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The high-dose aldesleukin (HD IL-2) "SELECT" trial in patients with metastatic renal cell carcinoma (mRCC).

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Abstract

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Background: HD IL-2 received FDA approval for mRCC in 1992, producing a 14% major response (CR + PR) rate and durable remissions in phase II trials. The Cytokine Working Group conducted the present trial to identify patients (pts) likely to respond to treatment in order to improve the therapeutic index of HD IL-2.

Methods: In this multicenter, prospective study pts with histologically confirmed RCC that was metastatic or unresectable, measurable disease, age ≥ 18 years, ECOG PS 0-1 and adequate organ function received HD IL-2 (600,000 U/kg/dose intravenously every 8 hours on days 1 through 5 and 15 to 19 (maximum 28 doses) every 12 weeks. The primary endpoint of the study was to determine the major response rate (RR) of pts with "favorable" predictive features. All pts were consented to provide archived tumor tissue that would be used for pathology risk classification, carbonic anhydrase IX (CAIX) staining and in creation of a tissue microarray.

Results: One hundred twenty eligible pts enrolled between November 2007 and July 2009. Seventy-two percent had ECOG PS 0, 71% were MSKCC intermediate risk, 96% had clear cell RCC and 99% had prior nephrectomy. No unanticipated toxicities were observed. There were two treatment-related deaths. At the time of this analysis, the investigator assessed RR was 29% (35/120) (7 CR, 28 PR) and was significantly greater than the historical RR (95% CI = 21%-38%, p=0.0009). The median PFS was 4.4 months (mo) and 20 responses are ongoing (range 4-35+ mo). The RR for pts with clear cell RCC was 30% (35/115) (95% CI = 22%-40%, p=0.0004). Response to IL-2 was not associated with any pre-treatment clinical factor or seen in pts with non-clear cell histology (5 pts) and high UCLA SANI (survival after nephrectomy and immunotherapy) score (8 pts). Tumor (98%) and blood (94%) samples were collected on most eligible pts.

Conclusions: The RR to HD IL-2 in this trial was significantly better than the historical experience. Clear cell histology may select pts who respond to IL-2. Analysis of tumor (central pathology review and staining for CAIX) and blood based predictive markers is ongoing to further improve the selection criteria for HD IL-2 in pts with mRCC and will be updated at the meeting.

Author Disclosure

Employment or Leadership Position	Consultant or Advisory Role	Stock Ownership	Honoraria	Research Funding	Expert Testimony	Other Remuneration
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