marrow cells. Methylation changes will be correlated with clinical responses and potential predictive markers explored. In addition, a number of immunologic and apoptotic assays will aim to further our knowledge of mechanisms of action particularly of thalidomide including T/NK cell enumeration and activation and serum cytokine changes by means of a multiplex cytokine bead array.

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13 Treatment of acute myeloid leukemia (AML) and high-risk myelodysplastic syndromes (MDS) in the elderly with azacitidine and gemtuzumab ozogamicin (GO)

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AML and high-risk MDS in patients over the age of 60 carry a poor prognosis. With standard chemotherapy, about 46% achieve a complete remission (CR) and treatment-related mortality approaches 30%. In 2005, we began a pilot trial for elderly patients with newly diagnosed AML or high-risk MDS, using hydroxyurea to lower the white cell count followed by azacitidine and GO. This combination was chosen for its non-overlapping mechanisms of action, low toxicity and ability to deliver treatment in the outpatient setting. There are several reasons to believe that the proposed sequence of treatment may be beneficial: (1) Azacitidine may increase CD33 expression and decrease p-glycoprotein expression, (2) Degree of CD33 positivity is associated with response to GO, (3) P-glycoprotein plays a significant role in resistance to GO therapy, (4) Lowering of WBC count increases uptake of GO by marrow blasts, thus allowing use of a lower dose of GO. The treatment regimen is as follows: If initial WBC count was >10,000/ul, patient was started on hydroxyurea 1500 mg orally twice daily. Once WBC count was <10,000/ul, the patient received azacitidine 75 mg/m^2 s/cu daily for 7 days. On D8, GO 3 mg/m^2 iv infusion was administered. A bone marrow was performed on D14 and the induction therapy was repeated if patient had residual disease. Those who achieved a CR went on to receive one consolidation treatment with azacitidine and GO in the same doses. Subsequent treatment was left to the discretion of the treating physicians. A total of 15 patients have been treated so far. Median age was 77 (62–83) and 7 were males. Two had RAEB and 13 AML. Four patients with AML had previous history of MDS. Nine had cytogenetic abnormalities at presentation. Eleven (73%) achieved a CR. Eight patients developed neutropenic fever including 1 typhlitis, all requiring hospitalization. There were no treatment–related deaths during induction therapy. Median survival is 10 months (1–20 mo) and 7 remain alive at this time. The trial is ongoing with an accrual goal of 20 patients. Two patients with relapsed AML were treated with this regimen off protocol. Both achieved CR, one lasting 11 months, the other >12 months. Thus, cytoreduction with hydroxyurea and leukapheresis followed by azacitidine and GO therapy appears to be a safe and effective regimen for elderly patients with AML and high-risk MDS. These preliminary results need to be confirmed in a larger Phase II study.

14 Cytogenetics of myelodysplastic syndromes and detection of del 5q

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Over 50% of all myelodysplastic syndromes (MDS) patients have cytogenetic abnormalities at the time of diagnosis [1,2]. These include a wide array of cytogenetic changes, such as monosomy, partial deletions and insertions of chromosomes, and trisomies. The type and complexity of cytogenetic abnormality closely relates to survival and the risk of progression to acute myeloid leukaemia (AML) [2]. Partial or complete deletion of the long arm of chromosome 5 (called deletion 5q; del 5q) is the most common cytogenetic abnormality found in MDS patients, occurring in 10–15% of all *de novo* MDS patients [1,2]. Prognosis of MDS patients with del 5q worsens with additional cytogenetic changes and increases in blast percentages [3,4]. Therefore, in the subgroup of del 5q patients with the 5q– syndrome (who have isolated del 5q and a blast percentage below 5%), prognosis is better than for other patients with del 5q [3,4]. Newer methods of cytogenetic testing in MDS patients, besides conventional metaphase karyotyping, are rapidly evolving. These methods include, among others, fluorescent *in situ* hybridization (FISH), chromosome painting (multicolour FISH and spectral karyotyping (SKY)), whole chromosome painting (WCP), loss of heterozygosity (LOH), comparative genomic hybridization (CGH), and gene expression analysis by the Affymetrix array. All these methods have their own pros and cons in clinical practice, and understanding these is important in optimal clinical decision making. Lenalidomide has shown to be highly effective in transfusion-dependent Low-/Int-1 IPSS risk MDS patients with del 5q in particular [5]. Newer cytogenetic detection techniques can detect del 5q more easily and accurately, and may therefore be very useful in the selection of patients for lenalidomide treatment, as well as prediction of response to lenalidomide [6]. In conclusion, understanding cytogenetics in MDS and the techniques to detect abnormalities such as del 5q accurately and easily, is