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Autologous haematopoietic stem cell transplantation in multiple myeloma patients from ethnic minority groups in an equal access healthcare system

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High-dose melphalan followed by autologous haematopoietic stem cell transplantation (ASCT) became part of the standard of care for most patients with multiple myeloma (MM) under the age of 65 years in the mid-to-late 1990s (Attal *et al*, 1996; Barlogie *et al*, 1997). While two smaller single-institution studies from the US reported better progression-free survival (PFS) but comparable overall survival (OS) in black compared with white MM patients following ASCT (Saraf *et al*, 2006; Verma *et al*, 2008), a recent large study by the Center for International Blood and Marrow Transplant Research (CI-BMTR) did not observe any significant differences in PFS, OS, relapse rate, or non-relapse mortality (Hari *et al*, 2010). No systematic study has compared the outcome of Asians with blacks or whites.

To address this gap in the literature, we evaluated the characteristics and outcomes of all MM patients who underwent a first ASCT at Hammersmith Hospital (HH), later Imperial College Healthcare NHS Trust (ICHNT), over a 16-year period. This patient population came from a large multiethnic community of almost two million people in an equal-access healthcare system.

We identified all patients with MM who underwent a first ASCT at HH/ICHNT between 1994, when the ASCT programme for MM was initiated, and 2009. Over the study period,

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Author contributions

HWA and AR designed the study. HWA, CG, JP, and RS collected and analysed data. EK, DMacD, DM, DMil, JFA, KR, JMG, and AR provided patient care, contributed to data analysis and revised the manuscript. OL contributed to data analysis and revised the manuscript. HWA and AR wrote the manuscript.

Conflict of interest

The authors declare no conflict of interest.

HH/ICHNT was the tertiary referral centre for haematopoietic stem cell transplantation for Northwest London. The 2001 UK Census recorded a Northwest London population of 1.73 million, consisting of 1.13 million whites (65%), 0.35 million Asians (20%), 0.15 million blacks (9%) and 0.1 million others (6%). Patients diagnosed with MM by primary and secondary healthcare providers who were considered eligible for ASCT were referred to HH/ICHNT upon completion of induction therapy. In accordance with the 2001 Census, we classified patient ethnicity as white (British, Irish, or other white ethnic background), black (Caribbean, African, or other black), or Asian (Indian, Pakistani, Bangladeshi, Middle Eastern, or other Southeast Asian). A reduced dose of melphalan was used at the transplant physicians' discretion in patients over the age of 65 years, those with severe renal impairment, or those with other co-morbidities. Tandem ASCT was performed in patients considered to have chemo-refractory disease. Responses were defined based on previously published criteria (Blade *et al.*, 1998). Groups were compared using a Mann–Whitney test for continuous data and a Chi-squared test for categorical data. Probabilities for OS and PFS were calculated according to the Kaplan–Meier method and differences were tested with the log-rank test, and all analyses were carried out using the Statistical Package for the Social Sciences (spss) software (version 12.0.1, IBM, New York, NY, USA). *P*-values < 0.05 were deemed statistically significant.

A total of 363 patients with a diagnosis of MM underwent a first ASCT at HH/ICHNT between 1994 and 2009. Of those, 270 (74.4%) were white, 56 (15.4%) were black, and 37 (10.2%) were Asian (Table I). There were no significant differences between the three ethnic groups in terms of gender, age, immunoglobulin subtype, bone marrow plasma cell content at diagnosis, serum beta-2-microglobulin levels at diagnosis, karyotypic abnormalities at diagnosis, time from diagnosis to ASCT, disease status at the time of ASCT, and number of CD34+ cells infused (Table I). Similar proportions of patients in the ethnic groups received a reduced dose of melphalan or a tandem ASCT (Table I). From the first 8-year bracket of the observation period (1994–2001) to the second (2002–2009), the number of whites, blacks, and Asians undergoing ASCT increased 1.5-, 2.3-, and 5.2-fold, respectively (Table I). Consequently, the proportion of patients from the three ethnic groups that underwent ASCT changed significantly from the first to the second half of the observation period (Table I, *P* = 0.006). At 3 months after ASCT, the proportion of patients failing to achieve at least a partial response (PR) was higher in blacks and Asians than in whites (*P* = 0.045, Table I). However, this did not translate into differences in PFS (Fig 1A) between whites (median 22.8 months, 95% confidence interval [CI] 20.4–25.2 months), blacks (median 19.1 months, 95% CI 12.1–26.2 months), and Asians (median 18.0 months, 95% CI 14.4–21.5 months; *P* = 0.59). Consistently, OS (Fig 1B) between the ethnic groups did not differ significantly (whites: median 59.1, 95% CI 50.0–68.1 months; blacks: median 61.2, 95% CI 55.2–67.2 months; Asians: median 44.1, 95% CI 31.9–56.3 months; *P* = 0.28).

This study is the first to directly compare characteristics and outcome of ASCT for white, black, and Asian MM patients. Our findings, that patients from the three ethnic groups had similar PFS as well as OS, support the notion that race should not affect decisions regarding ASCT for MM. However, our observation that the ethnic groups differed slightly with regard to response rates at 3 months after ASCT could indicate subtle ethnic differences in the responsiveness to high-dose melphalan. The potential for ethnic disparity in responses to

anti-myeloma therapy has recently been suggested as a possible explanation for the poorer improvement in MM survival rates in blacks compared with whites in the US (Waxman *et al*, 2010). Thus, systematic molecular studies with sufficient patient numbers as part of prospective clinical trials will be needed to determine whether differences in MM biology or in the response to therapeutic regimens between ethnic groups might still exist.

The absence of registries recording all diagnoses of MM in the catchment area during the observation period and the possibility of demographic fluctuations over time preclude any conclusions about the reasons for the disproportionate increase in the number of Asian patients undergoing ASCT in 2001–2009 compared to 1994–2000. Considering that minority race has been shown to affect receipt of standard care for various cancers, including MM, in the US (Mandelblatt *et al*, 1999; Rohatgi *et al*, 2007; Joshua *et al*, 2010), our findings may suggest that Asian MM patients could have been less likely to progress to ASCT in the years when this treatment was becoming a new standard of care. The establishment of suitable registries and systematic studies that address the possibility of ethnic disparity in the receipt of standard care for haematological malignancies in general, and for MM in particular, are warranted.

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Fig 1. Treatment outcomes. ASCT, autologous haematopoietic stem cell transplantation. (A) Progression-free survival. (B) Overall survival.

Table I.

Patient- and treatment-related characteristics.

	White	Black	Asian	<i>P</i>
Total (%)	270 (74.4)	56 (15.4)	37 (10.2)	
Sex (%)				ns
male	176 (65.2)	27 (48.2)	22 (59.5)	
female	94 (34.8)	29 (51.8)	15 (40.5)	
available	270 (100)	56 (100)	37 (100)	
Age (years)				ns
median (range)	57.2 (27–71)	58.0 (26–70)	55.9 (38–72)	
available	270 (100)	56 (100)	37 (100)	
Subtype (%)				ns
IgG	138 (51.1)	41 (73.2)	21 (56.8)	
IgA	63 (23.3)	4 (7.1)	6 (16.2)	
IgD	2 (0.7)	1 (1.8)	1 (2.7)	
IgM	2 (0.7)	0 (0.0)	0 (0.0)	
light chain	52 (19.3)	8 (14.3)	7 (18.9)	
non-secretory	13 (4.8)	2 (3.6)	2 (5.4)	
available	270 (100)	56 (100)	37 (100)	
BM plasma cells (%)				ns
median (range)	40 (1–100)	60 (4–99)	40 (3–95)	
available	211 (78.1)	49 (87.5)	31 (83.8)	
Karyotype (%)				ns
normal	53 (19.6)	13 (23.2)	7 (18.9)	
abnormal	32 (11.9)	12 (21.4)	6 (16.2)	
failed	72 (26.7)	10 (17.9)	12 (32.4)	
not done	113 (41.9)	21 (37.5)	12 (32.4)	
t(4;14)	7	1	1	
t(4;16)	0	0	1	
–17p	1	0	0	
del 13	15	4	2	
t(11;14)	5	3	2	
Beta-2-microglobulin (mg/l)				ns
median (range)	3.6 (0–22.5)	3.2 (0–7.2)	3.0 (0–9.1)	
>3.5 mg/l (%)	41 (34.5)	11 (36.7)	5 (29.4)	
available (%)	119 (44.1)	30 (53.6)	17 (45.9)	
Number of ASCTs (%)				0–006
1994–2000	109 (82.6)	17 (12.9)	6 (4.5)	
2001–2009	161 (69.7)	37 (16.9)	31 (13.4)	
Diagnosis to ASCT (months)				ns
median	10.5 (3.3–196.6)	11.1 (5.9–93.5)	10.6 (4.6–112.6)	

	White	Black	Asian	<i>P</i>
(range)				
available	270 (100)	56 (100)	37 (100)	
Status at ASCT (%)				ns
VGPR or CR	15 (5.6)	1 (1.8)	1 (2.7)	
PR	208 (77)	41 (73.2)	27 (73.0)	
<PR	47 (17.4)	14 (25)	9 (24.3)	
available	270 (100)	56 (100)	37 (100)	
Melphalan dose (%)				ns
140mg/m ²	69 (35.6)	18 (32.1)	14 (37.8)	
200mg/m ²	174 (64.4)	38 (67.9)	23 (62.2)	
CD34+ cells/kg × 10 ⁶				ns
median (range)	3.1 (0.9–19.2)	3.3 (1.9–10.7)	2.9 (1.0–15.5)	
available	265 (98.1)	52 (92.9)	36 (97.3)	
Response at 3 months after ASCT (%)				0.045
VGPR or CR	42 (15.6)	4 (7.1)	3 (8.1)	
PR	189 (70.0)	38 (67.9)	25 (67.6)	
<PR	34 (12.6)	14 (25.0)	9 (24.3)	
available	265 (98.1)	56 (100)	37 (100)	
Tandem ASCT (%)				ns
received	8 (3.0)	2 (3.6)	1 (2.7)	
ASCT for relapse/progression (%)				ns
received	62 (23.0)	10 (17.9)	10 (27.0)	

ASCT, autologous haematopoietic stem cell transplantation; BM, bone marrow; CR, complete response; PR, partial response; VGPR, very good partial response.