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Combination of antiangiogenic therapy and cytotoxic chemotherapy for sarcomatoid renal cell carcinoma.

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Background: Numerous treatment options exist for metastatic renal cell carcinoma (mRCC), but optimal treatment for patients (pts) with sarcomatoid features remains undefined. Sarcomatoid differentiation is a particularly unfavorable prognostic feature in mRCC. Cytotoxic chemotherapy has modest activity, with a response rate of 16% for doxorubicin plus gemcitabine (Gem). Retrospective data has suggested a response rate of 10% for antiangiogenic therapy. We prospectively studied the combination of antiangiogenic therapy, sunitinib (Su), with Gem chemotherapy in this mRCC subpopulation. **Methods:** Pts with mRCC and sarcomatoid differentiation were enrolled in a phase 2 clinical trial at 3 institutions. Treatment consisted of 21-day cycles of Su, 37.5 mg on a 2 weeks on/1 week off schedule, along with Gem 1000 mg/m2 on days 1 and 8. The primary endpoint was radiographic response rate (RR) by RECIST. Secondary endpoints included time to disease progression (TTP), safety, and overall survival (OS). **Results:** Among 35 pts treated in total, 7 were classified as MSKCC good risk, 26 as intermediate risk, and 2 as poor risk. There were 10 partial responses and 1 complete response, for a confirmed RR of 30%. An additional 10 pts exhibited stable disease (clinical benefit rate 60%). Among the 10 pts who had progressive disease as their best

response, the majority had underlying non-clear cell histology. Median TTP was 3.5 months (range 0.5-12). Eight pts discontinued due to adverse events (AEs). The most common treatment-emergent grade 3 or higher AEs were neutropenia (8 pts), fatigue (5), anemia (2), and hypertension (2). No treatment-related deaths occurred. Median OS was 11 months (range 1-38+). **Conclusions:** To our knowledge, this is the largest prospective trial combining cytotoxic chemotherapy and antiangiogenic therapy in patients with RCC and sarcomatoid features. Our results suggest that combination therapy may be more efficacious than either treatment alone in this subtype of mRCC and supports an ongoing intergroup trial (NCT01164228). Further research is necessary to define prognostic factors, including histologic and molecular biomarkers, for distinct subpopulations within this heterogeneous disease. Clinical trial information: NCT00556049.
