

CIBMTR Infection Data and the New Infection Inserts....

Marcie Tomblyn, MD, MS
Scientific Director, CIBMTR
Infection and Immune
Reconstitution Working Committee



Overview

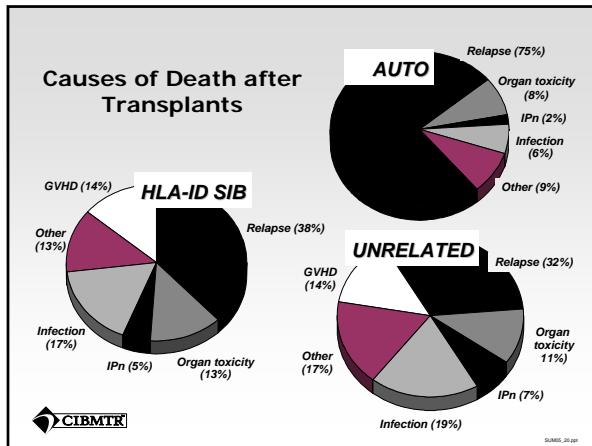
- ◆ Indication for expanded data collection
- ◆ Definitions
- ◆ Infection inserts
 - Fungal Infection
 - Viral Hepatitis B and/or C
 - Human Immunodeficiency Virus (HIV)



Indications for more work....

- ◆ Infection remains significant cause of morbidity and mortality after transplant
- ◆ Patients with chronic infections are living longer and may be transplanted for concomitant illness
- ◆ Newer drugs result in improved outcomes with certain infections





Infection Prophylaxis

- ◆ Usually include:
 - Antibiotics
 - Quinolones
 - Bactrim (TMP/SMX)
 - Antifungals
 - Antivirals
- ◆ Generally started about the time of conditioning to PREVENT infections

CIBMTR

Infection Prophylaxis

357. Did the recipient receive any of the following agents for infection prophylaxis after the start of the preparative regimen? (Report prophylaxis immunoglobulins at questions 63-64.) [L]

1 yes
2 no
3 unknown

Specify

358. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Systemic antibacterial antibiotics	
359. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Nonabsorbable oral antibiotics	
360. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Amphotericin (Fungizone) (non-lipid formulation)	
361. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Amphotericin (e.g. Abelcet, AmBisome, Amphotec) (lipid formulation)	
362. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Caspofungin	
363. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Fluconazole	
364. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Itraconazole	
365. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Micalungin	
366. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Posaconazole	
367. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Ravuconazole	
368. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Voriconazole	
369. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Other systemic antifungal agent	→ 370. Specify agent: _____
371. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Acyclovir	
372. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Foscarnet	
373. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Ganciclovir (DHPG)	
374. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Valganciclovir (Valcyte)	
375. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Valacyclovir	
376. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Other antiviral agent	→ 377. Specify agent: _____
378. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Atovaquone (Mepron)	
379. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Dapsone	
380. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Pentamidine inhaled	
381. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Pentamidine IV	
382. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Trimethoprim/sulfamethoxazole (Bactrim/Septtra)	
383. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Other pneumocystis prophylaxis	→ 384. Specify agent: _____
385. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	Other agent	→ 386. Specify agent: _____

“Clinically Significant Infection”

- ◆ Identified infections that result in a change of therapy with systemic antimicrobial agents
 - ◆ Suspected infections with supporting clinical or radiographic findings (i.e. pulmonary infiltrate on chest CT)
- **NOTE:** Fever without documented infection (i.e. culture negative neutropenic fever) is NOT an infection



So What’s NOT an Infection?

- ◆ Culture-negative neutropenic fever without clear source
- ◆ Upper respiratory infections that are presumed viral but no virus identified
- ◆ Stool Candida



Infections

388. Did the recipient develop a clinically significant infection after the start of the preparative regimen? 1 yes
 2 no

Report each infection organism, site and date of diagnosis. (see page 16 for organism and site codes)

Organism †§	Site *	Date of Diagnosis		
		Month	Day	Year
389. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 390. If other, specify: 391. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 392. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				
393. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 394. If other, specify: 395. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 396. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				
397. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 398. If other, specify: 399. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 400. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				
401. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 402. If other, specify: 403. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 404. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				
405. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 406. If other, specify: 407. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 408. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				
409. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 410. If other, specify: 411. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 412. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				
413. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 414. If other, specify: 415. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> 416. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				

† The codes for “other organism, specify” (codes 198, 209, 219, 259, 329 and 409) should rarely be needed; check with your microbiology lab or HSCT physician before using them.
 § For fungal infections marked with a section symbol (codes 210, 211, 212, 213, 219, 230, 240, 241, 242 and 503), also complete a Fungal Infection insert (SUP-FNG).
 * Do not report fever in the absence of infection. Report the most specific site of infection.

Fungal Insert

- ◆ To obtain more specific information about mold infections

- ◆ Requests detailed information of
 - Diagnosis
 - Prophylaxis
 - Therapy



Mold Infections of Interest

- ◆ Aspergillus
- ◆ Fusarium
- ◆ Mucormycosis
- ◆ Rhizopus
- ◆ Zygomycetes
- ◆ Molds not otherwise speciated
 - "branching hyphae"



Key Data Elements

- ◆ Date of infection
- ◆ Site of infection
- ◆ Diagnostic test
- ◆ Treatment
 - Fungal drugs at the time of diagnosis
 - Therapy up to 6 months after diagnosis



Mold infection

Information for this report should come from an actual examination by the Transplant Center physician, or the physician who is following the recipient post-HSCT, or abstraction of the recipient's medical records. Information reported here should reflect the date of last contact as reported in the data collection form, or immediately prior to death.

1. Did the recipient have a history of clinically significant fungal infections either within 6 months prior to the start of the preparative regimen or post-HSCT? (Report only Aspergillus, Fusarium, Mucormycosis, Rhizopus, Zygomycetes, or suspected fungal infections.)

1 yes
2 no
3 unknown

Specify the fungal infection(s):

2. Aspergillus

1 yes
2 no

Specify the following for the first evidence of Aspergillus infection:
(If not Aspergillus, specify the organism and site of infection.)

3. Specify the Aspergillus species. (see codes on page 6)

4. If code 219, specify:

5. Specify the site of infection: (see codes on page 6)

6. Specify date of onset:
Month Day Year

7. Specify the diagnostic test used to confirm infection: (see codes on page 6)



Mold Diagnostic Test Options

- ◆ Biopsy
- ◆ Culture
- ◆ Cytology
- ◆ KOH/Calcofluor stain
- ◆ Aspergillus galactomannan
- ◆ Unknown



Therapy Example

For the therapy table below, see "Reason Started" codes on page 6. Therapy paused for < 1 week should not be considered as "Therapy Stopped." If > 3 courses of therapy were given, copy this section and complete for each additional course.

Therapy Given?	Date Started	Daily Dose	Reason Started	Therapy Stopped?	Date Stopped
48. First course 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	49. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	50. <input type="text"/> <input type="text"/> mg	51. <input type="text"/> <input type="text"/> Code	52. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	53. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
54. Second course 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	55. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	56. <input type="text"/> <input type="text"/> mg	57. <input type="text"/> <input type="text"/> Code	58. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	59. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
60. Third course 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	61. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	62. <input type="text"/> <input type="text"/> mg	63. <input type="text"/> <input type="text"/> Code	64. 1 <input type="checkbox"/> yes 2 <input type="checkbox"/> no	65. <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

*If treatment held for less than 7 consecutive days and then restarted, do not consider as "Therapy Stopped"



Antifungal Drugs

- ◆ Fluconazole
- ◆ Itraconazole
- ◆ IV Amphotericin
- ◆ IV Amphotericin Lipid Formulation
- ◆ Caspofungin
- ◆ Micafungin
- ◆ Voriconazole
- ◆ Posaconazole
- ◆ Other, specify



Viral Hepatitis Insert

- ◆ Viral Hepatitis may be a chronic infection of the liver
 - Viral particles can be found in the blood stream
 - May lead to cirrhosis or hepatocellular carcinoma
 - May be lymphomagenic
- ◆ Goal: Collect detailed information on antiviral therapy and viral loads in HCT patients



Hepatitis B

- ◆ Diagnostic tests for prior infection
 - Hepatitis B core Antibody (HBcAb)
 - Hepatitis B surface Antigen (HBsAg)
 - Hepatitis B envelope Antigen (HBeAg)
- ◆ Diagnostic test for prior infection OR prior immunization
 - Hepatitis B surface Antibody (HBsAb)



Examples

- ◆ Patient AB:
 - HBcAb positive
 - HBsAb positive
 - HBsAg negative
- ◆ Patient YZ:
 - HbcAb negative
 - HBsAb positive
 - HBsAb negative

Which patient had a prior infection with Hepatitis B?



Hepatitis C

- ◆ Diagnostic test for infection
 - Hepatitis C Antibody (HCAb)
- ◆ No immunization available
 - If HCAb is positive, patient has an infection with viral Hepatitis C



Key Data Elements

- ◆ Diagnostic test
- ◆ Viral Load levels
- ◆ Request for pathology of liver biopsies
- ◆ Treatment
 - Lamivudine
 - Interferon
 - Other, specify



PreHCT vs PostHCT

- ◆ PreHCT forms
 - Request Hepatitis testing performed
 - Collect Recipient AND Donor information

- ◆ PostHCT forms
 - Recipient only



Example: Hepatitis B

PreHCT

Provide all documented hepatitis B viral load levels obtained within 3 months prior to the preparative regimen. If no values were obtained in the 3 months prior to the preparative regimen, provide and date the most recent values obtained prior to the preparative regimen.

5. Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	6. Hepatitis B viral load level: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Specify units: <input type="checkbox"/> log IU <input type="checkbox"/> IU/mL <input type="checkbox"/> copies/mL <input type="checkbox"/> pg/mL
7. Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	8. Hepatitis B viral load level: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="checkbox"/> log IU <input type="checkbox"/> IU/mL <input type="checkbox"/> copies/mL <input type="checkbox"/> pg/mL
9. Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	10. Hepatitis B viral load level: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="checkbox"/> log IU <input type="checkbox"/> IU/mL <input type="checkbox"/> copies/mL <input type="checkbox"/> pg/mL

PostHCT instructions:

Viral loads obtained since the last report



Example: Hepatitis C PreHCT

PreHCT

Provide all documented hepatitis C viral load levels obtained within 3 months prior to the preparative regimen. If no values were obtained in the 3 months prior to the preparative regimen, provide and date the most recent values obtained prior to the preparative regimen.

11. Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	12. Hepatitis C viral load: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Specify units: <input type="checkbox"/> log IU <input type="checkbox"/> IU/mL
13. Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	14. Hepatitis C viral load: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="checkbox"/> log IU <input type="checkbox"/> IU/mL
15. Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	16. Hepatitis C viral load: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="checkbox"/> log IU <input type="checkbox"/> IU/mL

PostHCT instructions:

Viral loads obtained since the last report



HIV Insert

- ◆ For recipients that are HIV-positive
- ◆ Requests information on
 - Dates of diagnosis
 - Relation of HIV diagnosis to disease for which HCT performed
 - Information on prior Opportunistic Infections
 - Viral loads
 - CD4 counts
 - Therapy



Relation of HIV to Diagnosis for HCT

- ◆ HIV was known prior to the diagnosis for HCT
- ◆ HIV and diagnosis for transplant occurred at the same time
- ◆ Diagnosis for HCT found then subsequently found to be HIV+
- ◆ HIV found incidentally during pre-HCT evaluation and testing



What is HIV-Associated?

- ◆ AIDS defining malignancies in HIV+ patients
 - Kaposi's Sarcoma
 - Non-Hodgkin Lymphoma
 - Cervical cancer
 - Anal cancer
- ◆ HIV-associated
 - Hodgkin Lymphoma
 - Lung cancer
 - Pediatric leiomyosarcoma
 - Lung cancer



Opportunistic Infections

- ◆ CMV
- ◆ Invasive fungal infections
- ◆ *Pneumocystis jiroveci*
 - formerly *Pneumocystis carinii* (PCP) pneumonia



Highly Active Anti-Retroviral Therapy (HAART)

- ◆ Became standard about 1996
- ◆ Multi-drug therapy
 - 16 different anti-retroviral medications currently listed on the insert



HIV Viral Loads

PreHCT

Provide all documented HIV viral load levels obtained within 3 months prior to the preparative regimen. If no values were obtained in the 3 months prior to the preparative regimen, provide and date the most recent values obtained prior to the preparative regimen.

134. Date: <input type="text"/> / <input type="text"/> / <input type="text"/>	135. HIV viral load level: <input type="text"/> . <input type="text"/> . <input type="text"/> . <input type="text"/>	Specify units: 1 <input type="checkbox"/> copies/mL 2 <input type="checkbox"/> log ₁₀ /mL
136. Date: <input type="text"/> / <input type="text"/> / <input type="text"/>	137. HIV viral load level: <input type="text"/> . <input type="text"/> . <input type="text"/> . <input type="text"/>	1 <input type="checkbox"/> copies/mL 2 <input type="checkbox"/> log ₁₀ /mL
138. Date: <input type="text"/> / <input type="text"/> / <input type="text"/>	139. HIV viral load level: <input type="text"/> . <input type="text"/> . <input type="text"/> . <input type="text"/>	1 <input type="checkbox"/> copies/mL 2 <input type="checkbox"/> log ₁₀ /mL
140. Date: <input type="text"/> / <input type="text"/> / <input type="text"/>	141. HIV viral load level: <input type="text"/> . <input type="text"/> . <input type="text"/> . <input type="text"/>	1 <input type="checkbox"/> copies/mL 2 <input type="checkbox"/> log ₁₀ /mL
142. Date: <input type="text"/> / <input type="text"/> / <input type="text"/>	143. HIV viral load level: <input type="text"/> . <input type="text"/> . <input type="text"/> . <input type="text"/>	1 <input type="checkbox"/> copies/mL 2 <input type="checkbox"/> log ₁₀ /mL

PostHCT instructions:

Viral loads obtained since the last report



CD4⁺ Lymphocyte Counts

PreHCT

Provide all documented CD4 counts obtained within 3 months prior to the preparative regimen. If no values were obtained in the 3 months prior to the preparative regimen, provide and date the most recent values obtained prior to the preparative regimen.

	Month	Day	Year												
124. Date:	<input type="text"/>	<input type="text"/>	<input type="text"/>	2	0										
125. CD4 counts:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
126. Date:	<input type="text"/>	<input type="text"/>	<input type="text"/>	2	0										
127. CD4 counts:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
128. Date:	<input type="text"/>	<input type="text"/>	<input type="text"/>	2	0										
129. CD4 counts:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
130. Date:	<input type="text"/>	<input type="text"/>	<input type="text"/>	2	0										
131. CD4 counts:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
132. Date:	<input type="text"/>	<input type="text"/>	<input type="text"/>	2	0										
133. CD4 counts:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

PostHCT instructions:

CD4⁺ counts obtained since the last report