Combination of dual immune checkpoint inhibition (ICI) with stereotactic radiation (SBRT) in metastatic renal cell carcinoma (mRCC) (RADVAX RCC).

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Abstract Disclosures

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Background:
Dual ICI with nivolumab/ipilimumab (N/I) has become a standard of care (SOC) for patients (pts) with mRCC. Since the failure to respond to ICI may be due to a lack of immune recognition, novel vaccination approaches and stimulation of the innate immune system (e.g. stimulator of interferon genes (STING) agonists) are being pursued in clinical trials. Because preclinical studies using SBRT have demonstrated the a.) release of tumor antigens, b.) STING pathway activation and c.) synergy with ICI, we have conducted a study to explore the safety and efficacy of this approach in mRCC pts.

Methods:
Pts with clear cell mRCC were screened and enrolled at two sites (UT Southwestern and Johns Hopkins). Prior treatment with tyrosine kinase inhibitors (TKI) and IL2 were allowed. Enrolled pts received standard of care dosing with Nivolumab (3 mg/kg) and Ipilimumab (1mg/kg) IV q3weeks followed by nivolumab monotherapy. SBRT was administered to 1-2 disease sites with a dose of 50 Gy in 5 fractions between the first and the second dose of N/I. The primary goals of this exploratory study were to determine the safety and tolerability as well as the objective response rate (ORR) by RECIST 1.1 of non-irradiated lesions.

Results:
A total of 29 pts were screened and 25 pts were enrolled. 11 (44%) of pts received at least one prior systemic therapy: 4 (16%) pts received IL2 and 7 (28%) TKI therapy. The cohort was primarily intermediate and poor risk pts (favorable risk n = 2 (8%), intermediate risk n = 20 (80%), poor risk n = 3 (12%)). 10 (40%) pts required immune suppressive therapy with prednisone for classic immune related adverse events as seen with dual ICI. Radiation pneumonitis limited to the radiation field (grade 2) was seen in 2 pts and responded promptly to oral steroids. At the time of analysis, partial responses (PR) were observed in 14/25 patients with an ORR of 56%. Additional analyses including duration of response, progression free survival and overall survival will be presented.

Conclusions:
Dual ICI with SBRT showed an acceptable safety and encouraging antitumor activity in mRCC warranting further investigations. Clinical trial information: NCT03065179