

A phase I study of Amrubicin (AMR) and Cyclophosphamide in patients with advanced solid organ malignancies: A trial from the Hoosier Oncology Group

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Background: AMR is a synthetic anthracycline with activity in small cell lung cancer (SCLC). Cyclophosphamide is an alkylating agent commonly combined with anthracyclines in diseases such as breast cancer and lymphoma. We conducted a phase I study to determine the maximum tolerated dose (MTD) of the combination. **Methods:** Eligible patients (pts) had refractory solid organ malignancies, PS 0-1, and adequate organ function. The primary endpoint was MTD and dose limiting toxicities (DLTs). Secondary endpoint was to assess response. Pts were enrolled in sequential dose escalation cohorts in a standard 3+3 design. Treatment consisted of cyclophosphamide IV at 500mg/m² on day 1 with escalating doses of AMR IV on days 1-3 (25-40mg/m² with increments of 5mg/m² per cohort). Cycles were repeated every 21 days. **Results:** Eligible and treated pts (n=36) received a median of 4 cycles (range 1-6). Pt characteristics: M: F 47.2%:52.8%, median age 61(range 21-80), PS 0:1 47.2%:52.8%. Eighteen of 36 pts had SCLC. The remaining pts had NSCLC (22%), extrathoracic small cell or neuroendocrine carcinoma (5.56%), and other malignancies (22%). MTD was determined to be dose level 2 (cyclophosphamide 500mg/m², AMR 30mg/m²) due to grade 4 thrombocytopenia. Incidence of grade 3-4 neutropenia, anemia, thrombocytopenia and febrile neutropenia was 33.3%, 16.7%, 19.4% and 5.56% respectively. Efficacy data was available for 34 pts. PR, SD and PD rates in the overall study population were 20.6% (all in small cell cancers), 38.2% and 41.2% respectively. PR, SD and PD rates in small cell cancer pts were 37%, 26%, and 37% respectively. Of the pts achieving PRs on our study, 4 were platinum sensitive, 3 were refractory. Three of the 7 PRs were of longer duration than observed with first line chemotherapy. Median number of prior therapies in pts with PRs was 3.4 (range 1-6). Median duration of response on our study in pts with PR was 3.4 months. **Conclusions:** AMR (30mg/m²) and cyclophosphamide (500mg/m²) can be safely combined with significant activity observed in a heavily pretreated SCLC population.