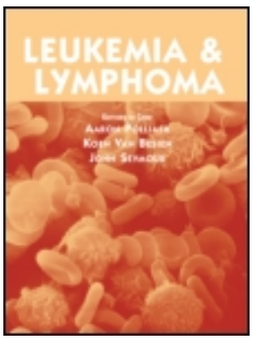

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LETTER TO THE EDITOR

A home-care, early discharge model after autografting in multiple myeloma: results of a three-arm prospective, non-randomized study

Massimo Martino[1], Letteria Russo[1], Tiziana Martinello[1], Giuseppe Alberto Gallo[1], Roberta Fedele[1], Tiziana Moscato[1], Giuseppe Console[1], Donatella Iolanda Vincelli[2], Francesca Ronco[2], Maurizio Postorino[3], Giuseppe Irrera[1] & Giuseppe Messina[1]

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Several articles on the outpatient management of patients with aplastic multiple myeloma (MM) after high-dose chemotherapy have been published, and have demonstrated that the outpatient program is feasible and safe [1,2]. There are various reasons for transferring support in the aplastic phase to the outpatient setting, including patient preference [3], reduced exposure to hospital micro-organisms [4], better use of available hospitals and cost saving [5–9]. In this model, however, patients experience time-consuming daily travel to the outpatient clinic for blood tests and physician check-ups.

"Hospital at home" is an alternative, designed to reduce hospital outpatient admissions by providing hospital-equivalent care to patients in the home setting [4,10–13]. By this means, patients may access the hospital at home service as an early discharge model (EDM) from hospitalization, and receive active treatment from healthcare professionals of a condition that otherwise would require acute hospital inpatient care.

We conducted a preliminary three-arm, prospective, non-randomized study to demonstrate and evaluate the clinical feasibility and efficiency of an EDM and home-care (HC) treatment for patients with *de novo* MM receiving high dose melphalan (HDM) (200 mg/m^2) with hematopoietic progenitor cell (HPC) rescue.

Patients who lived within a 20 min drive from hospital (HC group) were discharged to their private home the day after HPC infusion (day 1). Patients at home had to meet the requirements of: a caregiver who was willing to stay at home and help, and approval of the home by the medical staff of the bone marrow transplant unit. The medical staff required that there be no pet animals at home, the sheets be changed once a day and that the home be cleaned once a day. At home, patient management was regulated by an agreement between the local hospital and the Italian Association against Leukemia (AIL), Reggio Calabria section. In this model, every clinical and therapeutic activity performed at the patient's home was considered as a hospital activity. Therefore, all related costs (drugs, disposable items, equipment and insurance) were sustained by the hospital and national health system. When transplant physicians and nurses were not on duty, they spent their own time on the HC project and were paid by AIL funds. Transplant staff delivered all supportive care at home until hematological recovery. The program provided clinical examination performed twice daily (in the morning and in the afternoon), daily physician oversight of all evaluations, daily registered-nurse evaluations in the home, blood sampling for laboratory investigations and cultures, transfusion of blood products and infusion of parenteral antibiotics, monitoring of checklists completed by patients and relatives, recording of temperature and drug and fluid intake, and dealing with any complaints. Health professionals reached the patient's home by their own means. Blood samples and units of packed red blood cells were transported in insulated blood transport bags designed for inter- or intra-hospital transfer of blood products. With a starting temperature of 4°C when using the cool-packs included with the bag, the temperature takes more than 4 h to reach the 10°C maximum for the transport of blood. Blood tests were performed in the hospital analysis laboratory and results were available on the same day, within about 1 h. Healthcare professionals provided the supply of medications, and performed pulse oximetry for monitoring the patient's O_2 saturation as well as electrocardiography, in the home.

Patients who lived more than a 20 min drive from hospital were discharged to a residential facility near the hospital on day 1, and visited and were treated in the conventional outpatient clinic until hematological recovery (OUT group). Patients in this group were also required to have a caregiver with them all day. Both HC and OUT patients were admitted to the inpatient unit for chemotherapy and HPC infusion

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Table I. Main patient characteristics and outcome of different types of patient management after high dose melphalan and autografting.*

	Inpatient regimen	Outpatient regimen	Home-care regimen	*p*-Value
No. of patients	33	17	8	
Age (years)†	62 (43–67)	59 (42–65)	55 (45–60)	0.002
Sex				
Male	20	13	5	
Female	13	4	3	
No. of transplants	44	25	15	
CD34+ cell dose ($\times 10^6$/kg)†	4.9 (2.1–5.8)	5.0 (2.1–5.9)	5.1 (2.5–5.5)	NS
No. of days in hospital†	19 (15–27)	4 (4–21)	4 (2–15)	0.001
Day of discharge†‡	16 (12–14)	1 (1–17)	1 (1–3)	0.001
No. of days of evaluation†§	—	9 (0–12) (at outpatient clinic)	10 (1–11) (at patient's home)	
No. of erythrocyte transfusions (units)†	0 (0–6)	0 (0–2)	0 (0–3)	NS
No. of platelet transfusions (units)†	1 (0–4)	1 (0–4)	0 (0–5)	NS
Days to reach neutrophils $> 0.5 \times 10^9$/L†	9 (8–12)	9 (9–11)	9 (8–10)	NS
Days to reach platelets $> 20 \times 10^9$/L†	13 (9–20)	13 (10–17)	12 (9–14)	NS
Fever > 38°C				0.001
No vs. yes	11 (25%) vs. 33 (75%)	18 (72%) vs. 7 (28%)	9 (60%) vs. 6 (40%)	
Fever origin				
FUO	30	7	5	
CVC related	2			
Biologically documented	1		1°	
No. of days of fever > 38°C†	3 (0–12)	0 (0–7)	0 (0–14)	0.001
No. of days of i.v. antibiotics†	6 (0–18)	0 (0–7)	0 (0–23)	0.001
Mucositis				
No vs. yes	2 (4%) vs. 42 (95%)	5 (20%) vs. 20 (80%)	2 (13%) vs. 13 (87%)	NS
Grade 1–2 vs. grade 3–4	38 (86%) vs. 4 (9%)	19 (75%) vs. 1 (4%)	13 (87%) vs. 0	0.05
Nausea				NS
No vs. yes	8 (18%) vs. 36 (82%)	3 (12%) vs. 22 (88%)	3 (20%) vs. 12 (80%)	
Grade 1–2 vs. grade 3–4	34 (77%) vs. 2 (5%)	22 (88%) vs. 0	12 (80%) vs. 0	
Vomiting				NS
No vs. yes	9 (21%) vs. 35 (79%)	9 (36%) vs. 16 (64%)	5 (33%) vs. 10 (67%)	
Grade 1–2 vs. grade 3–4	34 (77%) vs. 1 (23%)	16 (64%) vs. 0	10 (67%) vs. 0	
Diarrhea				NS
No vs. yes	17 (39%) vs. 27 (61%)	7 (28%) vs. 18 (72%)	6 (40%) vs. 9 (60%)	
Readmitted to hospital¶				NS
No vs. yes	38 (86%) vs. 6 (13.6)	23 (92%) vs. 2 (8%)	13 (93%) vs. 2(13%)	
Readmitted to hospital reason¶				
Infection biologically documented**	3 (6.8%)	1 (4%)		
Fever – FUO	1 (2.3%)	1 (4%)		
Fever – clinically established	2 (4.5%)		1 (6.7%)††	

NS, not statistically different; FUO, fever of unknown origin; CVC, central venous catheter.
*Data were analyzed by descriptive statistical methods and group differences were calculated using Fisher's exact test.
†Values are expressed as median (range).
‡Day of discharge after transplant, i.e. day 0 is the day of stem cell reinfusion.
§After discharge and before hematological engraftment.
¶After hematological reconstitution and before day + 60 post-stem cell infusion.
**Cytomegalovirus reactivation without clinical signs.
††A-N1H1 virus.

for a minimum of approximately two nights to guarantee maximum reimbursement according to the Italian diagnosis related group (DRG) system. After discharge, they were provided with 24 h telephone access to a registered nurse and physician. Family caregivers were well informed about the care the patient required.

Patients who refused the HC or OUT program or lacked available caregivers were managed in hospital during the HPC post-infusion period, and these patients were registered as the inpatient (IN) cohort.

HC and OUT patients were regarded as equivalent to hospital inpatients, receiving the same critical elements of hospital service, including medicines and appropriate diagnostic and therapeutic procedures. The prophylaxis program included oral ciprofloxacin and acyclovir, and a dose of 6 mg of pegfilgrastim was administered subcutaneously on day 1. Indications for readmission or no discharge after HPC infusion included uncontrolled nausea, vomiting and/or diarrhea, severe mucositis requiring continuous fluid replacement or parenteral alimentation, pneumonia, cardiac and/or respiratory distress, fever unresponsive to first-line antibiotic therapy, and some other toxicity judged unmanageable at home by medical staff. Finally, patients were also admitted or not discharged on their own request. A bed was kept empty for readmission of OUT or HC patients.

Table I summarizes the main patient characteristics and outcomes of different types of patient management after transplant. Fifty-eight patients were treated with 84 cycles of HDM and stem-cell rescue: in the IN cohort, 33 patients received 44 transplants; in the OUT cohort, 17 patients received 25 transplants; and in the HC cohort, eight patients received 15 transplants. Thirty-three patients followed the IN model because 18 of them refused the HC or OUT program and 15 did not have available caregivers. Patients presented no differences in terms of disease status at the time of transplant.

In the 40 transplant cycles in the non-IN cohort, the median day of discharge was day 1 after reinfusion. Three patients did not leave hospital during the aplastic period, due to toxicity in two cases (vomiting) and refusal in one case.

Table II. Transplant data for each of 15 home-care patients following high-dose therapy with melphalan and autografting until hematological recovery.

Patient	Transplant	Sex	Age (years)	Day of discharge*	No. of days of evaluation†	Neutropenic fever‡	Fever origin	Days with fever	No. of days of i.v. antibiotics	Mucositis (WHO)	Readmission (reason)	Day of readmission§ (days of hospital stay)	Neutrophil/platelet¶ engraftment	No. of erythrocyte/platelet transfusions (units)
1	First	F	59	1	10	Yes	FUO	7	6	Yes (1)	No		8/9	0/0
2	Second	F	60	1	10	Yes	FUO	7	8	Yes (2)	No		9/12	0/0
3	First	M	57	1	10	Yes	FUO	3	4	Yes (1)	No		10/14	0/2
4	First	F	57	1	10	No		0	0	Yes (1)	No		9/14	0/0
5	Second	M	58	1	4	Yes	A-N1H1 virus	14	23	Yes (1)	Yes (fever)	7 (30)	9/13	3/5
6	Second	F	57	1	1	Yes	FUO	9	14	Yes (2)	Yes (fever)	2 (17)	9/9	0/0
7	First	M	46	1	10	Yes	FUO	6	4	Yes (1)	No		10/12	0/0
8	First	F	52	1	10	No		0	0	Yes (2)	No		9/11	0/1
9	Second	F	52	3	10	No		0	0	Yes (2)	No		9/12	0/1
10	Second	M	46	1	8	No		0	0	Yes (1)	No		9/12	0/2
11	First	F	51	1	10	No		0	0	No	No		10/14	0/0
12	First	M	55	3	7	No		0	0	Yes (1)	No		9/13	0/0
13	First	F	52	1	11	No		0	0	Yes (2)	No		10/12	0/2
14	Second	M	60	1	8	No		0	0	Yes (2)	No		9/11	0/1
15	Second	M	51	1	7	No		0	0	No	No		9/10	0/0

FUO, fever of unknown origin; WHO, World Health Organization.
*Day of discharge after stem cell infusion.
†At patient's home.
‡Neutropenic fever was defined as an axillary temperature exceeding >38.2°C on at least two consecutive occasions or a persistent temperature of equal to or greater than 38.0°C for at least 1 h, in the absence of any documented non-infectious cause.
§Day of readmission after stem cell infusion.
¶Neutrophil and platelet engraftment were defined as the first of 3 consecutive days of an absolute neutrophil count $\geq 0.5 \times 10^9$/L and the first of 3 days of a platelet count $\geq 20 \times 10^9$/L.

Median time to engraftment (granulocytes $\geq 0.5 \times 10^9$/L and platelets $\geq 20 \times 10^9$/L) was similar among the three groups. No intergroup differences in mucositis (yes vs. no) were observed. Febrile neutropenia (FN) incidence was lower in the OUT (28%) and HC cohorts (40%) than in IN cases (75%). In the aplastic period, FN occurred for a median of 3, 0 and 0 days for patients in the IN, OUT and HC settings, respectively. All patients with fever were managed with single daily-dose broad-spectrum antibiotics (intravenous ceftriaxone). Biologically documented infections were recorded in two of 46 febrile episodes, one with *Staphylococcus epidermidis* and other with A-N1H1 virus infection. In two courses, cultures indicated a central venous catheter (CVC)-related infection (coagulase-negative staphylococci). In 38 procedures FN was absent for all of the aplastic period (11, 18 and nine in the IN, OUT and HC cohorts, respectively). No gram-negative sepsis was observed, and there were no infectious deaths. No systemic fungal infections were documented. During the aplastic phase readmissions occurred in two of 25 (8%) OUT and two of 15 (13%) HC courses; all readmissions were caused by fever. Table II shows transplant data for each of the 15 HC patients from discharge until hematological recovery.

After hematological reconstitution and before day 90 post-HPC infusion, three of the above 40 (15%) patients were admitted secondarily (one because of cytomegalovirus reactivation without clinical signs and two due to fever). Six (14%) patients of the conventional IN group were also admitted secondarily before day + 90, after initial discharge (three because of cytomegalovirus reactivation and three due to fever). No transplant-related death was observed.

HC is mainly used for palliative care in patients with end-stage cancer and in geriatric patients. In this study, a HC-EDM was addressed to patients with significant prospects of care and subjected to medical treatment considered at high risk of complications. The main reason for the project was to allow the patient to be treated at home instead of in hospital, and the first aim was to determine whether HC was safe and useful for such patients. In this preliminary evaluation, we found that HC patients had fever less often, spent fewer days with fever and had fewer days on intravenous antibiotics than IN patients. In our opinion these results indicate that care at home could be not only safe and feasible, but better in many respects than isolation in hospital.

Patient approval was universal, and the main advantage was the opportunity to be with their family in a non-medical environment; studies to further document quality of life are under way and will be reported elsewhere.

The approach may be particularly appealing because it could provide an indication to change the public health system in Italy, with a reconstruction of the global outpatient care model. Currently, healthcare providers are obliged to carry out their own work schedule within the hospital. The "hospital at home" should be considered not as an independent service, but should be viewed as part of a comprehensive continuum of services. This perspective makes it possible to seek the appropriate niche for a

service that provides some of the hospital's roles, albeit outside the hospital walls [14]. Moreover, it is plausible that HC is cost-effective in the transplant setting, and in the future a cost comparison should be carried out.

In conclusion, HC following an EDM in patients with MM could be a novel approach, and more robust prospective studies are now required.

Potential conflict of interest: Disclosure forms provided by the authors are available with the full text of this article at www.informahealthcare.com/lal.

References

[1] Martino M, Montanari M, Bruno B, et al. Autologous hematopoietic progenitor cell transplantation for multiple myeloma through an outpatient program. Expert Opin Biol Ther 2012:12:1449–1462.
[2] Martino M, Montanari M, Ferrara F, et al. Very low rate of re-admission after an early discharge outpatient model for autografting in multiple myeloma patients: an Italian multi-center retrospective study. Biol Blood Marrow Transplant 2014;20:1026–1032.
[3] Summers N, Dawe U, Stewart DA. A comparison of inpatient and outpatient ASCT. Bone Marrow Transplant 2000;26:389–395.
[4] Fernandez-Aviles F, Carreras E, Urbano-Ispizua A, et al. Case-control comparison of at-home to total hospital care for autologous stem-cell transplantation for hematologic malignancies. J Clin Oncol 2006;24:4855–4861.
[5] Barosi G, Marchetti M, Alessandrino P, et al. A model for analysing the cost of autologous peripheral blood progenitor cell (PBPC) transplantation. Bone Marrow Transplant 1999;23:719–725.
[6] Mishra V, Vaaler S, Brinch L. Cost analysis of autologous peripheral blood stem cell transplantation for multiple myeloma. Clin Lab Haematol 2003;25:179–184.
[7] Meisenberg BR, Ferran K, Hollenbach K, et al. Reduced charges and costs associated with outpatient autologous stem cell transplantation. Bone Marrow Transplant 1998;21:927–932.
[8] Holbro A, Ahmad I, Cohen S, et al. Safety and cost-effectiveness of outpatient autologous stem cell transplantation in patients with multiple myeloma. Biol Blood Marrow Transplant 2013;19:547–551.
[9] Faucher C, Le Corroller Soriano AG, Esterni B, et al. Randomized study of early hospital discharge following autologous blood SCT: medical outcomes and hospital costs. Bone Marrow Transplant 2012; 47:549–555.
[10] Westermann AM, Holtkamp MM, Linthorst GA, et al. At home management of aplastic phase following high-dose chemotherapy with stem-cell rescue for hematological and non-hematological malignancies. Ann Oncol 1999;10:511–517.
[11] van Tiel FH, Harbers MM, Kessels AG, et al. Home care versus hospital care of patients and chemotherapy induced cytopenia. Ann Oncol 2005;16:195–205.
[12] Svahn BM, Remberger M, Myrbäck KE, et al. Home care during the pancytopenic phase after allogeneic hematopoietic stem cell transplantation is advantageous compared with hospital care. Blood 2002;100:4317–4324.
[13] Ringdén O, Remberger M, Törlén J, et al. Home care during neutropenia after allogeneic hematopoietic stem cell transplantation in children and adolescents is safe and may be more advantageous than isolation in hospital. Pediatr Transplant 2014;18:398–404.
[14] Bentur N. Hospital at home: what is its place in the health system? Health Policy 2001;55:71–79.