patients with overt interaction have been described, previous studies have not definitely excluded a possible interference of vancomycin with oral anticoagulants.[3] As with other drugs, the mechanism responsible for the teicoplanin-warfarin interaction in our patient is probably represented by an increase of warfarin clearance.[4,5] In view of this report, we recommend strictly monitoring the INR value when administering teicoplanin to patients who are adequately anticoagulated.

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Early autologous stem cell transplantation in Hodgkin disease in partial remission or in relapse

Sir,

With MOPP/ABVD like protocols, is possible to achieve a 70-80% cure rate in patients with different stages of Hodgkin's disease (HD). Prognosis is still poor for patients who never achieve a complete remission (CR) or relapse within one year, or for patients who are in resistant relapse.[1,2]

The poor therapeutic results observed in such patients treated with standard chemotherapy suggested investigating the alternatives for intensive treatment, such as high-dose chemotherapy (HDC) and autologous stem cell transplantation (ASCT). Several HDC regimens like CBV (CPM + BCNU + VP16), BEAM (BCNU + VP16 + ARA-C and melphalan), BEAC (BCNU + VP16 + ARA-C + CPM), or CPM ± VP16 + TBI etc. are currently employed with HD patients. The cure rate is extremely low (10-15%) when HDC and ASCT are delayed, resulting in an increasing drug resistance. Better results are obtained if patients are grafted early on in the first relapse or in significant partial remission (sPR), with 30-50% of continuous CR.[3-5]

This report concerns 31 patients with HD in partial remission (PR) or in relapse, treated with BEAM (19 pts), CBV (8 pts) and high-dose sequential chemotherapy (HDS) (4 pts), with bone marrow (ABMT) in 21 subjects (67.7%) and peripheral blood stem cell (PBSCT) rescue in 10 (32.3%). Twenty patients (64.5%) were treated in PR or significant PR (sPR>=70%), 9 (29.1%) were treated in relapse and 2 in refractory disease. The histology presented nodular sclerosis in 21 pts (67.7%), mixed cellularity in 9 (29.1%) patients and lymphocyte depletion in 1 (3.1%). The median age was 28.5 years (16-53). Stage III+IV was present in 24 pts (77.4%) and IIB with bulky disease (mediastinal or subdiaphragmatic) was present in 7 patients. B-symptoms in 23 subjects (74.2%), bulky disease (>10 cm) in 19 (61.3%), extranodal disease in 12 (38.7%), LDH >500 UI/L in 20 (64.5%) patients, β_2-microglobulin >2.5 mg/mL in 7 (22.6%) were the most frequent adverse prognostic factors at the time of diagnosis.

The CR rate was 71% (CR+PR=90.4%) and the median duration of CR was 15.2 months. No treatment-related deaths were

CR	2	71%
PR	6	19.4%
NR	3	9.7%
CR duration *(median)*	15.2 months	
Follow-up *(median)*	17 months	
Relapse	3	
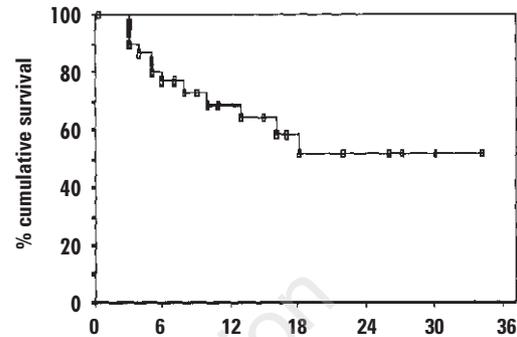
Figure 1. HDC and ASCT in 31 HD pts: response post-autograft and EFS.

reported, but Gram+ sepsis in six pts and grade 1 cardiotoxicity in 8 pts were documented. No difference in terms of response rate and median duration of CR was observed between the ABMT and PBSCT group. In the BSCT group, the median MNC reinfused was 3.2×10^8/kg; the median CD34+ CD38- cells was 28.8×10^6/kg and median CFU-GM was 135.5×10^4/kg. The median time to $\geq 0.5\times10^9$/L PMN following transplantations was 11 days in PBSC autografts and 13 days in the BM group. A platelet count $\geq 30\times10^9$/L was reached at day +9 for the PBSC group and at day +13 for the BM group. The median follow-up was at 17 months, and 24-months projected event-free survival from graft was 53% (Figure 1).

The knowledge that a survival rate at 5 years is about 30% in HD pts with more than three adverse prognostic factors, encouraged research regarding use of HDC and ASCT in the early phase of therapeutic approach, in the attempt of increasing survival and DFS. The treatment with several regimens of HDC followed by ABMT for relapsed or refractory HD achieved a response rate of about 50% with 20 to 30% of long-term DFS. Considering our group of patients (31), the median follow-up (17 months) and the median duration of CR (15,2 mths), our results confirm the possibility of achieving long-term EFS (53% at 24 months) and a high percentage of CR (71%) with ASCT in patients with advanced stage HD (77.4% of cases) and adverse prognostic factors (B-symptoms in 74.2%, bulky disease in 61.3%, elevated LDH in 64.5% of the cases).

ASCT has become a more and more frequent and safe procedure in HD patients and toxicity is very mild. This approach, in the early phase of a treatment plan, may be recommended for partial responders or early relapsing HD patients.[2] More investigative research, including prospective randomized trials, are needed in order to assess the efficacy of HDC and ASCT in treating patients with HD in PR or in relapse.[3-5]

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Probable ticlopidine-induced severe aplastic anemia and cholestatic hepatitis

Sir,

Ticlopidine is a thienopyridine derivative with platelet-inhibitor capability used to reduce the risk of stroke. The most common adverse effects are mild and transitory: diarrhea, nausea, dyspepsia and rashes. More serious side effects are less frequent; they include: neutropenia, thrombocytopenia, purpura and cholestatic hepatitis, whose pathogenesis is not fully understood.[1-3]

A 67-year-old man with no history of liver or hematological disease was admitted to the hospital on February 12, 1996. He had been suffering for ten days from acholia, choluria, fever, weakness and painless jaundice. His medical antecedents included chronic auricular fibrillation, hiatal hernia and duodenal ulcer with gastrointestinal bleeding. Treatment on admission consisted of digoxin, ciprofloxacine (for the last 3 days), occasionally acetaminophen and ticlopidine (250 mg po bid) for 69 days. The patient was markedly icteric, with 39°C fever and crepitation at both pulmonary bases. He had no abdominal tenderness and no palpable gallbladder or lymph nodes. The urine was dark brown and the stool was light. On admission, WBC count was 0.6×10^9/L (90% lymphocytes), hemoglobin 13 g/dL, platelets 79×10^9/L, reticulocytes 0%, ALAT 24 iu/L (5-40), γGT 321 iu/L (5-53), alkaline phosphatase 512 iu/L, bilirubin 18 mg/dL (conjugated 10 mg/dL) and abdominal ultrasound showed hepatomegalia, but no evidence of biliary obstruction. Coagulation tests, renal functions, immunoglobulin level, complement, autoantibodies and sucrose hemolytic tests were normal; viral screening was negative for AHV, BHV, CHV, HIV, CMV, and EBV; the bacterial blood cultures and parasitic investigation were negative as well. A chest x-ray displayed a minor cardiomegaly. The trephine biopsy showed a pattern of severe aplastic anemia with very hypoplastic cellularity and an absence of granulocyte, erythroid and megakaryocytic cells, presenting mainly mononuclear cells. On day 3 his blood cell counts were: 0.3×10^9/L (0% neutrophils), 9.4 g/dL hemoglobin, platelets 16×10^9/L and 0% reticulocytes. Our diagnosis was very severe aplastic anemia and intrahepatic cholestasis, probably due to ticlopidine. We suspended ticlopidine and began with empirical broad-spectrum iv antibiotic, antifungal agents, G-CSF (Linograstim®, Chugai-Rhone-Poulenc, 150 mcg/m²) isolation, transfusion and hydration. On the fifth day we started immunosuppressive therapy with ATG (Atgam® Upjohn, 15 mg/kg iv daily for 8 days). The clinical evolution was excellent: on the twelvth day WCB count was 5.7×10^9/L, platelets were 93×10^9/L, hemoglobin 9 g/dL, reticulocytes 32×10^9/L, bilirubin 3.7 mg/dL, alkaline phosphatase 402 iu/L and γGT 268 iv/L. All the analyses were normal after three weeks and on the fourteenth day, the patient was discharged. Sixty days later his tests were clinically and biologically normal.

In our study, we describe one of the first cases of the association of ticlopidine and severe aplastic anemia in addition to intrahepatic cholestasis. We believe the combination of general supportive and specific therapy probably determined the positive clinical evolution, as spontaneous normalization is usually observed within three to five weeks after suppression of ticlopidine.[4,5] We conclude that patients receiving ticlopidine should be monitored closely with a complete blood cell count and should be instructed to look for signs and symptoms of liver damage.

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Desferrioxamine in the treatment of myelodysplastic syndromes

Sir,

For many patients with myelodysplastic syndrome (MDS) refractory anemia is the main clinical problem. Unfortunately, only some patients benefit from treatment with hematopoietic growth factors.[1-3] Unresponsive individuals often have a high transfusion requirement and need iron chelation treatment. In some of these patients, desferrioxamine (DFO) has been reported to be effective not only as an iron-chelating agent but also in reducing the transfusion requirement.[4,5] In the last few years, we have treated three MDS patients with DFO. All three patients presented isolated anemia (see Table 1). All patients received 30 mg/kg of DFO three days per week, by subcutaneous infusion over a 12-hour period via a disposable infusor. No other medication was given. On each transfusion day, transfusion (of red cell concentrate, RCC) was given if Hb was below 9 g/dL; the transfusion requirement was estimated using the following formula:[4,5]

$$\frac{[(A \times BV + B \times 75) - (C \times BV)] \times 31}{D}$$

where A = pre-transfusional Hb (g/dL) at start of a transfusion episode; B = number of RCCs supplied on that day; C = pre-transfusion Hb at a subsequent transfusion episode; BV = blood volume; 75 = mean Hb content (g) in one RCC; D = number of days between A and C; and 31 = 31 days/month. The results are summarized in Table 1. Patients 1 and 2 showed steady improvement as regards both transfusion requirement and Hb concentration, and no longer needed transfusion after 12 and 15 months of treatment respectively. Patient 3 continued to require transfusions after 20 months of treatment. Serum ferritin levels did not decrease in patients 1 and 2.

The results for patients #1 and #2 show a reduction in transfusion requirement following DFO treatment, in accordance with previous reports.[4,5] These authors observed that the reduction in transfusion requirement correlated with the efficacy of iron chelation (as indicated by the reduction in the hepatic iron concentration), but not with the degree of attainment of normal iron stores.[5] In our patients, improvement was observed