-Cysteine

- The treatment of VOD:

1) 150 mg/kg in 200 ml of D5W IV bolus given over 15 minutes, then:
   50 mg/kg in 500 ml of D5W IV given over 4 hours

2) The following day start:

   150mg/kg/day in 1000 ml of D5W continuous infusion

******Drug is available as 800 mg per 4 ml******

- Prevention of Radiocontrast-Induced Nephropathy (RCIN)

developed by T. Mehta, Pharm.D.

Patient-related risk factors for RCIN:
- Pre-existing renal insufficiency (SCr >1.2 mg/dL or CrCl<50 mL/min)
- Anticipated contrast volume > 140 mL
- Dehydration
- Heart failure: NYHA Class III/IV
- Age>65 years
- Concurrent administration of nephrotoxic drugs (ex. NSAIDs, metformin, ACE inhibitors, diuretics, aminoglycoside, vancomycin)
- Sickle cell disease
- Multiple myeloma
- Previous contrast exposure within 72 hours

Dose: 600 mg po BID, starting the day before procedure and continued for total of 4 doses.

- At least 2 doses should be given on day of procedure
- Inhalation formulation diluted in carbonated drink (i.e. gingerale, juice, etc.) to mask taste
- AEs: Nausea, vomiting

+

Hydration: .45% or 0.9% Saline @ 1 ml/kg/hr starting 6-12 hours prior to contrast administration, maintain during and continue for at least 6-12 hours after procedure if no contraindication to volume administration.

Consider 0.45% or 0.9% Saline @ 0.5 ml/kg/hr in patients with volume restriction.

10. MESNA

- Mesna IV **10 mg/kg** bolus before Cyclophosphamide administration, followed by **continuous infusion** at **60%** of the total daily Cyclophosphamide dose, to continue for **24 hours** post last Cyclophosphamide dose.
- Maintain hyper-hydration per protocol (literature supports at least ~3 $L/m^2/d$).
- At the clinician's discretion, consider increasing ↑ mesna dose (e.g., by 40%) in the face of repeated diuretic administration.

11. URSODIOL

for the prevention of hepatic complications associated with ***Allogeneic*** Hematopoietic Stem Cell Transplantation

❖ Adult dose

12 mg/kg/day po into 2 divided doses

Round daily dose ***upward*** to the closest available formulation (available as a 300-mg capsule). Initiated on the day preceding the first dose of conditioning and continued until day 90 after transplantation (Rutu et *al*. *Blood* 2002; 100; 1977-1983)

❖ Pediatric dose

12 mg/kg/day *solution OR capsule* into 2-3 divided doses

Round daily dose ***upward*** to the closest available formulation (available as a 300-mg capsule and 20 mg/ml suspension).Initiated on the day preceding the first dose of conditioning and continued until day 90 after transplantation (Rutu et *al*. *Blood* 2002; 100; 1977-1983)

COMPOUNDING:
1. Empty contents of capsules into a mortar and reduce to a fine powder. Add a small amount of sterile water to saturate powder and mix well.
2. Add 20ml of Ora-Sweet/Ora-Plus 1:1 and mix to a uniform paste.
3. Add vehicle in geometric portions to almost desired volume while mixing.
4. Transfer to a graduate and qs to volume with vehicle. Transfer to an amber bottle and label.

Stability: 90 days

Label: Shake Well & Refrigerate

11. LINKS

- Blood Pressure management in adult and pediatric BMT patients

  http://intraweb/pharmweb/harper/clincommunications/Heme-Onc_and_BMT/default.htm

- Drug removal in plasmapheresis

  http://intraweb/pharmweb/harper/clincommunications/Heme-Onc_and_BMT/default.htm

- Dialysis of Drugs

  http://nephrologypharmacy.com/downloads/us_dod_2004.pdf