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for response thus far (13/13 [100%]) have achieved at least PR. Of these, 7/13 (54%) have achieved VGPR (with nCR/CR in 31%). The median time to PR was 2 cycles or 42 days. Maximum response occurred by cycle 4 for 12/13 (92%) pts. Overall, both components of the sequential regimen were very well tolerated. One pt had a ruptured colonic diverticulum related to dexamethasone, but recovered well and achieved nCR on trial. There have been 24

therapy attributed toxicity events \geq Grade 2 of which 11 have required drug/schedule adjustments: 3 each for cyclophosphamide (neutropenia), dexamethasone (hyperglycemia, pneumonia, perforated viscus) and Thalidomide (neuro related) plus 2 for Bortezomib (neuropathy). No deep vein thromboses (DVT) have occurred in the study. 3 pts have already proceeded to successful stem cell harvest with transplant planned.

Conclusion

The addition of cyclophosphamide and Thalidomide to Bortezomib/dexamethasone combination has improved the depth of response with \geq VGPR (54%) and CR/nCR (31%) compared to our previous 2-drug experience which produced \geq VGPR (38%). This very well tolerated new regimen is potentially an important step forward with further results and confirmation available by December 2007. ★

[300] CONTINUED LOW-DOSE DECITABINE (DAC) IS AN ACTIVE FIRST-LINE TREATMENT IN ALL CYTOGENETIC SUBGROUPS OF OLDER AML PATIENTS: RESULTS OF THE FRO0331 MULTICENTER PHASE II STUDY.

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Few therapeutic options exist for older, unfit AML patients (pts) who often have poor cytogenetics. We initiated a phase II trial in untreated AML pts >60 years ineligible for induction. 1° endpoint was best response: complete (CR) or partial remission (PR) or an antileukemic effect (ALE, >25% bone marrow [BM] blast reduction). 2° endpoints: overall survival (OS), toxicity. Low-dose DAC was given as for MDS (i.e. 135 mg/m² i.v. over 72 hrs), repeated q 6 weeks for up to 4 courses, with all-trans retinoic acid (ATRA, 45mg/m²/day for 28 days) given during course 2 in pts with ALE or stable disease (SD). Maintenance with 20 mg/m² DAC i.v. over 1 hour on 3 days (total dose 60mg/m², outpatient administration) q 6-8 weeks was offered to pts completing all 4 courses. Pts with a WBC of >20,000/ μ l received a short course of hydroxyurea (HU) prior to DAC. Pts requiring HU beyond day 28 of course 1 and/or showing blast increase had progressive disease (PD). In pts with

high absolute peripheral blood blasts, RNA from these cells was isolated sequentially (day 0, 2, 5), with CD34 selection in 2 pts, for global expression studies. At time of this analysis, 155 fully evaluable pts have been recruited (median age 72.5 yrs, range 56-85). 39% of pts were >74 yrs. Poor-risk cytogenetics and/or preceding MDS were present in 32 and 49%, respectively. Median WBC before treatment was 4800/ μ l (range, 400-241,000, >20,000/ μ l in 25%, >50,000/ μ l in 10%). Median BM blasts were 56% (25-100). A median of 2 courses was given. 69 pts received ATRA. 41 pts received a total of 162 maintenance courses (median 3, range 1-11). Best response was CR in 23 pts (15%) and PR in 15 pts (10%). An ALE occurred in 45 pts (29%), resulting in a 54% overall response rate. SD was seen in 37 pts (24%), 15 had PD (10%), 20 pts early death (13%). CR+PR rate by cytogenetic subgroups: with normal karyotype 18/51 (35%), with poor-risk 9/46 (20%) and with

other abnormalities 6/36 (17%). Toxicities of inpt DAC were very similar to those described for MDS (neutropenia, fever/infection, pancytopenia). No unexpected toxicities or ATRA syndrome were observed with the combination of DAC+ATRA. Median OS from start of treatment was 5.5 months (range, 0.3-38+), the 1-year survival 26%. Cytogenetic subgroups did not differ in median OS. Affymetrix HG-U133 Plus 2.0 microarrays of 9 pts revealed transcription changes (both induction and repression of large sets of genes): between 53 and 256 previously silent genes were reexpressed. Conclusions: low-dose DAC is very well tolerated by older AML pts ineligible for more aggressive treatment, with myelosuppression being the major toxicity. In vivo reexpression of genes was noted in leukemic blasts. Complete and partial remissions occurred in 25% of pts. A frequent antileukemic effect and the good feasibility of outpatient maintenance support continued DAC treatment. ★