To: Transplant Center Medical Directors and Data Managers

From: Douglas Rizzo, MD, MS

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RE: Preparative Regimen Data Reporting - UPDATE

Some drugs used as part of the preparative regimen are administered with guidance of serum pharmacokinetic testing to determine the recipient’s metabolism of the drug. This allows for “customization” of the drug dosing to the individual to optimize the desired effect and minimize the toxicity. Depending upon how the dose of the drug used to monitor drug levels is given, it can be reported in one of two different ways on the CIBMTR Pre-TED (2400) and Baseline (2000) forms.

Busulfan represents a common example of this situation. In some cases, the first dose of the drug is given in the usual fashion as part of the preparative regimen, serum drug levels are drawn after this first dose and sent to a reference lab, and the drug is continued at the starting dose with adjustment of later doses once the lab results are reported. In other situations, a “test dose” of the drug is given before the actual preparative regimen is started, and this dose is used for acquiring drug levels that are used to adjust the dose that will be used in the preparative regimen.

When a drug is used for the preparative regimen where pharmacokinetics will be tested, it is important to distinguish whether the testing will be done using the first dose of the preparative regimen or if the drug will be given with a “test dose” distinct from the beginning of the preparative regimen. The reporting of the dosing for the CIBMTR forms depends upon this distinction. This helps distinguish whether the dose is part of the therapeutic regimen, or not.

1. The first dose of therapeutic dosing is used for monitoring.
   - Example: Patient with MDS receives allogeneic HCT from an unrelated donor using Busulfan and Fludarabine preparative regimen. He is admitted to the hospital 7 days before his HCT, and receives a dose of Busulfan at 0.8 mg/kg IV at 6 AM. Serum samples are drawn every 30 minutes until the next dose of Busulfan at 0.8 mg/kg IV is given at 12 noon. His blood is sent to a reference lab, and he continues to receive Busulfan every 6 hours. On day -6, the lab calls with his drug levels, and it is determined that the current dose is correct. No adjustment is made, and he completes all 16
doses of Busulfan. Since the dose of Busulfan (0.8 mg/kg) that was used for drug testing was ALSO his first dose of the preparative regimen, it should be included in the amount of drug that was given for preparative regimen.

- If the first dose of the preparative regimen will be used to determine pharmacokinetics, the following should be reported:
  a. On the Pre-TED (2400) form, the total prescribed dose per protocol would include the dose used for monitoring.
  b. On the Baseline (2000) form, the start date of the chemotherapy agent should be reported as the date the first dose was administered. The actual dose received would include the dose used for monitoring.

2. The test dose is given ≥ 24 hours prior to the intended therapeutic dosing.

- **Example:** Patient with AML undergoes allogeneic HCT from sibling using Busulfan and Cyclophosphamide preparative regimen. The patient presents to clinic 9 days before the HCT, where a dose of Busulfan at 0.5 mg/kg is given intravenously. Blood samples are drawn for the next 6 hours, after which the patient leaves the clinic. His samples are sent to a lab, results are returned the next day and an adjusted dose of Busulfan is calculated. He returns to the hospital 6 days before HCT, and begins to receive Busulfan at the adjusted dose intravenously for 4 days, followed by Cyclophosphamide and proceeds to receive his cells. Since he received 0.5 mg/kg as a “test dose”, this would not be reported in his total preparative regimen dose.

- If a test dose is given, where the dose is distinct from the therapeutic dosing preparative regimen (often 1-2 or more days prior to the initiation of regular dosing), the following should be reported.
  a. On the Pre-TED (2400) form, the total prescribed dose per protocol would NOT include the test dose.
  b. On the Baseline (2000) form, the start date of the chemotherapy agent should be reported as the date the first therapeutic dose was administered. The actual dose received would NOT include the test dose.

Test doses must be reported consistently at your center. Since most centers follow a consistent approach to pharmacokinetic testing, it should be straightforward for the center to adopt a consistent approach to the reporting of “test doses.”