

In this issue, we explore novel approaches in three different populations. New treatment options in myelodysplastic syndrome are discussed including two agents for the complications associated with low risk MDS, and two strategies for higher risk MDS using decitabine and clofarabine. The emerging problem of imatinib resistance in CML is addressed by studies of dasatinib as frontline therapy and SKI606 in imatinib failures. And, finally, the issue of maintenance therapy in AML remission is discussed in a randomized study of decitabine versus observation.

Myelodysplastic Syndromes (MDS): What is new?

The hallmark of myelodysplastic syndromes (MDS) is ineffective hematopoiesis resulting in low peripheral blood counts that may affect one or more of the three lines (red cells, white cells, platelets). The cytopenias cause symptoms, particularly fatigue or easy bruisability. The predominant pathologic feature is dysplasia, an expression of exaggerated cell death (apoptosis) of early hematopoietic cells. MDS may evolve into an acute myeloid leukemia (AML). However, most patients suffer from consequences

Table 1.

Lower Risk (blasts<10%)	Higher Risk (blasts?10%)
Growth Factors – EPO ± G-CSF	5-azacytidine
Immune Rx - steroids, Cyclosporine, ATG	Investigational- decitabine, clofarabine
Lenalidomide (5q31)	Intensive chemotherapy (younger, diploid karyotype)
5- azacytidine	Allogeneic transplantation
Investigational – decitabine, tipifarnib, clofarabine, homoharringtonine	
g Iron chelation	
g t(5;12) or 5q33 variant (PDGFR-B) - imatinib	

of cytopenias.

MDS is heterogeneous and represents many different disease forms. Although current classification and prognostic schemes are valuable, a simple approach is to categorize MDS into lower risk (blasts < 10%) and higher risk categories. General strategies in each subset are summarized in Table 1. Until recently, supportive care was considered the standard of care. Recently, growth factors, immune therapy, oral chelation, FDA approved drugs such as azacytidine (for all MDS and CMML) and lenalidomide (for low risk, 5q-, transfusion dependence) have improved outlook in MDS. Novel and targeted therapeutic agents such as inhibitors of farnesyl trans-

ferases (RAS inhibitors) and receptor tyrosine kinases, or angiogenesis inhibitors are being developed in clinical trials. The current edition of Leukemia Insights provides a summary of some new treatment options for patients with MDS at M. D. Anderson Cancer Center.

New Strategies in Lower Risk MDS

AMG531, a thrombomimetic agent, for the treatment of lower risk MDS and thrombocytopenia

(continued on page 2)

In This Issue

1 Myelodysplastic Syndromes

- 1 New Strategies - Lower Risk
 - AMG531 for thrombocytopenia
 - FG-2216 for anemia
- 2 New Strategies - Higher Risk
 - Decitabine based strategies
 - Clofarabine

3 Dual Src & Abl Tyrosine Kinase Inhibitors for CML

4 Frontline therapy with dasatinib

4 Use of SKI606 after imatinib failure

4 Randomized study of Decitabine versus observation as maintenance therapy in AML

Myelodysplastic Syndromes (MDS): What is new?

(continued from page 1)

AMG531 is a thrombopoiesis stimulating protein which targets the thrombopoietin receptor, thus stimulating megakaryopoiesis. However, its structure is different from endogenous thrombopoietin (eTPO), therefore if AMG531 produces antibodies, they will not bond to eTPO and cause thrombocytopenia. AMG531 has shown positive results in patients with immune mediated thrombocytopenic purpura (ITP) producing platelet improvements in over 2/3 of patients.

This study will evaluate the activity of AMG531 in patients with lower risk MDS (blasts < 10%; IPSS low or intermediate-1) with thrombocytopenia ($< 50 \times 10^9/L$), particularly life threatening thrombocytopenia. Other eligibility criteria are standard: age ≥ 18 years, performance 0-2, adequate renal and liver functions. Patients with a history of cardiac problems and thrombotic events are excluded. Patients will receive AMG531 subcutaneously weekly at 4 dose levels: 300, 700, 1000, and 1500 mcg. Up to 25 patients will be treated at the MTD. Responding patients can continue on therapy. For further information, please contact Dr. Hagop Kantarjian or any other leukemia physician.

FG-2216 for the treatment of lower risk MDS and anemia or red blood cell (RBC) transfusion-dependence

The most common complication of MDS is anemia and its consequences, including the need for RBC transfusion. This problem can be treated with

erythropoietin with or without growth factors, RBC transfusions, oral chelation (to prevent iron overload), and a new agent, lenalidomide, if they have a chromosome 5q abnormality. These treatment options have limited efficacy with a response rate of 30% to 35%.

Hypoxia inducible factor (HIF) is a key element in the body's oxygen sensing mechanism. HIF-responsive genes are key regulators of erythropoiesis, iron metabolism, angiogenesis, cell cycle progression, and apoptosis. FG-2216 is an orally active small molecule inhibitor of HIF-PH enzymes. It appears to increase erythropoietin levels, reduce TNF- α levels, and favorably mediate efficient iron mobilization. Thus, FG-2216 is viewed as an agent that stimulates "total erythropoiesis" and could improve on anemia and RBC transfusions. FG-2216 has shown positive results in anemia of renal failure and of chronic inflammation.

FG-2216 is now being evaluated in patients with lower risk MDS and anemia or RBC transfusion-dependence. Eligibility criteria are: MDS IPSS low or intermediate-1 risk, age ≥ 18 years, hemoglobin < 10 g/dl or transfusion-dependence (≥ 2 units within 8 weeks), and failure of procrit or aranesp. Other eligibility criteria are standard. Patients with secondary MDS, platelets $< 30 \times 10^9/L$ and ANC $< 0.75 \times 10^9/L$, are excluded.

FG-2216 is given at 1250 mg orally TIW. Dose escalation to 2000-2500 mg is allowed for lack of response. Responding patients

will continue on therapy. For further information, please contact Dr. Hagop Kantarjian or any leukemia physician.

New Strategies in Higher Risk MDS

Decitabine Based Strategies

An emerging concept in cancer is that tumor-suppressor genes (the "brakes" in cellular growth) responsible for the normal differentiation of cells can be silenced through DNA methylation and histone deacetylation. Thus, a potential treatment strategy in cancers, including MDS, is to use 2 new classes of agents, hypomethylating agents and histone deacetylase inhibitors, to re-express the silenced genes, and reestablish the normal differentiation process.

Two drugs with hypomethylating properties are in different phases of investigation. 5-azacytidine (5-AZA) has been approved by the FDA for the treatment of MDS. Decitabine is another hypomethylating agent, which is 10x more potent than azacytidine in vitro.

Decitabine has shown significant activity in AML, CML, and MDS. In MDS, Wijermans et al. treated 169 patients with decitabine 45-50 mg/m² daily X 3 (135-150 mg/m² per course) every 6 weeks. The CR rate was 20% and overall response rate 49%. Induction death was 7%. Median response duration was 9 months and median survival 15 months. Response rates by IPSS risk were: intermediate-1 46%; intermedi-

(continued on page 3)

ate-2 52%, high 51% (Blood 100: abst 355, 3134, 2002). A randomized study of decitabine versus supportive care has been completed demonstrating the benefits of decitabine in relation to response rates, time to AML or death, and improvements in transfusion needs. However, the median number of courses given was 3; 48% received 2 courses.

We had observed that lower-dose longer exposure schedules of decitabine might induce optimal hypomethylation and improve on the therapeutic: toxic ratio of decitabine. We tested in a randomized study 3 different schedules of decitabine in MDS (same total dose per course): 20 mg/m² IV over 1 hour daily x 5, 10 mg/m² over 1 hour daily x 10, and 20mg/m² SQ daily x 5. Courses were given every 4 weeks for at least 3 courses; if there is a response, up to 24 courses are given.

Ninety-five patients were treated. Their median age was 65 years. Cytopenias were present in 96%; 56% had chromosomal abnormalities; secondary MDS was present in 32%; median MDS duration was 3.2 months; 61% had received therapy for MDS. Diagnosis was MDS in 77 (International Prognostic scoring System [IPSS] risk high in 19%, intermediate-2 in 46%, and intermediate-1 in 34%) and chronic

myelomonocytic leukemia in 18. Overall 32 patients (34%) achieved CR, and 69 patients (73%) had an objective response by modified IWG criteria. The 5-day IV schedule was selected as optimal after the 65th patient; the CR rate in that arm was 39%. The median overall survival was 19 months with an 18 month estimated survival rate of 56%. Extramedullary grade 3-4 side effects were uncommon. Myelosuppression-associated febrile episodes resulted in hospitalization in 19% of courses. Compared with intensive chemotherapy, decitabine was associated with significantly lower early induction mortality rates (p<.01) and significantly better survival (p<.01), confirmed by multivariate analysis (hazard ratio 0.73; p= 0.0009). A multivariate analysis among patients receiving decitabine confirmed the independent association of pretreatment high methylation status with worse prognosis.

We are currently studying several programs involving decitabine or azacytidine with histone deacetylase inhibitors including valproic acid, SAHA, LBH589, and MGCD. These studies are open and accruing in MDS and AML. For further information, please contact any leukemia physician.

Clofarabine

Clofarabine, an adenosine nucleoside analogue, has shown activity in ALL (FDA approval for pediatric ALL), and AML. Several studies are ongoing with clofarabine including: in elderly newly diagnosed AML, clofarabine with low dose cytarabine; in ALL salvage, clofarabine and cyclophosphamide; and in AML first salvage, a randomized study of higher-dose cytarabine ± clofarabine.

Clofarabine has also shown preliminary positive results in MDS. Among patients with higher risk MDS receiving clofarabine 40 mg/m² daily x5, 2 achieved CR and 2 had CRp. To further explore the efficacy of clofarabine in MDS, we have developed 2 studies. The first study compares 2 schedules of IV clofarabine 15mg/m² vs 30 mg/m² IV daily x5 every month. The second study investigates oral clofarabine 40 mg/m² daily x5 every month. Eligibility for these studies requires high risk MDS (intermediate-higher risk IPSS). Other eligibility criteria are standard. Patients need to be in Houston weekly x4 in the first month. For further information, please contact Drs. Stefan Faderl, Hagop Kantarjian, or any other leukemia physician.

Dual Src and Abl Tyrosine Kinase Inhibitors for CML

Nearly 70% to 90% of patients with CML in early chronic phase treated with imatinib achieve complete cytogenetic response. With a median follow up of 5 years, the annual rate of resistance/progression is 3-4% and of mortality 1-2%. However, most

patients maintain some levels of minimal residual disease and some patients may eventually develop resistance to imatinib, thus the need to develop new agents for patients with CML. There is a second generation of tyrosine kinase inhibitors that are

significantly more potent than imatinib and are able to overcome resistance by most of the mutations seen in patients who fail imatinib. Some of these agents, such as nilotinib (AMN107), are more selective

(continued on page 4)

Dual Src and Abl Tyrosine Kinase Inhibitors for CML

(continued from page 3)

inhibitors of ABL, while others, such as dasatinib (BMS354825), SKI606 and INNO406, are dual inhibitors of Src family of kinases and abl. These agents have already demonstrated significant activity and a very good toxicity profile in patients that have failed prior therapy to imatinib or have been intolerant to imatinib. Hematologic responses have been observed in 60% to 90% of these patients treated with dasatinib after failing imatinib, and cytogenetic responses in 40% to 60%.

Frontline therapy with dasatinib (BMS354825)

We have an ongoing clinical trial of dasatinib as frontline therapy for patients with CML in early chronic phase. Based on the significant potency of this agent, the objective of this trial is to improve the rate of molecular responses achieved at 12

months, an endpoint that has been shown to be associated with improved progression-free survival. To be eligible patients must be previously untreated or should have received no more than 1 month of therapy with imatinib and be in chronic phase. To date we have treated 20 patients and preliminary reports show a complete cytogenetic response rate of 80% at 3 months. This compares favorably to the approximately 30% with standard-dose imatinib. There has also been a rapid decrease in the transcript levels measured by PCR. The tolerance has been very good, with no grade 3 non-hematologic toxicity observed to date and only a couple of instances of mild pleural effusion that have resolved with medical intervention. If you are interested in this trial, please contact Drs. Jorge Cortes or Hagop Kantarjian.

Use of SKI606 after imatinib failure

SKI606 is another dual Src and Abl inhibitor that has been recently introduced to the clinic in a phase I study. Like dasatinib, it has been shown in vitro to overcome the most common mutations seen after imatinib failure and to be more potent than imatinib. This agent has been overall well tolerated in patients with solid tumors with no pleural effusions seen. A dose finding study has been initiated in patients with CML who failed imatinib and the early evidence shows that patients with different mutations have achieved complete hematologic responses and are starting to show evidence of cytogenetic response. In addition, there is minimal toxicity at the doses explored to date. For information on this trial, please contact Drs. Jorge Cortes or Hagop Kantarjian.

Randomized study of Decitabine versus observation as maintenance therapy in AML

Treatment of adult patients with unfavorable risk (poor and intermediate risk cytogenetics) acute myeloid leukemia (AML) remains unsatisfactory. Although achieving CR continues to be challenging in a significant proportion of these patients, relapse after achieving CR remains to be one of the major factors responsible for treatment failure. Similarly, treatment of patients with relapsed AML remains difficult and although a number of these patients can be

rescued with an allogeneic stem cell transplant, limited availability of donors and the complications associated with transplant restrict its use to a minority of patients.

Therefore strategies to increase the duration of CR are likely to be beneficial both in the first and subsequent remissions. Relapse in AML is likely to be due to a population of residual cells left behind after completion of therapy whose eradication or suppression

through maintenance therapy is likely to be beneficial. The role of post-remission therapy has been long-established in treating adult patients with AML. [Cassileth, et al, J Clin Oncol 1988;6:583-7]. However, several studies have suggested that there is no role for maintenance therapy in this disease. An ECOG study randomized patients after receiving standard induction therapy into 2 arms; one

(continued on page 5)

receiving 2 further courses of attenuated induction followed by maintenance, versus maintenance therapy only for 2 years. [Cassileth, et al, Blood 1984;63:843-7]. This study demonstrated that a more intensive post-remission therapy is necessary and questioned the role of maintenance. [Cassileth, et al, Blood 1984;63:843-7]. A randomized CALGB study demonstrated that protracted maintenance for 36 months was not superior to 8 months of maintenance and led to further questioning of the role of maintenance. [Preisler, et al, Blood 1987;69:1441-9]. However, the regimens used in these trials were based on the traditional cytotoxic chemotherapy agents with their attendant toxicity and difficulties in administration.

Despite the significant problems associated with these regimens, several other studies have convincingly demonstrated the benefit of maintenance therapy in adult patients with AML. In a study by the German AML cooperative group patients achieving CR after receiving a standard induction regimen were randomized to receive either a protracted maintenance therapy or 'observation only'. [Buchner, et al, J Clin Oncol 1985;3:1583-9]. Disease free survival at 3 years was 30% versus 17% (p=0.003) in favor of the maintenance arm. As a result of this study, maintenance therapy was established as an integral part of front-line therapy in AML patients by the German group. [Buchner, et al, Blood 1999;93:4116-24]. Another study conducted by SWOG confirmed the benefit of maintenance in prolonging the disease-

free survival in these patients. [Hewlett, et al, Leukemia 1995;9:562-9].

Therefore, although maintenance therapy appears to be effective, its precise role has not been well defined. Such strategy is more likely to be beneficial in older adults with unfavorable risk disease than in younger adults who are able to tolerate more intensive forms of post-remission therapy. The establishment of a role for maintenance therapy in AML has been difficult to achieve because of the toxicity associated with the cytotoxic drugs and the other agents that have been evaluated in this setting. For example, studies of interleukin-2 (IL-2) were largely unsuccessful particularly due to the difficulty in delivering the drug due to its significant toxicity. [Cortes, et al, Cancer 1999;85:1506-13], [Farag, et al, Clin Cancer Res 2002;8:2812-9], [Sievers, et al, J Clin Oncol 1998;16:914-9].

Decitabine has been used successfully to treat patients with myeloid disorders and at the lower doses has been associated with very limited extramedullary toxicity. As such, decitabine is an ideal agent to be investigated in this setting. Furthermore, the hypomethylating effects of decitabine require an extended period of therapy and are likely to be more beneficial in the setting of a minimal disease burden.

We will soon be initiating a clinical trial examining the role of decitabine in maintenance therapy of patients with unfavorable risk AML in first CR or relapsed patients who have achieved second or subsequent CR. The objectives of the study

will be to evaluate the benefit in prolonging the duration of relapse-free and overall survival as compared with the control patients and to assess the toxicity of decitabine in this setting. Adult (> 18 years) patients with AML in first or subsequent CR who have received any induction or salvage therapy, who are interested in further therapy, and have an adequate performance status and organ function are eligible to participate in this randomized study. Relapsed patients in second or subsequent CR will be evaluated separately. Patients in first CR will be stratified based on their age (< 60 years vs. ≥ 60 years) and their bone marrow cytogenetics (poor vs. intermediate risk). All patients will be randomized to two arms:

Arm 1: First group will receive decitabine 20 mg/m² intravenously over approximately 1 hour daily x 5 days.

Arm 2: The second group will be monitored or continue current therapy at the discretion of their treating physician.

Decitabine therapy will be repeated every 4 to 8 weeks for a total of 12 cycles or until unacceptable and irreversible grade 3 or 4 toxicity develops or until disease relapse. Patients will have repeat bone marrow evaluations before every three courses of therapy or at 3 to 6 month intervals for the control arm. If you have patients who may be interested in continuation of therapy after receiving the initial induction and consolidation please contact Dr. Farhad Ravandi or any other leukemia physician.

CLL Treatment Priorities

1. Untreated

- Fludarabine + Cytosan + Mitoxantrone + Rituximab (2005-0106)
- Rituximab + Sargramostin (2004-0102)
- CFAR (2005-0269)
- Kinetic Biomarker (2005-0528)
- Idiotype-KLH + GM-CSF (2005-1013)

2. Prior Therapy

- Fludarabine + Cytosan + Rituximab (ID99-338)
- CFAR (DM02-593)
- CI Campath/SQ Campath (ID02-424)
- PT100 + Rituximab (2004-0276)
- Clofarabine (2004-0134)
- Campath + Rituximab (ID02-368)
- Anti CD40 MoAb (2005-0025)
- Cloretazine (2005-0249)
- Forodesine HCL (2005-0290)
- XL844 (2005-0368)
- OFAR (2004-0373)
- Lenalidomide (2005-0175)
- CNF2024 (2005-0452)

3. Other

- T-cell LPD:
 - Alemtuzumab + Pentostatin (2004-0408)
 - Forodesine HCL (2004-0800)
- Hairy Cell: 2CDA + Rituximab (2004-0223)

AML/MDS Treatment Priorities

1. Newly Diagnosed

A. Acute Promyelocytic Leukemia: cytogenetic feature: t(15;17): ATRA + Arsenic Trioxide (ID01-014)

B. Cytogenetic feature: Inv16 or t(8;21): Fludarabine + Ara-C

C. Age <60

- Ida + Ara-C + Zarnestra (2003-0563)
- Decitabine (ID03-0180)
- Dauno + Ara-C + PKC 412 (2003-0645)

Age >60

- Clofarabine ± LD Ara-C (2004-0183)
- Decitabine (ID03-0180)
- 5-aza + Valproic Acid + ATRA (2004-0799)
- IV Clofarabine (2005-0535)

2. Salvage Programs

- Clofarabine ± Ida ± Ara-C (ID03-0181)
- Ida + Ara-C + EL625 (2003-0475)
- VNP + Hydrea (2004-0140)
- Arsenic Trioxide + ATRA + Mylotarg (ID00-424) in APL
- Mitoxantrone + Etoposide + Ara-C ± CEP-701 (2003-0719)
- PTK 787 + Gleevec (2004-0248)
- Troxatyl (2005-0283)
- Cloretazine + Ara-C (2004-0639)
- Low dose Decitabine (2004-0468)
- HuM195/rGel (DM98-342)
- Pixantrone (2004-0840)
- AVE9633 (2004-0756)
- Ida + Ara-C + AEG (2005-0384)
- Oral Clofarabine (2005-0536)
- Lovastatin + Ara-C (2005-0473)
- 5-aza+Valproic Acid (2005-0177)
- 5-aza + Ara-C (2005-0291)
- Zarnestra + Ara-C (2006-0021)

List of Leukemia Service Attendings

ANDREEFF, MICHAEL	(713) 792-7260	ISSA, JEAN-PIERRE	(713) 745-2260
BERAN, MILOSLAV	(713) 792-2248	KANTARJIAN, HAGOP	(713) 792-7026
BORTHAKUR, GAUTAM	(713) 563-1586	KEATING, MICHAEL	(713) 745-2376
BURGER, JAN	(713) 792-1865	KOLLER, CHARLES	(713) 792-7747
CABANILLAS, MARIA	(713) 745-0654	KORNBLAU, STEVEN	(713) 794-1568
CORTES, JORGE	(713) 794-5783	MATTIUZZI, GLORIA N.	(713) 745-2723
ESTEY, ELIHU	(713) 792-7544	O'BRIEN, SUSAN	(713) 792-7543
ESTROV, ZEEV	(713) 794-1675	RAVANDI, FARHAD	(713) 745-0394
FADERL, STEFAN	(713) 745-4613	THOMAS, DEBORAH	(713) 745-4616
FERRAJOLI, ALESSANDRA	(713) 792-2063	TSIMBERIDOU, APOSTOLIA	(713) 792-4259
FREIREICH, EMIL	(713) 792-2660	VERSTOVSEK, SRDAN	(713) 745-3429
GARCIA-MANERO, GUILLERMO	(713) 745-3428	VU, KHANH	(713) 745-0655
GILES, FRANCIS	(713) 792-8217	WIERDA, WILLIAM	(713) 745-0428

- CHIR-258 (2005-0674)
- ABT-869 (2005-0474)
- MGCD + Aza (2005-0659)

3. Low Risk MDS and CMML with <10% Blasts

- Cytokine Immunotherapy (2004-0253)
- Low dose Decitabine (ID03-0180)
- VNP + Hydrea (2004-0140)
- Oral SCIO-469 (2004-0790)
- Thymoglobulin + Cyclosporin (2005-0115)
- Deferasirox (2005-0233)
- PR1 vaccine (DM97-325)
- FG-2216 (2005-0721)
- AMG531 (2005-0577)

ALL Treatment Priorities

1. Newly Diagnosed or Primary Refractory (one non-hyper-CVAD induction)

- Modified Hyper CVAD (ID02-230)
- Burkitt's: Hyper CVAD + Rituximab (ID02-229)
- Ph+: Hyper CVAD + Gleevec (ID01-006)

2. Salvage Programs

- Ph+:LBH 589 (2005-0898)
- Ph+:AMN107 (2004-0251)
- Augmented Hyper CVAD (ID03-0166)
- Liposomal Vincristine (ID01-572)
- L-Annamycin (2004-0675)
- Forodesine HCL (2005-0449)
- IMTOX 19 + 22 (2005-0271)
- Clofarabine + Cytosar (2005-0552)

CML Treatment Priorities

1. CML Chronic Phase

- Early (Diagnosis < 12 months); no prior IFN
 - Gleevec +/- Peg Intron + GM-CSF (ID02-534)
 - BMS-354825 (2005-0422)
 - Imatinib 400/800 (2005-0325)
- Early; prior IFN- α or late (Diagnosis >12 months)
 - No prior IFN- α :
 - High-dose STI571 (ID01-292)
 - STI571 failures:
 - BMS-354825 (2005-0428)
 - AG-858 + Gleevec (2005-0119)
 - AMN107 (2004-0251/2005-0754)
 - R115777 + STI571 (ID02-169)
 - Decitabine (DM02-134)
 - KOS-953 + Gleevec (2004-0282)
 - HHT + Gleevec (2005-0067)
 - SKI-606 (2005-0813)

2. CML Accelerated Phase

- AMN107 (2004-0251)
- STI571 + Decitabine (ID02-205)
- Decitabine (DM02-133)
- KOS-953 + Gleevec (2004-0282)

- HHT + Gleevec (2005-0067)
- SKI-606 (2005-0813)
- BMS-354825 (2005-0394)

3. CML Blastic Phase

- Myeloid or undifferentiated
 - BMS-354825 (2005-0394)
 - AMN107 (2004-0251)
 - STI571 + Decitabine (ID02-205)
 - STI571 + Idarubicin + Ara-C (ID01-300)
 - Decitabine (DM02-135)
 - PTK787 + Gleevec (2004-0248)
 - KOS-953 + Gleevec (2004-0282)
 - HHT + Gleevec (2005-0067)
 - SKI-606 (2005-0813)
- Lymphoid
 - BMS-354825 (2005-0394)
 - Hyper CVAD + STI571

4. Philadelphia-negative Myeloproliferative Disorders (MF, ET, PV, CEL/HES, Ph-neg CML)

- BMS-354825 (2004-0817)
- Pegasys (DM03-0109)
- PTK787 + Gleevec (2004-0248)
- AP23573 (2004-0362)
- ONTAK (2004-0142) (Mastocytosis only)
- Azacitidine (2005-0033) (MF only)
- STI571 (ID01-167) (HES only)
- 2CDA + Ara-C (DM97-232) (HES only)
- Oral IFN (2004-0919) (ET, PV)
- AMN107 (2004-0251)
- Velcade (2005-0284)

Phase I/II Agents for Hematologic Malignancies

- Rosiglitazone + Targretin (ID02-587)
- SAHA (ID03-0044)
- XL119 (2003-0909)
- XK469R (2004-0154)
- AP23573 (2004-0362)
- MGCD0103 (2004-0748)
- ZIO101 (2004-0865)
- ALIMTA (pemetrexed) (2004-0873)
- SNS-595 (2005-0295)
- MK-0457 (2005-0330)
- RTA 401 (CDDO) (2005-0469)
- MPC-2130 (2005-0532)
- Perifosine (2005-0793)
- SAHA + Ida (2005-0031)
- PT523 (Talotrexin) (2005-0122)
- GX15-070 MS (2005-0584)
- SJG-136 (2005-0607)
- AVN-944 (2005-0609)
- Sapacitabine (2005-0768)
- LBH-589 (2005-0898)

The University of Texas
M. D. Anderson Cancer Center
1515 Holcombe Boulevard
Houston, Texas 77030-4009

Non-Profit Org.
U.S. Postage
Paid
Permit No. 7052
Houston, Texas

Leukemia Insights
and other valuable information are
now available via the World Wide Web.
Our address is:
<http://www.mdanderson.org/leukemia>
Or you may E-mail us at:
ckoller@mdanderson.org

Editor:
Hagop Kantarjian, M.D.

WebMaster:
Charles A. Koller, M.D.

Administrator:
Vicky Zoeller

Associate Editor:
Sherry Pierce, R.N.