''focus on...'' session: transplantation

027 THE GICAT (ITALIAN COOPERATIVE GROUP ON AIDS AND TUMORS) EXPERIENCE WITH HIGH DOSE THERAPY AND PERIPHERAL BLOOD STEM CELL TRANSPLANTATION AS SALVAGE TREATMENT FOR HIV-RELATED LYMPHOMA: LONG-TERM RESULTS AND MULTIVARIATE ANALYSIS FOR PROGNOSTIC FACTORS

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Introduction: The introduction of highly active antiretroviral therapy (HAART) has allowed the use of intensive treatment in HIV-related lymphoma (HIV-Ly).

Materials and methods: In 2000 we started a prospective study of HDT and PBSCT in HIV+ pts with primary refractory or relapsed HIV-Ly.

Results: From 2000 to 2007 50 pts entered the study. 31 had NHL and 19 HL; 20 had refractory disease, 5 PR, 22 1st and 3 2nd relapse; 60% stage IV and 26% bone marrow (BM) involvement. CD4 count was 218/mcl (17-561) and 11 pts had CD4 < 100. Pts first received 2-4 cycles of debulking chemotherapy (CT) followed by PBSC collection: 2 died from toxicity and 10 had progressive disease (PD); 1 pt retracted and 6 failed PBSC mobilization. 31 pts collected PBSC (median CD34+ 5.9x10e6/kg); 4 had PD soon after collection and 27 (54%) received HDT (BEAM) according to the protocol. Treatment-related toxicity was low with no toxic deaths. All pts received HAART during the entire treatment program. CD4 count decreased after treatment and recovered few ms after PBSCT (median 190 pre PBSCT and 119 at +3, 157 +6 and 285 +12). 3 pts had PD after PBSCT and 3 relapsed after CR; 21 are alive and disease free, after a f-up of 44 ms (2-70), with OS 75% and PFS 76%. Failure to achieve CR was the only independent prognostic factor for OS [HR 7.6 (1.3-43.5); p= 0.02] and PFS [HR 8.2 (1.4-47.3); p= 0.01] in pts receiving transplant. According to the intention to treat analysis, the median survival of the entire series (50 pts) was 33 ms (OS 50% and PFS 49%; f-up 45 ms). Stage IV [OR 5.7 (1.2-26.3); p= 0.02] and CD4 < 100 [OR 25.4 (2.2-284.7); p= 0.008] were the only factors significantly associated with a lower possibility to receive transplant, in multivariate analysis. The multivariate analysis of prognostic factors showed that BM involvement [HR 5.2 (2.0-13.9); p= <0.001], PS 2 [HR 3.8 (1.6-8.8); p= 0.001] and CD4<100 [HR 6.7 (2.5-18.0); p= <0.001] were associated with poorer OS and BM involvement [HR 3.4 (1.3-8.9); p= 0.009] and CD4< 100 [HR 6.1 (2.3-15.9); p< 0.001] with poorer PFS.

Conclusions: This study demonstrates the feasibility, safety and long-term efficacy of HDT with PBSCT as salvage treatment in HIV-Ly. Fiftyfour % of eligible pts underwent PBSCT with low CD4 count and advanced stage lymphoma associated with a lower possibility to complete the treatment program. Both HIV-related factors (CD4 count <100) and lymphoma-related factors (bone marrow involvement), together with poor PS, were associated to poorer outcome in an intention to treat analysis.

028 EVALUATION OF MYELOABLATIVE THERAPY FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION IN FIRST REMISSION IN PATIENTS WITH ADVANCED STAGE FOLLICULAR LYMPHOMA AFTER INITIAL COMBINED IMMUNO-CHEMOTHERAPY (R-CHOP) AND CONVENTIONAL CHEMOTHERAPY (CHOP): ANALYSIS OF 540 PATIENTS TREATED IN PROSPECTIVE RANDOMIZED TRIALS OF THE GERMAN LOW GRADE LYMPHOMA STUDY GROUP (GLSG)

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Background: the anti-CD20 antibody rituximab has dramatically changed the treatment paradigms for advanced stage follicular lymphoma (FL) and has allowed to improve overall survival in this patient group for the first time. One of the key current questions is whether myeloablative treatment followed by autologous stem cell transplantation (ASCT) in first remission still adds clinical benefit in the era of initial rituximab/chemotherapy induction.

Methods: we now report on the treatment outcome of 540 patients with advanced stage FL, treated with ASCT versus IFN-alpha maintenance in first remission after initial therapy with CHOP versus Rituximab/CHOP (R-CHOP) in two consecutive prospective trials of the GLSG.

Results: 137 pts and 104 pts were treated with CHOP or R-CHOP, respectively, followed by ASCT; CHOP or R-CHOP followed by IFN-maintenance was applied in 160 pts and 139 pts, respectively. Patient characteristics were well balanced between the different groups. The estimated progression free survival 5 years after the end of initial (R-)CHOP induction therapy was 27% for CHOP followed by IFN-alpha maintenance, 65% for CHOP followed by ASCT, 68% for R-CHOP followed by IFN-alpha maintenance and 80% for R-CHOP followed by ASCT.

Conclusions: Also the differences between ASCT and IFN-alpha maintenance are not significant after initial R-CHOP at the time point of analysis, the data indicate that ASCT in first remission might be able to further improve PFS after initial immunochemotherapy. Our observations encourage prospective randomised trials to test the role of ASCT in first remission in the era of rituximab in FL.

029 MYELOABLATIVE THERAPY FOR RECURRENT HODGKIN LYMPHOMA: GOOD SUCCESS RATES IRRESPECTIVE OF PREVIOUS TREATMENTS IN THE UKLG LY09 TRIAL (ISRCTN97144519)

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Introduction: This randomised trial compared ABVD with two multi-drug regimens (MDR) for initial therapy of advanced Hodgkin Lymphoma (HL). The results of salvage therapy have been examined.

Methods: Patients (pts) with advanced HL were randomised to standard ABVD or one of two MDRs: Alternating ChlVPP/PABlOE or Hybrid ChlVPP/EVA. Pts who developed recurrence, or in whom remission was not achieved, were advised to undergo high dose therapy (HDT).

Results: 807 pts were randomised; 406 allocated ABVD and 401 MDRs. At 65 months median follow-up, 220 PFS events were reported. 101 pts were treated with HDT as the first treatment after initial therapy: 27 after inadequate response and 74 for recurrence. Median time from diagnosis to HDT was 11 months. At median 48 months follow-up, 87% (95%CI 79%, 93%) pts remain alive at 2 years after HDT and 66% (95%CI 54%, 75%) at 5 years. In univariate analyses, prior use of ABVD or MDR had no influence upon survival after HDT (Hazard ratio (HR) 0.817 (95% CI 0.398, 1.678) There is limited evidence that radiotherapy after initial chemotherapy is associated with poorer survival after HDT (HR 0.56, 95%CI 0.25, 1.28) and a suggestion that pts who receive 6 cycles of chemotherapy do better after HDT than pts who receive more (HR 1.35, 95% CI 0.62, 2.93) but less well than those who had fewer (HR 0.45, 95%CI 0.15, 1.41). Results for pts with primary refractory disease (81% alive at 2 years) are similar to those treated for recurrence (90% alive at 2 years) (HR 0.97, 95%CI 0.44, 2.15).

Conclusion: Results of HDT-based salvage are good for pts with HL, with durable remissions obtained in a high proportion. In this sample of 101 pts, statistical power is limited but there is no clear evidence that outcome after HDT is affected by the complexity of initial therapy or the timing of HDT.

030 ALLOGENEIC STEM CELL TRANSPLANTATION IN MATURE T-CELL LYMPHOMA - AN ENCOURAGING ALTERNATIVE

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Introduction: Patients (pts) with mature T-cell lymphoma (TCL) are known to have high rates of primary progressive disease and relapse with a poor outcome. We here report on 91 pts with TCL who underwent allogeneic stem cell transplantation (SCT) in EBMT centres between 2000 and 2005.

Patient characteristics: Histological subtypes were anaplastic large cell lymphoma (ALCL, 26.8%), peripheral TCL (59.3%) and TCL unspecified (12.1%), respectively. From the ALCL pts 5 were ALK pos and 6 ALK neg (15 unknown). Median age at SCT was 42 years (yrs, 18-66); median time from diagnosis to SCT was 18 months. 72.5% of pts had stage III/IV disease. Data on IPI were available for 47 pts, 2/3 had an IPI >=2. At SCT 64.8% of pts had chemosensitive and 22% chemorefractory diesease, respectively. 68.1% of pts had failed at least one treatment regimen (other than CR 1 [15.4%] or PR1 [11%] or unknown); 48.4% of pts had had more than 1 relapse or were considered progressive or refractory, and 35.2 % had had a previous auto SCT. Donors were HLA identical siblings in 60.4%, matched unrelated (MUD) in 23.1% and

others in 16.5%. Stem cell source was peripheral blood in 73.6%. 53.8% of pts received a reduced intensity conditioning (RIC).

Results: This analysis was restricted to 74 pts transplanted from siblings or MUD. The cumulative incidence of aGvHD at day 100 was 56.7% and for cGvHD at 2 yrs was 56.4%, respectively. At the same time the non relapse mortality (NRM) was 32%, relapse rate (RR) 29%, PFS 40.6% and OS 44.7%, respectively. In multivariate analysis, poor performance status (PS) at SCT (p<0.001) and ex vivo T-cell depletion (p=0.001) were associated with a higher NRM, and RIC (p=0.03) was associated with a higher RR, respectively (trend for refractory disease p=0.06). Adverse factors for PFS were poor PS, ex vivo T-cell depetion and CMV status other than neg-neg. cGvHD caused a higher NRM (p=0.01) but had no significant impact on RR.

Conclusion: With a high percentage of very poor prognosis pts (68% failure of first treatment, 48% refractory, progressive or worse than 1st relapse) a PFS of 40.6% at 2 yrs can be considered quite encouraging. Prospective trials are necessary to further define the role of allogeneic SCT in TCL pts.

031 GRAFT VERSUS LYMPHOMA EFFECT FOR AGGRESSIVE T-CELL LYMPHOMAS IN ADULTS: A STUDY FROM THE SFGM-TC (SOCIÉTÉ FRANÇAISE DE GREFFE DE MOELLE ET DE THÉRAPIE CELLULAIRE)

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Aggressive T-cell Lymphomas (ATCL) represents 10-15 % of non-Hodgkin's lymphoma (NHL) in adults. We conducted a retrospective analysis which included 77 ATCL patients who underwent allo-SCT. The diagnosis included: Anaplasic Large Cell Lymphoma (ALCL) (n=27), Peripheral T-cell Lymphoma Not-Otherwise Specified (PTCL-NOS) (n=27), Angioimmunoblastic T-cell Lymphoma (AITL) (n=11), Hepatosplenic g/d lymphoma (HSL) (n=3), T-cell granular lymphocytic leukemia (T-GLL) (n=1), nasal NK/T-cell lymphoma (nasal-NK/L) (n=3) case or non-nasal NK/T-cell lymphoma (non nasal-NK/L) (n=2), enteropathy-Type T-cell (n=1) and HTLV-1 lymphoma (n=2). Fifty-seven patients received a myeloablative conditioning regimen. Donors were HLA-matched in 70 cases and related in 60 cases. Thirty-one patients were in CR at the time of allo-SCT while 26 were in PR. Five-years toxicity-related mortality (TRM) incidence was 33% (95%CI, 24 to 46%). The 5-year estimates overall and event-free survivals were 57% (95 %CI, 45 to 68%) and 53% (95%CI, 41 to 64%), respectively. In multivariate analysis, a chemo-resistance disease at time of allo-SCT and occurrence of severe grade 3-4 acute graft-versus-host disease (aGVHD) were the strongest adverse prognostic factors for OS ($p= 0.03$ and $p=0.03$, respectively). Disease status at transplantation significantly influenced the 5-years EFS ($p= 0.003$) and a HLA-mismatched donor increased TRM ($p= 0.04$). Allo-SCT is a therapy in T/NK lymphomas patients and is worth further investigation in prospective clinical trials.

032 HLA-IDENTICAL SIBLING ALLOGENEIC STEM CELL TRANSPLANTATION (ALLOSCT) FOR PATIENTS WITH PRIMARY CUTANEOUS T-CELL LYMPHOMA (CTCL).

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Patients (pts) with aggressive forms of Mycosis Fungoides (MF), Sézary syndrome (SS) and other subtypes of primary CTCL have a dismal prognosis with conventional therapy. We have now conducted a retrospective analysis of 46 recipients of an alloSCT from a HLA-Identical sibling for advanced CTCL reported to EBMT between 1997 - 2006 (30 male; median age 46; median reported follow up in survivors, 27 months). AlloSCT was performed at a median of 23 (3-313) months from initial dx, following a median of 3 (1-8) prior lines of therapy, and with a reduced-intensity (RIC) alloSCT conditioning in 31 (67%) cases. Only 17% of pts were in CR at the time of alloSCT, while the rest were primary refractory (27%), in progression (34%), or in PR (22%). Non-relapse mortality at 1 year was 20.1%, and appeared significantly poorer in patients receiving myeloablative conditioning (MAC) than in those RIC alloSCT (43.8% vs 9.7%; p=0.02). Acute graft versus host disease (GVHD) occurred in 41% of patients at risk, and chronic GVHD in 56% of patients alive at day +100. The CI of disease relapse was 33.9% at 2 years after alloSCT (RIC 37.5% vs MAC 26.7%; ns). Postransplant first-progression free survival (PFS) was 46% at 2 years (RIC 52.8% vs MAC 29.3%; ns). Out of 16 patients who relapsed, 9 remain alive and 3 of these are in CR at last follow up, indicating that a proportion of patients can achieve a better control of their CTCL following relapse after alloSCT. Estimated four-year overall survival (OS) for the whole series was 56.7%, with a trend towards an improved OS in RIC than in MAC alloSCT (60.5% vs 47.1%; p=0.1). Overall, this outcome appears superior to the expected median OS for these patients with conventional therapy.