



Weight based dosing of drugs for overweight and obese patients undergoing blood and marrow transplantation

Background

Although pharmacokinetic assays have been developed for a number of chemotherapeutic agents used in cancer medicine, the dosing of the majority of drugs, including most of those used in conditioning regimens for allogeneic HCT, is done according to patient weight. With obesity emerging as an increasing public health problem, more overweight and frankly obese patients are being considered as allogeneic transplant candidates.

The chemotherapeutic agents used in conditioning regimens, particularly in myeloablative regimens, have narrow therapeutic windows and the risk of non-hemopoietic toxicity is high. The dosing of conditioning regimen agents in overweight patients has been highly controversial, since there is little evidence on which to base rational policies. However, a recently published position statement from the Practice Guidelines Committee of the American Society for Blood and Marrow Transplantation has reviewed available evidence and made recommendations for modifying drug doses in overweight BMT patients¹. In addition, a recent publication has made recommendations on dosing of antimicrobials in morbidly obese patients².

It is acknowledged that the evidence for recommendations re dosing of drugs in overweight and obese patients undergoing stem cell transplant in the cited papers is not of high quality. Therefore the recommendations outlined in this document should be regarded as suggestions based on the best available data and should not be considered as a definitive policy statement. It is hoped that this document may act as a starting point for consideration of drug dosing and may lead to a better harmonised approach to prescribing in overweight and obese patients undergoing stem cell transplant.

The Bone Marrow Transplant Society of Australia and New Zealand encourages all physicians prescribing for this group of patients to consider these recommendations and to make final decisions about drug dosing based on the available evidence and their own clinical experience.

Abbreviations

A variety of measures of weight and degrees of obesity are available and are in common usage. These include:

BMI: body mass index (mass (kg)/height (m)²)

TBW: total body weight

IBW: ideal body weight

ABW: adjusted body weight

- ABW 25, IBW + 0.25(TBW-IBW)
- ABW 40, IBW + 0.40(TBW-IBW)

A variety of web based tools are available to calculate BMI and IBW. Examples include

https://qxmd.com/calculate/calculator_30/bmi-and-bsa-du-bois

Definitions

WHO definitions based on BMI

- overweight: BMI 25 to 29.9
- obese: BMI 30 to 39.9
- severely obese: BMI >40.

Suggested dosing for drugs commonly used in stem cell transplant in overweight and obese patients

1. **Busulphan.** Dose on ABW25 for obese and non-obese adults receiving per kilogram dosing, with subsequent pharmacokinetic targeting.
2. **Carmustine.** Dose on body surface area based on TBW up to 120% IBW, then on ABW25.
3. **Cyclophosphamide.** For CY120, dosing can be either IBW or TBW up to 120% IBW, then ABW25.
4. **Cytarabine.** Dose on TBW.
5. **Etoposide.** Dose on TBW for surface area based dosing.
6. **Fludarabine.** Dose on TBW.



7. **Melphalan.** Dose on TBW.
8. **Thiotepa.** Dose on surface area based on TBW, unless >120% IBW, then ABW40.
9. **Alemtuzumab.** Flat dose according to protocol.
10. **Antithymocyte globulin.** Dose on mg/kg based on TBW.
11. **Aciclovir.** Dose on IBW.
12. **Ganciclovir.** Dose on IBW.
13. **Foscarnet.** Dose on IBW or ABW25.

References

1. Bubalo J et al. BBMT, 2014, 20: 600.
2. Polso A et al. J Clin Pharmacy and Therapeutics, 39:584.