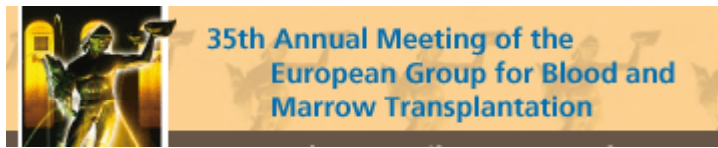


# EBMT 2009 MM Abstracts and Posters



29 March - 1 April 2009, Göteborg, Sweden

## Abstracts related to Myeloma

### Physicians Abstracts

O157

Post-transplant immunotherapy with donor-lymphocyte infusion and novel agents to upgrade partial into complete and molecular remission in allografted patients with multiple myeloma

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Several studies suggest that patients with multiple myeloma who achieved a complete or even a molecular remission after allogeneic stem cell transplantation enjoy prolonged disease-free survival. We investigated post-transplant immunotherapy with escalating donor-lymphocyte infusions (DLI) to target complete remission in 32 patients with multiple myeloma who achieved only partial remission after allogeneic stem cell transplantation. If no complete remission was achieved by DLI one of the novel agents (thalidomide, bortezomib, and lenalidomide) were added. CR defined either by EBMT-criteria, by flow-cytometry, or by molecular methods as assessed by patient specific IgH-PCR or plasma cell chimerism PCR was accomplished in 59%, 63%, and 50% of patients, respectively. Achievement of CR resulted in an improved five-year-progressive-free and overall survival according to EBMT criteria (53% vs. 35%;  $p=0.03$  and 90% vs. 62%  $p=0.06$ ), flow-cytometry (74% vs. 15%;  $p=0.001$  and 100% vs. 52%;  $p=0.1$ ), or molecular methods (84% vs. 38%;  $p=0.001$  and 100% vs. 71%;  $p=0.03$ ). Molecular CR was achieved in 47% with DLI or single novel agent alone, and in 40% with combination of DLI and novel agents, while in 13% DLI and two agents were required to obtain molecular CR. Our finding demonstrates the clinical relevance of post-transplant therapies to upgrade remission, and of remission's depth of for long-term survival in myeloma patients.

O158

Long-term follow-up of a comparison of non-myeloablative allografting with autografting for newly diagnosed myeloma

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We previously published a study where the treatment assignment of 162 newly diagnosed patients was based on the presence/absence of an HLA-identical sibling (Bruno et al, N Engl J Med). First-line treatment plans included a cytoreductive autograft followed by a nonmyeloablative allograft (Tandem auto-allo) or a second melphalan-based autograft (Doubleauto). Primary endpoints were overall (OS) and event-free (EFS) survivals by intention-to-treat analysis. The 80 patients with a sibling donor were offered a Tandem auto-allo and the 82 without a Double-auto after high (140-200 mg/m<sup>2</sup>) or intermediate dose melphalan (100 mg/m<sup>2</sup>). Importantly, neither induction or maintenance therapies with so-called “new drugs” were part of the treatment protocol. First statistical analyses were carried out at a median follow up of 45 (range 21-90) months, OS and EFS were significantly longer in patients with donors: 80 versus 54 months (p=0.01) and 35 versus 29 months (p=0.02). Median OS was not reached in the 58 (out of 60 enrolled, 97%) patients who completed Tandem auto-allo and was 58 months in the 46 (out of 59 enrolled, 78%) who completed high-dose doubleauto (p=0.03).

Here, we report an update at a median follow up of 6 years: OS was not reached for the 80 patients with an HLA-identical sibling and was 52 months for those without (HR 0.53, CI 95% 0.34-0.81, p=0.004). EFS remained significantly longer in patients with HLA-identical siblings: 35 versus 29 months (HR: 0.63; 95% CI: 0.44-0.89, p=0.009). Median OS was not reached in the 58 patients who completed Tandem auto-allo and was 64 months in the 46 who completed high-dose double-auto (HR 0.54, CI 95% 0.31-0.96, p=0.04). EFS was 37 and 33 months (HR 0.65, CI 95% 0.41-1.02, p=0.06).

After a median follow-up of 75 months, Attal et al. (N Engl J Med) reported median OS of 48 and 58 months after one and two autologous transplants respectively. EFS of the entire cohort was 30 months. These data are consistent with our results (OS: 63 months; EFS: 33 months). We can safely conclude that Tandem auto-allo allow better clinical outcomes than

standard Double-auto.

We point out, however, that Double-auto is not universally regarded as “standard therapy” since the introduction of new agents such as bortezomib and lenalidomide. Thus, it is imperative to thoroughly explore their roles in the setting of allografting and compare clinical outcomes with those obtained with new drugs with/without autografting.

#### O159

#### Bortezomib induction prior to reduced-intensity autologous transplantation followed by lenalidomide consolidation/maintenance in elderly untreated myeloma patients

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Background and objectives: Bortezomib and lenalidomide have shown significant antitumor activity in clinical studies. In this phase II, single-arm, multicenter study we evaluate a sequential approach with bortezomib as induction prior to autologous transplant, followed by lenalidomide as consolidation/maintenance. Primary endpoints were safety (incidence of grade 3-4 adverse events) and efficacy (response rate).

Methods: Newly diagnosed multiple myeloma (MM) patients, aged 65-75 years, were eligible. The induction included four 21-day cycles of bortezomib (1.3 mg/m<sup>2</sup> days 1,4,8,11), pegylated liposomal doxorubicin (30 mg/m<sup>2</sup> day 4) and dexamethasone (40 mg: days 1-4, 8-11, 15-18, cycle 1; days 1-4, cycles 2 to 4) (PAD). Autologous transplant was tandem Melphalan 100 mg/m<sup>2</sup> and stem-cell support (MEL100). Consolidation included four 28-day cycles of lenalidomide (25 mg/day days 1-21) plus prednisone (50 mg every other day) (LP) and was followed by maintenance with lenalidomide alone (10 mg/day days 1-21 every 28 days) (L) until relapse.

Results: One-hundred and two pts have been enrolled. After induction with PAD, 58.8% of patients achieved at least at least very good partial response (VGPR), including 12.7% complete response (CR). After MEL100, 87.0% achieved at least VGPR and 42.9% CR. After LP/L consolidation/maintenance, 95.0% of patients achieved at least VGPR rate and 72.5% CR. In all patients, 3-year progression-free and overall survival rates were 73.7% and 84.6%, respectively. Patients aged < 70 years showed longer 3-year PFS than patients aged over 70 (P=0.05). There

were no significant differences in 3-years PFS of patients presenting with del(17) or t(4;14) or t(14;16) compared to patients who did not show any of these abnormalities (P=0.5). During PAD induction, grade 3-4 adverse events included thrombocytopenia (16.7%), neutropenia (9.8%), peripheral neuropathy (15.7%), and pneumonia (12.8%). During LP consolidation grade 3-4 adverse events were neutropenia (16.1%), infections (10.7%) and cutaneous toxicity (7.14%). The other grade 3-4 toxicities and all the toxicity during maintenance occurred in no more than 5% of patients. Conclusion: Bortezomib as induction before transplantation, followed by lenalidomide as consolidation /maintenance induced a high response rate. Further evaluation of this promising sequential regimen is warranted in newly diagnosed disease.

#### O160

##### Allogeneic stem cell transplantation for multiple myeloma with a T-cell depleted reduced-intensity conditioning regimen using both unrelated and related donors

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In multiple myeloma, myeloablative alloSCT studies have shown that potentially curative effects are offset by high mortality due to infections and GvHD. Reduced intensity conditioning (RIC) regimens may improve survival by reducing transplant related mortality (TRM).

In Leiden a RIC regimen consisting of fludarabine, busulphan and ATG is used combined with T cell depletion of the graft with alemtuzumab. Donor lymphocytes are infused after 6-9 months in case of residual myeloma or mixed bone marrow chimerism. Between 2002 and 2007, we transplanted 15 patients with a related and 13 patients with an unrelated donor (median age of 52 years, range 36-61). Seventy five percent of patients were transplanted for relapsed disease, 25% directly following initial induction chemotherapy and autologous SCT. Disease status at transplantation was: 8% PD, 23% SD, 35% PR, 11% VGPR, 23% CR.

TRM was 11% (related donor 7%, unrelated donor 15%). All patients alive at 6-9 months (n=23) showed mixed chimerism for which donor lymphocyte infusion (DLI) was given. In the unrelated group all patients and in the related group 81% of patients converted to full donor chimerism. Of the patients with measurable disease at the time of DLI, 88% showed a complete response in the unrelated group as opposed to 28% in the related group. Acute GvHD was observed in 67% of patients transplanted with an unrelated (33% grade 3-4) and 36% of patients transplanted with a related donor (9% grade 3-4). One patient died from acute GvHD. Chronic GvHD developed in 81% of patients in the unrelated group (63% limited, 18% extensive) and 27% of patients in the related group (18%

limited, 9% extensive). Chronic GvHD resolved in most patients within a few months, one patient died from extensive chronic GvHD. Only two patients have ongoing limited chronic GvHD. In the related group 6 patients died from relapse, in the unrelated group only one.

With a median follow up time of 2.3 years, overall survival in this group of patients transplanted mainly with relapsed disease and mostly not in remission is 76% in the unrelated and 40% in the related group ( $p=0.11$ ).

In conclusion, T cell depleted RIC alloSCT for myeloma results in limited TRM and hardly any persisting GvHD. Complete antimyeloma responses can be induced with DLI, especially in patients transplanted with an unrelated donor. There is a trend towards a better survival in patients transplanted with an unrelated donor compared to a related donor.

#### O161

##### Impact of genetic abnormalities after allogeneic stem cell transplantation in multiple myeloma: report of the Société Française de Greffe de Moelle et de Thérapie Cellulaire (SFGM-TC)

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Background and aim: Del (13q), t (4;14) and del (17p) are wellrecognized poor prognostic genetic abnormalities in multiple myeloma after standard chemotherapy and autologous stem cell transplantation (SCT). We investigated the impact of these genetic abnormalities, detected by fluorescence in situ hybridization (FISH), on the outcome of patients who underwent allogeneic SCT, in a retrospective study of the SFGM-TC.

Patients and methods: Data were collected from 15 centers for a total of 160 patients. The median age of the population at diagnostic was 52 years (range, 30-64 years). Most patients had advanced myeloma: beta2microglobuline was > to 4 mg/L in 48% and more than 90% had received at least one autologous SCT. The median time from diagnostic to allogeneic transplantation was 14 months (range, 4-175 months).

Chromosomal abnormalities were found in 117 of 160 patients

(73%), distributed as follows (in percent of patients analyzed for the abnormality): 61% for del (13q), 24% for t (4;14), 26% for del (17p), 24% for t (11;14) and 4% for t (14;16). Seventy three percent of patients received a reduced intensity conditioning regimen; the source of stem cells was peripheral blood in 79% of patients and 69% of donors were HLA-identical siblings. Results: With a median follow-up of 20 months, the 2-year progression, progression free survival (PFS) and overall survival (OS) were respectively 51%, 34% and 57%. One-year transplant-related mortality was 21%. Grade II to IV acute graft-versus-host disease (GvHD) was present in 34%. Limited and extensive chronic GvHD occurred respectively in 28% and 32% of evaluable patients. In univariate analysis, the del (13q), t (4;14) and del (17p) had no impact on PFS (2y PFS: 36% for del (13q) versus 32% for non-del (13q) (P=0.35); 36% for del (17p) versus 21% for non-del (17p) (P=0.89); 20% for t (4;14) versus 34% for non-t (4;14) (P=0.37)). Better PFS was associated with younger age at transplant (P=0.04), chemo sensitive disease at transplant (P=0.02) and a short delay from diagnostic to transplant (P=0.02). In multivariate analysis, the diagnosis-transplant interval was the only factor associated with better PFS (P=0.017, OR: 1.6, CI 1.1-2.4).

Conclusion: These data suggest no impact of genetic abnormalities after allogeneic SCT for multiple myeloma. Contrary to published data (Schilling et al., Leukemia, 2008), multiple myeloma with t (4;14) does not seem to benefit from allogeneic SCT.

#### O162

High-dose therapy/autologous stem cell transplantation increases complete remission rate in multiple myeloma irrespective of the induction regimen used: TD (Thalidomide/dexamethasone), VTD (bortezomib/thalidomide/dexamethasone) or VBMCP/VBAD plus bortezomib

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Background: The benefit of autologous stem cell transplantation

(ASCT) in multiple myeloma (MM) is associated with the degree of tumour decrease with the initial induction chemotherapy. In April 2006, the Spanish Myeloma Group (PETHEMA/GEM) activated a phase III trial comparing TD vs. VTD vs. VBMCP/VBAD/Velcade in patients 65 years-old or younger with newly diagnosed MM, followed by ASCT with MEL-200.

Aim: response rate after induction and after ASCT.

Patients and Methods: TD consisted of thalidomide 200 mg daily and dexamethasone 40 mg on days 1-4 and 9-12 at 4-week intervals for 6 cycles. The VTD regimen was identical to TD plus Velcade 1.3 mg/m<sup>2</sup> on days 1,4,8,11 of each cycle. Combination chemotherapy plus Velcade consisted of 4 cycles of VBMCP/VBAD followed by 2 cycles of Velcade.

Results: As of February 15, 2008, 190 patients (median age: 57 yrs., M:96, F:94; IgG:107, IgA:50, light chain:25, others: 9) entered the study. 29 (16%) patients had soft-tissue cytogenetics, were similar in the 3 arms. 183 patients (TD:63, VTD:56 and VBMCP/VBAD/Velcade:64) were evaluable for response and toxicity to induction therapy. The PR rate was 66%, 80% and 72% with TD, VTD and VBMCP/VBAD/Velcade, respectively (p=NS). The CR rate was significantly higher with VTD (30% vs. 6%, p=0.0006) and with VBMCP/VBAD/Velcade (20% vs. 6%, p= 0.01) compared to TD. Progressive disease was significantly higher in patients with EMP (34% vs. 11%, p=0.03). This higher PD rate was similar in the three arms. In patients with poor cytogenetics t(4;14), t(14;16), del(17p) there was a trend towards a higher response rate with VTD than with the two others arms (79% vs 45%, p=0.09). The incidence of = grade 3 thrombotic events was higher in the TD arm (13% vs 1.7% and 5%, p=0.02) while = grade 3 peripheral neuropathy was higher with VTD (16% vs. 0% and 1.5%, p=0.005). 102 patients were evaluable for response after ASCT. The post-ASCT CR rate were higher with VTD (49%) and with VBMCP/VBAD/Velcade (43%) compared to the TD arm (34%) although the difference did not reach statistical significance.

Conclusions: Our preliminary analysis shows that:

- 1) VTD and VBMCP/VBAD plus Velcade result in a higher CR rate than TD,
- 2) in patients with poor cytogenetics there is a trend towards a higher response rate with VTD,
- 3) intensification with ASCT increases the CR rate in 28%, 19% and 23% in the TD, VTD and VBMCP/VBAD/Velcade arms, respectively.

O163

Autologous stem cell transplantation in elderly patients with multiple myeloma: age per se does not affect outcome

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Autologous stem cell transplantation (auto-SCT) is an effective therapy for multiple myeloma (MM) patients that can provide superior outcome to standard treatments. Since its introduction, auto-SCT has usually been limited to MM patients aged up to 60-65 years. This retrospective single centre analysis assessed the outcome of 186 consecutive MM patients aged over 60 y. treated with auto-SCT, with the specific aim to compare the outcome of the 82 “elderly” (age>65 y.) patients subgroup, with their 104 “younger” mates aged between 60 and 65 years treated in the same period and in the same auto-SCT program. Median age among the total 186 patients population was 64 (range, 60-77). Except for age, both groups were comparable (P=NS). The majority of patients (91%) received homogeneous “induction” VAD chemotherapy, with this being comparable between the “elderly” (87%) and “younger” (94%) group. In this population, and prior to auto-SCT, the comorbidity index was also comparable between both groups (77% of the “younger” patients with a 0-1 index, vs. 74% in the “elderly” group; P=NS; 97% of the patients received high-dose melphalan conditioning for auto-SCT. 33% of the “younger” and 28% of the “older” group (P=NS) completed a second auto-SCT. ANC and platelets recovery, the median length of hospitalization for the first auto-SCT, infectious and other serious auto-SCT-related complications were comparable between both groups (P=NS); With a median follow-up of 41 (range, 5-227) months after auto-SCT, 120 patients are still alive. Disease progression (n=40; 61%) was the main cause of death. Auto-SCT-related mortality was 3.8% (n=4/104) in “younger” and 3.7% (n=3/82) among “older” subjects. Disease response rate after the first auto-SCT was comparable (CR, VGPR and PR rates: 88% vs. 90%, P=NS), and overall survival (OS) was also comparable (57% vs. 54% at 5 years, P=NS; 32% vs. 24% at 10 years, P=NS). In a Cox multivariate analysis model, none of the relevant characteristics was shown to be a critical prognostic features for OS. Of note, age was insignificant for both OS and transplant-related mortality. We conclude that there is no biological justification for an age-discriminant policy for MM therapy. “Physiologic” aging is likely more important than “chronologic” aging. Thus, all treatment options, including auto-SCT in the “elderly” population, must be rigorously evaluated, as age does not appear to be an adverse parameter for selected MM patients receiving high-dose melphalan therapy with peripheral blood stem cell support.

## Physicians Poster Sessions

P585

### Lenalidomide therapy increases the frequency of activated T- and NK-cells in patients with relapsed multiple myeloma following allogeneic stem cells transplantation

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Recent data suggest the significant success of lenalidomide therapy in patients with multiple myeloma (MM) who show relapse after allogeneic stem cells transplantation (allo-SCT). This might be explained by its immunostimulatory properties. The ability of lenalidomide to enhance natural killer (NK) cells and to stimulate cytotoxic activity of T-lymphocytes was shown in vitro and in murine models but however has not been systematically addressed in patients with MM.

In this study we performed analysis of cellular immune response in eight MM patients (7 males and 1 females; median age: 54,3 years, range: 39-68) who relapsed  $\approx$ 6 months (median: 19,6 month, range: 6-81) after allo-SCT and were treated with lenalidomide. Lenalidomide was administered for 21 days at 10-25 mg/day, followed by 1 week interruption. Peripheral blood samples were collected before and during lenalidomide therapy at two time-points: (i) between day 30 and 60 and (ii) between day 90 and 120 after start of treatment). Using cell counting and four-colour multiparameter flow cytometry (MFC) the following parameters were determined: the number of white blood cells (WBC) and lymphocyte (Ly) per  $\mu$ l whole blood; frequency of T (CD3+), CD3+CD4+, CD3+CD8+, activated T (CD3+HLA-DR+), T-regulatory (CD4+CD25+CD127lo) and NK (CD3-CD56+) cells in common lymphocyte population and representation of different surface receptors (CD94, CD158a/h, CD158b, CD158e, CD226, NKp30, NKp44, NKp46) on the NK cell membrane.

There were no significant changes of WBC numbers, frequency of T-, CD3+CD4+, CD3+CD8+, or NK cells, and the expression of all investigated NK-cells surface markers (except NKp44) during lenalidomide therapy (Student's t-test) (Table 1). In contrast, the number of Ly ( $p=0.012$ ; Fig. 1, A), the frequency of activated ( $p=0.0048$ ; Fig. 1, B), and regulatory ( $p=0.036$ ; Fig. 1, C) T-cells as well as of activated NK-cells (NKp44+) ( $p=0.0008$ ; Fig. 1, D) were significantly increased under lenalidomide.

These data suggest for the first time that lenalidomide may not only enhance the number of common lymphocyte population, but also significantly increases the frequency of activated T- and NK-cells in peripheral blood of MM patients after allo-SCT. This immunostimulatory effect seems to be an important mechanism for antimyelomatous activity of lenalidomide.

P586

Thalidomide + dexamethasone as maintenance after single autologous stem cell transplantation improves progression-free survival in advanced multiple myeloma. A prospective Brazilian randomised trial

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Introduction: Autologous stem cell transplantation (ASCT) remains the mainstay of treatment of multiple myeloma (MM) in patients <65 years old. However, most patients relapse after ASCT suggesting that additional treatment is needed. The Brazilian Multiple Myeloma Group designed a study to evaluate the impact of thalidomide maintenance after ASCT.

Methods: From October 2003 to July 2008, 212 untreated patients <70 years old were enrolled in a prospective randomized multicenter study. All patients signed an informed consent and the protocol was approved by the Ethical Committees of each center. The treatment consisted of 3 phases: (1) induction with 3-5 cycles of VAD; (2) high-dose cyclophosphamide (4g/m<sup>2</sup>) plus G-CSF for stem cell mobilization; (3) melphalan 200 mg/m<sup>2</sup> and ASCT. On day +60 post ASCT patients were randomized to receive dexamethasone (40 mg/d x 4 days every 28 days) with (arm A) or without (arm B) thalidomide (200 mg daily) for 12 months or until disease progression.

Results: The median age was 55 years (27-70), 52% were male, the median serum beta-2 microglobulin was 3.66 mg/dl, 33% were ISS stage 3, 36% were ISS stage 2 and 24% had deletion of chromosome 13. In July of 2008, 93 patients (44%) were randomized: 54 in arm A and 39 in arm B. Reasons for nonrandomization were: treatment related deaths during phases

1-3 (n= 39), disease progression (n= 22), ineligible or refused ASCT (n= 7), SMD after ASCT (n= 1), protocol violation (n= 3), abandoned (n= 19), and still in phases 1-3 (n= 28). Clinical characteristics of each group were similar. The median followup from diagnosis was 15 months. Progression-free survival (PFS) in arms A and B were 42% (95% confidence interval [CI] 22-62) and 25% (95% CI 5-45), p= 0.07. A multivariate analysis that included baseline serum beta-2-microglobulin and deletion of chromosome 13 showed that maintenance with thalidomide was significantly associated with better PFS (hazard ratio 2.43, 95% CI 1.10-5.35, p=0.03). Overall survival was 65% in arm A (95% CI 35-95) and 74% in arm B (95% CI 44-100), p= NS.

Conclusions: A high proportion of MM in Brazil has advanced disease at diagnosis, and this explains the high number of

patients who did not reach the maintenance phase. This study shows that the addition of thalidomide to dexamethasone improves PFS after a single ASCT.

#### P587

#### Application of the propensity score matching method to the estimation of survival benefit of non-myeloablative allogeneic transplantation in patients with multiple myeloma relapsing after a first autologous transplantation

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Despite recent advances, Multiple Myeloma (MM) is still an incurable disease with a poor prognosis at relapse. The use of conventional allogeneic hematopoietic stem cell transplantation (SCT) is limited by a high transplantation-related mortality (TRM). Allografting with nonmyeloablative conditioning (NMA-C) has therefore been considered to improve survival. We retrospectively studied a series of 23 patients with relapsing MM who underwent allogeneic transplantation after NMAC and compared their outcome with those of patients who relapsed but were not allografted. The propensity score (PS) methodology was used to correct for potential recruitment bias. The idea was to model, for each patient with MM alive at 6 months after relapse, the probability of receiving NMA-C transplantation, according to a set of baseline characteristics (age, serum beta2 microglobulin level (beta2M), and time to progression (TTP) after the first autologous SCT). This PS was estimated using logistic regression and was then used to match 1:1 patients with similar propensity to receive allograft. Data of patients treated in the MAG-95 and -02 trials were used. Twenty-three patients with MM in first (n=21) or second (n=2) relapse were treated with high dose therapy followed by Autologous SCT preceding allogeneic SCT with a 2 Gy TBI NMAC. Donors were HLA-identical siblings in 13 (56%) patients. Median age at allograft was 50 years. Median follow-up after allograft was 27.4 months. Post-allograft response was CR in 9 patients, VGPR in 8, PR in 4 and progressive disease (PD) in 2. TRM at one year was 13%. Two patients died from PD in the year after allograft. Acute GvHD occurred in 19 patients (15 grade I/II, 4 grade III/IV) and chronic GvHD in 11. Among the 10 patients (41.6%) who relapsed with a median of 10,7 months, 6 are alive with a median survival of 38.3 months. So far, 8 patients (34,7%) including 5 in CR and 3 in VGPR are still alive without relapse with a median follow-up of 36.8 months. From the 23 allografted patients, 21 matched pairs were successfully constituted. Based on these matched pairs, the estimated hazard ratio of death was 0.35 (95% confidence interval: 0.14-0.88, p=0.027) for allografted patients compared with non allografted. In conclusion, PS matching method here suggests

that NMA-C allograft in MM patients in first relapse provides a high and durable response rate with a low TRM. These promising results must be further evaluated in clinical trials.

P588

Outcomes in patients with multiple myeloma following autologous stem cell transplantation using intravenous busulfan and melphalan: a matched comparison to a double autologous transplant strategy conditioned with melphalan and CBV

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Introduction: In multiple myeloma (MM) we have reported a high response rate with a novel conditioning regimen using intravenous busulfan and melphalan (ivBuMel). We present results of a retrospective matched-pair analysis comparing outcomes of MM patients transplanted using the ivBu-Mel conditioning regimen with matched controls receiving an autologous hematopoietic stem cell transplant (ASCT) after standard melphalan followed by a second ASCT for patients not achieving complete remission (CR) after the first transplant (Control group).

Material and Methods: Forty three cases and 86 matched controls were available for comparison. Patients in the Control group were transplanted from 2002 to 2005, while patients in the ivBuMel group underwent transplant between 2005 and 2008.

Controls were selected to match on sex, age, Durie-Salmon and ISS stage at diagnosis, and disease status at transplant. ivBuMel conditioning regimen consisted of a single dose of 3.2 mg/kg (days -5 to -3) followed by Mel at a dose of 140 mg/m<sup>2</sup> (day -2). Standard melphalan 200 mg/m<sup>2</sup> was the conditioning regimen administered to the Control group in the first ASCT.

The preparative regimen administered to those patients in the Control group undergoing a second transplant consisted of cyclophosphamide, BCNU and etoposide (CBV).

Results: There were no differences in the hematopoietic recovery and mild or moderate mucositis was the toxicity most frequently observed in both groups. Fever was seen in 35 cases

in the ivBuMel group and in 66 cases in the Control group, (p = NS). No patient developed sinusoidal occlusive syndrome.

Two patients died due to transplant-related complications in the ivBuMel group and 1 in the Control group. Overall, 14 (16%) patients in the Control group underwent the planned second ASCT. After ASCT, 49% of patients were in complete remission in the ivBuMel group vs. 51% in the controls. Thirty-months overall and progression free survival was 79±8% and 47±1% in the ivBuMel and 74±5% and 46±1% in the Control group, respectively.

Conclusions: These results suggest that the use of ivBu-based regimen for ASCT in patients with MM is a well tolerated conditioning regimen associated with a low transplant-related morbidity and mortality that compares favourably with a double transplant strategy with melphalan and CBV. Further follow-up is necessary to ascertain whether ivBu will favourably influence time to progression and overall survival.

P589

Effect of plerixafor plus G-CSF on tumour cell mobilisation in patients with multiple myeloma

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Tumor cell mobilization (TCM) can occur following G-CSF (G) mobilization of hematopoietic stem cells (HSC), as well as other mobilization methods such as chemotherapy. Given that plerixafor is administered in combination with G to enhance HSC mobilization, it is important to understand whether or not plerixafor results in TCM at levels above that observed with G alone. The purpose of this report is to assess the effect of plerixafor plus G on TCM in patients with multiple myeloma (MM) enrolled in EU 21.

EU21 was a Phase II study in patients with MM and non-Hodgkin's lymphoma (NHL) which examined the safety and preliminary efficacy of plerixafor when given in combination with G.

Thirty-five patients (31 MM and 4 NHL) received a mobilizing regimen of G (10 mcg/kg) each morning for 4 days. Starting the evening of Day 4, patients received plerixafor 240 mcg/kg. Apheresis was initiated in the morning, 10 to 11 hours following the dose of plerixafor. Tumor cell mobilization was evaluated using a very sensitive polymerase chain reaction (PCR)-based technique in a sub-population of 7 patients with MM. Patient bone marrow (BM) samples were collected to establish the primer for the PCR assay. Patient BM and peripheral blood (PB) samples were collected at three time points to assess TCM: screening (pre-G), after G treatment but before plerixafor, and following G and plerixafor. Quantitative allele specific oligonucleotide PCR was performed to detect and assess the mobilization of MM tumor cells for each patient at all three time points. This result was then used to calculate the frequency of tumor cells compared to total peripheral blood mononuclear cells (PBMCs).

In the overall patient population, all patients collected =  $2 \times 10^6$  CD34+ cells/kg. Following treatment with G alone, just prior to administering plerixafor, mobilization of tumor cells was detected with a minimum of  $9.70 \times 10^{-6}$  and a maximum of  $1.38 \times 10^{-3}$  tumor cells per total PBMC. After plerixafor treatment, 3/7 patients had a small increase and 4/7 patients a small decrease in PB tumor cells. The observed fold increase in tumor cells from before plerixafor administration to pre-apheresis ranged from

0.11 fold to 1.08-fold.

In a sub-group analysis, plerixafor did not appear to contribute to TCM above that which occurs with G mobilization alone. These findings are consistent with other phase II clinical studies, which reported negligible TCM after plerixafor treatment.

#### P590

##### Outpatient stem cell transplantation for multiple myeloma

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Introduction: The aim of this study was to explore the feasibility and safety of performing autologous stem cell transplantation (ASCT) on an outpatient basis.

Methods: Total of 134 patients affected by multiple myeloma (MM) in complete remission (CR) or partial remission (PR) were selected to receive ASCT on an outpatient or inpatient basis. Our analysis consist of 100 patients. Median age was 50.2 years (ranged 27-68) with 70% male. In the inpatient group 34 patients received 200 mg/m<sup>2</sup> and 21 patients received 140 mg/m<sup>2</sup> melphalan as conditioning regimen respectively. In outpatient group 13 patients received 140 mg/m<sup>2</sup> and 32 patients received 200 mg/m<sup>2</sup> melphalan. In outpatient group all the patients were programmed to go home the day after ASCT and to be re-hospitalized in the case of febrile neutropenia or other sever toxicities. We used caregiver, general physician, staff nurse as an outpatient and visit team and also unequipped routine house of the patients during neutropenia.

Results: Median hospital stay were 25 days in inpatient and 4.8 days in outpatient respectively (p<0.01). There were not significant differences between these groups in apheresis days, granulocyte colony stimulating factor requirement for mobilization and mononuclear cell, There were also significant reduction (p<0.001) in parenteral antibiotic, blood product requirement and need for total parenteral nutrition. The most frequent causes of re-admission in 6 patients (outpatient group) were febrile neutropenia and sever mucositis need TPN. 2 years overall survival rate was 98.2% (SE=2%) in inpatient groups and 86.6% (SE=5.7) in outpatient groups.

Conclusion: The ease of administration of high dose melphalan as well as the lack of excessive extramedullary toxicity including nausea and vomiting renders patients with MM more suitable for outpatient management, in the present study, we describe an outpatient program based on management of the patient in his/her house during aplastic phase. Our results clearly indicate that such a procedure is feasible and safe in a patient population with an assessable caregiver.

P591

Detrimental effect of platelet contamination on the quality of stem cells products collected to autograft patients with multiple myeloma

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Patients with Multiple Myeloma (MM) in our institution receive Velcade and Dexamethasone (VD) for induction and are then consolidated with high dose melphalan followed by one or two autografts according to the IFM protocols.

We monitor the ratio CFUGM 104/ CD34 106/Kg (sup 8) in all apheresis products as an indicator of quality for the graft. In recent months, we were alarmed by several unexpected low ratios (< 5) which led us to cancel the graft procedure and initiate new aphereses.

We retrospectively studied the quality of the apheresis products in relation to the induction treatment VD or VAD (vincristine, adryamycine and Dexamethasone) and the mobilisation procedure Cyclophosphamide (CY) (4g/m<sup>2</sup>) plus growth factor (GF).

We focussed on the leukaphereses (LK) in the different groups with a ratio CFUGM 104/ CD34 106/kg under 5.

Patients and methods: 114 MM treated between the years 2000-2006 at Hopital Saint-Antoine Paris were analyzed..

Three groups were identified: group 1 (CY and GF) – Group 2 (VAD and 5 days GF) – Group 3 (VD and 5 days GF). During this period the procedure to harvest cells was not modified and performed on a Spectra equipment (Gambro BCT).

Results (median): Group 1/2/3. Number of patients 47/29/38. Number of LK : 73/59/79. Granular cells % 44.5/21/29. Total granular cells per LK : 149.5/91.13/143.63. CD34 106/Kg/LK: 2.81/3.37/2.70. Total CD34 106/mobilization: 6.76/8.21/7.69. Ratio CFUGM/CD34: 9.53/9.55/8.24. Platelet 1011/LK: 2.28/5.71/5.56.

Patients presenting a Low ratio (<5) were identified in each group: number of patients: 3/1/8. ratio: 1.72/3.85/3.27. platelets 1011/LK: 6.40/8.62/9.19. Stored overnight before freezing LK: 2/1/8.

Conclusions: Leukapheresis products with a very low ratio are highly contaminated with platelets. The overnight storage at 4°C of such a quantity of platelets in a small volume may induce various damages, such as modification of the cell oxygen metabolism and diminution of pH . We recommend harvesting and freezing the MM apheresis products the same day, especially for patients under VD who have a higher level of platelets before harvesting.

P592

Is there a curative potential of autologous stem cell transplantation in multiple myeloma? Long-term results from a single-centre series

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Background: Autologous stem cell transplant (ASCT) is the gold standard in the upfront therapy of younger patients with multiple myeloma (MM). It is considered that ASCT is not curative. However, Barlogie et al (Br J Haematol 2006;135:158) reported that 16 out of the 231 (7%) patients enrolled in the Total Therapy I, including tandem ASCT, were in continued CR after a median follow-up of 12 years, suggesting a possible cure.

Objective: To report the long-term outcome of patients who underwent a single ASCT at our institution.

Patients and Methods: From March 31st 1994 to December 31st 2003, 95 patients (median age: 54 yrs; M: 57, F: 38; IgG: 55, IgA: 21, light chain: 15, others: 4) underwent a single ASCT at our institution and had a minimum possible follow-up of 5 years. The initial chemotherapy treatment consisted of VBMCP/VBAD (40 patients), VCMP/VBAP (15 patients), VAD (11 patients), others (27 patients). Sixty-seven patients received the ASCT as intensification of an initial response (upfront group) while in 28 the ASCT was performed for relapsed or refractory disease (relapse/refractory group). The high-dose regimens consisted of: MEL-200 (49 patients), MEL140-TBI (31 patients) and Busulphan-12/MEL-140 (BU/MEL) (15 patients). Response, relapse and progression were evaluated according to the EBMT criteria.

Results: The response after ASCT was: CR (31%), PR (63%), MR (2%), SD or PD (3%). The median time to progression (TTP) from transplant was 30 months (40 vs. 17 months for the upfront and the relapsed/refractory groups, respectively,  $p = 0.01$ ) and the median overall survival (OS) 59 months (78 vs. 30 months for the upfront and the relapsed/refractory groups, respectively,  $p = 0.03$ ). The median TTP for patients who achieved CR and PR was 78 vs. 18 months, respectively,  $p < 0.001$ ). After a median follow-up of 8.2 years, 11 of the 95 patients (11%) remain in continued CR from 8 to more than 14 years post-ASCT, this resulting in a PFS and OS plateau. Eight of these 11 patients received the ASCT as part of the upfront therapy (in continued CR from 8 to 14 years) while the remaining three underwent the ASCT for relapsed/refractory disease (in continued CR from 10 to 14 years).

Conclusions: The long-term results of the present series with 11% of patients surviving in continued CR at 8 to 14 years from ASCT suggest that, a portion of patients with MM can be cured with a single ASCT.

P593

**Autologous peripheral blood stem cell transplantation in 5 patients affected by POEMS syndrome**

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POEMS is a multisystemic paraneoplastic syndrome, the acronym refers to Polyneuropathy, Organomegaly, Endocrinopathy, M protein, Skin changes. We treated 5 pts affected by POEMS syndrome with high dose chemotherapy and autologous peripheral blood stem cell transplantation (aPBSCT). Pts were M/F 3/2, median age 54ys (range 44-62). All pts had a severe, rapidly progressive sensory-motor peripheral neuropathy, involving extremities, with inability to walk. All pts had M component IgA-lambda and 1 had also M component IgG-lambda, all had plasmacytosis (7-10%) in bone marrow. Endocrinopathy was present in all pts as thyroid disease and in 1 patient as hypogonadotropic Hypogonadism, in 1 pts as hypophysary adenoma, in 1 pts as glucose intolerance. All pts presented melanosis. 2 patient had splenomegaly, and 3 hepatomegaly. A patient had sclerotic bone lesion. One patient had significantly abnormal pulmonary function before aPBSCT. All pts received Cyclophosphamide 1500 mg/m<sup>2</sup> on day 1,3 and Methylprednisolon 250 mg from day 1-4 for 2 cycles and G-CSF 5 mcg/kg/day was added after 2° cycle for mobilization. 3 pts were previously treated with high dose Ig i.v. and steroids in the neurologic unit. Time from diagnosis to aPBSCT was 4 months (range 3-7). Conditioning regimen was HDMel (Melphalan 100 mg/m<sup>2</sup> for 2 consecutive days). Engraftment was rapid and sustained. After a median follow-up of 55 months (range 3-67), all pts are alive with slow but progressive improvement in neurological disease, skin changes, organomegaly, performance status and without evidence of plasmacytosis. Negativization of M component was observed in 4 pt. Pt with sclerotic bone lesion also received radiotherapy. VEGF level was only performed after aPBSCT, but in our results (see table) this parameter was not correlated with clinical and laboratoristics improvement. Our experience confirms that HDMel and aPBSCT is feasible and efficacious and should be the treatment of choice for POEMS, arresting and even reversing the disease course. Early diagnosis is important to obtain best response and improve clinical outcome. aPBSCT might be safely performed at experienced transplant centres combined to neurological expertise. We did not observe correlation between VEGF level and clinical improvement, but this data should be confirmed in the follow-up to clarify the role of bevacizumab, anti-VEGF antibody, as new therapeutic option for patients who can not perform transplant or relapse after aPBSCT.

P594

**Bortezomib and lenalidomide for multiple myeloma patients relapsed after allogeneic stem cell transplantation**

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Allogeneic stem cell transplantation (allo-HSCT) represents an effective treatment for multiple myeloma (MM). However, clinical relapse or progression after allo-HSCT are common and new therapeutic strategies are needed. New drugs, in particular bortezomib and lenalidomide, are appealing for several reasons: 1) their toxicity is not overlapping with chemotherapy; 2) the mechanism of antitumor activity is different from that of chemotherapy; 3) their activity encompass also modulation of immune cells, with potential effects on the graft versus-myeloma effect. In order to evaluate the clinical role of bortezomib and lenalidomide after allo-HSCT, we reviewed data from 23 patients treated at 4 Italian institutions. Median age at transplantation was 53 years (range 35-64). Twenty-one patients underwent a reduced-intensity, and 2 a myeloablative conditioning regimen. Donors were HLA-identical siblings in 17 patients, and matched unrelated donor in 6 patients. Eleven (48%) patients developed acute GVHD, and 15 (65%) chronic GVHD (9 limited, 6 extensive). All patients relapsed or progressed after allo-HSCT. Eight patients were treated with bortezomib, 7 with lenalidomide, and 8 received bortezomib and, subsequently, lenalidomide. The median interval between allo-HSCT and bortezomib was 31 months (range 7-144), and 27 months (range 7-71) for lenalidomide. The 16 patients treated with bortezomib received a median number of 3 courses (range 1-7), in all cases with dexamethasone, in 8 cases also with thalidomide, and, in one case, in association with doxorubicin. The responses to bortezomib were as follows: 5 CR, 4 VGPR, 4 PR, 2 SD, and 1 PD. The median duration of response (DOR) was 10 months (range 1-43). Longer DOR were observed in patients also receiving thalidomide. The 15 patients treated with lenalidomide received a median number of 5 courses (range 2-14), in all cases with dexamethasone. The responses to lenalidomide were as follows: 2 CR, 2 VGPR, 6 PR, one SD, and 4 PD. The median DOR was 6 months (range 2-14). Toxicities were neuropathy for bortezomib, and neutropenia for lenalidomide. Only a reversible grade III lenalidomide-associated hepatic toxicity was reported. No grade IV toxicities were observed. In one case GVHD worsened during treatment with bortezomib. In conclusion bortezomib and lenalidomide are

promising treatments for MM patients in the allo-HSCT setting. It is reasonable to explore their use, also in combination with immunological manoeuvres.

P595

#### Ethnicity and autologous stem cell transplantation in myeloma

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The results of previous observations indicate that access to and outcome of autologous stem cell transplantation (ASCT) for multiple myeloma may be different for African Americans compared to white Americans. The effect of Asian ethnicity is unknown, and the role of ethnic background on myeloma treatment has not been investigated outside the US. We have analysed the impact of ethnicity on ASCT in all myeloma patients referred to a large UK transplantation centre over a 15-year period. Hammersmith Hospital is a tertiary open-access referral centre for SCT with a catchment area that primarily covers Northwest London. A total of 311 patients with a diagnosis of myeloma were referred to our institution between 1994 and 2008 for ASCT. 235 were Caucasians, 47 were of African, and 29 of Asian background. All patients received single Melphalan-conditioned ASCTs. There were no differences in baseline patient demographics and disease status at the time of ASCT between the ethnic groups. The proportion of ethnic minorities undergoing ASCT for myeloma more than doubled from 14% in the first to 31% in the last 5-year observation period, while the absolute number of Caucasians receiving ASCT for myeloma remained stable. For the entire study group, PFS after ACST was 19.7 months, and OS from diagnosis was 71.3mo. Progression-free survival (PFS) after ASCT was significantly shorter in Africans (14.9m) compared to Caucasians (21.7m,  $p=0.02$ ). In Asians, there was a trend towards shorter PFS after ASCT (15.9m), but this was not significant. Overall survival (OS) from diagnosis (Africans, 65m; Asians, 76m; Caucasians, 73.8m) and from the time of ASCT (Africans, 46.1m; Asians, 36.4m; Caucasians, 56.9m) were not significantly different between the ethnic groups. These observations suggest that access to ASCT for myeloma has improved for ethnic minorities in the UK, probably because of improved referral rates rather than changes in population demographics. Although patients of African ethnicity have a significantly shorter PFS after ASCT, OS after transplantation and from diagnosis is not different. Further studies are required to investigate if myeloma patients of African background benefit from ASCT to the same extent as other ethnic groups.

P596

Vinorelbine and pegfilgrastim for mobilization of peripheral blood progenitor cells in patients with multiple

myeloma: a predictive and cost-effective procedure

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Several mobilization regimens are used to mobilize stem cells for transplantation in multiple myeloma, but timing of collection is often difficult and the rate of side effects is quite high. To optimize timing of collection of peripheral blood stem cells, to reduce side effects and costs of the procedure, we evaluated vinorelbine, a drug shown to have activity in multiple myeloma, with a single dose of pegfilgrastim as mobilizing regimen. Thirty consecutive patients with newly diagnosed stage I to III multiple myeloma received 2 - 4 cycles of VAD (vincristine, adriamycin, dexamethasone) induction therapy at two transplantation centers. This was followed by one dose of vinorelbine 35mg/m<sup>2</sup> iv in an outpatient setting on day one and a single dose of pegfilgrastim 6mg s.c. on day 4. On day eight a median count of 52.5 CD34+ stem cells/microliter (range 2 - 320) was measured in the blood of 28 patients. Two patients already showed CD34+ cells of 51 and 60 at day 7. One stem cell apheresis was sufficient to collect a median of 8.9 x10<sup>6</sup> CD34+ cells/kg body weight (range 1.2 -36.6). Four patients (13%) needed two stem cell aphereses to achieve a sufficient number of stem cells for transplantation. Twenty-one (70%) of the 30 patients mobilized had their first apheresis on day 8, 2 (7%) on day 7, and 7 patients (23%) on day 9. No episodes of fever in neutropenia or other side effects were observed during mobilization. After high dose chemotherapy with melphalan and stem cell transplantation, recovery of neutrophils was within the expected range, indicating no harmful effect of the mobilization scheme to the stem cells collected. The combination of vinorelbine and pegfilgrastim is an effective alternative to cyclophosphamide in the mobilization of stem cells for autologous transplantation in multiple myeloma. Results are reliable and day of apheresis is highly predictable. As all the mobilizing and collection procedures were done in an outpatient setting, this mobilization scheme is cost saving compared to the mobilization with cyclophosphamide, that usually requires hospitalization. In addition, a single dose of pegfilgrastim averts the problem of non-compliance of daily filgrastim injections and improves acceptance of the treatment by the patient.

**P597**

**Genetic prognostic factors and the outcome of autologous stem cell transplantation in plasma cell disorders**

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Between December 1999 and May 2008 104 autologous stem cell transplantations were performed in 103 patients with plasma cell disorders in our transplant center in Hungary. The patients mean age was: 54.48 years. Sex distribution: 56 males, 47 females. The diagnosis was multiple myeloma in 98, multiple plasmocytomas in 4, acute plasma cell leukemia in 1 patient. The conditioning regimen was 200 mg/m<sup>2</sup> melphalan in 100 cases, 120-160 mg/m<sup>2</sup> melphalan in 3 patients with kidney failure and in 1 case with a second transplantation. We administered the median of 4.9x10<sup>6</sup>/kg CD34 positive cells on transplantation. Neutrophil engraftment (ANC>1.0 G/l) occurred on day +10, platelet engraftment (PLT > 20.0 G/l) on day +13. According to bone marrow morphology on day 100 and immunofixation CR rate was 76%, VGPR occurred in 21%, 2 patients were considered as non-responders. 80% of the 103 patients are still alive. The median observation time from diagnosis was 38.4 months and from transplantation 28.9 months. The day 100 non-relapse mortality was 0%. The progression free survival according to Kaplan-Meier analysis was 63.17 ± 6.1 (95% CI: 51.0 – 75.3) months, the overall survival was 83.2 ± 5.7 (95% CI: 71.9- 94.5) months.

The results of interphase cytogenetical examinations (FISH) were available in 45 patients. In 74% of them genetical abnormalities have been identified. Del(13q) was proved in 41.9%, del(17p) in 9.7%, abnormalities in the IgH gene in 58% of the cases (overlaps). Among IgH gene abnormalities t(11;14) occurred in 16.7%, t(4;14) in 22.2% and t(14;16) in 5.6%, in 55.5% of the cases no partner gene has been identified. Three prognostic categories were distinguished: good prognosis (t(11;14)), intermedier prognosis (normal FISH results, IgH gene abnormalities without identification of a partner gene, t(11;14) + the presence of a poor prognostic marker) and poor prognosis (the presence of any unfavorable genetic prognostic marker). 22% of the patients belonged to the good, 33% to the poor and 45% to the intermedier prognostic category. There were significant survival differences (p= 0.01) between the different genetic prognostic groups of patients.

Autologous stem cell transplantation definitely improves survival in patients with multiple myeloma. Cytogenetical examinations play an important role in the definition of different prognostic categories that represent significant survival differences of these patients.

P598

CD66A expression on plasma cells from multiple myeloma patients

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Background: Expression of CD66, a member of the carcinoembryonic

antigen (CEA) and immunoglobulin superfamilies, has been reported on granulocytes. Phase I and II clinical trials at our centre utilise this property for the delivery of targeted radiotherapy as part of the conditioning regimen for transplantation in acute leukaemias and multiple myeloma. In these studies the vector for the application is conjugated to one of two radioisotopes: Indium-111, a gamma radiation-emitting isotope for imaging to demonstrate bone marrow targeting and Yttrium-90, a beta-emitter which delivers therapy. Previous studies revealed abnormal expression of CD66 and its isoforms (CD66a to CD66e) in tumour cells. Preliminary studies at our centre suggested the presence of CD66 antigen on normal and malignant plasma cells. However, little is known about the differential expression pattern of its variants on plasma cells from patients with multiple myeloma.

**Objective:** We performed flow cytometry on myeloma cell lines and plasma cells from patients with multiple myeloma to evaluate the expression of the CD66 variants.

**Methods:** Fresh bone marrow samples were obtained from patients at Southampton General Hospital between 2007 and 2008. Mononuclear cells expressing CD138, a specific plasma cell marker, were either positively selected (Easysep magnetic separation kit) or incubated with saturating amounts of CD138 and a single CD66 monoclonal antibody (CD66a and d: R&D, Genovac; CD66b and e: AbD Serotec; CD66c- Santa Cruz). Similar analysis was performed on two human myeloma cell lines, U266 and ARH77.

**Results:** Data acquisition and analysis were performed using the FACScalibur, CellQuest Software (Becton Dickinson).

Plasma cells were gated according to forward and side scatter characteristics and CD138 expression.

In all clinical bone marrow specimens, positive expression for CD66a was identified (range 69% to 100%) with a median fluorescence ranging from 54 to 673. Expression of CD66a was also identified in cell lines, with no detectable expression of the other isoforms of CD66. Positive but weaker expression was seen with utilisation of the panCD66 monoclonal antibody (CD66a/b/c/e) in primary samples and the cell lines.

**Conclusion:** CD66 expression, in particular CD66a expression, was detectable on cell lines and CD138+ plasma cells. These findings may help in optimisation of future radio-immunotherapeutic strategies in patients with multiple myeloma.

**P599**

**Regional differences in haematopoietic stem cell activity in South East England: a multi-centre investigation of inequalities in utilisation and inequity of access to treatment for multiple myeloma**

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International variations in haematopoietic stem cell transplant (HSCT) rates are widely documented but few comparative studies exist at national levels. Studies from the USA have examined differences in HSCT rates between States, often in the context of socioeconomic and ethnic differences between populations. Little is known about the differences in transplant activity within a universal healthcare system such as the UK. This study investigated inequalities in HSCT activity between 9 strategic health authorities in the Pan Thames region of the UK, and the extent to which this is suggestive of an inequity of access. Data was obtained from the British Society for Blood and Marrow Transplant (BSBMT) for transplants carried out from 2004 to 2007 inclusive, in 4 South East England and 5 London health authority regions. Each region is served by a single transplant centre. Collectively, these centres perform 20% of the annual volume of HSCT in the United Kingdom. Transplant rates per million population were calculated for 1900 patients aged 18-72, receiving first transplants for haematological malignancies. Rates were directly age and sex standardised to the 2001 UK census population. Utilisation was examined in relation to regional deprivation scores, ethnicity and level of educational attainment of the patient. Transplant rates in general, increased during this period but differences were noted between regions seemingly matched for size and economic status. The transplant rate in one particular region increased in association with the expansion of the local transplant unit. There was also an overall increase in transplantation for ethnic minorities. Following standardisation, we found inequalities in stem cell transplantation rates for different indications between age and ethnicity matched regions. Low educational attainment was associated with low transplant rates in both deprived and affluent regions and in regions with different ethnic compositions. Our results suggest that factors related to ethnic background, education level and the referral process may be associated with underuse of HSCT, particularly by populations resident in Essex and North East London. Further research with emphasis placed on quantifying need, is required in order to assess the extent to which these factors can be interpreted as evidence of inequity of access to HSCT in the Pan Thames region.

#### P600

Plerixafor plus G-CSF is effective without significant toxicity in PBSC mobilisation from myeloma patients with dialysis-dependent renal failure who have failed to mobilise by conventional means: an initial series of three patients

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Objectives: Myeloma patients with dialysis-dependent renal failure may benefit from autologous transplant, but PBSC mobilisation may prove challenging. The unlicensed small molecule chemokine inhibitor plerixafor is available on a named-patient basis for PBSC mobilisation from patients failing conventional mobilisation. Plerixafor is renally excreted & has not initially been used in patients with renal failure. However, on the basis of encouraging toxicity data in patients without renal failure, we have recently used plerixafor at reduced dosage for PBSC mobilisation from three myeloma patients with dialysis-dependent renal failure who had failed to mobilise PBSC by conventional means.

Methods: Prospective audit. The regime used initially consisted of Plerixafor 160 micrograms/kg/day following 4 days of G-CSF 10 micrograms/kg/day, with apheresis initiated at 11-12 hours after each plerixafor dose, and plerixafor and G-CSF repeated daily until a transplantable PBSC dose was achieved (where possible). Plerixafor was administered post-dialysis, as it is predicted to be removed by dialysis.

Results: All 3 patients were female, aged 58-61, & had myeloma presenting in dialysis-dependent renal failure. All had failed to mobilise PBSC by conventional means (cyclophosphamide plus G-CSF in 1 patient; G-CSF only in 2 patients). Following plerixafor plus G-CSF on the regime described above, 2 patients mobilised a transplantable PBSC dose of  $>2 \times 10^6$ /kg CD34+ cells after 1 and 2 apheresis procedures respectively. The third patient mobilised a suboptimal CD34+ dose of  $0.36 \times 10^6$ /kg after the first apheresis procedure, and the plerixafor dose was therefore increased to 240 micrograms/kg/day. After 3 apheresis procedures, the total dose collected remained inadequate for transplant at  $0.86 \times 10^6$ /kg. In view of this, a second treatment cycle of G-CSF and plerixafor was initiated approximately 4 weeks later, with the plerixafor dose escalated to 240 micrograms/kg/day. On this occasion, a total CD34+ dose of  $2.12 \times 10^6$ /kg was collected in 3 apheresis procedures, giving a total cumulative CD34+ dose of  $2.98 \times 10^6$ /kg which is adequate for transplant. No immediate plerixafor toxicities were experienced by any of the three patients. All 3 patients are now scheduled for transplant in early 2009.

Conclusions: In our initial experience, plerixafor is effective in PBSC mobilisation from myeloma patients with dialysis-dependent renal failure, without undue toxicity.

P601

Severe renal impairment is not a major limit for autologous stem cell transplantation in patients with multiple myeloma or amyloidosis

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High-dose therapy using Melphalan (200mg/mq) followed by autologous stem cell transplantation (auto-HSCT) is the most

common treatment for multiple myeloma (MM) and Amyloidosis. Reducing Melphalan dose allows to offer this procedure to patients with severe renal impairment. From 2003 to 2008, nine patients (6 MM, 2 Amyloidosis, 1 Crystalcryoglobulinemia) with renal impairment underwent auto-HSCT: six were males, three females, median age was 55 years (range 30-65), median creatinine value was 5.4 mg/dl (range 1.5-8.65), median creatinine clearance was 19 ml/min (range 10-48). Status of disease at transplant was near complete remission (nCR) in two patients, very good partial remission (VGPR) in one patient, partial remission (PR) in three patients, while three patients had active disease. Median Melphalan dose was 140 mg/mq (range 100-160), administered at day -2 and followed by autologous peripheral stem cells infusion at day 0 after DMSO removal (median number of CD34+ : 4.61 x 10<sup>6</sup> cells/Kg, range 3.74-7.87). All patients engrafted, with a median time to engraftment of 12 days (range 10-15); they all developed fever with only two positive blood cultures (Staphylococcus aureus and Staphylococcus warnerii). Median duration of hospitalization was 22 days (range 18-30). We observed grade II oral mucositis in four patients, ARDS-like pulmonary toxicity in one patient, severe gut mucositis in one patient. At day +90 (data available for 7 patients) six patients achieved a favourable response (2 CR, 3 VGPR, 1 PR). All patients are alive with a median follow up of 12 months (range 1-60 months); three out of six patients on haemodialysis at transplant became haemodialysis independent (50%). Median duration of response (available for 7 patients) is 14 months (range 4-27). This study confirms that Melphalan followed by auto-HSCT is feasible in patients with severe renal impairment; a dose of 140 mg/mq is well tolerated and this reduction doesn't jeopardize the efficacy of the procedure.

#### P602

Short-course pretransplant velcade, thalidomide and dexamethasone regimen induces high complete response rate without compromising CD34+ cell collection in untreated multiple myeloma patients: preliminary results of a single-centre experience

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Background: High-dose chemotherapy with autologous stemcell support has significantly improved progression-free and overall survival of patients with untreated multiple myeloma (MM). Pre-transplant complete response (CR) and tumor reduction have been identified as most relevant prognostic factors for long-term survival in untreated MM. Recently, thalidomide and bortezomib both given as single agent shown to be effective in previously treated MM. Since they have target different molecular pathways their combination is waited to be highly effective

to induce high CR rate and tumor reduction before HDT with stem-cell support. We present early data of this regimen in untreated symptomatic MM patients.

Patients and Methods: From March 2007 to October 2008 16 pts (M/F: 12/4) were enrolled in the study; median age was 57 years (range: 42-71), 47% were older 60 years; Most of pts had stage III according to Durie & Salmon (76%) and ISS score 2-3(76%). M-component was IgG 69% (11/16), IgA 19%, and non secretory 12%.

Regimen: Bortezomib was given at 1.3 mg/m<sup>2</sup> on days 1,4, 8, 11, thalidomide at dose of 100 mg PO daily, and dexamethasone (40 mg/die PO) was given the day of bortezomib and the day after (320 mg td for each cycle). All patients received 3 cycles of VTD every 4 weeks before CD34+ cell collection and high-dose melphalan (200 mg/m<sup>2</sup>). Deep-venous thrombosis prophylaxis was established in all pts consisting of aspirin 100 mg daily in 44% of pts, low-molecular weight heparin (28%) or low dose warfarin (28%).

Results: all pts are evaluable for response to Velcade, Thalidomide and Dexamethasone (VTD) regimen and PBSC collection; 13 pts have been transplanted. After three VTD 88% of pts achieved PR including 47% of CR. VTD regimen was well tolerated with main toxicity consisting of WHO grade III peripheral neuropathy in 12% of pts. There was no chemotherapy reduction or delay due to toxicity. A median of 6.5 x 10<sup>6</sup>/kg of CD34+ cells (range: 2.7-11.6) was collected in 15 of 16 pts. The median CD 34+ cells infused was 3.2 x10<sup>6</sup>/kg (range: 2.0 - 4.3). Times to platelet (20x10<sup>9</sup>/L) and granulocyte (500x10<sup>9</sup>/L) recovery were 13 and 10 days respectively. After VTD and transplant 10 of 13 patients achieved CR (75%) and 2 (15%) a VGPR. Conclusion: These very preliminary data suggest that VTD is effective and well tolerated regimen; high response rate without compromising PBSC collection makes it a good option for initial treatment of MM although more pts and longer follow-up are required.

#### P603

#### 11 years of single-centre experience with stem cell transplantation for multiple myeloma

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Introduction: Autologous stem cell transplantation (ASCT) became standard of care for patients with multiple myeloma (MM) under the age of 65 years. We routinely perform ASCT for newly diagnosed MM since 1996 in our department.

Patients and methods: We retrospectively analyzed all 225 transplants in 136 patients done for MM from 1996 till 2007. 210 transplants were autologous (195x Mel200, 15x Mel100 for elderly patients), 15 transplants were allogenic (13x reducedintensity conditioning Bu-Flu-ATG or Flu-Cy, 1x myeloablative

Bu-Mel, 1x twin sibling). Median age of patients was 56 years (27-74). We analyzed overall survival (OS) and progressionfree survival (PFS) regarding conditioning, stage, complete or very good partial remission (CR, VGPR) achievement, renal impairment, single vs. double transplant and use of new drugs (thalidomide and bortezomib).

Results: Estimated 10-years survival of the whole set of patients is 38% (median survival 55 months). Patients who underwent allogeneic transplantation upfront had lower PFS ( $p=0.0001$ ) and OS ( $p=0.018$ ) compared to those who had only ASCT. Patients with renal impairment had significantly shorter OS than those without ( $p=0.03$ ). Patients with Mel100 conditioning had trend towards worse OS than those with Mel200, however statistical significance was not reached ( $p=0.08$ ). We observed trend towards better outcome in patients treated with new drugs but significance was not reached ( $p=0.052$ ). Reaching CR or VGPR was surprisingly not translated into better OS ( $p=0.29$ ) and PFS ( $p=0.27$ ). Also stage of the disease and whether single or double transplant was used did not make any significant difference in the outcome.

Conclusion: Stem cell transplantation greatly improves outcome of patients with MM. Poor outcome of allogeneic transplantation in our group of patients is related to high transplant related mortality (20% vs. 0.4%) and unexpected high relapse rate. However in this group are two long term survivors who are disease free for more than 10 years. There is a trend towards better survival, when new drugs are incorporated at any time in the course of the disease as an addition to ASCT. This fact supports hypothesis that use of new drugs with ASCT should translate into better long-term outcome. Our results also suggest that Mel100 regimen is insufficient and other treatment options should be offered to older patients. This is in good agreement with results of recent clinical trials.

Supported by project MZO00179906.

P604

Autologous haematopoietic progenitor cell transplantation followed by a reduced-intensity conditioning and allotransplantation in de novo multiple myeloma patients: an update

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We evaluated an up-date of the combination of high-dose therapy and autologous hematopoietic progenitor cells transplantation (AHPCT) followed by a reduced intensity conditioning and allotransplantation (RICT) in de novo multiple myeloma (MM) patients (Martino et al. AJH 81:973–978, 2006). 20 subjects with stage III MM (median age 52 years, range 40–64) received high dose melphalan (200 mg/m<sup>2</sup>) followed by AHPCT previously

collected after cyclophosphamide (4 g/m<sup>2</sup>) and granulocyte colony-stimulating factor (G-CSF). After 3–4 months from APBSCT, the patients underwent RICT, consisting of fludarabine 90 mg/m<sup>2</sup> + cyclophosphamide 900 mg/m<sup>2</sup> on days. Graft-versus-host disease (GVHD) occurred in 12 patients (8 patients developed chronic GVHD); 5 patients developed CMV antigenemia and were treated pre-emptively with ganciclovir. No transplant related mortality was shown. Response was simultaneously measured by both electrophoresis (EP) and immunofixation (IF); when IF was negative, patients were classified in complete remission (CR) and when it remained positive, near CR (nCR). After a median follow up of 62.2 months post AHPCT, the OS and EFS are 62.2 and 36.2 months, respectively. Overall, the CR + nCR rate after dose-reduced allograft was enhanced from 30 to 70%. A correlation not statistically significant between GVHD and EFS was found. In conclusion, this up-date confirms that an up-front tandem strategy with RICT following autografting is feasible and induces high CR/nCR rate in MM. It is open the debates around the results gotten in terms of OS and EFS.

#### P605

#### Impact of low-dose thalidomide as maintenance therapy in advanced multiple myeloma patients following high-dose therapy

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Introduction: Multiple Myeloma (MM) is a fatal disease with a median survival of 3-4 years. The standard therapy in pts aged <65 years was, in the last years, VAD or VAD-like regimens followed by high dose Cyclophosphamide (Cy) and Alkeran (L-PAM) with support of peripheral stem cells (PBSC). Thalidomide (Thali) alone or associated to chemotherapy (CT) has showed considerable activity. Its efficacy as maintenance therapy is still under investigation.

Patients and methods: We considered a conventional CT (3 cycles of VAD or VAD-like regimen), high dose Cy (7 g/m<sup>2</sup> i.v.) and PBSC harvest, followed by single or tandem (when disease still present) high dose L-PAM (200 mg/m<sup>2</sup> i.v.) with rescue of PBSC (CD34+>4x10<sup>6</sup>/Kg). All pts were in stage II/III, according to Durie and Salmon. Thali (100 mg/day) was given to all pts regardless the response and discontinued at the time of relapse or progression or because of toxicities. No anti-thrombotic prophylaxis was administered. Between January 1999 and October 2007, 95 consecutive pts were treated, 90 valuable, median age 55 (33-66), male/female 50/40, M component IgG/IgA/IgD/monoclonal light chain and non-secretory MM were 51/22/3/12 and 2, respectively. All pts completed induction and high dose CT. One toxic death occurred. Thali (100 mg/day)

was started within 3 months from transplant in 68 pts; 22 could not be treated because of refusal (4), progression disease (9), allergic reactions (3) or neurological toxicities (6).

Results: At transplant, 13/90 (14%) were in very good partial remission or complete remission (VGPR+CR according to EBMT criteria), further 33 pts (30%) reached the CR after transplant, for a total of 46/90 CR (51%) at the end of the program.

We compared the number of responses (VGPR+CR), the treatment-free interval (TFI) and overall survival (OS) in the 2 groups of pts. The median follow up was 42 months. The VGPR+CR rate was 64% (44/68) in the group treated with Thali versus 50% (11/22) in the remaining pts. With Thali we obtained further 9 CR+VGPR/33 pts not in remission after transplant (27%). Comparing the 2 groups, the TFI was 37 and 22 months, the OS was 47 and 37 months, respectively ( $p < 0.08$ ).

Conclusions: Low dose Thali following single or tandem autotransplant appears to be a safe and feasible treatment not only as maintenance, but also as consolidation therapy, improving the rate of response (VGPR+CR), delaying the need of subsequent therapy and improving the OS, with an acceptable toxicity.

#### P606

##### Impact of pretransplantation, mobilisation and graft variables on transplant outcome after autologous haematopoietic stem cell transplantation for patients with multiple myeloma

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We studied 197 autologous HSCT performed in 132 patients (53 F, 79 M, median age of 57 years) treated for multiple myeloma in our center. At diagnosis there were 71 IgG (49 kappa, 22 lambda), 26 IgA (15 kappa, 11 lambda), 2 IgD (1 kappa, 1 lambda), 27 light chain (18 kappa, 9 lambda), 2 plasma cell leukemia, 3 non secretory, 1 non secretory with 11 stage I, 12 II, 96 III (13 were not classified). At diagnosis, 24/98pts had a del(13), and 65/179 had high levels of beta2microglobulin. PBSC were mobilized in steady state in 135 cases, after cyclophosphamide alone in 53 cases or associated with other drugs in 9 cases. The number of apheresis were 1 (n=65), 2 (n=31), 3 (n=16), 4 (n=18), 6 (n=1) and 8 (n=1). During mobilization, we used G-CSF in 179 cases, GM-CSF in 5 cases, SCF in 4 cases and associations of GM-CSF or SCF with G-CSF in 9 (4.5%) cases. The median number of infused cells were: TNC  $5 \times 10^7$ /kg (1-59), CFU-GM  $70.5 \times 10^4$ /kg (0-2616) and CD34+cells  $3 \times 10^6$ /kg (0-27); 115 (58%) received a number of CD34+cells  $< 4 \times 10^6$ /kg and 82 (42%) =  $4 \times 10^6$ /kg. After transplantation, 156 (79%) received growth factors [1 GM-CSF, 148 G-CSF and 7 SCF]. The median number of RBC and Pt transfusions were 0 [0-23]

and 1 [0-20] respectively. The median number of days with neutrophils  $<0.5\text{G/L}$  was 6 (0-33) and with  $\text{Pt}<50\text{G/L}$  17 (2-104) and the median length of hospitalization was 18 days (14-54). The probability of 5-year overall and event-free survival were 64.3% (56.3-73.4%) and 32.4% (24.9-42.2%). The variables studied were age, disease status at transplant, infused TNC,  $\text{CD34+cell}$  and CFU-GM, growth factor use during mobilization and after transplantation, mobilization chemotherapy and interval Diag-T. Using a conditional logistic-regression model, we observed a significant negative impact of interval diagnosis-T ( $p=0.05$ ) on length of hospitalization and RBC transfusions. A multivariate analysis showed a significant positive impact of CFU-GM number [HR=1 (1000-1.002) ( $p=0.03$ )] and growth factor use after transplantation [HR=0.55 (0.36-0.85) ( $p=0.005$ )] on the number of days with less than 0.5 G/L neutrophils and a significant negative impact of  $\text{CD34+cell}<4 \times 10^6/\text{kg}$  on the number of days with less than 50G/L Pt ([HR=1.65 (1.09-2.50) ( $p=0.01$ )]). In conclusion, we did not show any apparent impact of the pretransplant, mobilization and graft variables but a significant influence of the diagnosis-T interval on platelet transfusion and of the use of GCSF post-transplant, the  $\text{CD34+}$  and CFU-GM numbers on the length of aplasia.

#### P607

##### Lenalidomide as salvage therapy after allogeneic transplant for primary plasma cell leukaemia: a case report

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Primary Plasma Cell Leukemia (PPCL) is an aggressive and rare variant of Multiple Myeloma (MM). Allogeneic haematopoietic stem-cell transplantation (HSCT) results in sustained longterm OS, suggesting a possible graft-versus-leukemia (GVL) effect. Relapse or progression after HSCT are common and outcome is poor. No data are available about Lenalidomide as salvage therapy for PPCL relapsed after HSCT. We report a 41 year-old woman with PPCL (IgA kappa monoclonal component (MC), 32% immature plasmacells in peripheral blood, 50% immature plasmacells  $\text{CD38/CD138/slgkappa+}$ ,  $\text{CD19/CD56/CD45-}$  in the bone marrow). She received six Hyper-CVAD courses achieving Complete Remission (CR) and, after blood stem cells collection, underwent ASCT (Melphalan  $200\text{mg}/\text{m}^2$  followed by reduced intensity conditioning HSCT from HLA identical brother (thiotepa  $5\text{mg}/\text{Kg}$ , fl udarabine  $30\text{mg}/\text{m}^2$ , melphalan  $140\text{mg}/\text{m}^2$ . Full donor chimerism was documented at day +90. At day +138 she relapsed with cytogenetics showing

a complex hyperdiploid karyotype. Bortezomib (1,3mg/m<sup>2</sup>) and Dexamethasone (40mg) (days 1,4,8,11) were started without response; as a second-line, cyclophosphamide (300 mg/m<sup>2</sup> on days 1,8,15) was added to Bortezomib and Dexamethasone. Nevertheless disease progressed and full donor chimerism was lost; therefore Lenalidomide (25mg/day, 1-21) and Dexamethasone (40 mg/day 1,8,15,22) were administered. At the end of the first course the patient developed a skin rash, hyperbilirubinemia and increased liver enzymes, compatible with acute GVHD, treated with methylprednisolone (2 mg/Kg/day). The patient showed a quick improvement with reduction of MC and abnormal plasmacells in the bone marrow. After six courses of Lenalidomide the patient is in CCR, with complete donor chimerism and normal cytogenetics; a mild cGVHD persists, requiring low dose steroids. We describe here the first case of a patient with relapsed and chemorefractory PPCL after allogeneic HSCT, who achieved a CCR with Lenalidomide; moreover, this is the first case of response to Lenalidomide associated with development of GVHD. The mechanism of the GVL/GVM is largely unknown. T and NK cells might exert an alloimmune reaction. In this case we hypothesize that the strong antiproliferative effect of Lenalidomide could have reduced the leukemia burden, making the GVL effect stronger. Furthermore Lenalidomide could have stimulated donor T/NK cells, as suggested by experimental data.

#### P608

Tolosa-Hunt-like syndrome in a myeloma patient receiving palifermin shortly after high-dose melphalan therapy

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Oral mucositis is a common adverse effect in subjects with haematological cancers receiving high-dose (HD) therapy and autologous peripheral blood progenitor cell (APBC) transplantation. Palifermin, a recombinant human keratinocyte growth factor, has been approved to decrease incidence and severity of oral mucositis and is associated with rash, edema/erythema and sensations of increased tongue thickness. We report on a 65 year-old female patient with IgG kappa myeloma in ISS I stage who underwent chemomobilization of APBCs followed by HD melphalan 140 mg/m<sup>2</sup>. She was included in an open-label study to receive palifermin from day -6 to +2 with APBC retransfusion on day 0. On day +10 the patient complained of severe unilateral headache and diplopia. On clinical examination she had ophthalmoplegia, partial visual loss down to 0.1 and exophthalmos of the left eye. Initial cranial MRI revealed inflammation in the ethmoid and sphenoid sinuses while the subsequent one showed diffuse enhancement of superior orbital fissure and orbital apex consistent with Tolosa Hunt syndrome. Painful ophthalmoplegia as well as exophthalmos responded to high-dose

dexamethasone with a quick recovery of visual acuity to 0.8. Extensive radiographic and laboratory work-up including CSF did reveal neither signs of specific infection nor of recurrence of myeloma. Following haematological recovery both typical signs of palifermin-induced adverse effects as well as elevated CRP levels normalized while several attempts in tapering corticosteroid doses were followed by prompt worsening of visual loss. Eight weeks from APBC transplantation the patient was in excellent clinical shape except persistent Tolosa Hunt syndrome. We repeated bone marrow and serological assessments of myeloma that was confirmed to be in VGPR, cranial MRI and, eventually, performed an 18F FDG positron emission tomography (PET) to exclude possible extramedullary involvement. Testing for infectious agents was uneventful. Findings in the latter examinations were consistent with unspecific inflammation of the orbital apex. The patient received local irradiation that allowed cessation of corticosteroid treatment. We conclude Tolosa Hunt-like syndrome in this case to be secondary due to a specific pharmacologic adverse effect of palifermin rather than an immune-mediated inflammation since myeloablative treatment is considered to be one of the most effective means of immunosuppression.

P609

#### Autologous peripheral blood stem cell transplantation in patient in advanced stage of POEMS syndrome

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Introduction: POEMS syndrome is a rare plasmatic cell dyscrasia, which is associated with overproduction of VEGF and characterized by polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes. A specific treatment for this disease is not established. In recent reports, high dose chemotherapy followed by autologous peripheral blood stem cell transplantation (APBSCT), performed in early stage can improve clinical symptoms, especially for polyneuropathy. We describe the clinical course of a patient with POEMS syndrome in advanced stage and unresponsive to standard chemotherapy, treated successfully with APBSCT.

Case report: A 47-year-old man was admitted to Department of Haematology and Bone Marrow Transplantation of Medical University in Lublin with quadriparesis, hepatosplenomegaly, sclerotic bone lesion, acrocyanosis, IgG lambda gammopathy and thrombocytosis. There was no increased number of plasmatic cells in bone marrow smear. The first symptoms of disease were appeared three years ago and diagnosis of POEMS was established 18 months ago. The patient was unresponsive to chemotherapy consisted with cyclophosphamide and prednisone, so we decided to perform APBSCT. Peripheral blood stem cells were collected after mobilization by cyclophosphamide (4g/m<sup>2</sup>) and G-CSF. The number of collected CD34+

cells was  $12 \times 10^6/\text{kg}$ . The conditioning regimen was high dose melphalan ( $140 \text{ mg}/\text{m}^2$ ). The number of transplanted CD34+ cells was  $4 \times 10^6/\text{kg}$ . The post-transplantation course was complicated by fever with no identifiable infectious etiology, diarrhoea, cutaneous rash and swelling without hypoalbuminaemia (engraftment syndrome?). Neutrophil ( $0.5 \text{ G}/\text{l}$ ) and platelet ( $20 \text{ G}/\text{l}$ ) engraftment occurred on days 11 and 13, respectively. The improvement was manifested by disappearance of gammopathy and organomegaly. The correction of neurological symptoms was unsatisfactory. Therefore thalidomide in a dose of  $50 \text{ mg}/\text{day}$  was applied. The second autologous transplantation is planned in January 2009.

Conclusion: Our experience suggests that APBSCT may be valuable method of treatment even in advanced stage of POEMS syndrome. The effect of thalidomide and second transplantation will be presented during EBMT meeting.

## Publication only

R1289

Bortezomib treatment in autologous transplanted patients in a university department of internal medicine, Debrecen, Hungary

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Objectives: Bortezomib (B) was accepted by the Food and Drug Administration in 2003 for treating refractory multiple myeloma (MM) patients. There were 150 patients (pts) who underwent autologous transplantation during the period between September 2003 and August 2008 at the authors' clinic. MM: 74, NHL: 44, Hodgkin lymphoma: 27, Leiomyosarcoma: 1, Autoimmune disease: 4. Our purpose here is to compare the survival rate of the MM patients without and with B therapy.

Patients and methods: The survival probability of the 74 MM patients was 80%. From the 1st group: 20 patients were treated without B. The follow-up period was 23 months. 8 patients died (40%) during this time. From the 2nd group 54 patients were treated with B in 18 months, six of whom died (11%). The following therapy-form was used pre-transplantation (pre-tx):

partly vincristine+adriamycin+dexamethasone, vincristine+idarubicin+dexamethasone, interferone, etoposide+dexamethasone+adriamycin+prednisolon, melphalan+prednisolon, B+adriamycin+dexamethasone (PAD). The B group had a post-tx maintenance therapy with B 4 weeks: 1,3 mg<sup>2</sup> iv doses weekly + dexamethasone 20 mg 4 days.

Results: Length of survival times (OS) without and with B were significantly different. Further analysis of the curves in complete remission indicated 100% survival probability and 90% disease free survival (DFS) in 19 patients in a 50-month period. In the very good partial remission (VGPR) group (12 pts) the OS was 100%, however, the DFS was only 60%. The survival curves were significantly worse when tx was made in partial remission (OS: 55%, DFS: 50% by 23 pts).

Conclusions:

1. The authors' data support the finding that lasting survival can be expected when tx is performed in CR or VGPR.
2. In the interest of this, in cases of a more aggressive disease, the first line PAD protocol before tx is the best therapy. After the tx a consolidation therapy with B+dexamethasone is very useful.
3. In a slightly less aggressive disease or with accompanying diseases a thalidomide+dexamethasone first therapy may also be possible.
4. Tx performed in partial remission may be dangerous. At this time needed put in „the therapy arsenal”.

R1290

Acute renal failure in myeloma patients during mobilisation procedures for autologous transplantation

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During the last 30 years blood cell separation, generally referred to aphaeresis, has established a central role in both blood donor programmes and therapeutics. The technological advances in aphaeresis equipment have made procedures safer, faster and more effective. We present 3 cases (2 males and 1 female) with multiple myeloma treated at our department during 2007 until 2008. Initial chemotherapy treatment was provided with thalidomide based regimens (C-Thal dex 4 cycles or ThalDex in 4 cycles) or 4 cycles of VAD in one patient. All 3 patients before diagnosis and during initial treatment had normal and stable renal function. After completing remission in all, mobilisation of PBSC was preformed with G-CSF 10mcg/kg in duration of 5 days. The number of WBC count prior collection was median  $42 \times 10^9/L$  (30-51) with median lymphomonocyte percent 13, 43 (4-22). Aphaeresis was preformed at day 5 with Cobe Spectra cell separator and large volume aphaeresis. In all 3 patients after finishing the first procedure we registered increase of renal degradation products in the serum during the first 6 hours post aphaeresis and complete anuria which revealed in acute renal failure (renal type) treated with haemodialysis in several consecutive occasions. One month after resolving the renal impairment the patients continued with second mobilisation procedure with the same regimen and obtained a minimal MNC count of  $2,0 \times 10^8/kg$ . Autologous transplantation followed by Melphalan reduced dose conditioning  $100mg/m^2$ . Engraftment was registered for  $Ne > 0,5 \times 10^9/L$  and  $Plt > 20 \times 10^9/L$  on median day + 10 (8 to 12). The patients had no need for blood transfusions. All 3 are in CR med 7 mths (3-11) after transplant. In one patient 4 months after, a double transplant was preformed. Concerning the small group of patients, we can evaluate the possible impact of large volume aphaeresis in the renal impairment in these patients or the influence of cytokine mobilised cells on renal tubules.

## Posters related to Myeloma

- ❑ 1. [\[P589\] Effect of plerixafor plus G-CSF on tumour cell mobilisation in patients with multiple myeloma](#)  
**Authors:** S. Fruehauf, J. Topaly, S. Muller, M. Moos, H. Goldschmidt, A.D. Ho, G. Calandra  
**Session:** Physicians Poster Session: Multiple myeloma
  
- ❑ 2. [\[P592\] Is there a curative potential of autologous stem cell transplantation in multiple myeloma? Long-term results from a single-centre series](#)  
**Authors:** M. Rovira, L. Rosinol, F. Fernandez-Aviles, C. Martinez, E. Gine, J. Esteve, M.T. Cibeira, P. Marin, E. Carreras, J. Blade  
**Session:** Physicians Poster Session: Multiple myeloma
  
- ❑ 3. [\[P604\] Autologous haematopoietic progenitor cell transplantation followed by a reduced-intensity conditioning and allotransplantation in de novo multiple myeloma patients: an update](#)  
**Authors:** M. Martino, G. Console, E. Spiniello, D. Marcuccio, G. Messina, G. Irrera, R. Fedele, E. Massara, I. Bova, T. Moscato, M. Cuzzola, P. Iacopino  
**Session:** Physicians Poster Session: Multiple myeloma
  
- ❑ 4. [\[P506\] Transplanted CD34+ cell dose is associated with long-term platelet count recovery following autologous haematopoietic stem cell transplant in patients with non-Hodgkin's lymphoma and multiple myeloma](#)  
**Authors:** P.J. Stiff, I.N. Micallef, A.P. Nademanee, E.A. Stadtmauer, R.T. Maziarz, B.J. Bolwell, G. Calandra, G. Bridger, J.F. DiPersio  
**Session:** Physicians Poster Session: Stem cell source
  
- ❑ 5. [\[P482\] Results of two phase III, multicentre, randomised, placebo-controlled trials of plerixafor + G-CSF versus G-CSF + placebo for mobilisation and engraftment of non-Hodgkin's lymphoma and multiple myeloma patients undergoing autologous transplantation](#)  
**Authors:** J.F. DiPersio, I.N. Micallef, A.P. Nademanee, P.J. Stiff, E.A. Stadtmauer, R.T. Maziarz, B.J. Bolwell, J. Angell, G. Bridger, G. Calandra  
**Session:** Physicians Poster Session: Stem cell source
  
- ❑ 6. [\[P485\] Efficacy of plerixafor plus G-CSF compared to G-CSF plus placebo for mobilisation of CD34+ haematopoietic progenitor cells in patients older than 60 years with non-Hodgkin's lymphoma or multiple myeloma](#)  
**Authors:** I.N. Micallef, J.F. DiPersio, A.P. Nademanee, P.J. Stiff, E.A. Stadtmauer, R.T. Maziarz, B.J. Bolwell, J. Angell, G. Bridger, G. Calandra  
**Session:** Physicians Poster Session: Stem cell source
  
- ❑ 7. [\[P600\] Plerixafor plus G-CSF is effective without significant toxicity in PBSC mobilisation from myeloma patients with dialysis-dependent renal failure who have failed to mobilise](#)

[by conventional means: an initial series of three patients](#)

**Authors:** K.W. Douglas, P.J. Hayden, M.E. O'Dwyer, A. Rahemtulla

**Session:** Physicians Poster Session: Multiple myeloma

- ❑ 8. [\[P598\] CD66A expression on plasma cells from multiple myeloma patients](#)  
**Authors:** C.H. Lee, B. Guinn, S. Brooks, D. Richardson, K. Orchard  
**Session:** Physicians Poster Session: Multiple myeloma
- ❑ 9. [\[P596\] Vinorelbine and pegfilgrastim for mobilization of peripheral blood progenitor cells in patients with multiple myeloma: a predictive and cost-effective procedure](#)  
**Authors:** M.J. Bargetzi, T. Pabst, A. Schoenenberger, J. Burger, P. Fernandez, P. Moosmann, A.R. Huber, M. Wernli, M. Heizmann  
**Session:** Physicians Poster Session: Multiple myeloma
- ❑ 10. [\[P890\] Use of ciprofloxacin to prevent bacterial infection in patients receiving high-dose chemotherapy and autologous stem cell transplantation for multiple myeloma, AML, and lymphoma/solid tumours](#)  
**Authors:** E. Bauernschmitt, T. Szislo, C. Peschel, H. Menzel  
**Session:** Physicians Poster Session: Infectious complications
- ❑ 11. [\[P586\] Thalidomide + dexamethasone as maintenance after single autologous stem cell transplantation improves progression-free survival in advanced multiple myeloma. A prospective Brazilian randomised trial](#)  
**Authors:** A. Maiolino, V. Hungria, G. Oliveira-Duarte, D. Mercante, E.C.M. Miranda, A. Quero, A. Miguel Peres, P. Tanaka, L. Oliveira, R. Magalhaes, E. Rego, M. Nucci, I. Lorand-Metze, C. Lima, I. Zalberg, E. Braggio, C. de Souza  
**Session:** Physicians Poster Session: Multiple myeloma
- ❑ 12. [\[P590\] Outpatient stem cell transplantation for multiple myeloma](#)  
**Authors:** A. Ghavamzadeh, K. Alimoghaddam, A. Karimi, A. Manookian, M. Asadi, R. Maheri, A.R. Shamshiri  
**Session:** Physicians Poster Session: Multiple myeloma
- ❑ 13. [\[P585\] Lenalidomide therapy increases the frequency of activated T- and NK-cells in patients with relapsed multiple myeloma following allogeneic stem cells transplantation](#)  
**Authors:** M. Lioznov, P. Freiberger, Y. Hildebrandt, U. Bacher, A. Zander, N. Kroeger  
**Session:** Physicians Poster Session: Multiple myeloma
- ❑ 14. [\[P587\] Application of the propensity score matching method to the estimation of survival benefit of non-myeloablative allogeneic transplantation in patients with multiple myeloma relapsing after a first autologous transplantation](#)  
**Authors:** L. Karlin, B. Arnulf, S. Chevret, M. Robin, R. Peffault de Latour, M. Malphettes, N. Kabbara, B. Asli, L. Ades, V. Rocha, J.-P. Fermand, G. Socie  
**Session:** Physicians Poster Session: Multiple myeloma

- ☐ 15. [\[P1142\] Autologous transplant in cardiac amyloidosis: nursing care](#)  
**Authors:** S. Davila Quintana, M.R. Ortega Carrion, M.R. Munoz Montano, I.M. Duran Sanchez, R.M. Torres Munoz, J. Jimenez Martinez, V. De la Osa Garcia, M. Aguilar Roman  
**Session:** Nurses Poster Session: Standards of care
- ☐ 16. [\[P490\] Immediate plasma removal and cryopreservation in HAS/DMSO corrects reduced CD34+ cell viability in cryopreserved cell harvests from patients with systemic amyloidosis](#)  
**Authors:** R. Krishna, V. Day, J. Snowden, D. Pawson, C. Birchall, K. El-Ghariani, G. Cook, A. Lubenko  
**Session:** Physicians Poster Session: Stem cell source
- ☐ 17. [\[P997\] Timing of G-CSF injection for effective autologous stem cell collection](#)  
**Authors:** J.E. Kim, C.W. Suh, E.K. Kim, B.S. Sohn, I. Park, D.H. Yoon, C. Yoo, G. Jang, D.H. Lee, S.-W. Kim, J.S. Lee  
**Session:** Physicians Poster Session: Cytokines
- ☐ 18. [\[P1201\] Palonosetron \(Aloxi\): a single-centre experience in the prevention of emesis in patients affected by haematological malignancies](#)  
**Authors:** D. Basile, A. Assanelli, C. Soliman, F. Ciceri, V. Matozzo  
**Session:** Nurses Poster Session: Impact of new therapies
- ☐ 19. [\[P1162\] Changing landscapes in haematopoietic stem cell transplantation for haematological malignancy](#)  
**Authors:** M. Kenyon, G. Mufti  
**Session:** Nurses Poster Session: Management issue
- ☐ 20. [\[P576\] Addition of anti-thymocyte globulin could reduce the GvHD and not increase mortality in unrelated stem cell transplantation](#)  
**Authors:** T.-D. Tan  
**Session:** Physicians Poster Session: Graft-versus-host disease - clinical
- ☐ 21. [\[P665\] Activation of haemostasis after transfusion of cryopreserved haematopoietic stem cells containing dimethylsulfoxide](#)  
**Authors:** J. Studt, S. Meyer-Monard, C. Arber, M. Stern, D. Heim, G. Marbet, A. Gratwohl, D. Tsakiris  
**Session:** Physicians Poster Session: Early side effects / Late effects and quality of life
- ☐ 22. [\[P771\] Haematopoietic stem cell transplantation in mantle cell lymphoma patients between 2001 and 2008 – A single-centre experience](#)  
**Authors:** A. Barta, A. Batai, Z. Csukly, V. Goda, L. Gopcsa, B. Kapas, L. Lengyel, N. Lovas, S. Lueff, Z. Matrai, G. Milkala, S. Nahajevszky, M. Peto, A. Sipos, E. Torbagyi, R. Rasonyi, M. Reti,

A. Tremmel, P. Remenyi, T. Masszi  
**Session:** Physicians Poster Session: Lymphoma

- 23. [\[P869\] Monitoring strategy of adenovirus infections in allogeneic stem cell transplant patients](#)  
**Authors:** H. Omar, G. Avetisyan, P. Ljungman  
**Session:** Physicians Poster Session: Infectious complications
  
- 24. [\[P603\] 11 years of single-centre experience with stem cell transplantation for multiple myeloma](#)  
**Authors:** J. Radocha, V. Maisnar, P. Zak, A. Zavrelva, M. Cermanova, M. Kmonicek, L. Jebavy, J. Maly  
**Session:** Physicians Poster Session: Multiple myeloma
  
- 25. [\[P841\] Respiratory syncytial virus infection in recipients of allogeneic stem cell transplantation: retrospective study of the incidence, clinical features and outcome](#)  
**Authors:** G. Avetisyan, J. Mattsson, P. Ljungman  
**Session:** Physicians Poster Session: Infectious complications
  
- 26. [\[P872\] Treatment of respiratory syncytial virus infection with nebulised ribavirin and the humanised monoclonal antibody palivizumab in eight haemopoietic stem cell transplant recipients](#)  
**Authors:** D.A. Tsitsikas, H. Oakervee, J. Cavenagh, S. Agrawal, J. Gribben, F. Mattes  
**Session:** Physicians Poster Session: Infectious complications
  
- 27. [\[P548\] Extracorporeal photopheresis for the treatment of steroid-resistant acute graft-versus-host disease](#)  
**Authors:** S. Fritsch, J. Tischer, G. Ledderose, B. Maier, R. Reibke, A. Rank, H.J. Kolb  
**Session:** Physicians Poster Session: Graft-versus-host disease - clinical
  
- 28. [\[P575\] Assessment of bioequivalence of a generic cyclosporine \(Equoral™\) by a prospective randomised controlled trial in allogeneic stem cell transplant \(ASCT\) recipients](#)  
**Authors:** T. Ben Othman, N. Ben Fredj, A. Klouz, A. Abdelkefi, S. Ladeb, L. Torjeman, A. Lakhali, M. Lakhali  
**Session:** Physicians Poster Session: Graft-versus-host disease - clinical
  
- 29. [\[P664\] Prognostic impact of serum ferritin concentration on survival following reduced-intensity conditioned allogeneic haemopoietic stem cell transplantation](#)  
**Authors:** R. Oakes, N. Sood, R. Pearce, G. Cook, M. Gilleece  
**Session:** Physicians Poster Session: Early side effects / Late effects and quality of life
  
- 30. [\[P519\] Human iNKT compartment homeostasis after haematopoietic stem cell allograft](#)  
**Authors:** A. Rossignol, A. Yip-Fa, C. Giraud, M. Charron, N. Maillard, A. Chauvineau, A. Barra, A. Herbelin, J.M. Gombert, F.

Guilhot

**Session:** Physicians Poster Session: Graft-versus-host disease - preclinical and animal models

- ❑ 31. [\[P1145\] Enteral nutritional support: to audit the effectiveness of percutaneous endoscopic gastrostomy tube with jejunal extension in patients undergoing allogeneic haematopoietic stem cell transplantation](#)  
**Authors:** S. Pattni  
**Session:** Nurses Poster Session: Standards of care
  
- ❑ 32. [\[P1189\] Ongoing prospective clinical trial on primary prevention of cardiac damage induced by intensive chemotherapy with angiotensin-converting enzyme inhibitors and beta-blockers: central role of a nurse as coordinator](#)  
**Authors:** A. Domenech, M. Rovira, J. Esteve, N. Borrás, A. Ciurana, M. Valverde, X. Bosch  
**Session:** Nurses Poster Session: Symptom management
  
- ❑ 33. [\[P508\] High-dose G-CSF is safe and effective for mobilisation of haemopoietic cells for autologous stem cell transplantation with clinical utility in the majority of sub-optimal mobilisers](#)  
**Authors:** A. Alfred, S. Mahmood, D.A. Jones, D. Hess, J. Wright, J. Snowden, A. Mijovic  
**Session:** Physicians Poster Session: Stem cell source
  
- ❑ 34. [\[P609\] Autologous peripheral blood stem cell transplantation in patient in advanced stage of POEMS syndrome](#)  
**Authors:** M. Cioch, J. Manko, A. Dmoszynska  
**Session:** Physicians Poster Session: Multiple myeloma
  
- ❑ 35. [\[P744\] EPO and MIP-1 alpha are associated with increased levels of vascular progenitors in autologous haematopoietic stem cell grafts](#)  
**Authors:** L. Labonte, C. Li, L. Yang, A. Gillingham, M. Halpenny, A. Giulivi, D. Allan  
**Session:** Physicians Poster Session: Non-haematopoietic tissue repair
  
- ❑ 36. [\[P867\] Serum vascular endothelial growth factor in adult haematological patients with neutropenic fever: a prospective comparison with C-reactive protein](#)  
**Authors:** E. Jantunen, S. Haemaelaenen, I. Matinlauri, T. Kuittinen, I. Koivula, A. Juutilainen  
**Session:** Physicians Poster Session: Infectious complications
  
- ❑ 37. [\[P504\] Plerixafor is highly effective in the mobilisation of PBSC for autologous transplantation from patients failing to mobilise by conventional means: the initial Scottish experience in three transplant centres](#)  
**Authors:** W.C. Gordon, P.R.E. Johnson, P.H. Roddie, P.C.A. Shepherd, F.M. Scott, J.M. Davies, L.M. Manson, D. Culligan, Y.-L. Chee, A.N. Parker, I.G. McQuaker, A. Clark, R.L. Soutar, K.W. Douglas  
**Session:** Physicians Poster Session: Stem cell source

- ❑ 38. [\[P856\] Prospective study of oral valganciclovir for pre-emptive therapy of cytomegalovirus after allogeneic stem cell transplantation](#)  
**Authors:** R. de la Camara, L. Vazquez, J. Lopez, C. Solano, D. Serrano, A. Garcia Noblejas, J.M. Ribera Santasusana, C. Ferra  
**Session:** Physicians Poster Session: Infectious complications
  
- ❑ 39. [\[P649\] Donor-derived alveolar macrophages are the effector cells in cryptogenic organizing pneumonia after SCT](#)  
**Authors:** M. Ito, M. Fujino, D. Kajiura, A. Kominami, T. Yokoyama, F. Nomura, K. Miyamura  
**Session:** Physicians Poster Session: Early side effects / Late effects and quality of life