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

A. Ghavamzadeh, K. Alimoghaddam, S.A. Ghaffari, S. Rostami, M. Jahani, M. Iravani, R. Hosseini, A. Khodabandeh, S.A. Mousavi, E. Eini. *Hematology oncology and stem cell research centermedical sciences/university o, Hematology, Tehran, Iran*

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?

J. Sherriff, C. Brammer. *New Cross hospital, Oncology, Wolverhampton, United Kingdom*

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

[1] Ribrag V et al. Primary breast lymphoma: a report of 20 cases. Br J Haematol 2001; 115(2): 253−6.

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

M.A. van Lierde[1], K. Vermeylen[1], F. Serra[1], L. De Rop[1], K. MacDonald[2], E. Strobbe[1], M. Geelhand[1], S. Vancayzeele[3], S. De Geest[4], I. Abraham[5]. *[1]Novartis, Oncology, Vilvoorde, Belgium; [2]Matrix45, Scientific Consulting, Earlysville, USA; [3]Novartis, Medical Affiars, Vilvoorde, Belgium; [4]University of Basel, Institute of Nursing Science, Basel, Switzerland; [5]Matrix45, & University of Pennsylvania, Earlysville, USA*

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