carcinoma thyroid patients and follicular thyroid were 87[12.7%]. Out of 20 males who had follicular carcinoma thyroid 11 [55%], majority of them were in the third and fourth decades. Out of 67 females who had follicular carcinoma thyroid 16[23%] had bone metastases, majority of them were in the fifth and sixth decade.
Results: Out of 87 patients with bone mets, 27 (31.03%) presented with bone metastases, the commonest being skull and pelvis. 4 patients (14.81%), had metastasis in more than one site. 10 (37.03%) patients presented primarily as bone metastases. 3 (11.11%) patients had external radiotherapy to the bone for palliative pain relief. 7 patients (29.92%) lost follow up. 9 (33.33%) had two year follow up with an average ablation dose of 190MCIU and the disease remains static. 3 (11.11%) patients with an average 400MCIU as ablation dose had progressive disease. 8 (29.62%) patients had regression of the lesion with an average dose of 270MCIU and they were followed up for an average of 6 years. All the patient had residual disease in the neck for which I131 ablation was done with an average dose as 90 mciu. The commonest site of regression were spine and long bones. All patients with static or progressive disease had initial high thyroglobulin value of more than 300.
Conclusion: Bone metastases more common in males in third and fourth decades and they have more chance of having bone Mets with follicular carcinoma thyroid. 30% of the patients can have regression of their bone metastases with repeated I-131 ablation up to 1000MCIU and initial high thyroglobulin is an indicator of poor prognosis. External radiotherapy can be given to alleviate bone pain.

Haematological Malignancies

Oral presentations (Wed, 26 Sep, 09.00−11.00)
Leukaemia, lymphomas, transplantation (adults)

6000 ORAL

Quality assessment of FDG PET imaging in clinical trials: definition of standard indicators and longitudinal assessment in patients treated for lymphoma

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Introduction: F-18 FDG PET is widely applied in clinical oncology. It remains a heterogeneous process. A recent consensus was unable to provide a solution for quality assessment (Juweid et al, 2007). We developed a method for quality control (QC) and validated it longitudinally in a cohort of patients treated for lymphoma.
Material and Methods: PET scan was performed in 79 subjects using a PET/CT Biograph 16. Careful and reproducible protocols of acquisition and analysis were applied. QC method was based on data of 30 normal subjects and further validated using longitudinal data of 153 PET scans/49 patients under treatment for lymphoma and followed for up to 32 months. Mean standardized uptake values (SUVm) were obtained for normal tissues (lung, liver, and trabecular bone of L4 vertebral body). Two observers performed blind analyses in order to calculate %CV and least significant changes for a 95% level of confidence (LSC-95%). QC corresponded to lower/upper limits of acceptance (mean SUV ± 2 SD). These limits were compared to LSC-95% values. Longitudinal QC was performed by identifying SUV changes larger than LSC-95% between exams.
Results: Tissue specific SUVm of PET averaged (1SD) was 0.43 (0.10), 2.21 (0.44) and 1.72 (0.48) for liver, lung and bone in normal subjects while, for patients with lymphoma, it was 0.41 (0.11), 2.03 (0.45) and 1.94 (0.72). For normal subjects, LSC-95% was 0.3, 1.3 and 1.2, enabling to calculate the lower/upper limits: 0.90/3.52, 0.12/0.74 and 0.28/3.16. Among the 153 PET exams analyzed, only 2 exams with pulmonary SUVm and 12 exams with bone SUVm values were above the defined upper limit. All hepatic SUVm were within normal range. Simultaneous changes in the 3 parameters were never found. Intra-subject longitudinal QC identifies 12 patients with transient significant changes of normal bone SUVm and only 1 patient with transient significant change of normal pulmonary tissue SUVm. For bone reference, transient increase was correlated to administration of GCSF while for lung tissue, it was related to occurrence of pulmonary infectious disease. Chemotherapy never altered SUVm of hepatic tissue.
Conclusion: Quality assessment of FDG PET imaging is feasible using SUVm of reference tissues (lung, liver and bone). Applying the calculated lower/upper limits of references, QC enables to identify inappropriate PET scans. When applying LSC-95%, discrimination between effect of treatment and non-specific technical effect can be performed.

6001 ORAL

Immunosuppressive TLI-based reconditioning regimens enable engraftment after graft rejection or graft failure in patients treated with allogeneic hematopoeitic stem cell transplantation

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Background: Primary non-engraftment/ early graft rejection after allogeneic hematopoietic stem cell transplantation (HSCT) is a rare but life-threatening complication after allogeneic HSCT. Standardized treatment protocols addressing the type of the reconditioning regimen are lacking. As total lymphoid irradiation (=TLI) confers substantial immunosuppression with relatively little toxicity we speculated that a TLI-based approach could be useful for reconditioning prior to a second allogeneic HSCT.
Materials and Methods: We identified a cohort of 14 patients (7 adults – $\geqslant$18 years, median age 48 years, range 27−53 years – and 7 children – <18 years, median age 9 years, range 4−16 years) with primary non-engraftment (n = 7) or early graft rejection (n = 7) after conventional myeloablative allogeneic HSCT for different hematologic diseases. Patients were treated with a TLI-based reconditioning regimen with 7 Gy single dose application (median dose rate 1.18 Gy/min, range, 0.55−2.13 Gy/min) plus anti-T lymphocyte antibody OKT3 (n = 11) and/or antithymocyte globulin (n = 7)/fludarabine (n = 9), and/or thiotepa (n = 5), followed by an infusion of peripheral blood stem cells (n = 13) or bone marrow stem cells (n = 1) from related/unrelated donors.
Results: The median interval between initial transplantation and retransplantation was 38 days (range, 23–173 days) for the overall group, 36 days (range, 23–173 days) for adults and 41 days (range, 31−61 days) for children. All patients were transplanted in aplasia. 11/14 recipients were evaluable for engraftment following TLI-based reconditioning as three adults died early (day 2/5/15) after second transplantation due to infectious complications. Engraftment in four adults was seen after a median of 12 (range 10−18) days. In seven children engraftment occurred after a median of 10 (range 9−32) days. TLI-based reconditioning was well-tolerated with no severe organ toxicity. Median overall survival/ disease-free survival for the whole cohort was 140 days (range 5–1268 days). After a median follow-up of 681 days, in children disease-free/ overall survival are 85.7%/ 85.7%, respectively. Despite engraftment in 4 adults none of them survived due to fatal GvHD (n = 1), infection (n = 1), disease relapse (n = 1) and acute respiratory distressed syndrome (n = 1).
Conclusion: In patients with graft failure or graft rejection after allogeneic HSCT, TLI-based reconditioning regimens allow sustained engraftment paralleled by favourable toxicity profile potentially leading to long-term survival.

6002 ORAL

Involved-field radiotherapy (IFRT) and involved-nodal radiotherapy (INRT) as a component of combination therapy for limited stage Hodgkin lymphoma: a question of field size

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Background: Combination therapy is the standard of care for limited stage Hodgkin lymphoma (HL). The radiotherapy component has evolved from extended-field (EFRT) to involved-field radiotherapy (IFRT), lowering radiation-induced toxicity whilst maintaining high cure rates. Recent publications suggest a further reduction of field size to involved-nodal radiotherapy (INRT). Although guidelines have been published, there is no uniform consensus on the optimal definition for radiotherapy field size. Furthermore, there is no published evidence to demonstrate that field size can be reduced from IFRT to INRT while maintaining treatment efficacy.
The aim of this study is to determine the influence of field size on patterns of relapse in limited stage HL treated with combination therapy. Is INRT associated with increased marginal recurrences?
Materials and Methods: Using the BC Cancer Agency Lymphoid Cancer Database, 325 eligible patients were identified: limited stage HL diagnosed between 5/1/89 and 4/1/05, and treated with combined chemo/radiotherapy. According to prospective protocols, patients were treated with EFRT until

1996, IFRT from 1996 to 2001, and INRT from 2001. Exclusion criteria were age <16 years, non-ABVD-like chemotherapy, >4 cycles of chemotherapy, use of PET to guide treatment, or co-morbidities that precluded accurate staging or treatment.
Results: At diagnosis, the median age was 32 (16−81) years, 52% were male, Ann Arbor stage was IA in 29% and IIA in 71%, and 10% had extra-nodal disease. Chemotherapy consisted of 2 cycles of ABVD-like chemotherapy in 95%, 3 cycles in 3% and 4 cycles in 2%. Three radiotherapy treatment groups were identified: EFRT in 127 (39%), IFRT with 10 cm margin in 96 (30%), and INRT with 5 cm margin in 102 (31%). Median follow-up for living patients was 73 (14–207) months.
The median time to relapse was 3.1 (0.8−8.8) years. A total of 12 relapses occurred (4%): 4 after EFRT (3%); 5, IFRT (5%); and 3, INRT (3%) (P = 0.9). Loco-regional relapse (LRR) occurred in 5 patients: 3 in the EFRT, 2 in the IFRT and none in the INRT groups. Of note, no marginal recurrences occurred after INRT. Distant-only relapses were less common after EFRT (1 vs 3, IFRT vs 3, INRT).
At 5 years, progression-free survival (PFS) was 97%, and overall survival (OS) was 95%. At 10 years, PFS and OS were 95% and 89%, respectively.
Conclusion: Reduction in field size appears to be safe, without an increased risk of LRR in patients receiving INRT.

6003 ORAL

Phase II trial of oral vorinostat (suberoylanilide hydroxamic acid, SAHA) in relapsed diffuse large B-cell lymphoma (DLBCL)

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Background: The histone deacetylase inhibitor (HDACI) vorinostat (Zolinza™) was approved in the US in October 2006 for the treatment of cutaneous manifestations in patients (pts) with cutaneous T-cell lymphoma who have progressive, persistent or recurrent disease on or following 2 systemic therapies. Oral vorinostat has demonstrated activity in pts with DLBCL in a Phase I trial.
Methods: An open-label, Phase II trial of oral vorinostat 300 mg bid (initially 14 d every 3 wks; amended to 3 d per wk) until progressive disease (PD) or intolerable toxicity was conducted. Pts with measurable, relapsed/refractory DLBCL and adequate hematologic, hepatic and renal function, who had received ⩾2 prior systemic therapies were eligible. Exclusion criteria included: prior HDACI treatment, allogeneic transplant, or failure on >3 prior therapies. The primary end point was the objective response rate (ORR) measured by CT/PET. Assessment of response duration (DOR), time to progression (TTP), time to response (TTR) and safety were secondary end points.
Results: Eighteen pts (median age, 66 y [range, 59–86 y]) who had received a median of 2 prior systemic therapies were enrolled from May 2005 to March 2006 at 8 centers. Initially, 7 pts received 300 mg bid 14 d every 3 wks, however 4 had DLT (Gr 3 muscle spasms; Gr 4 thrombocytopenia, n = 3). On the amended schedule (300 mg bid 3 d per wk), no pts had DLT, but 1 achieved a complete response (TTR = 85 d; DOR = 331+ d). The ORR was 5.6%. One pt had stable disease for 301 d. Sixteen pts discontinued for PD and the median TTP for all pts was 44 d. The median number of treatment cycles was 2 (range, 1−19+). Two pts received >6 cycles (126 d). Common drug-related adverse experiences (AE; mostly Gr 1/2) were diarrhea (61%), fatigue (50%), nausea (39%), anemia (33%) and vomiting (33%). Three pts had dose reduction (from 300 to 200 mg bid 14 d every 3 wks) and none discontinued for drug-related AE. Drug-related AE ⩾Gr 3 included thrombocytopenia (n = 3; 300 mg bid 14 d every 3 wk) and asthenia (n = 2; 300 mg bid 3 d per wk). Two pts died on study of causes unrelated to drug: PD + GI hemorrhage (d 40) and acute myocardial infarction (d 95).
Conclusion: Vorinostat showed limited activity in pts with relapsed DLBCL and is well tolerated at 300 mg bid 3 d per wk or 200 mg bid 14 d every 3 wks. The optimal dose and schedule as well as predictive response biomarkers require further investigation.

6004 ORAL

Oblimersen plus fludarabine/cyclophosphamide (FC) significantly increases complete remission and overall survival in non-refractory patients (Pts) with relapsed chronic lymphocytic leukemia (CLL): results from a prospective randomized phase 3 trial

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Background: Oblimersen (Genasense® [G]) decreases Bcl-2, an anti-apopotic factor linked to pathogenesis and progression in CLL. Addition of G to fludarabine and cyclophosphamide (FC) significantly increased the primary endpoint of the rate of complete and nodular partial response (CR/nPR: 17% vs. 7%; P = 0.025) and durability (median not reached; estimated 36+ mos vs. 22 mos; P = 0.035) of these response in pts with relapsed or refractory CLL who had prior F. To identify pts deriving maximal benefit, we conducted additional analyses on prospectively defined non-refractory pts who remained sensitive (S) to F.
Methods: Eligible pts were treated with up to six 28-day cycles of FC (25 mg/m^2/d and 250 mg/m^2/d × 3 d) with or without G (3 mg/kg/d × 7 d by CIV, beginning 4 days before FC). Clinical and bone marrow data were blindly reviewed and graded by NCI-WG criteria. CT or ultrasound was required to confirm CR/nPR in pts with pre-existing abnormalities. All randomized pts have been followed >3 years or until death or withdrawal of consent.
Results: Out of 241 pts in the study, 101 (FCG = 51, FC = 50) were in the S population. Demographics were exceptionally well-balanced, including age (median 64 years, each arm), time from diagnosis (66 and 69 mos, respectively) and prior treatment history (mean 6 cycles F, each). Among S pts, G disproportionately increased the CR/nPR rate (25% vs 6% in the FC group, P = 0.016) and significantly increased overall survival (estimated 39+ mos vs. 33 mos; P = 0.05). No difference was observed in time-to-progression (both ITT and S analyses). Among grade 3−4 events in the S population, pts in the FCG group had significantly less neutropenia and anemia (P = 0.03), and no significant increase in thrombocytopenia or non-hematologic toxicities. Patients in the G arm had fewer opportunistic infections and secondary malignancies. No S pts experienced tumor lysis and/or cytokine release or autoimmune events.
Conclusions: The addition of G to FC significantly increased CR/nPR in pts with relapsed CLL. Pts who were not F-refractory derived maximal benefit with significant increases in CR/nPR and survival and significantly less myelosuppression.

6005 ORAL

Are we changing the survival of follicular lymphomas? Patterns of outcome in the patients treated at the Oncology Institute of Southern Switzerland from 1979 to 2006

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Background: The natural history of follicular lymphoma (FL) was believed not to have changed over the last 30 years of the previous century. Median survivals of about 10 years were reported from many centres and the disease was considered incurable. Several new treatment options have been developed in the last decade, but it still remains to be clarified whether patterns of outcome in FL patients have changed.
Patients and Methods: We analyzed the outcome of the 258 patients with FL treated at the Oncology Institute of Southern Switzerland (IOSI) from 1979 to 2006. Three diagnostic eras were taken into consideration according to the major changes in the available therapeutic armaments: 1979 to 1989 ("alkylating agents' era", N = 73), 1990 to 1999 ("aggressive regimens and G-CSF era", N = 118), and 2000 to 2007 ("rituximab era", N = 67). Median survival times, Kaplan-Meier survival curves, and relative survival rates were calculated.
Results: The median age of the entire group was 57 years (range 21−92). The distribution of the main prognostic factors (including age, stage, international prognostic index, LDH and beta-2 microglobulin levels) was similar in the three eras. A significant improvement in the cause-specific survival of all patients with FL was observed between the three eras by log-rank test (p = 0.018). The median cause-specific survival was 12.5 years for patients with FL diagnosed between 1979 and 1989 but was not reached in the two more recent groups. Estimated cause-specific survival rate at