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Immunogenic chemotherapy: The basic and the clinical application

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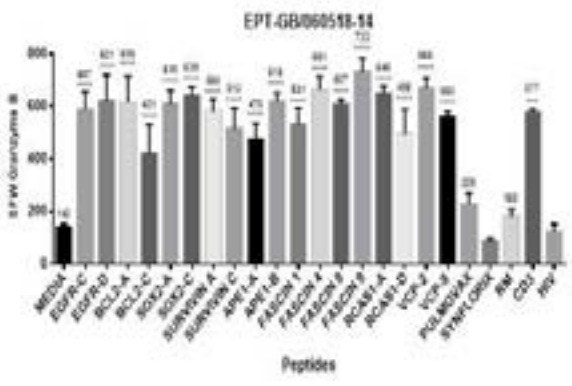
The two main cancer treatment modalities recognized for many years are cancer chemotherapy and radiotherapy. However, by performing dose-response and time-effect curves we can find clinically potential classic cytotoxic cancer chemotherapy that in the past was even fatal for some patients because the toxicity and some of them even required hospitalizations and internal medicine care. Examples of very useful drugs now recognized in many pre-clinical studies as an example 5-Fluorouracil, Cyclophosphamide, Adriamycin, Oxaliplatin, Carboplatin, Paclitaxel and many ones including old alkylant agents and new like temozolamide etc. So, with this in mind we performed *in vitro* several studies using 10-15% of the original dose used in the standard of care treatment. We found in this pilot clinical study just by adjusting the doses of Adriamycin, Oxaliplatin in particular showed significant clinical improvement in patients with challenge neoplasias such as refractory different subtypes of breast cancer, ovarian cancer, sarcomas and neurotumors in both adults and pediatric patients. Since 2011, the medical oncology initiated to recognize the power of training the right immune cells with different approaches including immunogenic chemotherapy to improve PFS and OS with limited clinical and economical toxicity. The concept of immunogenic chemotherapy occurs with some cancer classic cytotoxic chemotherapy are able to kill Cancer Stem Cells (CSC's), augmenting the anti-tumor immune response mainly relay on CD8, Th1, and augmenting the "flavor" of the tumor cells and became more attractive by the mentioned cells. 16 patients were treated with 20 mg total of Adriamycin and 30 mg total dose of Oxaliplatin. We treated the patients having as end point the granzyme B ELISPOT and by cytotoxicity assays to evaluate the tumor cells death and correlate with the clinical by CT-Scan and the immunological assays. 16/10 patients improve statistically significant the Granzyme B production against four recall antigens and 10 tumor-associated antigens after one month of treatment. The treatment was well tolerated, and we continued the treatment until tumor progression. With one month of treatment 60 % of the patients undergo tumor reduction demonstrated by CT scan. Responder patients had high-production of Granzyme against a cocktail of four tumor-associated antigens (p=0.005). Clinical immunogenic chemotherapy with Adriamycin and Oxaliplatin will be a feasible protocol in combination with standard of care treatment, checkpoint inhibitors and multi-peptide active antigen specific immunotherapy in patients with good Karnofsky despite being refractory.



Biography

Dr. Pedro Alejandro Lucero Diaz, MD was born and raised in Peru. He received his medical degree from the National University of San Marcos in Peru. Then he was trained in internal medicine and eventually in medical oncology at the National Medical Center in Mexico City (XXI century medical center) where he started clinical projects about the effects of cisplatin and magnesium in the beginning of the Cisplatin era. Afterwards he went back to Peru to become the chairman of the Department of Medical Oncology of the Air force Military Hospital in Lima Peru where he served for six years. He decided to go back to Mexico, and he got a position in Sonora in the Pacific Northwest Medical Center in Ciudad Obregon, Sonora where he was an attending medical oncologist and radiotherapist. In 2002 he started a project in coordination with several oncologists in order to create a cancer research center, now named the Sonora Cancer Research Center in Seattle, Washington, United States and Ciudad Obregon, Sonora (CICS USA and CICS Sonora). Since then he has been presented and published several clinically relevant data in ovarian, TNBC, inflammatory breast His research interest is the immunomodulation in refractory tumors and he found that refractory patients including but not limited to ovarian, breast, sarcomas, neuro-tumors and GI tumors even in refractory conditions as long they have an Karnofsky >80% who in some cases are good candidates to receive therapies such as immunogenic chemotherapy, which is his main line of research interest.

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