**TPS280** **Trials in Progress Poster Session (Board #48C), Mon, 8:00 AM - 12:00 PM**

# An early-phase study of azacitidine and lenalidomide for untreated elderly acute myeloid leukemia (AML) patients.

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**Background:** Induction therapy results in suboptimal outcomes in elderly AML patients (pts). CpG hypermethylation of tumor suppressor gene (TSG) promoters can reduce expression and contribute to these poor outcomes. Azacitidine (aza) prevents DNA methyltransferase from methylating CpG cytosines, allowing transcription of previously silenced genes. Lenalidomide (len), an immunomodulatory agent, upregulates SPARC, a hypermethylated TSG with reduced expression in AML (Pellagatti A, et al. PNAS USA. 2007;104:11406). In addition, len was recently shown to activate demethylation of the promoter histone of p21, allowing expression of this TSG (Escoubet-Lozach L, et al. Cancer Res. 2009;69:7347). Therefore, we hypothesize that the low-intensity combination of aza and len will be a well-tolerated, mechanistically logical regimen that can synergistically upregulate TSG expression in elderly AML pts. **Methods:** Pts $\geq$60 with newly diagnosed untreated AML are eligible. In phase I, cohort 1 receives 75 mg/m$^2$ aza SC/IV on days 1-7. After 3 weeks off, pts receive the same dose and schedule of aza, plus len, 5 mg PO on days 8-28 of a 42-day cycle. Cohorts 2, 3, and 4 receive 10, 25, and 50 mg of len, respectively, with the same dose and schedule of aza, for 42-day cycles. Once the maximum tolerated dose (MTD) is determined, the MTD cohort will roll over to an expanded phase II efficacy study. Sub-MTD cohort pts may continue at the same dose if they respond and tolerate the regimen. Pts may receive a maximum of 12 cycles. Disease assessments in both phases occur after cycles 1, 3, 6, and 12 by bone marrow biopsy. Using a Simon two-stage design with $\alpha$= 0.05, power= 0.8, null hypothesis=20% complete remission (CR) (based on reports of use of aza alone) and alternative hypothesis=40% CR, phase II requires 33 pts. The primary endpoints for phase I and II are MTD and CR rate, respectively. Correlative studies to identify molecular features that predict responsiveness, including investigations of Cdc25C and PP2Ac$\alpha$ phosphatase expression, TET2 mutations, and genome expression profiling, are planned. As of January 1, 11 pts, 6 with secondary AML, have enrolled in phase I (5, 3, and 3 in cohorts 1, 2, and 3), receiving a median of 2 cycles.