7 of 59 patients (11.9%) have relapsed, and 10 of 59 patients (16.9%) developed a secondary malignancy in our cohort.
Summary/Conclusions: Herein, we summarize our single-institution experience with acute promyelocytic leukemia treated over the last fifteen years. A comparison of the adverse events and efficacy of ATRA and chemotherapy *versus* ATRA and arsenic needs further exploration.

PB1664

SUCCESSFUL BL-8040 TREATMENT FOR RELAPSED AML PATIENTS SINGLE CENTER EXPERIENCE

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Background: BL-8040 is a high-affinity antagonist of CXCR4, a chemokine receptor that is directly involved in tumor progression, angiogenesis, metastasis, and cell survival. BL-8040 binds to CXCR4 on leukemic cells, inhibiting its function, thus releasing them from the protective microenvironment of the bone marrow (BM) resulting in amplification of their sensitivity to chemotherapy. BL-8040 also has a direct anti-tumor effect by selectively inducing apoptosis of malignant cells.
Aims: To assess the effectiveness of BL-8040 in combination with cytarabine (Ara-C) in three patients with relapsed AML who were treated under compassionate protocol.
Methods: Treatment of relapsed AML patients with SC BL-8040 1.25mg/kg on days 1-7 together with Ara-C 1.5 gr/m^2 from day 3-7.
Results: Case 1: A 75 year old male with relapsed AML, 7 years after initial diagnosis. At the time of diagnosis he had normal karyotype and treated successfully with 7+3 followed by consolidation with Ara-C. At time of relapse he presented with dysplastic changes and additional chromosome 13 karyotype. At relapse the patient was treated with Ara-C and BL-8040. On day 35 his BM was in complete remission (CR) with less than 5% blasts. Maintenance therapy with azacitidine began three months later. Nine months post induction the patient is still in CR. Case 2: A 23 year old male with a history of Hodgkin lymphoma at age 17. At the age of 20 he was diagnosed with AML with the t(8;21) chromosomal abnormality. He was treated with 7+3 followed by consolidation with Ara-C. A year later he relapsed and received an allogeneic transplant (allo-HSCT). Two years post-transplant the patient relapsed with intra and extramedullary disease represented by a large chest wall mass. He was treated with BL-8040 and Ara-C as a salvage treatment. There was some resolution of the extramedullary mass on the first 2 days of monotherapy treatment with BL-8040 (before the onset of Ara-C). The patient experienced severe injection site pain and generalized muscle pain which required narcotics for analgesia. The patient entered CR on day 34 and underwent a second allo-HSCT. Almost a year and half post BL-8040 salvage treatment the patient is still in CR. Case 3: A 66 years old female with relapsed AML, 14 months after first diagnosis. At the time of diagnosis she presented with a complex karyotype. She received induction treatment followed by allo-HSCT but relapsed 3 months later. She was then treated with Ara-C and donor lymphocyte infusion (DLI) reaching CR; 7 months later she relapsed again. A second salvage treatment with BL-8040 and Ara-C was provided. During treatment she suffered from severe muscle pain (chest and legs). The patient didn't reach response showing 52% myeloblasts on day 24 BM examination. Two days later the patient died. The direct cause of her death is likely to be disease related.
Summary/Conclusions: Three patients were treated with BL-8040 and Ara-C as salvage therapy for relapsed AML. The safety profile was similar and the adverse events were well managed. These were characterized by injection site reactions and severe muscle pain. BL-8040 in combination with Ara-C can be administered safely to relapsed, heavily pretreated, AML patients. BL-8040 in combination with Ara-C has been shown to be an effective regimen for bone marrow as well as extramedullary AML. BL-8040 in combination with Ara-C should be considered as a bridging therapy for allo-HSCT.

PB1665

IMPACT OF GRANULOCYTE COLONY STIMULATING FACTOR FOR OUTCOMES OF NON-M3 AML PATIENTS TREATED WITH ANTHRACYCLINE-BASED INDUCTION (7+3 REGIMEN) CHEMOTHERAPIES

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Background: Currently most guidelines recommend primary granulocyte colony-stimulating factor (G-CSF) prophylaxis in patients with solid cancer who have an approximately 20% or higher risk for febrile neutropenia. However, these recommendations are not as clear for patients with acute myelogenous leukemia (AML).
Aims: To identify the role of G-CSF in induction treatment in patients with newly diagnosed AML, we analyzed the efficacies of administration based on clinical situations such as the development of neutropenia or fever, and investigated the impact of G-CSF exposure on the anti-leukemic efficacies of induction chemotherapy.
Methods: A total of 285 patients enrolled in the Korea University AML registry from September 2001 to March 2015 were analyzed and classified based on G-CSF administration: (1) no G-CSF exposure during induction (no G-CSF group), (2) administration initiated immediately after the development of neutropenia (absolute neutrophil counts, <1000/μL) but before the development of febrile neutropenia (preemptive group), and (3) administration initiated after the development of febrile neutropenia (therapeutic group).
Results: G-CSF administration resulted in faster ANC recovery compared to that in the no G-CSF group (p <0.001), but did not significantly affect the duration of neutropenia or chemotherapy-induced febrile neutropenia (CIFN) in both the preemptive and therapeutic group. In treatment-related mortality (TRM) multivariate analysis, the therapeutic group had higher TRM than the preemptive group (OR 5.921, 95% confidence interval 1.316–26.634, p=0.020), with no significant difference between the preemptive and no G-CSF groups (OR 2.454, 95% CI 0.482-12.495, p=0.280). Only quinolone prophylaxis was shown to be effective in reducing the incidence of CIFN (p=0.001). There were no significant differences in remission rate, cumulative incidence of relapse, overall survival, and relapse-free survival among the groups (Table 1).

Table 1. Univariate and multivariate analysis for risk factors associated with treatment-related mortality.

Factors	Treatment-related mortality			
	Univariate	Multivariate		
	P value	OR	95% CI	P value
Group(Ref. Pre-emptive G-CSF)	**0.040**			**0.022**
Pre-emptive G-CSF vs. No G-CSF	0.076	2.454	0.482 – 12.495	0.280
Pre-emptive G-CSF vs. Therapeutic G-CSF	**0.014**	5.921	1.316 – 26.634	**0.020**
Age< 60 (Ref.) vs. Age≥ 60	**<0.001**	2.366	0.979 – 5.716	0.056
Sex	0.139			
ECOG 0-1(Ref.) vs. ECOG≥ 2	**0.001**	3.392	1.239 – 9.288	**0.017**
CCI 0-1(Ref.) vs. CCI ≥ 2	**0.001**	2.813	1.093 – 7.237	**0.032**
Cytogenetic risk	0.558			
Type of anthracyclin	0.481			
Prophylactic quinolone	0.836			

Abbreviations: G-CSF, Granulocyte-stimulating factor; CCI, Charlson comorbidity index; HR, Hazard ratio; CI, Confidence interval; NA, Not applicable

Summary/Conclusions: G-CSF administration during induction chemotherapy in non-M3 AML patients can accelerate neutrophil recovery without affecting treatment outcomes. It is best administered at least before the development of febrile neutropenia in order to prevent TRM. Quinolone prophylaxis might be effective in reducing CIFN.

(11)

PB1666

ADULT BIPHENOTYPIC ACUTE LEUKEMIA: THE EGYPTIAN NATIONAL CANCER INSTITUTE EXPERIENCE

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Background: Biphenotypic acute leukemia is a rare form of leukemia. Knowledge concerning the clinical and biological presentation, as well as the outcome of treatment, in adult is limited
Aims: Our objective was to analyze the biological features and outcome of patients diagnosed with BAL in our institute.
Methods: This is a retrospective analysis of the clinical, biological, and immunophenotypic features of 30 biphenotypic acute leukemias (BALs), fulfilling modified EGIL's score, and treated in the medical oncology department at the National Cancer Institute (NCI-Cairo) between 2005& 2010. Myeloid and T-lineage features were demonstrated by cytoplasmic myeloperoxidase and CD3; B-lineage features were demonstrated by CD19, CD22 and CD10.

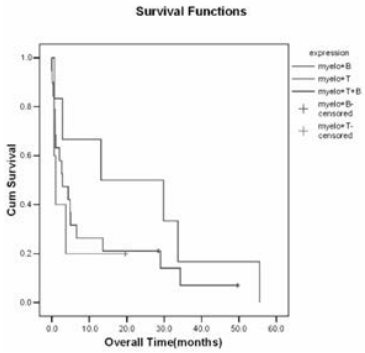

Figure 1.

Results: There were 18 men and 12 women; all were adult with a male to female ratio 3:2. The median age of the patients at diagnosis was 40 years (range, 19-62).The median white blood cell (WBC) count, hemoglobin concentration and platelet count were 31x10^3/dl (range, 2-275), 7g/dl (range, 4.1-11) and 53x10^3/dl (range, 14-539), respectively. Morphological assessment showed myeloid features in 14, and undifferentiated in sixteen patients. According to the EGIL classification, there were 20 cases of myeloid+B-lymphoid leukemia (66.7%), 5 cases of myeloid+T-lymphoid (16.7%), and 5 cases of trilineage myeloid+B+T-lymphoid leukemia (16.7%). The most common phenotypic feature was the expression of CD45 antigen which was positive in 27 (93.1%) patients. Cytogenetic results were available for only 4 patients. Eight patients received ALL-tailored therapy, 14 received AML-tailored therapy while 8 were either unfit for chemotherapy or died before induction treatment. Patients that received ALL-tailored chemotherapy had a better CR achievement rate (87.5%) over the patients that received AML-tailored chemotherapy (35.7%). The 6, 12 & 24 months overall survival (OS) were 33.3%, 30.0% & 26.6% respectively. Although patients with trilineage phenotype had better OS at 6, 12 & 24 months this was not of statistical significance (Figure 1).
Summary/Conclusions: Biphenotypic acute leukemia is a poor-risk disease. Despite the progress in the treatment of acute leukemia there are no uniform criteria about whether to treat BAL patients as ALL or AML. Further prospective collaborative studies are needed to investigate proper treatment protocols for this entity.

PB1667

SALVAGE REGIMENT WITH FLAT FOR REFRACTORY AND RELAPSED AML: EXPERIENCE A SINGLE CENTRE

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Background: Outcomes in patients with acute myeloid leukemia (AML) who are primary refractory or early relapsed are dismal, and there is not one standard therapy for all patients. Allogeneic hematopoietic stem cells transplantation (HSCT) is the treatment with the highest probability of cure when is possible to reduce the leukemia burden with salvage chemotherapy regimen prior to transplantation.
Aims: In this study, we report our experience of salvage chemotherapy regimen with fludarabine 30 mg/m^2, cytarabine 2 g/m^2 and topotecan 1.5 mg/m^2 on days 1 to 4 (FLAT), for refractory or relapsed AML treated in our institution.
Methods: Analytical, observational and retrospective study. We included all patients treated with FLAT from 2008 to 2016 in our center. We studied disease status prior to salvage therapy (refractoriness to one or two previous regimens *Vs* early or late relapse), cytogenetic risk profile (favorable, intermediate or adverse), response (complete response [CR], partial response [PR] or refractory disease [RD]) and survival (overall survival [OS]).
Results: Twenty-four patients were treated with FLAT in the last eight years in our center. Median age at time of treatment was 55 years old (range 39-69). AML was the underlying condition in all individuals. Cytogenetic risk profile at diagnosis (ELN) was favorable in 2 patients, intermediate in 10 and adverse in 9 of them. It was not determinate in 3 patients. Ten patients received FLAT salvage course for primary refractory AML, 1 for secondary refractory AML, 11 for relapsed AML after chemotherapy and 2 for relapsed AML after stem cell transplant (allo-SCT). Median OS was 16 months (range 1-86), with median follow up of 41 months. OS in primary refractory AML was 20 months (1-84) and 14 months (3-86) in relapsed AML. RC rate after FLAT was 45.8% (11 patients), higher in refractory disease (7 out of 11). Treatment related mortality was 16%. After reaching CR or PR, 7 patients underwent allogeneic transplantation. In this group, OS was 23 months (2-84). Four patients did not undergo transplantation despite reaching CR because of infection complications or early relapse while unrelated donor search was activated. Four patients underwent a sequential approach with a third salvage chemotherapy and allo-SCT despite refractoriness to FLAT; two of them could reach CR with this approach.
Summary/Conclusions: FLAT is an efficient salvage regimen for refractory and relapse AML. An acceptable CR rate allowed patients to continue with allogeneic-SCT and a longer overall survival. This combination has an acceptable safety profile, even for the patients who were treated after transplant.

(12)

PB1668

KINETICS OF WT1 OVER-EXPRESSION IN ACUTE MYELOID LEUKEMIA PATIENTS WHO RECEIVED STANDARD CHEMOTHERAPY OR UNDERWENT ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Wilms' tumor 1 (WT1) gene expression is well-known pan leukemia marker which overexpressed in more than 90% of newly diagnosed acute myeloid leukemia patients. However, the clinical utility of WT1 monitoring has been somewhat controversial.
Aims: The aim of this study is to compare WT1 transcript level kinetic changes in patients with AML either received standard chemotherapy (Arm A) or underwent allogeneic stem cell transplantation (Arm B).
Methods: Peripheral blood samples collected from 26 patients diagnosed with AML at initial diagnosis. Further samples collected from 9 patient who received standard chemotherapy (Arm A) at post-induction and post-intensification time points. Further samples collected from 8 patients who underwent allogeneic stem cell transplantation (Arm B) before conditioning, at day 30 and at day 100. The remaining 9 patients were not included in the analysis due to either early death or a negative WT1 at diagnosis. Quantitative RT-PCR detection of WT1 gene transcript level using Ipsogen WT1 profile Quant was performed on peripheral blood samples in both arms at the different time points mentioned before.
Results: We observed significant difference in the median values of WT1 transcript level at the 3 time points for patients with Arm A (P value 0.011) while for allogeneic arm B the median values were nearly the same at the 3 time points (P value 0.687). We found that WT1 level post-induction correlates with morphologic response (P value: 0.04). The median values for WT1 level were more for relapsed rather than non-relapsed cases in both arms at the 3 time points, but this difference was statistically insignificant except at D100 in arm B (P-value 0.046) and about to be significant at post-intensification (P value was 0.064) in arm A (Figure 1).

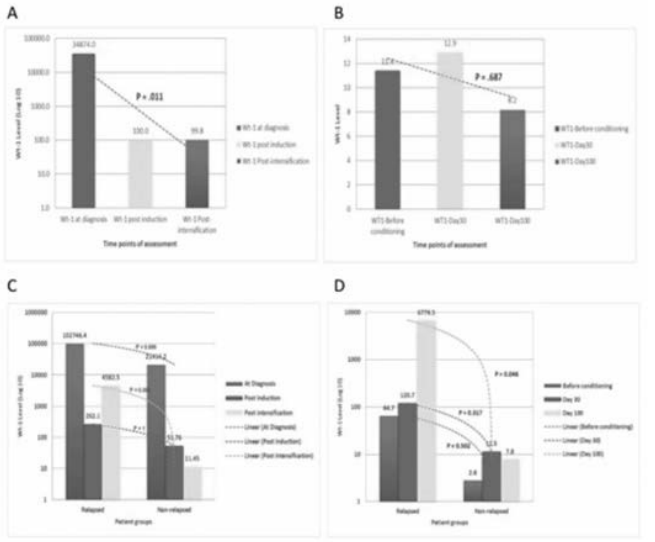

Figure 1. WT1 kinetics. A: WT1 kinetics for arm A. B: WT1 kinetics for arm B. C: WT1 transcript level between relapsed and non-relapsed case in arm A. D: WT1 transcript level between relapsed and non-relapsed case in arm B.

Summary/Conclusions: We identified a positive correlation between WT1 transcript level and morphological response. Therefore, elevation or rising WT1 transcript levels after intensifications or beyond day 100 post-transplant may be a marker of impending relapse that if validated in larger studies, may warrant either close observation or pre-emptive intervention. Although our results are poorly reaching the level of significance, probably due to the small sample size, WT1 transcript level showed dynamic changes with treatment and may be a marker for relapse. We recommend further studies with larger number of patients in different centers to confirm these results.

PB1669

STANDARD INDUCTION CHEMOTHERAPY IN CHILDREN WITH MLL-AF9 ACUTE MYELOID LEUKEMIA AND SEVERE DISSEMINATED INTRAVASCULAR COAGULATION IS ASSOCIATED WITH HIGH MORTALITY

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Background: MLL-AF9 AML is a rare subgroup of unfavorable prognostic leukemia secondary to t(9;11)(p22;q23) with particular clinical aspects, mainly severe coagulopathy.
Aims: To analyze the clinical, hematological and coagulation parameters at diagnosis and correlation with the outcome after chemotherapy initiation in children with MLL-AF9 leukemia treated according to a BFM 2004 AML protocol in a single center.