

as a control group. CD95 (FAS) and P53 were studied by flowcytometry, BCR/ABL gene was studied at the cytogenetic and molecular level by RT PCR and ultrastructural apoptotic changes were studied by EM.

**Results:** Mean level of P53% was highly increased in the all CML patients compared with controls ( $p=0.04$ ). Mean level of CD95% expression was higher when measured on the whole cell population in the (accelerated and/or blastic crisis) compared with chronic phase and controls ( $p=0.14$ ). By selecting CD34+ve cells, lower levels of CD95% expression were found in the (accelerated and/or blastic crisis phase) compared with the levels expressed on the whole cell population in the same phase. Mean level of P53% in the treated cases was higher compared to newly diagnosed cases (before treatment) showing a statistically significant difference ( $p>0.01$ ). Higher mean levels of CD95% on whole cell population, and on CD34+ve selected cells were detected after treatment ( $p=0.30$ ,  $p=0.83$ ). The mean levels of P53% and CD95% were higher in BCR/ABL fusion gene positive cases than BCR/ABL fusion gene negative cases but didn't reach significant levels respectively ( $p=0.21$ ,  $p=0.62$ ).

**Conclusions:** P53% and CD95% levels expression in the accelerated and blastic crisis phases of CML patients were higher than those in the chronic phase. Comparative studies for the apoptotic markers with cytogenetic analysis and RT PCR techniques revealed higher levels of P53 and CD95 in BCR/ABL positive cases than BCR/ABL negative cases. Also P53 and CD95 levels were higher in treated cases than newly diagnosed cases.

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POSTER

### Fatal trichosporon fungemia in patients with hematologic malignancies

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**Background:** Invasive *Trichosporon* infection is becoming increasingly recognized in patients with hematologic malignancies, whereas most studies have been sporadic case reports and little is yet known about details of this infection. Our study aims to clarify the clinical characteristics and management of this disease.

**Materials and Methods:** We studied 32 consecutive patients with hematologic malignancies who developed *Trichosporon* fungemia (TF) treated at 7 regional tertiary care hospitals in Japan over a 15 years period (1992 to 2007).

**Results:** Age ranged 4–85 years (mean, 56). Male predominated (91%). Underlying disease included acute myeloid leukemia (AML) in 30 patients (94%), acute lymphoblastic leukemia in 3, chronic myeloid leukemia in 2, and mature lymphoid neoplasms in 3. Thirty patients (94%) had received intensive chemotherapies, and 5 of them undergone allogeneic hematopoietic stem cell transplantation. Twenty-six patients (81%) had neutropenia at the onset. Breakthrough TF occurred in 29 patients (91%) during the use of antifungals, 18 of whom (62%) were receiving micafungin (MF). Attributable death was seen in 24 patients (75%) and 21 of them (88%) died within 10 days after the onset. Univariate analysis revealed that neutrophil recovery was associated with patient survival ( $p<0.01$ ), and the presence of pneumonia ( $p=0.04$ ) and hyperglycemia ( $p=0.01$ ) were correlated with poor prognosis. Overall survival was longer in patients treated with azole containing regimen than in those without azole (log-rank test,  $p<0.01$ ). TF tended to occur like an epidemic disease in certain hospitals; however, modification of the antifungal regimen, including limited use of MF, produced satisfactory results.

**Conclusion:** Since TF is mostly lethal at present unless neutrophil recovery occurs, we should pay attention to the occurrence of this infection in patients with hematologic malignancy, particularly AML. When we encounter TF, we should treat with azole and revise the use of agents lacking anti-*Trichosporon* activity to prevent breakthrough infection. This is the largest study of proven invasive trichosporonosis in patients with hematologic malignancies.

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POSTER

### Safety of romiplostim for treatment of chemotherapy-induced thrombocytopenia (CIT) in patients with advanced non-small cell lung cancer (NSCLC)

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**Background:** CIT is a potentially serious side effect of chemotherapy with limited treatment options. Romiplostim is an Fc-peptide fusion protein (peptibody) that increases platelet production by the same mechanism as thrombopoietin.

**Methods:** This was a phase 2, randomized, double blind, placebo-controlled study with the primary objective to evaluate the safety of romiplostim in NSCLC patients (pts) receiving myelosuppressive chemotherapy. Eligible pts were >18 years old with stage IIIB or IV NSCLC receiving Q21 day gemcitabine and platinum chemotherapy and had experienced a transient platelet count decrease to  $<100 \times 10^9/L$  in a previous treatment cycle. Pts were randomized 4:1 to romiplostim or placebo and received one s.c. administration of romiplostim at 250, 500, or 750  $\mu g$  or placebo on day 2 for up to 5 chemotherapy cycles.

**Results:** Overall, 63 pts were randomized. The table contains safety and efficacy parameters for romiplostim. Romiplostim treated pts showed similar rates of adverse events (AEs) and thrombotic AEs as placebo pts. The rate of serious AEs was numerically higher in romiplostim treated pts than in placebo pts, but there were no dose-dependent trends in any AE category. The most common serious AEs were anemia and thrombocytopenia. No pts tested positive for neutralizing antibodies to romiplostim or eTPO. Two non-treatment related deaths were reported: one in the 500  $\mu g$  group (sepsis) and one in the 750  $\mu g$  group (progression of NSCLC). There was no evidence that administration of romiplostim had a beneficial impact on platelet count related efficacy endpoints.

**Conclusion:** Romiplostim appeared to be a well-tolerated treatment in NSCLC pts with CIT. Sample size was limited and additional studies are necessary to define the optimal dose and schedule of romiplostim in this setting.

Overall pt incidence of AEs and first on-study treatment cycle findings

	Placebo (N = 12)	Romiplostim*		
		250 $\mu g$ (N = 16)	500 $\mu g$ (N = 18)	750 $\mu g$ (N = 16)
Overall AEs				
Any AE, n (%)	12 (100)	16 (100)	18 (100)	14 (88)
Serious AEs n (%)	1 (8)	7 (44)	5 (28)	5 (31)
Thrombotic AEs, n (%)	0	1 (6)	1 (6)	1 (6)
First on-study treatment cycle				
Grade 3 or 4 thrombocytopenia, n (%)	5 (42)	7 (47)	7 (39)	7 (44)
Duration of grade 3 or 4 thrombocytopenia, days	2	4	3	2
Platelet transfusions, n (%)	1 (8)	4 (27)	1 (6)	1 (6)
Chemotherapy dose reduction, day 8, n (%)	2 (17)	4 (27)	4 (22)	5 (31)

\*a pt in the 750mcg cohort was not dosed and a pt in the 250mcg cohort did not complete the first cycle so they were not included in the safety and/or efficacy analysis sets.

ClinicalTrials.gov Identifier NCT00413283. Trial status: complete. Trial sponsor: Amgen Inc.

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POSTER

### Single vs double dose palonosetron for the prevention of acute and delayed nausea and vomiting in patients undergoing high dose chemotherapy and autologous stem cell transplantation

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**Objectives:** The vast majority of patients (pts) undergoing high dose chemotherapy (HDT) and autologous stem cell transplantation (ASCT) still experience major acute and delayed chemotherapy-induced nausea and vomiting (CINV), showing how emesis control in the ASCT setting remains sub-optimal. Palonosetron (PALO), a new 5-hydroxytryptamine receptor antagonist with long half-life and high receptor binding affinity, achieves

a significant control of CINV in pts receiving moderately/highly emetogenic chemotherapy. We prospectively evaluated the efficacy of a single or double i.v. dose PALO in pts undergoing HDT and ASCT.

**Methods:** A total of 60 pts (M/F = 32/28), median age 45 yrs (r16–64), with diagnosis of lymphoma (29), myeloma (24), sarcoma (5), acute leukemia (1), breast cancer (1) were accrued. The first cohort (30 pts) received a single iv PALO dose (0.25 mg) plus 8 mg of dexamethasone (DMS) 30' before starting of HDT while in the second cohort (30 pts) the first dose was followed by a further PALO (0.25 mg)/DMS (8 mg) injection 48h after HDT. The distribution of conditioning regimens (high-dose melphalan = 28, BEAM = 25, MitoMel = 6, ThioEpiCTX = 1) was comparable between the two cohorts. Acute (24h) and delayed (120h) CINV episodes were rated by the visual analogic scale (MASCC/MAT) while CINV impact on daily activities was self-assessed by pts (at 120h from starting of HDT), through the Functional Living Index-Emesis (FLIE) tool.

**Results:** No significant differences between the two groups (single vs double PALO) emerged as to acute CINV evaluation (MAT) since 98% of pts achieved a complete response (CR=no emesis, no need for rescue therapy) with only 17 pts (28%) experiencing moderate nausea (median intensity = 5, r 1–10). Double-dose PALO displayed a trend for a better control of delayed nausea which occurred in 53% vs 77% of pts ( $p=0.0581$ ). In addition, double PALO dosing had a highly significant impact on nausea-related modifications of daily activities. FLIE nausea score was of a median value of 55.26 (r47.5–58.9) in pts receiving two doses of PALO vs 40.92 (r35–45.2) for pts treated with the single PALO dosing ( $p=0.0009$ ).

**Conclusion:** Our results indicate that double dose PALO achieves an optimal control of acute/delayed CINV and significantly reduces the detrimental impact of nausea on daily activities in patients undergoing HDT. The impressive activity of PALO in the ASCT setting might be possibly improved by combination with NK1 receptor antagonists.

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## POSTER

### Secondary malignancies after stems cell transplantation – a single centre experience

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**Background:** It is considered that patients (pts) submitted to Stem Cell Transplantation (SCT) are at increased risk of develop secondary primary malignancies which may be related to several factors, such as primary malignant disease, radiation/chemotherapy treatment or graft-versus-host disease. Authors aim to report a single centre experience on this issue.

**Material and Methods:** Retrospective analysis of pts who developed secondary malignancies (SM), selected from all stem cell transplanted patient, from June 1989 to December 2008, in the Portuguese Oncology Institute, Porto. Statistical analysis was performed using SPSS v16.0.

**Results:** A total of 1026 patients underwent 1190 SCT during this period - 599 autologous (AutoSCT) and 591 allogenic (AlloSCT). SM after SCT were identified in 28 pts (2.7%) – 16 in autoSCT and 12 in alloSCT. 78.6% of pts were male and median age was 38 years (range: 3–66). Conditioning plan did not predict total body irradiation or any other radiation strategy. Most common primary malignancy was hodgkin lymphoma (7 cases), followed by non-hodgkin lymphoma and acute myeloid leukaemia (6 cases each). Secondary malignancies, according to their frequency, were: oral cavity/tongue, colon, sarcoma, acute myeloid leukaemia, and myelo-displastic syndrome (3 cases each); thyroid, urinary tract and cervix (2 cases each); breast, esophagus, PNET, skin (basocellular carcinoma), renal, gastric and hepatocellular cancer (1 case each). Four pts developed a third malignancy (sarcoma, esophagus, thyroid and non-hodgkin lymphoma). SM was responsible for 12 (42.9%) of the 16 deaths observed in this set of patients. Ten years overall survival after SM diagnose was 41.7% (31.2% in AutoSCT and 60% in AlloSCT). Median time from SCT to SM was 51.5 months (range: 1–177). Hodgkin lymphoma seems to be related with secondary myelo-displastic syndrome ( $p=0.055$ ). No statistical significant independent prognostic factor was found.

**Conclusions:** A low incidence of SM was found, particularly in AlloSCT pts. It is important to conduct larger studies in order to determinate possible risk factors and better manage these events.

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## POSTER

### Hepatitis B virus (HBV) reactivation in patients with resolved prior HBV according to HBV profiles in the era of immunochemotherapy

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**Background:** The epidemiology and factors affecting HBV reactivation in patients with resolved prior HBV (HBsAg -ve; anti-HBc +ve) has not been defined. We aim to analyse the HBV profiles of patients with resolved prior HBV and correlate them with the risk of reactivation, particularly in those receiving immunochemotherapy.

**Materials and Methods:** 374 patients from 2005–09 were included. HBsAg, anti-HBc, anti-HBs and HBV DNA were tested. HBV reactivation was defined as the reappearance of HBsAg with an increase in HBV DNA levels when compared with baseline.

**Results:** 374 had both HBsAg and anti-HBc tested, 124 (33.2%) had resolved prior HBV. The proportion of resolved HBV increases with age, rising from 12.5% in patients 10–20 yrs to 58.5% in 70–80 yrs, ( $p<0.01$ ). 95 were tested for anti-HBs, which was positive in 67 (67.4%). 87 were tested for HBV DNA, which was detectable in 5 (5.7%), 2 were anti-HBs positive, 2 were negative and 1 was not tested. Overall, 103 patients with prior HBV received systemic treatment and 3 reactivated (2.9%). Of note, 1 reactivated despite having high anti-HBs titer (90mIU/ml). Among patients receiving Rituximab-based treatment and no anti-viral prophylaxis, the reactivation rate was 3.1% (2/65). Of note, 4 patients received maintenance-Rituximab and 1 (25%) reactivated. Of the 5 patients with detectable HBV DNA, 1 reactivated (20%).

#### Conclusions:

1. In 3 lymphoma patients in an endemic area have prior HBV, although the prevalence appears decreasing in younger patients, possibly due to an active immunization program;
2. 6% of our patients were viraemic despite being HBsAg negative, suggesting that a polyclonal EIA (enzyme immunoassay) for HBsAg may have a role in detecting HBV mutants, compared to the current monoclonal EIA;
3. The rate of reactivation in patients with resolved HBV is relatively low, even among patients treated immunotherapy without antiviral prophylaxis. This coupled with the high prevalence of resolved HBV suggest that routine prophylaxis may not be feasible or indicated in all;
4. Nonetheless, our data caution that patients receiving maintenance-Rituximab or having detectable HBV DNA may be at increased risk of reactivation and the role of prophylaxis further evaluated;
5. Anti-HBs appears to have a limited immune-protective role as 2 patients were viraemic despite having high anti-HBs titers (values). Further, 1 patient without viraemia reactivated despite having high anti-HBs titer;
6. These results are novel.

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## POSTER

### Influence of bevacizumab on platelet function in vivo

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**Background:** Haemorrhage, as well as arterial and venous thromboembolism are well known side effects associated with bevacizumab. The pathophysiological mechanisms involved are poorly understood. We hypothesized from preclinical data, that platelet function may be a possible site of interaction of vascular endothelial growth factor (VEGF) and bevacizumab. We aimed at testing this hypothesis in a clinical observational study.

**Material and Methods:** Platelet adhesive and aggregatory functions were tested with a platelet function analyzer (PFA-100) inducing platelet activation with either epinephrine (EPI) or adenosinediphosphate (ADP). Soluble P-selectin (sP-sel) as a marker of platelet activation was measured using a commercially available immunoassay-kit. In 22 patients with advanced metastatic disease treated with cytostatic chemotherapy and bevacizumab, PFA-100 closure times (CTs) and sP-sel plasma levels were assessed before and immediately after first treatment with bevacizumab and after 6 weeks of treatment.

**Results:** Mean PFA-100 CTs (with 95% confidence interval (CI)) before, after first bevacizumab application and after 6 weeks were 112.6 sec (99.8–125.4), 110.9 sec (98.5–123.3) and 110.8 sec (94.0–127.7) respectively with EPI ( $p>0.05$ ). CTs for ADP were 79.7 sec (71.9–86.7), 82.1 sec (72.7–90.8) and 81.0 sec (72.8–89.2), respectively ( $p>0.05$ ).