Novel applications of growth factors in solid tumors
Westermann, A.

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At home management of aplastic phase following high dose chemotherapy with stem cell rescue for hematological and non-hematological malignancies

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Chapter 7

Abstract

Background After high-dose chemotherapy with autologous stemcell transplant support long hospital stays in the aplastic phase are expensive, lead to increased risk of hospital infections and to increasing pressure on available hospital beds. We developed a home care regimen that allows patients to be at home for most of the aplastic period, without daily hospital visits.

Patients and methods Between October 1995 and December 1997, transfer of supportive care to the home setting took place in three phases for patients undergoing high-dose chemotherapy with stem-cell transplant for malignant lymphoma (one course of BEAM), breast cancer or germ cell cancer (3 courses of lCTC). In the inpatient cohort, the supportive care designed for at home use was administered in the hospital until neutrophile recovery to 0.5 x 10^9/l. In the second, outpatient cohort, patients were discharged the day after stem-cell reinfusion but the supportive care was delivered daily in hospital. The third, home care cohort, consisted of patients who were discharged the day after stemcell reinfusion, after which specialized home care professionals delivered all supportive care including transfusions and parenteral antibiotics at home, with once weekly check-up in hospital by the transplant physician.

Results 42 patients were treated with 81 cycles of high dose chemotherapy (11, 18 and 13 patients and 17, 40 and 24 courses in the inpatient, outpatient and home care cohorts respectively). Inpatients were hospitalized in the aplastic phase for a median of 14 days. Patients in the outpatient cohort were at home in the aplastic phase for a median of 5 days (with a median of 6 days in hospital), and in the home care cohort for a median of 10 days (with a median of 1.5 days in hospital). Unscheduled readmissions and hospital visits were frequent in the outpatient and home care cohorts, mostly due to fever, central indwelling catheter malfunctioning or chemotherapy-related toxicity. However, patients could usually be discharged again after observation and treatment. No infectious deaths or unexpected emergencies occurred in the outpatient or home care cohort. Neither was there any suggestion of an increased number of fevers, infections, or other complications.

Conclusions At home management in the aplastic phase after high dose chemotherapy and stemcell transplant by community-based professionals is feasible without signs of increased toxicity or infections.
Introduction

High dose chemotherapy with autologous stem-cell support is a potentially curative treatment option for patients with relapsed or poor-risk malignant lymphomas, leukemias and certain pediatric tumors. It is, however, in breast cancer in the adjuvant high-risk or disseminated setting that this intensive treatment has been most frequently used, even though this indication has not yet proven its worth in randomized controlled trials. Trials examining the efficacy of this therapy in ovarian cancer and small cell lung cancer patients are in progress. These developments have led to a marked increase in the number of patients undergoing high-dose chemotherapy with stem-cell support.

Traditionally, patients undergoing high-dose treatment have been admitted to intensive nursing care units from the start of chemotherapy till substantial bone marrow recovery, usually leading to prolonged hospital stays (average 21 days). Clinical care incorporates the administration of high dose chemotherapy with hydration and antiemetic regimens, with support in the aplastic phase in the following weeks. This support consists of the monitoring of bacterial colonization, daily blood counts and blood chemistry, the administration of fluids, antiemetics and prophylactic as well as therapeutic parenteral and oral antibiotics. In addition, blood and platelet transfusions are frequently delivered.

The feasibility of this procedure has greatly increased in recent years due to several simultaneous developments: The use of hematopoietic colony-stimulating factors in both priming of peripheral blood stem-cells before collection and after stem-cell reinfusion has resulted in a marked reduction in the duration of absolute myelosuppression. The improvement in oral prophylactic antibiotic regimens and the once daily dosing of parenteral antibiotics have simplified management of febrile neutropenia. Outpatient parenteral antimicrobial treatment has been proven feasible and safe with modern intravenous catheters and infusion devices.

There are strong arguments for transferring support in the aplastic phase to the outpatient setting: patient preference, diminished exposure to hospital microorganisms, better use of available hospital beds and lower costs. For selection of patients for outpatient treatment the type of regimen, since for instance significant mucositis-producing regimens might compromise the success of outpatient treatment, and availability of adequate residence facilities close to the hospital are important. A stand-by hospital bed for emergency inpatient care is mandatory. In recent years, papers on the outpatient management of the aplastic patient after high dose chemotherapy have been published but in all reports patients had to visit hospital once a day. To avoid this, specialized home care should be available in order to take over some of the traditional in-hospital care, such as the administration of parenteral antibiotics and transfusions.
We report the results of an outpatient, home-treatment program for patients receiving one or more high dose chemotherapy courses with stem-cell rescue. Well-specialized home care could be organized in close co-operation with a community-based team involving specialized district nurses and a pharmaceutical home care association.

Patients and methods

Between October 1995 and December 1997 supportive care in the aplastic phase after peripheral blood progenitor transplant was transferred from the hospital to the home setting in three phases.

Eligible patients included patients treated with a single course of the BEAM regimen (BCNU 300 mg/m², etoposide 800 mg/m², cytarabin 800 mg/m² and melphalan 140 mg/m²) followed by stem-cell reinfusion for relapsed malignant lymphoma. Another group of eligible patients underwent the triple tCTC (carboplatin 1066 mg/m², thiotepa 320 mg/m² and cyclophosphamide 4 g/m² q. 4 weeks) regimen with triple stem-cell reinfusions for advanced breast cancer or relapsed germ cell cancer. Both regimens do not usually lead to very severe mucositis or prolonged vomiting, and were therefore deemed suitable to pilot this approach.

Because of our unfamiliarity with this novel approach, we first protocolized a supportive care regimen with oral prophylactic antibiotics and once-daily empirical broad-spectrum antibiotics (in order to later facilitate outpatient management) in hospitalized patients (inpatient cohort). Since it almost immediately transpired that this was a reasonable and safe protocol, we then discharged patients the day after stem-cell transplant, and had them visit the hospital every day for medical and nursing care (outpatient cohort) until neutrophile recovery. After the feasibility of this approach was established, we subsequently assigned most of the care to the specialized district nurses in the home setting (home care cohort).

In the outpatient and home care cohorts, patients were required to have an available caregiver at home to help monitor patient's condition and drug and fluid intake. In case of patient refusal to the outpatient treatment, lack of available caregivers or prohibitive sickness after reinfusion, the protocolized supportive care was administered in hospital and these patients were registered in the inpatient cohort from the first transplant cycle.

The supportive care regimens for the inpatient, outpatient cohorts and the home care cohort are summarized in table 1.
<table>
<thead>
<tr>
<th>Table 1. Difference between inpatient, outpatient and home care cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inpatient cohort</strong></td>
</tr>
<tr>
<td>Monitoring vital signs</td>
</tr>
<tr>
<td>Cultures</td>
</tr>
<tr>
<td>Blood sampling from central venous catheter</td>
</tr>
<tr>
<td>Blood and platelet transfusions</td>
</tr>
<tr>
<td>Evaluation of fever</td>
</tr>
<tr>
<td>Physical examination</td>
</tr>
</tbody>
</table>

**Prophylactic antibiotic regimen**
- ciprofloxacin 500 mg twice daily, orally
- itraconazole 200 mg twice daily, orally
- roxitromycin 150 mg twice daily, orally
- aciclovir 400 mg twice daily, orally

**Administration of empirical antibiotics**
- in hospital
- in outpatient clinic
- at home

**Empirical antibiotic regimen**
- ceftriaxon 2000 mg once daily, intravenously
- teicoplanin 400 mg once daily, intravenously

**Principal caregiver**
- hospital specialized nurse
- partner & specialized district nurse

**Day of discharge**
- when neutrophils > 0.5 x 10⁹/l
- day after transplant

**Place of residence during aplastic phase**
- hospital
- within 45 minute drive from hospital or at adjacent residential facility
- at home when living in Amsterdam, or at adjacent residential facility

**Outpatient cohort**
After chemotherapy and stem-cell transplant, patients were discharged if physical condition allowed, i.e. in the absence of fever, grade 3 or more vomiting or diarrhea leading to insufficient oral intake, or any other complication necessitating clinical observation or treatment. Patients were discharged to their private homes if they lived within 45 minutes of hospital, or to a residential facility (without medical, restaurant or other services) near the hospital. Infection control measures consisted of prophylactic antibiotics, surveillance cultures as described below, and simple hygienic instructions. No isolation was required and there was no limit to the number of visitors a patient could receive. Patients completed a daily monitoring checklist, to record temperature, drug and fluid intake, and any complaints. Every day patients were seen and treated in the hospital by transplant physicians and nurses on an outpatient basis. No home care was delivered. Patients who could not initially be discharged, were discharged as soon as their condition allowed.
Home care program

Patients were eligible for discharge the day after stem-cell reinfusion in the absence of the contraindications as mentioned above. Patients were discharged to their private homes when living in the Amsterdam area, or to the residential facility (without medical or other services) near the hospital, in order to be within the geographic limits of the specialized nursing team. The daily checklists were identical to those in the outpatient program, as were the infection control measures. Specialized district nurses, whose technical skills had been validated after instructions by the hospital transplant nursing staff, delivered all supportive care at home. Apart from more general nursing procedures, this included blood sampling from the central indwelling intravenous catheter for laboratory investigations and cultures, transfusion of blood products, and infusion of parenteral antibiotics. The nurse was present for the first 30 minutes of each erythrocyte transfusion, and for the duration of each platelet transfusion. Patients with known hypersensitivity reactions to transfusions were premedicated with clemastine and prednisone. One of the senior hospital transplant nurses visited the patients on a daily basis to monitor both patient symptoms and procedural security. Patients were seen once a week by their transplant physician in the outpatient clinic, but were not required to come to the hospital in the absence of complications for the rest of the week.

Supportive care

In case of unexpected problems, outpatients could consult the transplant physicians from 08:00 AM to 06:00 PM at the transplant center. Experienced transplant nursing staff was available in hospital for consultation at all hours with backup by a transplant physician. The same staff treated all three patient cohorts.

Daily blood counts and blood chemistry were performed, and patients received irradiated and filtered blood products to keep the hemoglobin level above 5.5 mmol/L and the platelet count above 10,000/μL. Antiemetics and mineral supplements were administered orally if necessary. Blood cultures taken via the indwelling intravenous catheter were done daily; surveillance cultures of stool, nose and throat were taken twice weekly. Blood cultures were incubated in an automated blood culture system (Vitek Biomerieux) for 7 days. Feces were cultured semiquantitatively for growth of aerobic gram negative bacteria and yeast. Nose and throat swabs were investigated for potentially pathogenic aerobic gram negative bacteria and yeast.

Patients were admitted to the hospital in case of insufficient oral intake due to uncontrolled vomiting or diarrhea, absence of a suitable caregiver, severe mucositis, or other situations at the discretion of the attending physician. Febrile neutropenia was initially evaluated in hospital and empirical once-daily therapy was initiated. In the absence of hypotension, pneumonia or other complications, patients were discharged the same day. Antibiotic treatment was continued on
an outpatient basis or at home, depending on the patient cohort. A home care pharmaceutical company prepared intravenous antibiotics for patients in the home care cohort. Only in case of complications or deteriorating physical condition would febrile patients be readmitted.

Antimicrobial regimens

The prophylactic antimicrobial regimen (Table 1) consisted of oral itraconazole, ciprofloxacin and aciclovir from day -10 before transplantation to neutrophile recovery to $0.5 \times 10^9/l$, and roxitromycin from day 1 after transplant to neutrophile recovery to $0.5 \times 10^9/l$. Empirical treatment of fever started after the temperature rose to $38\degree C$ on two separate occasions, or above $38.5\degree C$ once, and consisted of once daily teicoplanin and ceftriaxone. Patients with positive blood cultures taken from the indwelling intravenous catheter with coagulase-negative *Staphylococci* without fever or signs of infection at the catheter insertion site were treated with teicoplanin. Second line empirical antibiotics were generally started if fever persisted for 48 to 72 hours after the initiation of first line broad-spectrum antibiotics, depending on the patient's clinical condition and physician judgment. The antibiotic regimen is summarized in Table 1.

Analysis of results

Patient data collected consisted of gender, age, diagnosis and treatment in addition to number of days at home and in hospital. Days with fever, days on parenteral antibiotics, the number of transfusions of blood products and whether this happened in hospital or at home was also recorded. The number of unscheduled consultations and readmissions with their indications was carefully registered. Culture-positive fever episodes and microorganisms were documented. From September 1996, outpatient and at home patients and their partners were asked to fill out a questionnaire designed to detect inadequacies in the organization, patient perception of advantages and disadvantages of the procedure, unrecognized anxieties, and recommendations.

Results

Patient cohorts (Table 2)

Forty-two patients were treated with 81 cycles of high-dose chemotherapy and stem-cell rescue: 11 patients in the inpatient cohort receiving 17 transplants, 18 patients in the outpatient cohort receiving 40 transplants and 13 patients in the home care cohort for 24 transplants. Patient and treatment characteristics are given in Table 2. Overall median age was 44, with a slightly younger population in the home care cohort.

In the outpatient cohort, 15 patients stayed at home since they lived within 45 minutes of the
### Table 2. Patient and treatment characteristics in different cohorts

<table>
<thead>
<tr>
<th></th>
<th>Outpatient regimen provided during in-hospital stay</th>
<th>Outpatient regimen</th>
<th>Home care regimen</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>11</td>
<td>18</td>
<td>13</td>
<td>42</td>
</tr>
<tr>
<td>Age (in years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Median</td>
<td>46</td>
<td>44</td>
<td>39</td>
<td>44</td>
</tr>
<tr>
<td>- Range</td>
<td>33-55</td>
<td>24-53</td>
<td>24-55</td>
<td>24-55</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Male</td>
<td>-</td>
<td>5</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>- Female</td>
<td>11</td>
<td>13</td>
<td>9</td>
<td>33</td>
</tr>
<tr>
<td>Diagnoses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- breast cancer</td>
<td>6</td>
<td>11</td>
<td>6</td>
<td>23</td>
</tr>
<tr>
<td>- germ cell cancer</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>- malignant lymphoma</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td>Number of transplants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- tCTC</td>
<td>12</td>
<td>40</td>
<td>24</td>
<td>81</td>
</tr>
<tr>
<td>- BEAM</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>18</td>
</tr>
</tbody>
</table>

**Legend:** tCTC = carboplatin 1066 mg/m², thiotepa 320 mg/m², cyclophosphamide 4 g/m² q. 4 weeks; BEAM = BCNU 300 mg/m², etoposide 800 mg/m², cytarabin 800 mg/m², melphalan 140 mg/m².

hospital, and three stayed in the residential facility near the hospital as they lived further away from hospital. In the home care cohort three patients lived in Amsterdam within the reach of the home care team, and the other 10 rented a room in the residential building.

### Actual day of discharge (Table 3)

Of 40 transplant cycles in the outpatient cohort, in 26 cases the patient could be discharged the day after stem-cell transplantation. In five cases discharge was delayed to the second or third day after reinfusion for logistical reasons or because of transient toxicity, and in one case to the seventh day after transplant due to temporary lack of a caregiver at home. Eight patients did not leave hospital for most of the aplastic period, due to toxicity in seven cases (four cases of fatigue, all after 2nd or 3rd transplant, and one case each of nausea, hemolytic uremic syndrome and veno-occlusive disease), and because of lack of a caregiver at home in one case. In this cohort (including the patients that stayed in hospital) the median discharge was nevertheless on day 1 after stem-cell reinfusion.

In the 24 transplant cycles in the home care cohort, patients were discharged on the first day after stem-cell reinfusion in 18 cases. Five patients left hospital on the second or third day after
### Table 3. Outcome of different types of patient management after high dose chemotherapy and PBPC transplant

<table>
<thead>
<tr>
<th>Parameter per aplastic period after transplant [range]$^{1}$</th>
<th>In hospital courses (n=17)</th>
<th>Outpatient courses (n=40)</th>
<th>Home care courses (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median no. of days in hospital</td>
<td>14 [9-60]</td>
<td>6 [0.54]</td>
<td>1.5 [0.34]</td>
</tr>
<tr>
<td>Median no. of days at home</td>
<td>-</td>
<td>6 [0.22]</td>
<td>10 [0.20]</td>
</tr>
<tr>
<td>Median day of discharge$^{2}$</td>
<td>14.5 [9-60]</td>
<td>1 [1-54]</td>
<td>1 [1-19]</td>
</tr>
<tr>
<td>Median no. of unscheduled consultations</td>
<td>-</td>
<td>0 [0-1]</td>
<td>2 [0-5]</td>
</tr>
<tr>
<td>Median no. of unscheduled readmissions</td>
<td>-</td>
<td>1 [0-2]</td>
<td>1 [0-2]</td>
</tr>
<tr>
<td>Median no. of erythrocyte transfusions at home</td>
<td>-</td>
<td>-</td>
<td>2 [0-6]</td>
</tr>
<tr>
<td>Median total no. of platelet transfusion encounters</td>
<td>6 [2-113]</td>
<td>4 [1-37]</td>
<td>5.5 [1-42]</td>
</tr>
<tr>
<td>Median no. of platelet transfusion encounters at home</td>
<td>-</td>
<td>-</td>
<td>1 [0-8]</td>
</tr>
<tr>
<td>Median days of fever &gt; 38°C</td>
<td>4 [0-14]</td>
<td>5 [0-20]</td>
<td>3.5 [0-13]</td>
</tr>
<tr>
<td>Median days on broad spectrum antibiotics</td>
<td>7 [0-13]</td>
<td>6 [0.24]</td>
<td>5 [0.25]</td>
</tr>
</tbody>
</table>

$^{1}$ Defined as period starting on the day of stem cell reinfusion, and ending with the day of neutrophile recovery to $0.5 \times 10^9/\text{l}$.

$^{2}$ Day of discharge after transplant, i.e. day 0 is the day of stem cell reinfusion.

transplant, mainly because of logistical problems with home care. In one case a patient could not be discharged in the aplastic period, due to general malaise and fatigue in the third transplant cycle. The median day of discharge in this cohort was day one after reinfusion.

**Number of days at home versus in hospital (Table 3)**

In the aplastic period, defined as the period between the day of stem-cell transplantation and neutrophile recovery to $0.5 \times 10^9/\text{l}$, the patients in the hospital cohort were hospitalized for a median of 14 days. In the outpatient cohort, patients were at home for a median of six days, and were hospitalized for a median of six days. This includes the nine patients who had to stay in hospital for reasons delineated above. The home care patients spent most of the aplastic period at home, for a median of 10 days, with 1.5 days in hospital.

**Unscheduled consultations and readmissions**

In the outpatient cohort unscheduled visits to the hospital were rare, mainly because the transplant staff saw patients daily anyway, but in two cases patients were evaluated for fever...
that started in the night. In the home care cohort, where patients visited hospital only once weekly, unscheduled calls occurred twice per transplant cycle (median), for a total of 39 extra visits in 24 courses. Most of these consultations were prompted by fever (16 of 39 instances) or venous catheter-related problems (eight times). In the 15 other cases miscellaneous indications existed, such as stomatitis, diarrhea, skin lesions or transfusion related exanthema.

Readmissions were not uncommon, and occurred in the majority of both the outpatient (29 of 40) and home care (17 of 24) courses. However, most patients could be discharged again after a short period of observation and treatment. Over half of the readmissions were because of fever (18 in the outpatient cohort and nine in the home care cohort). Other indications were venous catheter-related (three and five respectively), vomiting (five in the outpatient cohort) and other chemotherapy related toxicity (three cases in each group).

Erythrocyte and platelet transfusions (Table 3)

The median number of units of erythrocytes transfused (Table 3) was eight per transplant procedure for all cohorts (8, 7.5 and 9 for the inpatient, outpatient and home care cohort respectively). A median of five platelet transfusions were administered per course (6, 4 and 5.5 for the inpatient, outpatient and home care cohort respectively, see table 3). In the home care cohort, although only a minority of transfusions was administered at home by the district nurse (median two erythrocyte transfusions and one platelet transfusion per transplant), in total this amounted to 55 erythrocyte transfusions and 42 platelet transfusion encounters. One of the patients in the home care cohort developed a major anaphylactic reaction on platelet transfusion. Because the transfusion coincided with a scheduled hospital visit, adequate supportive care was immediately delivered in our transplant unit and she was readmitted. However, all subsequent platelet transfusions in this patient were also administered in hospital, with clemastine and prednisone prophylaxis. In two cases patients were seen in the hospital at our request after platelet transfusion reactions with exanthema that occurred in the presence of the district nurse. In both cases admission was not necessary, and further transfusions were uneventfully administered with clemastine and steroid premedication, at home or in hospital depending on convenience.

Febrile neutropenia, days on antibiotics and infections

Febrile neutropenia occurred for a median of five days in the aplastic period (4, 5 and 3.5 days for patients in the hospital, outpatient and home care setting respectively, Table 3). All patients with fever received empirical broad-spectrum antibiotics, for a median of six days per course (7, 6 and 5 days in the in hospital, outpatient and home care cohort respectively, see Table 3). Second line broad-spectrum antibiotics were prescribed in 9, 18 and 8 cycles in the inpatient, outpatient and home care cohorts respectively. Bacterial infection could be documented in 18
of 61 febrile episodes, mostly with *S. epidermidis* (15 of 18 cases). The other infectious agents were α-hemolytic *Streptococci*, *C. xerosis*, and *Str. fecalis* (one each). Moreover, in 20 courses patients were treated with teicoplanin because surveillance cultures from the indwelling intravenous catheter had yielded coagulase-negative *Staphylococci*. In 20 procedures fever was absent for all of the aplastic period (2, 8 and 10 in the inpatient, outpatient and home care cohort respectively). No Gram negative sepsis was observed, and there were no infectious deaths. No systemic fungal infections could be documented, but surveillance stool cultures and throat swabs yielded one or more asymptomatic itraconazole-resistant *Torulopsis glabrata* and *Candida* species in 50 of 81 courses. In those individual cases oral amfotericin B suspension was added to the antifungal regimen. One case of itraconazole-resistant oral candidiasis was registered in the outpatient cohort.

It should be mentioned that there was one unexplained sudden death in an afebrile patient in the inpatient cohort, probably due to arrhythmia or thromboembolic complications, but unfortunately autopsy was refused.

**Questionnaires**

Nine of 18 patients and their partners filled out the questionnaire in the outpatient cohort, and nine were not asked because of relapse (4), psychosocial problems (1), or administrative reasons (4). None of the partners and only one of the patients felt unsafe or anxious about risks while at home. Although the hospital could easily be reached in case of need, seven of nine patients considered the waiting times in hospital in addition to the daily travelling times one of the major drawbacks of the outpatient regimen. Eight patients would recommend the procedure to a fellow patient in the same situation, or would elect to go home after transplant in a similar situation, but one would not because of the fatigue created by waiting and travelling. Primary advantages mentioned were the feeling of being with one’s family, in non-medical surroundings (7), increased privacy (2), free choice of food (3), free movement and therefore distraction (2).

In the home care cohort, nine of 13 patients and their partners filled out the list, and four were not asked for administrative reasons (3) or psychosocial problems (1). All patients and partners felt safe at home, and eight indicated that they would elect to go home in a similar situation, and so advise fellow patients. The one patient who would not again choose to be at home after transplant, was concerned about the room all the equipment took up in his small apartment, and the strain this put on his family. The organization of visiting nurses, checklists and medication, especially in the first days after discharge was mentioned as a disadvantage by two patients. Boredom was prominent in two of the patients staying in the residential facility near the hospital. For eight patients this did not outweigh advantages such as the non-medical environment (7), the quiet (1), the free choice of activity (2), increased privacy (2) and free choice of food (2).
Discussion

In this study we describe the development of a home care program for supportive care after peripheral blood progenitor cell transplant after high-dose chemotherapy. The approach seemed reasonable after the continuing improvement in supportive care measures after stem-cell rescue, such as antiemetics, oral and once-daily antibiotics and hemopoietic growth factors. The availability of professional home care nurses whose technical skills were validated by the transplant staff in hospital, greatly aided this development. The growing awareness of the shift of care from hospital to the home setting led to full reimbursement of this treatment by insurance companies.

Our strategy was to first protocolize a supportive care regimen in such a way that it could be transferred to the outpatient setting and to the home setting, and test its feasibility in hospital. After we were convinced that this was safe and without increased toxicity or infections, we treated patients in the outpatient clinic. Although they were at home during day and night, patients had to come to the outpatient hospital every day for blood tests and physician check-up. There was no suggestion of increased toxicity. Most patients appreciated the opportunity to be with their families in this period. However, occasionally long waiting times in hospital and the daily travelling times were experienced as uncomfortable and exhausting. This is further indicated by the fact that in four cases patients decided not to go home during the next aplastic period due to extreme fatigue and exhaustion. We therefore felt justified in taking the outpatient approach one step further by transferring supportive care to the specialized district nurse level assisted by the senior transplant nursing team at our hospital. In the home care cohort, patient approval was universal, and even though patients were well aware of the change from normal routine that the new approach engendered, there was no sign of increased anxiety in the home situation. For almost all patients and partners, the main advantage was the opportunity to be with one's family in a non-medical environment, and this outweighed possible disadvantages in all but two of 18 patients. Studies to further document quality of life are underway and will be reported elsewhere.

Our data suggest that outpatient and at home management of aplastic phase recovery following high dose chemotherapy with stem-cell rescue for both breast cancer and lymphoma patients is feasible. Discharge was possible the day after transplant in a majority of cases. Unscheduled consultations and readmissions, mostly for fever, were frequent in the home care cohort that was scheduled to come to the outpatient clinic only once weekly. In spite of this, patients spent most of the aplastic period following stem-cell reinfusion at home.

Home erythrocyte transfusions occurred 55 times, and were not associated with an increase in transfusion reactions or fever. The suggestion that home blood transfusion therapy, in a well-defined program with adequate practical guidelines, is a safe procedure confirms the findings of
At home supportive care after stem-cell transport

others although most reports were generated in the palliative setting.\textsuperscript{17,18} Although 42 platelet transfusions were safely administered in the home setting, the one patient with a serious adverse reaction convinced us once more of the necessity of delivering platelets in the presence of well instructed personnel only, as described in the methods section. Administration of clemastine, prednisone and if necessary adrenaline could in case of emergency be carried out by the professional home care nurses present at every platelet transfusion. We therefore saw no reason to change the protocol after the above reaction. Although minor urticarial reactions after platelet transfusions occurred twice at home, and both patients visited hospital at our request to check symptoms, no problems were encountered in subsequent transfusions after premedication with clemastine and prednisone.

The absence of infectious deaths in this population was reassuring. However, neutropenic fever occurred in a majority of cycles in all cohorts. In case of documented infection, the source was usually the central indwelling intravenous catheter, with \textit{S.epidermidis} as the causative agent. Also, a substantial proportion of patients developed colonization of the central venous catheter with coagulase negative \textit{Staphylococci}, especially in the outpatient and home care cohorts. We propose that this is the result of the increased number of times new catheter connections had to be established in patients who were not hospitalized. In hospitalized patients, a continuous intravenous infusion is often kept up for practical purposes. Fortunately, this did not lead to prolonged fever episodes or systemic antibiotics in the home care and outpatient cohorts.

Even though no systemic yeast infections occurred, the relatively frequent incidence of itraconazole-resistant yeast in surveillance stool cultures and throat swabs made us reconsider our prophylactic regimen. Subsequently, oral amfotericin suspension was substituted for itraconazole for all transplant patients.

In this feasibility study, no unexpected emergencies were encountered, and toxicity did not seem different from the full hospitalization schedule during the aplastic period. It should be noted that the success of our approach is probably also the result of selection of transplant regimens that do not produce severe mucositis. This side effect would very likely preclude the simple at home management (without continuous parenteral fluids) that we have piloted in our patients.

Because the allocation of different types of management was convenience-related rather than in any way random, a direct comparison of outcome or economic effects was not performed.

In conclusion, through the cooperation with home care professionals and insurance companies, it was feasible to take the outpatient approach one step further to the home situation than previously reported. We have not had to compromise on patient safety and have gained on quality of life and improved the allocation of available hospital beds. More study is necessary to determine the economic consequences of further expansion of home treatment to other patient groups.
References


