121P Radiotherapy as an immunological booster in patients with metastatic melanoma or renal cell carcinoma treated with high-dose Interleukin-2: Final data

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Background: High-dose interleukin-2 (HDIL-2) represents a curative treatment option in metastatic melanoma (MM) and renal cell carcinoma (RCC) patients, although still in need of improving its therapeutic efficacy. Radiotherapy (XRT) strongly synergizes with immunotherapy and may boost the effects of HDIL-2 allowing for less toxic schedules.

Methods: In this proof-of-principle phase II study, biological markers of immunological response were considered as primary endpoints in previously treated MM and RCC patients. The treatment consisted of 3 daily doses of XRT (6-12 Gy) delivered to one lesion before the first and third IL-2 infusion (18 MIU/m2/day by IV infusion for 72 h), repeated every 3 weeks for a maximum of 6 cycles. In a first stage, 4 out of 7 enrolled

patients showed an immunological response allowing the recruitment of a further 12 patients according to the minimax two-stage Simon design. The immunological efficacy of the combined XRT/HDIL-2 treatment was assessed measuring the proportion of circulating immune effectors specific for tumor antigens known to be expressed in MM and in RCC (i.e. Tyrosinase, gp100, Mart-1, 5T4, CAIX/G250, EGFR, survivin, MAGEA3 and NYESO1) by means of INF-γ Elispot assay. Moreover, the predictive value of pre-treatment serum biomarkers was also assessed.

Results: Since September 2012 a total of 19 patients have been enrolled (9 RCC and 10 MM patients of which 6 uveal, 2 mucosal and 2 cutaneous) with a median age of 55 years. Assessed clinical responses were 4 PR (3 RCC and 1 MM), 6 SD (2 RCC and 4 MM) and 9 PD. Median PFS was 3.2 and 2.9 months and median OS was 8.7 and 6.7 months, for RCC and MM respectively. According to CTCAE 4.0, the majority of toxicities was grade 1-2. IL-2 dose was never reduced, nor was the infusion interrupted. Interestingly, we found an enhancement greater than 10% of antigen-specific spot-forming cells (SFCs) for at least one tumor antigen after treatment in 16 out of 19 patients. Moreover, we detected much lower serum basal levels of IL-8 and IL-1b in responders (CR/PR/SD=10) compared to non responders (PD = 9).

Conclusion: HDIL2/XRT combined treatment is well tolerated and fairly active in the MM and RCC settings.

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