BSH 2020 VIRTUAL
9 -14 NOVEMBER
60 1960–2020
British Society for Haematology
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Real world experience of tandem autologous stem cell transplant for high risk multiple myeloma at a single UK centre

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INTRODUCTION

Optimal management of newly diagnosed patients with high risk multiple myeloma (MM) is challenging and these patients have poorer outcomes, despite novel agents.

Emerging data support tandem autologous stem cell transplant (ASCT) in patients with high risk cytogenetics or R-ISS II-III with improved progression free survival (PFS) and overall survival (OS).[1] Trial data suggest a high proportion of those assigned to tandem ASCT proceed as planned.

AIM

To examine our recent experience of high risk MM patients to assess efficacy and tolerability of tandem ASCT, including reasons for not proceeding.

METHOD

We undertook a retrospective analysis of high risk patients who underwent tandem or single ASCT between November 2017-November 2019.

High risk was defined as: adverse risk cytogenetics: (t(4;14), t(14;16), t(14;20), del 17p)), plasma cell leukaemia, extramedullary disease, or suboptimal response to induction therapy (≤partial response).

Patient characteristics and clinical outcomes were recorded from electronic patient records.. PFS was defined as time from D0 ASCT-1 to progression or death.

RESULTS

44 high risk patients were identified, of which 33 were considered for tandem. **Ultimately only 17 patients (39%) underwent tandem and 27 (61%) single ASCT**. Patient characteristics are included in Table 1. Reasons for not proceeding to tandem are shown in Figure 1 and included toxicity from 1st ASCT (n=4, 25%), performance status (n=4, 25%), and patient choice (n=4, 25%).

All patients received a proteasome inhibitor (PI) or immunomodulatory agent (IMiD) for induction, with PI+IMiD more common in the tandem vs single ASCT arm (88% vs 63%). Patients received a median of 2 lines of therapy (1-3) pre-ASCT in the tandem arm and 1 line (1-3) in the single ASCT arm. 11 tandem patients (65%) and 13 single ASCT patients (48%) required salvage pre-ASCT. At time of proceeding to ASCT, overall response rate (ORR) was 94% for tandem patients (vs 81% for single ASCT), with 47% achieving ≥ very good partial response (VGPR) (vs 44% for single ASCT). Median time to engraftment was unaffected by ASCT (12 days for both ASCT-1 and ASCT-2 in tandem arm), and 12 days for the single ASCT arm. In the tandem arm, Melphalan dose was more often reduced in ASCT-2 compared to ASCT-1 (41% vs 12%).

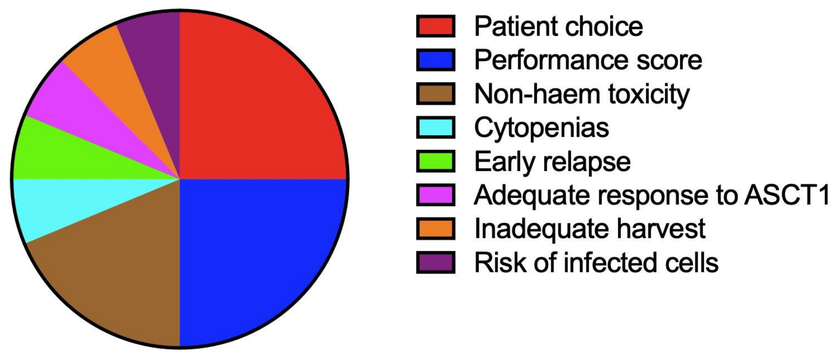
Overall response rate (ORR) at 3 months was 88% for tandem (vs 78% for single ASCT), 76% achieving ≥ VGPR (vs 50% for single ASCT). **5 patients (29%) in the tandem group had improvement in their response between ASCT-1 and ASCT-2**.

Median follow up was 17 months for tandem and 13 months for single ASCT patients. 1 year PFS was 69.1% (95% CI: 35.9% to 87.5%) for tandem and 68.8% (95% CI: 46.9% to 83.2%) for the single ASCT arm. 1 year OS was 86.9% (95% CI: 56.6% to 96.6%) for tandem and 87.1% (95% CI: 64.8% to 95.7%) for single ASCT patients. 1 patient (6%) in the tandem arm and 7 patients (26%) in the single ASCT arm relapsed early (<12 months post ASCT). There were 2 peri-transplant deaths in the tandem arm attributable to infection and acute lung injury, and 1 in the single ASCT arm from stroke. PFS and OS data remain immature due to short follow-up.

Table 1: High Risk Patient Characteristics

	Tandem ASCT		Single ASCT
Number of patients	17		27
Sex	Male: 10 (59%) Female: 7 (41%)		Male: 11 (41%) Female: 16 (59%)
Median age	52 years (29-69)		60 years (31-74)
ISS Stage			
Stage I	4 (24%)		5 (19%)
Stage II	6 (35%)		12 (44%)
Stage III	6 (35%)		5 (19%)
Unknown	1 (6%)		5 (19%)
FISH			
Adverse risk	9 (53%)		18 (67%)
Standard risk	7 (41%)		8 (30%)
Unknown	1 (6%)		1 (4%)
Extramedullary disease	2 (12%)		2 (7%)
Plasma cell leukaemia	3 (18%)		0 (0%)
At least 2 lines of therapy pre-ASCT	11 (65%)		13 (48%)
First line Induction therapy			
PI alone	2 (12%)		10 (37%)
IMiD alone	0 (0%)		0 (0%)
PI+IMiD	15 (88%)		17 (63%)
Median time from diagnosis to ASCT-1	9 months (7-25)		10 months (7-28)
Melphalan dose reduction	ASCT-1 2 (12%)	ASCT-2 7 (41%)	 8 (30%)
Maintenance/consolidation	3 (18%)		4 (15%)
Response at 3 months post ASCT	ASCT-1	ASCT-2	
CR	4 (24%)	6 (35%)	7 (26%)
VGPR	7 (41%)	7 (41%)	6 (22%)
PR	6 (35%)	2 (12%)	8 (30%)
PD	0 (0%)	0 (0%)	4 (15%)
Death	0 (0%)	2 (12%)	1 (4%)

Figure 1: Reasons For Not Proceeding to Tandem ASCT (n=16)



CONCLUSIONS

- Our data highlight the potential benefits and challenges of delivering tandem ASCT in the real world setting.
- ORR was favourable in the tandem arm, with deepened responses between 1st and 2nd ASCT in 29% of patients.
- However, 48% of patients considered for tandem did not proceed to 2nd ASCT, mainly due to toxicity, performance status and patient choice.
- Better understanding of the risks, benefits and feasibility of tandem ASCT will help define its place in the real world management of this high risk group.

ACKNOWLEDGEMENT

This work was undertaken at University College London Hospitals, which receives funding as a NIHR Biomedical research centre. We would like to thank all staff and patients.

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