values, [Bu+Clo], [Bu+Gem], [Mel+Clo], [Mel+Gem] and [Bu+Mel] combinations did not show synergistic cytotoxicity. However, a combination of [0.25 μM Clo + 3.5 nM Gem] resulted in about 60% inhibition of proliferation of p53-wild type NCI H929 and MM.1R cells; combination indexes = 0.1 – 0.6 suggested strong synergism. Two p53-mutated MM cell lines, RPMI 8226 and U266B1, were more resistant to these drugs. For example, exposure to [0.4 μM Clo+30 nM Gem] inhibited proliferation of RPMI 8226 only by 25%. To determine if the cytotoxicity of [Clo+Gem] is mediated by p53, H929 and MM.1R cells were pre-exposed to a p53-inhibitor, pifithrin α. More than 50% of the [Clo+Gem]-mediated cytotoxicity was reversed. The level of p53-regulated pro-apoptotic PUMA and p21 proteins increased with [Clo+Gem] but the effects were reversed in the presence of pifithrin α. ATM kinase was activated, further supporting involvement of the ATM-p53 pathway in activation of DNA-damage response. Phosphorylation of deoxycytidine kinase (DCK) increased, and proteins involved in DNA-repair and rRNA production were down-regulated. The activation of apoptosis is suggested by the cleavage of PARP1 and caspases 3 and 8. Further, mitochondrial membrane potential (MMP) decreased in cells exposed to [Clo+Gem] consistent with increased levels of proapoptotic factors cytochrome c, AIF and SMAC/DIABLO in the cytosol, suggesting mitochondrial leaks. These results show that the mechanism of synergistic cytotoxicity of [Clo+Gem] in p53-positive MM cells involves activated DCK, DNA-damage response, decreased MMP, inhibited DNA repair, and nucleolar stress through decreased rRNA. We are determining the effects of [Clo+Gem] in primary cell samples from MM patients; the data will be presented and discussed. Our investigation provides a basis for introducing nucleoside analog combination(s) in both cytoreductive induction therapy and pre-ASCT therapy in MM, and in individualizing therapy based on p53 status to avoid subjecting patients to ineffective therapy.

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Outcomes of Salvage Autologous Versus Allogeneic Hematopoietic Cell Transplantation for Multiple Myeloma Relapsed After Initial Autologous Hematopoietic Cell Transplantation

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Background: Standard therapy for multiple myeloma (MM) includes initial autologous hematopoietic cell transplantation (autoHCT1) but this is not curative and most patients will relapse. Data on salvage autoHCT2 or allogeneic HCT (alloHCT2) are limited and the optimal salvage strategy is unknown.
Methods: This is a retrospective study of MM patients >18 years of age who relapsed after autoHCT1 and underwent salvage autoHCT2 or alloHCT2 between 1995-2011 at our institution. Tandem auto-autoHCT or auto-alloHCT were excluded.
Results: Characteristics of autoHCT2 (N=27) and alloHCT2 (N=19) patients were not significantly different except the alloHCT2 median age was significantly ($P = .002$) lower (54 years) than for autoHCT2 (62 years) and more alloHCT2 patients had KPS ≥ 70% ($P = .031$). Complete and very good partial remission (CR/VGPR) improved from 7% to 56% after autoHCT2 and from 26% to 37% after alloHCT2. Of 15 patients with progressive disease (PD) at the time of autoHCT2, 5 achieved CR/VGPR and 7 PR. Nonrelapse mortality (NRM) at 3 years was 3.7% for autoHCT2 and 5.3% for alloHCT2 ($P = .901$). Median progression free survival (PFS) and overall survival (OS) for autoHCT2 (19 months, 23 months) and alloHCT2 (6 months, 19 months) were not significantly different. For those entering salvage autoHCT2 in PD, PFS at 3-years was 41.7% (15.2-68.1%) and OS at 3-years was 45% (16.1-73.9%). On multivariate analysis, time from autoHCT1 to relapse <1year vs. ≥1year (HR 24.81 [95% CI 2.4-249.9]) and no maintenance therapy vs. given after autoHCT2 (HR 12.19 [95% CI 2.5-249.9] impacted OS after autoHCT2. However, only time from autoHCT1 to relapse <1 year versus ≥1 year (HR 18.55 [95% CI 2.28-150.57]) impacted PFS after autoHCT2. For alloHCT2, no factors impacted NRM, PFS or OS. For those with relapse from autoHCT1 <1 year versus ≥1 year undergoing autoHCT2, median OS was 15 months (1-53) vs. not yet reached at 143 months and median PFS was 5 months (1-49) vs. not yet reached at 88 months. Major causes of death for alloHCT2 were PD (n= 5), GVHD (n=3), while for autoHCT2, PD (n=10), infection (n=3).
Conclusions: Salvage autoHCT2 and alloHCT2 are both feasible for patients with post autoHCT1 MM relapse. Relpase ≥ 1 year from autoHCT1 predicts for better PFS and OS in the autoHCT2 group. Those with progressive disease can also be salvaged by autoHCT2. Maintenance therapy after autoHCT2 is beneficial and should routinely be used.

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Lenalidomide Could Minimize an Engraftment Syndrome After Autologous Hematopoietic Stem Cell Transplantation in Patients With POEMS Syndrome

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Background: High dose chemotherapy followed by autologous stem cell transplantation (ASCT) is effective therapy for patients with POEMS syndrome. However, treatment before ASCT has not been standardized. In addition, patients are at high risk for an engraftment syndrome (ES) after ASCT, which is associated with morbidity. Lenalidomide has recently emerged as therapeutic options in patients with POEMS syndrome. The purpose of the present study is to evaluate the role of lenalidomide before ASCT.
Patients: Between December 2005 and May 2011, 7 patients (pts) with POEMS syndrome underwent ASCT at our institution (median age at ASCT: 54 years, range: 36-66). Peripheral blood stem cell (PBSC) was collected using cyclophosphamide (CY) and granulocyte colony-stimulating factor (G-CSF). PBSC was used in 6 pts, whereas bone marrow and PBSC were used in a patient. Patients were conditioned using melphalan (L-PAM; 200mg/sqm: n=5, 140mg/sqm: n=1, 100 mg/sqm: n=1).
Results: Of 7 pts, 5 have achieved neurologic improvement after ASCT and are alive with a median follow-up of 44 months (range, 20-81 months), whereas 2 were not evaluated for response because of early death. Interestingly, 2 pts who had received prior therapy, lenalidomide (Case6: 15-20mg per day for 53days, Case7: 15mg per day for 15days), have been alive without ES after ASCT. However, of 5 pts who had not received lenalidomide, 4 pts had ES after ASCT and consequently 2 pts died (5 and 7 months).

Case	Age	Sex	Mobilization regimen	Prior therapy	ES	Response after ASCT	Observation period (months)	Outcome
1	36	F	CY+ G–CSF	–	No	Yes	82	Alive
2	49	F	CY+ G–CSF	–	Yes	Yes	81	Alive
3	45	F	CY+ G–CSF	Dex	Yes	Yes	45	Alive
4	63	M	CY+ G–CSF	–	Yes	No	6	Dead
5	52	M	CY+ G–CSF	L–PAM+PSL	Yes	No	7	Dead
6	66	F	CY+ G–CSF	Len	No	Yes	25	Alive
7	54	M	CY+ G–CSF	Len+Dex	No	Yes	20	Alive

Conclusion: Lenalidomide has the advantage of being associated with a much lower risk of peripheral neuropathy than new agents such as bortezomib and thalidomide. In addition, lenalidomide could result in successful ASCT without severe ES through possible immunomodulating effects before ASCT.

POSTER SESSION 1: PEDIATRIC DISORDERS

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Treatment of High-Risk Pre-B Acute Lymphoblastic Leukemia in a Fanconi Anemia Patient With Reduced-Intensity Chemotherapy

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Fanconi anemia (FA) is an inherited bone marrow failure syndrome that is associated with multiple congenital anomalies and a predisposition to cancer, primarily acute myeloid leukemia and oropharyngeal cancers. Acute lymphoblastic leukemia (ALL) has also rarely been reported. Because of their rarity, there is no consensus on how to treat leukemias when they develop. We report an 8-year old boy with FA, who developed high-risk pre-B ALL due to an unfavorable DNA-index, and monosomy 7. Patient received low-risk ALL induction chemotherapy (vincristine 1.5 mg/m^2 iv, weekly $\times$ 4; prednisone 40 mg/m^2/day orally for 28-days then tapered; Peg-asparaginase 2500 IU/m^2 on day 3, intrathecal cytarabine on day 0, intrathecal methotrexate on day 14). Patient went in remission promptly by day 14. The patient developed liver dysfunction and a fungal infection, which were treated accordingly. Following induction, the patient developed prolonged myelosuppression that required regular platelet and PRBC transfusions. He was treated with non-myelosuppressive post-induction chemotherapy for 6 months prior to stem cell transplantation (SCT). His therapy consisted of two doses of Peg-asparaginase and two courses of oral dexamethasone for 5 days each. During this period, serial bone marrow biopsies showed that the patient remained in remission. Moreover, cytogenetic analysis showed a disappearance of monosomy 7. Because the patient had no matched donor, he was given T-cell depleted haploidentical SCT from his mother. The patient's lymphoid and myeloid donor cell chimerism was 100 % on day +47 of SCT. The patient's condition was complicated by a severe adenovirus infection to which he succumbed on day +60 post SCT. In conclusion, there is no standard chemotherapy treatment for patients with FA and ALL. Our patient's high-risk ALL appeared to respond to low-risk induction and minimal non-myelosuppressive post-induction chemotherapy. These observations suggest that minimal chemotherapy may be effective in these patients while awaiting SCT.

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Allogeneic Stem Cell Transplant for Children With Sickle Cell Disease Reduces Healthcare Utilization

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The lifelong health care cost of a patient with sickle cell disease (SCD) is estimated at ~$1 million (Kauf, AJH 2009). Allogeneic stem cell transplantation (alloSCT) remains the only curative option for SCD, but no data exists investigating health care utilization related to alloSCT. We hypothesize that alloSCT in children with SCD reduces health care utilization in comparison to children with SCD who do not receive alloSCT.

Financial data from 2002-2011 was analyzed across the two groups. The health care utilization was determined over three time periods: pre-alloSCT, during alloSCT (day 0 to day +365), and post-alloSCT. The control group consisted of patients referred for alloSCT and/or HLA typed without alloSCT. Subjects without inpatient or outpatient visits during the study time periods were included in the analysis with a value of 0. The number of inpatient/outpatient visits was compared with Poisson regression method, and health care cost was compared with un-paired t-test.

The alloSCT and control cohorts included 26 patients (mean age - 6.78yrs), and 47 patients (mean age - 5.15yrs), respectively. The 3-yr EFS for patients receiving HLA matched sibling alloSCT was 100% and 44.4% for unrelated cord blood transplant recipients. The mean total cost per patient during the alloSCT year was $414,000 inpatient and $28,000 outpatient. The average monthly inpatient visits were similar in pre and post-alloSCT time periods; while the number of inpatient visits in the post-alloSCT period was significantly lower than the control group (0.03 $\pm$0.10 vs. 0.13$\pm$0.13/month, $P = .0003$). The average number of outpatient visits was also significantly lower post-alloSCT compared to pre-alloSCT (1.08$\pm$1.05 vs. 3.84$\pm$4.33/month, $P < .0001$). When compared to controls, the post-alloSCT cohort had significantly higher outpatient visits (1.08 $\pm$1.05 vs. 0.26$\pm$0.29/month, $P < .0001$). Detailed health care utilization is described in the table below.

This analysis indicates that post-alloSCT health care utilization decreases when compared to pre-alloSCT. However, this does not translate into decreased cost when compared to controls. This may reflect the limitation of the study period to identify the actual changes in utilization over time. More detailed analysis is ongoing to determine variables contributing to the substantial alloSCT associated costs and the long term change in costs over time.