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Background: CMML is a clinically heterogeneous disease for which, according to recently reported experiences, hypomethylating therapies have provided significant clinical benefits.
Aims: Herein, we present the outcome of 11 patients (pts) who fulfilled the WHO 2008 criteria for CMML (CMML-2 in 7, CMML-1 in 2) or CMML-related acute myeloid leukemia (AML) with <30% bone marrow blast (2 pts) and have been treated with azacitidine (aza) at our institution between 2010 and 2014 after informed consent has been obtained.
Results: Median age at diagnosis was 76 years (range 62–86). Five pts had proliferative CMML. Four pts were transfusion dependent at some time point of disease course. Two out of 11 pts had abnormal kariotype (46,XY,Inv12 and 45,Y,-X, respectively). Two pts had secondary CMML; one to a 7-years lasting myelodysplastic syndrome (refractory anemia), whereas the other, who has undergone radio-chemotherapy for a solid tumor 3 years before, presented a likely therapy-related CMML. Prior therapies included cytoreductive therapy and erythroid stimulating agents. The MDAPS was low, Int-1, Int-2 and high in 1,2,4 and 2 CMML pts, respectively. Pts were treated with azacitidine, 75 mg/m^2 x 7 days, 5+2+2 schedule, every four weeks, subcoutaneously). Supportive care was given as required. Bone marrow (BM) response was assessed in 10 pts (following the sixth cycle in 9 pts and the fourth in 1); response was not assessed in 1 pt only, due to death (multiorgan failure) occurrence after second cycle. Responses were classified according to the modified IWG criteria; 5/9 evaluable pts achieved complete remission (CR) and 3 partial remissions (PR) with an overall response rate (CR+PR) of 73%; 2 pts maintained stable disease. No progressing pts continued the treatment. Two pts progressed to AML following the sixth and the fourteenth cycle respectively, after having obtained CR. With a median follow-up of 13 (2 – 31) months, 4 pts are alive and all of them continue to receive the treatment; six pts have died, 3 of AML, 2 of sudden cardiac death (with stable CMML), 1 of multiorgan failure (before response assessment); 1 patients was lost at follow up; median survival from therapy start was 15 months. Treatment was well-tolerated and no remarkable side effects were recorded.
Summary and Conclusions: In conclusion, despine the limited number of cases, our experience was encouraging; indeed, the use of aza in our hands achieved good responses in more than 70% of the treated pts, despite their high risk of disease and unfavorable prognostic profile.

PB1604

CYTOGENETIC ANALYSIS IN MYELODYSPLASTIC SYNDROME: AUDIT OF THE CURRENT PRACTICE IN A HAEMATOLOGICAL MALIGNANCY DIAGNOSTIC CENTRE. WHAT IS THERE TO BE LEARNT?

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Background: Identification of a clonal cytogenetic abnormality is essential for prognostic assessment of patients with Myelodysplastic Syndrome (MDS) (Revised International Prognostic Scoring System (IPPS-R)) and necessary for informing treatment decisions. According to the British Committee for Standards in Haematology (BCSH) guidelines (2013), cytogenetic analysis should be performed on all patients with suspected MDS having a bone marrow examination. Cytogenetic analysis is costly however, so it is crucial to ensure that the test is performed on appropriate samples. In many centres samples are cultured initially and subsequently analysed where needed. As significant numbers of these specimens are not analysed, we have implemented a procedure of immediate morphological screening of bone marrow aspirate samples prior to sending for cytogenetic culture.
Aims: We audited our current laboratory practice of immediate morphological screening of bone marrow aspirate samples before requesting cytogenetic analysis when investigating patients with possible MDS.
Methods: Using the Haematological Malignancy Diagnostic Links (HMDL) database, we reviewed 603 bone marrow samples received from the University Hospitals of Leicester NHS Trust, Kettering General Hospital NHS Foundation Trust and Northampton General Hospital NHS Trust over a 6 month period (March-August 2013). The key words 'myelodysplasia', 'uni-, bi-, pan-cytopenia', were used to select cases where MDS was suspected by the clinician. 116 bone marrows that met the criteria were assessed. Cytogenetic findings were reported in accordance with the International System for Human Cytogenetic Nomenclature Recommendations.
Results: Of the 116 samples, 52 were consistent with MDS according to the World Health Organisation (WHO) Revised Classification 2008 but only 29 of these were a new diagnosis and so appropriate for prognostic cytogenetic analysis. 14 samples were screened as possible MDS but this was not confirmed on detailed morphological reporting and in 7 of these cases cytogenetics were not subsequently analysed. As a result of bone marrow screening, 33 samples requested by clinicians were not sent for cytogenetic processing, as there was no evidence of dysplasia.
Of the 29 suitable cases cytogenetics could not be performed and as a result, the IPPS-R score could not be calculated for 5 new patients. For 3 of these no sample was received and in one case cytogenetic analysis failed. However, in 1 case the sample was rejected at the screening process resulting in the need for a repeat aspirate sample. Out of the 25 available reports, 10 showed an abnormal karyotype (40%). 10 cases were deemed intermediate or high risk by IPSS-R criteria and were considered for treatment with the nucleoside analogue, Azacitidine as per the TA218 National Institute for Health and Care Excellence (NICE) recommendations and the BCSH guidelines.
Summary and Conclusions: Immediate morphological screening of bone marrows referred as possible MDS has prevented the inappropriate processing of 43% of samples. This represents a significant cost saving. The audit has led to the introduction of a check procedure to ensure samples are not inappropriately rejected at screening.

PB1605

ASSISTED ADMINISTRATION OF SUBCUTANEOUS 5-AZACYTIDINE TO THE PATIENT'S HOME IS SAFE AND COST-EFFECTIVE

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Background: Administration of azacitidine is planned in-patient daily, there is no experience of its administration to the patient's home.
Aims: The aim of this work was to evalute the feasibility of a program of home administration of azacitidine capable of reducing the cost-of-illness, to increase adherence to treatment while maintaining the same safety of the therapy given in the hospital.
Methods: Between Jan 2005 and Dec 2012, 22 consecutive patents, (MDSs, n= 15; CMML, n= 4; AML, n= 3), were enrolled in the study.The pharmaco-economic analysis included assessment of direct costs (hospital inpatient, physician inpatient,physician outpatient, emergency department , nursing home care, specialists' and other health professionals' care,diagnostic tests, prescription drugs and drug sundries, and medical supplies),indirect costs incurred by care recipients and unpaid caregivers, induding time, productivity and travel cost.
Results: Azacitidine 75 mg/m2 day was administered as a subcutaneous injection for 7 consecutive days every 4 weeks.Median age of the patients was 71 years (range, 65-83. Median number of courses delivered to each patient was 9 (range, 3-31) Hematologic responses (CR/PR/mCR) were induced in 6 patients {27%} Median number of treatment courses to achieve any response was 2 (range 1 -6) Adverse events were evaluated for the first 6 courses for all patients, for a total of 124 courses. Major adverse events were cytopenia and cytopenia-related infection. Grade 3 or higher neutropenia was 64.4%) but incidence of febrile episode requiring intravenous antibiotics was 8,4% slightly lower than reported from the pivotal clinical study. Grade 3 or higher non-hematologic toxicities were infrequent. Injection site reaction 0.4 and site pain 0% Median follow-up duration of surviving patients was 46.9 months (range, 11.8-55-5). Of the 14 patients who where RBC transfusion dependent at baseline, 48.0% became RBC transfusion independent during the treatment period. Adherence to treatment was 100%>
Summary and Conclusions: In our experience, despite the high percentage of elderly patients of whom 36% living in rural area, it was possible to give treatment to all patients with total adherence. There has been a reduction in direct medical costs due to less use of hospitalization, a reduction of indirect costs by 63% due to the lower number of working days lost and a drastic reduction of travel costs with the same efficacy and safety of administration.

PB1606

MYELODYSPLASTIC SYNDROMES MANAGEMENT AND TREATMENT: A CONCEPTUAL FRAMEWORK

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Background: First-line treatment of myelodysplastic syndrome (MDS) patients with hypomethylating agents (HMAs) has been demonstrated in clinical trials to improve survival and/or delay progression to acute myelogenous leukemia (AML). However, most patients eventually relapse and, unless eligible for allogeneic hematopoietic cell transplant (HCT), face limited treatment options

and survival of only months. Despite the anticipated growth in the MDS population, little is known about the diagnostic and treatment decision-making undertaken by clinicians who treat non-transplantable MDS patients.
Aims: We sought to better understand MDS patient management and unmet needs by identifying clinicians' approaches for determining MDS: diagnosis; risk; progression; and treatment, particularly among higher-risk patients and after initial treatment failure.
Methods: We conducted in-depth, semi-structured interviews with nine hematology and/or oncology specialists (8 physicians; 1 nurse practitioner) in the US experienced in diagnosing and managing MDS patients.
Results: Diagnostic processes were consistent across providers and included blood work, physical examination, and often tests to rule out potential alternative diagnoses. Bone marrow biopsies (BMBs) were always performed to confirm the diagnosis. Providers calculated International Prognostic Scoring System (IPSS) and/or revised IPSS (IPSS-R) scores for almost all treatment-naïve patients. Some providers used just one system, while others used both due to specific trial protocol requirements and the limited real-world evidence regarding IPSS-R use in guiding treatment decisions. Initial treatment decision-making was driven by risk score, symptoms, transfusion dependency and, in some cases, performance status. Providers' management approaches were generally consistent for very low-risk (*e.g.*, active monitoring) and very high-risk (*e.g.*, HMA; HCT, if eligible) patients. There was substantial variation in response criteria (*e.g.*, change in BMB results, worsening cytopenias) used to determine progression from lower- to higher-risk MDS; several providers cited the need for a validated metric to address this inconsistency. Two-thirds of providers treated indefinitely with HMAs regardless of treatment response and given an absence of treatment-related adverse effects, citing long term or cyclical HMA benefits and lack of second-line options. Differences existed in methods used to determine HMA response, with the most common being periodic blood counts and/or BMBs. Providers noted that patients receiving HMAs either fail to respond or respond for some period of time and eventually experience treatment failure and MDS progression. Providers agreed that there is a significant unmet medical need for treating these second-line, non-HCT eligible MDS patients. Described as "limited," second-line treatments included clinical trials, cytotoxic induction chemotherapy, and supportive care. All providers stated that prognosis is poor regardless of approach.
Summary and Conclusions: The lack of treatment options for MDS patients, especially high-risk patients who do not respond to HMAs or have initial treatment failure, is an issue of profound importance. Providers use different approaches for these patients but agree that none offer significantly improved prognoses, leaving a considerable unmet need for second-line options. More research is required in determining optimal strategies for treating higher-risk and second-line MDS; assessing disease response in treated patients; and defining treatment failure.

PB1607

PROGNOSTIC SIGNIFICANCE OF CYTOGENETIC CATEGORIES IN MYELODYSPLASTIC SYNDROMES: SINGLE CENTRE STUDY FROM OMAN
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Background: Myelodysplastic syndromes (MDS) are clonal disorders of hematopoietic stem cells characterized by ineffective hematopoiesis, peripheral cytopenias and a variable risk of leukemic transformation. Chromosomal abnormalities play an important role in the underlying disease biology, predicting prognosis.
Aims: To investigate and compare IPSS-R prognostic stratification in MDS patients with the outcomes.
Methods: This retrospective study assessed 50 MDS patients (median age-60; range 1-86 years) with IPSS-R poor and very poor (n=5), intermediate (n=7) and good and very good (n=38) prognostic stratification. The median follow up was for 39.5months (range 1-70).They were analyzed for overall survival, leukemic progression, and according to the MDS associated cytogenetic abnormalities.
Results: 31 patients (62%) had normal cytogenetics. Amongst the MDS related abnormalities described, 4 (8%) had monosomy 7, 4 (8%) had trisomy 8 and one each had isochromosome 17q, del (11q) and del (5q). 14 had single abnormality, 3 showed double abnormalities, whereas one each had a complex abnormality and balanced translocation (t(5:12)). In the IPSS-R cytogenetic groups, the median survival was 34months for the good risk, 32 months for the intermediate group but 15.5 months for the poor risk subgroups($p<0.05$, chi square test). Although the overall mortality was 26%, it was 22%, 29% and 36% in the IPSS-R good, intermediate and poor subgroups respectively. Leukemic transformation was seen in 22% patients with an overall mortality of 55%. However, leukemic transformation occurred in 3%, 43% and 55% in the IPSS-R good, intermediate and poor subgroups respectively (Figure 1).

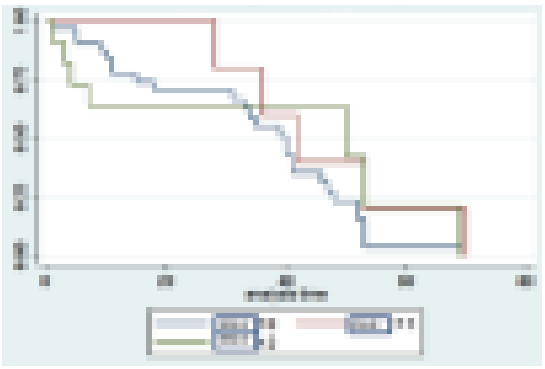

Figure 1. Kaplan-Meier survival estimates.

Summary and Conclusions: The IPSS-R can effectively stratify the prognosis of MDS based on cytogenetics even in a small single centre study of 50 patients with the three Kaplan Meier curves can be seen to diverge initially. However, with effective therapy like BMT, it was seen that progressively the lower curve superimposes with the first indicating the better long term outcomes.

PB1608

PEDIATRIC MYELODYSPLASTIC SYNDROMES: HOW DO THEY DIFFER FROM ADULTS?
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Background: Although uncommon, pediatric myelodysplastic syndromes [MDS] are not rare but its incidence is underestimated. Furthermore, unlike adults, it frequently presents as bone marrow failure syndrome in contrast to refractory cytopenias, and *per se* there is considerable difficulty in assigning the overlapping morphological features seen with bone marrow failure syndromes.
Aims: To study the clinical presentation, overall survival and correlate WHO 2008 Classification of MDS cytogenetic changes in childhood MDS *versus* Adults.
Methods: This retrospective study assessed 14 pediatric MDS patients (Median Age-11.5; range 1-16 years) and compared them with 39 adult MDS patients (Median age-65, range 23-86 years) from a single tertiary institution in Oman. Pediatric MDS patients were analyzed for initial presentation, type of progression, leukemic transformation and overall survival as well as according to the MDS related cytogenetic abnormalities. The median follow up was for 43 months (range 1-69).
Results: The commonest presentation was refractory cytopenia of childhood [RCC] in 43%, followed by RAEB-T [29%], RAEB [21%] and JMML [7%]. Seven patients (54%) had normal cytogenetics. Amongst the MDS related abnormalities described, four (31%) had monosomy 7 whereas, one each (8%) had trisomy 8 and trisomy21 with del (10q). Overall mortality in the pediatric MDS patients was 29%. Six patients [43%] demonstrated leukemic transformation with 50% mortality. Seven patients [50%] underwent Bone marrow transplantation (BMT) with six long term survivors [85%] (Figure 1).

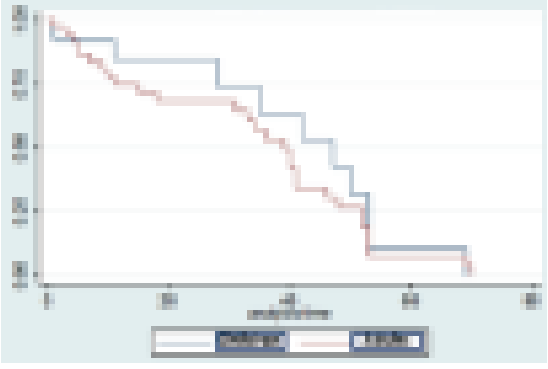

Figure 1. Kaplan-Meier survival estimates.

Summary and Conclusions: Although there are several fundamental differences between childhood and adult MDS patients, the overall survival in these MDS cohorts did not show any statistically significant differences in the