disrupted mitochondrial function, increased reactive oxygen species (ROS) production, modified signal transduction and anti-angiogenesis. ZIO-101 is active against diverse cancers in vitro and in animal models of AML and other leukemias. These features make ZIO-101 attractive for clinical evaluation in hematological malignancies.
Methods: Two studies a phase-1 study evaluating the safety and pharmacokinetic (PK) profile of ZIO-101and a phase II trial in patients with advanced hematological malignancies are ongoing. Patients received ZIO 101 IV for 5 consecutive days every 28 days until disease progression or significant toxicity.
Results: A total of 14 patients 13 with acute myelogenous leukemia (AML) (median 3 prior treatments) and 1 with MDS (median 2 prior treatments) Therapy with ZIO-101 has been well-tolerated to date. Preexisting anemia and thrombocytopenia increased by 1 grade in 4 and 3 patients each. Grade >3 neutropenia occurred in 2 subjects. No significant renal, hepatic or cardiac toxicity occurred. Six of the 13 evaluable AML patients, a decrease in the peripheral blood myeloblasts was noted. Bone marrow myeloblasts were unchanged. The studies are ongoing and continue to accrue patients.
Conclusions: Administration of ZIO-101 to patients with advanced AML was well tolerated and an antileukemic effect has been observed.

6017 POSTER

First line treatment of acute promyelocytic leukemia with arsenic trioxide without ATRA and chemotherapy

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Background: Standard treatment of APL is all-*trans* retinoic acid (ATRA) plus chemotherapy but arsenic trioxide (ATO) is most potent single agent against APL cells. Role of ATO in first line therapy of APL needs to clarify.
Material and Methods: Between may 2000 and September 2006, we treated 141 new cases of APL(Median age 28±12.8 y/o min = 11, max = 71) by 2 hours iv infusion of 0.15 mg/kg ATO until complete remission. Trial approved by IRB and consent form obtained. Diagnosis was by clinical and morphologic characteristics and confirmed by cytogenetic and RT-PCR for detection of t(15,17) and presence of PML-RAR?. After complete remission patients received consolidation by 28 days infusion of ATO for one or four courses (one consolidation one month after CR and for some patients second, third and forth consolidations one month after first one and two another, one year and two year after CR).
Results: complete remission observed in 121 cases (85.8%) and early mortality rate was14.9% (most common cause of early mortality was APL syndrome, 61.9%). Median follow up was 28 months. For patients who achieved complete remission, one-, two- and three-year disease free survival rates were 95.6±2%, 76.9±4% and 57±6%, respectively. Many relapsed patients salvaged again with ATO alone so, two- and three-year overall survival for this cohort was 95.6±2% and 83.7±4%. Increasing number of consolidation from one to four couldn't increase DFS or OS in one and two years after CR.
Conclusion: ATO is effective in treatment of new cases of APL. Introduction of ATO in first line treatment of APL (with or without ATRA plus chemotherapy) needs a multi center randomized clinical trial.

6018 POSTER

Primary breast lymphoma and the risk of central nervous system disease – Should all patients receive prophylactic intrathecal chemotherapy?

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Background: Primary breast lymphoma (PBL) is rare. Existing practice is based upon studies limited by small patient numbers. It has been shown in a small retrospective study of twenty patients presenting with PBL, that patients may go on to develop central nervous system disease. 25% of the patients in this study had relapses with proven CNS disease [1]. This has led to a gradual change in clinical practice favouring the increasing use of prophylactic intrathecal chemotherapy. There is currently little data considering whether patients with limited disease at presentation should receive prophylactic intrathecal chemotherapy. Our main objective is to evaluate the appropriate use of prophylactic intrathecal chemotherapy.
Material and Method: We report a series of fifteen cases of patients with PBL presenting at New Cross Hospital, Wolverhampton, UK between 1991 and 2006. Patient age, histology, stage at diagnosis, treatment and outcome were recorded. The patients were followed up to observe for relapses involving the central nervous system and any necessary further treatment.
Results: The fifteen patients identified consisted of fourteen females and one male. Age at diagnosis ranged from 28 to 88 years. Of the fifteen patients seven had stage I disease, two had stage II disease and six had stage IV disease. Those with stage IV disease had either a positive bone marrow biopsy or abdominal disease present on CT scanning. None of the patients were identified to have evidence of CNS disease at presentation. Ten patients received CHOP/R-CHOP chemotherapy with seven achieving a complete response and three a partial response. Six of the patients achieving complete response also received radiotherapy. Three of the five patients not receiving chemotherapy were treated with radiotherapy and two of these achieved a complete response. In total five patients had relapses after first line treatment. Two involved CNS relapses. Both of these patients had initially presented with advanced (Stage IV) disease. None of the patients who presented with limited disease (Stage I-II) in our cohort went on to develop CNS disease.
Conclusions: It is becoming increasingly common for patients with PBL to receive prophylactic intrathecal chemotherapy with first line treatment. Our data suggests that whilst the use of prophylactic intrathecal chemotherapy is justified in patients presenting with advanced PBL, there is little evidence demonstrating any benefit in patients presenting with stage I or II PBL. This treatment is expensive and associated with significant morbidity. Further studies with larger numbers are needed before the use of prophylactic intrathecal chemotherapy should become routine practice in patients presenting with stage I or II PBL.

References

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6019 POSTER

Background and methodology of the ADAGIO study – a prospective, observational, multicenter study to determine the prevalence, predictors, and mediators of non-adherence in patients treated with imatinib

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Background: We describe the rationale and methodology of the "Adherence Assessment with Glivec®: Indicators and Outcomes" (ADAGIO) study, which examines determinants of adherence with imatinib treatment in chronic myeloid leukemia (CML) and gastro-intestinal stromal tumors (GIST) patients. Imatinib should be continued indefinitely in responding patients. Patient adherence with long-term medication regimens is influenced by patient-, clinician-, disease-, treatment-, and health system-related variables. The tolerance margin for imatinib nonadherence is narrow due to the relapse risk. Determinants and dynamics of nonadherence must be studied to design adherence-enhancing interventions.

	Month	
	0	3
Patient recruitment (screening, eligibility, informed consent)	X	
Patient characteristics (demographics, medical history, current comorbidity)	X	
Disease-related information		
Disease history	X	
Current clinical status	X	X
Concomitant medications: risk for drug-to-drug interactions	X	X
Physician variables (demographics, education, specialty, practice environment, number of CML/GIST patients, time spent with patients in diagnosis and treatment, use of scientific information; use of patient awareness and support materials, perspectives on patient compliance)	X	
System-related variables	X	
Patient adherence (patient and collateral interviews, pill count, appointment adherence, physician rating of adherence)	X	X
Patient variables (medication behavior self-efficacy, assessment of chronic illness care, symptom experience/distress, understanding of disease and treatment, functional status, knowledge-seeking behavior)	X	X
Response parameters		
CML: hematological, cytogenetic and molecular response	X	X
GIST: clinical, CT and PET	X	X
Treatment-related: CML/GIST-related GP and specialist visits t1 to t2		X

Materials and Methods: Primary study aims are to (1) examine prevalence and severity of non-adherence with imatinib treatment in CML/GIST patients; and (2) identify (modifiable) variables that predict or mediate (non-)adherence. 229 patients from 46 centres in Belgium were enrolled in an observational study with assessments as listed in the table.
Results: With last-patient/last-visit scheduled in early May 2007, publication of results is anticipated for late 2007 and 2008.
Conclusions: ADAGIO should increase knowledge about (modifiable) patient-, physician-, disease-, treatment, and system-related determinants of CML and GIST patients' (non)adherence with imatinib treatment.

6020 POSTER

Prevalence of hepatitis C virus infection in B-cell non Hodgkin lymphoma patients in India

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The role of hepatitis C virus (HCV) infection in the pathogenesis of non-Hodgkin's lymphoma (NHL) is controversial. A prior study from our institute (Varma S et al., Gastroenterology 2004; 126: 1498−99) had suggested lack of this association among Indian patients. However, a weakness of this study was the use of serological markers alone to diagnose HCV infection. Hence the present study was undertaken to look for the presence of this association by doing HCV RNA in patients with B-cell NHL. We determined the prevalence of HBsAg, anti-HCV antibodies and HCV RNA in 57 consecutive chemotherapy naive patients with B-cell NHL diagnosed in our institution between January 2004 and June 2005. The control group comprised of 171 patients of non malignant disorders admitted in hospital during the same period. The diagnosis of lymphoma was made by lymph node fine needle aspiration cytology (FNAC), biopsy or bone marrow examination and demonstration of CD 20 positivity. Patients and controls with prior history of jaundice, intravenous drug abuse, Interferon α therapy, corticosteroid therapy and HIV infection were excluded. Antibodies against HCV were detected by a third generation ELISA ('LG HCD 3.0 Plus'; LG Chemical Ltd., Pharmaceutical division, Seoul, Korea), detecting antibodies against three kinds of fusion proteins which are constituents of the HCV nucleocapsid; core 518, E1E2NS4 and NS5. Detection of Hepatitis B surface antigen (HBsAg) was done by direct immunoenzymatic assay of the "sandwich" type ('Bioelisa HBsAg colour', Biokit, S.A., Barcelona, Spain) HCV RNA was detected by nested RT-PCR, involving 3 steps (RNA isolation, c DNA synthesis/Reverse transcription and nested PCR: HCV RNA genotyping). Chi-square test was used to compare the prevalence of HCV infection among patients and controls. Out of the 57 newly diagnosed patients with B-cell NHL enrolled in our study, 37 (64.9%) were males and 20 (35.1%) were females. The mean age was 48.7 years (range 18−80). Using the Ann-Arbor staging, 43 patients were in stage IV, 11 were in stage III and 3 were in stage II at presentation. In the NHL group, one patient tested positive for HBsAg (1.75%) while none tested positive for anti-HCV (0%). This patient had a history of blood transfusion in the past. Among all patients, only one patient tested positive for HCV RNA (1.75%). Among controls, one tested positive for HBsAg (0.58%) and two tested positive for anti-HCV (1.17%). Thus the prevalence of HBV and HCV were not different among patients and controls. We could not demonstrate relationship of any other factors with the presence of hepatitis B or C infection either in cases or controls. In conclusion, this study reconfirmed our earlier observations of no association between HCV infection and NHL in Indian patients.

6021 POSTER

Clinical features and treatment outcome of patients with myeloid antigen coexpression in acute lymphoblastic leukemia: a study of 214 Peruvian patients

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Aim: The purpose of the study was to evaluate the incidence of myeloid antigen coexpression and its prognostic significance in Peruvian patients with acute lymphoblastic leukemia (ALL).
Patients and Methods: A retrospective study was conducted of all ALL cases (between 14 to 57 years old) diagnosed and treated in Neoplasicas Institute (Lima-Peru) between 2002 and 2004, with available immunophenotype data. Presenting features and treatment outcome of 214 ALL patients was analyzed. The patients were similar in demographic, clinical and laboratory features and their treatment outcome. All patients were treated with a uniform treatment protocol (9904, intensive chemotherapy regimen). Myeloid antigen coexpression was defined as more than 30% isolated leukemic cells positive for CD13 and/or CD33 and/or CD15. Median age was 18.5 years. The incidence of myeloid antigen coexpression was 60 per cent.
Results: Presenting features were similar between My+ and My− with regard to age, gender, FAB morphology, white cell count, hemoglobin level, platelet count, mediastinal involvement, presence of lymphadenopathy, and proportion of blast cells detected in the marrow.
We found that only the patients with CD33(+) had difference statistically significant in terms of DFS and OS Vs My(−), DFS was 14% and OS was 18% (p: 0.032).
Conclusion: We observe smallest survival and DFS, stadistically significant among the patient with myeloid associated antigen expression CD33. This study demonstrates that myeloid antigen coexpression is common and constitutes 60% of patients ALL within the Peruvian population and that CD33 can be an adverse risk factor in Peruvian patients with ALL.

6022 POSTER

Examination of risk factors for mortality of patients with haematological malignancies admitted to intensive care

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Introduction: We examined potential risk factors for mortality of patients with haematological malignancy (including lymphomas) admitted to a cancer hospital critical care unit (CCU) over a 2 year period. Several factors that have been identified as poor prognostic factors in this group were considered for analysis, including renal replacement therapy (RRT).
Methods: Data from all patients with haematological malignancy admitted to the CCU over two years were collected retrospectively. In addition to RRT the following putative risk factors for mortality, identified from published data, were studied: mechanical ventilation, neutropenia, microbiological evidence of fungal infection, significantly deranged liver function tests (LFTs) and multiorgan failure. Outcomes were expressed in terms of CCU and hospital mortality. Univariate and multivariate analysis were used to assess whether risk factors were predictors of mortality.

Table 1: Individual risk factors and positive outcome.

Factor	N	Positive outcome	P
All patients	64	36(56.3%)	
Renal replacement therapy	19	10 (52.6%)	0.705
Ventilation	28	14 (50%)	0.375
High CRP	48	26 (54.2%)	0.562
Poor liver function	11	7 (63.6%)	0.589
Neutropenia	32	14 (43.8%)	0.046
Fungal infection	20	10 (50%)	0.498
Multi organ failure	28	14 (50%)	0.375

Results: 64 patients were identified. Overall CCU mortality was 44% after a mean stay of 9 days compared to survivor stay of 14 days. Overall hospital mortality was 64%. Individual disease mortality: Acute leukaemia (N = 24), CCU mortality 42%, Hospital Mortality 67%; Chronic leukaemia (N = 11) CCU mortality 64% Hospital Mortality 81%; Lymphomas (N = 24) CCU mortality 42% Hospital Mortality 50%; Myeloma (N = 5) CCU mortality 20% Hospital Mortality 80%
The significance of the individual risk factors was assessed by comparing the CCU mortality. A positive outcome was defined as a patient leaving CCU alive. Using primary binary regression each variable was considered separately as a prognostic factor for CCU mortality.
Conclusion: CCU mortality rates for patients with haematological malignancy were consistent with previously published. We found that only neutropenia is a significant poor prognostic factor for this population (P value 0.046, Odds ratio 0.354). None of the other risk factors assessed were shown to be significant. Further prospective study may identify other risk factors in this patient group.

6023 POSTER

Tissue microarrays method is useful for immunophenotyping analyses in patients with diffuse large B-cell lymphoma

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Introduction: Diffuse Large B-Cell Lymphoma (DLBCL) is the most common of the non-Hodgkin lymphomas. This lymphoma may de novo