

Supplement 1

Materials and Methods (full version)

Data collection

Data were obtained retrospectively from records kept by Anthony Nolan for the period 2005-11. 2591 HPC donations were made during this time by 2472 unrelated adult donors to 2493 recipients.

During this study period, 145 requests for subsequent donations were made, of which 25 (17.4%) were later cancelled by the transplant center. Of these 145 requests, 118 (81.4%) were from the same donor to the same patient (group A), 21 (14.5%) from one donor to a different patient (group B), and 6 (4.1%) from two donors to the same patient (group C).

For the purposes of assessing an association between donor and patient characteristics at initial donation and the need for a subsequent donation (whether from the same or a different donor), all patients where there was a request for a subsequent donation were reviewed (i.e. excluding those donors in group B where it was the first transplant for the patient). For the purposes of assessing harvest yields and adverse events related to a second donation, all donors who had donated more than once were reviewed (i.e. excluding those in group C where donors had donated only once).

13 (8.9%) of those making a subsequent donation during the study period made their initial donation before 2005. As statistical analysis relied on comparator data from those donors making only a single donation, this subgroup was excluded from all analyses, since comparator data from before 2005 was not obtained.

Donor factors considered in this analysis included degree of HLA match (10/10 allele matching being the ideal), CMV status, gender, age and route of

donation at first donation. Patient factors considered in the analysis included patient age, gender and disease type. The year of first donation was also included to account for changes in preference for HPC source in recent years. These characteristics are readily available to the donor registry. Other patient characteristics, including disease status at transplant and conditioning regimen intensity are generally not shared with the registry, and therefore were unavailable for this study.

Serious adverse reactions were defined according to standard criteria published by the Serious Events and Adverse Reactions (SEAR) committee of the World Marrow Donor Association (WMDA). A serious adverse reaction (SAR) is *'an unintended response, including a communicable disease, in the donor or in the recipient associated with the procurement or human application of tissues and cells that is fatal, life-threatening, disabling, incapacitating or which results in, or prolongs, hospitalization or morbidity.'* Each serious adverse reaction (in both first and subsequent HPC donors) was re-examined at the time of data collection to ensure this definition had been complied with historically. Rates of serious adverse reactions in those donors making two or more donations were compared to rates in those making just a single donation during the study period.

The study protocol was reviewed by the Institutional Review Board at Anthony Nolan, who deemed that ethical approval was not necessary.

Statistics

Donor variables that had more than two categories (degree of HLA match, and age) were summarized to dichotomous categorical variables in a fashion that reflects standard transplant practice.^{26, 27} These were: donor age ≤ 30 and > 30 and HLA match 0 or ≥ 1 mismatches. Patient age was similarly categorized using the median (46) as a cut-off, i.e. ≤ 46 and > 46 , and an analysis of pediatric (< 18 years old) vs adult was also performed.

Univariate analyses of donor and patient factors influencing subsequent HPC donation requests were performed using a chi-squared test for binomial variables and logistic regression for multinomial categorical variables (e.g. disease). Multivariate analysis was performed using binary logistic regression. Only those variables with at least a statistical trend towards association with subsequent donation request ($p \leq 0.1$) were entered into the multivariate analysis. Associations between variables that potentially predicted subsequent donation requests were examined to look for collinearity. A time-dependent cumulative hazard plot for subsequent HPC donation request was modeled using the Kaplan-Meier method, and Cox regression analysis was performed to compare the hazard of subsequent donation requests between PBSC and BM as route of initial donation. This latter analysis controlled for the potentially confounding effect of a change in graft selection practice (from BM to PBSC) over the study period. Rates of serious adverse events between first time and subsequent HPC donors were compared using a chi-squared test. Harvest yields between first and subsequent donations were compared using a paired t-test.

All statistical analyses were performed using PASW statistics v.18.0.