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MULTIPEPTIDE IMMUNOTHERAPY PLUS IMMUNOGENIC CHEMOTHERAPY IN REFRACTORY CANCER

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Background: Refractory tumors are a challenge. Tumor adaptive immune infiltration in several tumors, even when refractory, is not uncommon. It is clear that the future of oncology treatments is the combination of therapies to revert chemoresistance. We treat in pilot study 25 patients with refractory tumors using 22 peptides from biological and relevant proteins in combination with oxaliplatin and doxorubicin as immunogenic chemotherapy. After the end of the treatment, we observed an effective clinical response in 100% of the cases.

Methods: After approval by the local ethics committee, we treated patients such as high grade serous ovarian cancer (n=8), soft sarcomas (n=5), pancreatic cancer (n=2) and triple negative breast cancer (n=10). Blood was drawn before, during and after treatment to monitor the adaptive immune response by granzyme B and interferon-gamma ELISPOT. Also, we collected serum for ELISA. DTH was performed before and after treatment in leg and primary tumor area. 22 peptides were administrated subcutaneously (SC) every week for 4 weeks in the axillary and inguinal lymph nodes. Afterwards, the peptides were administrated subcutaneously in the areas with tumor activity according with CT and/or PET scan. Doxorubicin and oxaliplatin were administered at low dose (immunogenic chemotherapy) four times for every two weeks.

Results: The treatment was well tolerated in 100% of the patients with minimal local dermatological reactions in the peptide administration site. 100% of the subjects entered remission according with the CT scan. Importantly, the clinical remission correlated with the infiltration of CD8 cells in the DTH site. Also, all the patients had a statistically significant CD8 immune response against all the peptides. This was especially remarkable for fascin (p=0.0001), Ape-1 (p=0.0001), Bcl-2 (p=0.001) and VCP (p=0.005) peptides.

Conclusions: Combination therapy with multipeptide antigen specific active immunotherapy with immunogenic chemotherapy is feasible and demonstrated remarkable clinical results, as remission were reached even in refractory patients. We observed multiple lymphadenopathies in the CT scans that correlate with the clinical and the granzyme immune response.

Biography

Juan Pablo Marquez Manriquez is a Medical Oncologist with training in Mexico, California and Seattle, Washington. His passion for Immunology and Oncology emerged from the very early stages of his life, as he prepared in pre-medicine by studying Pharmaceutical Chemist Biologist and later Medicine. He is currently developing projects for the prevention of gastrointestinal cancer in the CICS, USA, Seattle campus. He is currently specializing in the prevention of recurrence of tumors of high clinical impact such as ovary, triple negative breast, inflammatory breast, colorectal and multiple myeloma. Since 2002, he has presented scientific papers at multiple international congresses, led by AACR, ASCO, AAI, SITC and ESMO. He worked as a Medical Doctor at the Tumor Vaccine Group of the University of Washington. He is a Director General of the Cancer Research Center in Sonora (CICS) both at the Ciudad Obregón Sonora campus and at the Seattle Washington campus (CICS USA), although his base is in Seattle. In coordination with CICS and various institutions at the international level, CICS is developing through the investigations of his and CICS scientific medical team preventive vaccines to prevent cancer and its recurrences. They are also generating the combination of therapies that will allow for longer remissions and fewer recurrences for different types of tumors.

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