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Alejandro Camacho Hernandez, J Cancer Sci Ther 2019, Volume 11
DOI: 10.4172/1948-5956-C1-158

32nd Euro Congress on

Cancer Science & Therapy

March 07-08, 2019 | Barcelona, Spain

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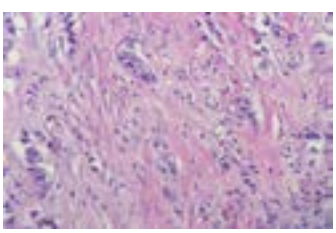
Treat locally equals treat systemically: Targeting the tumor microenvironment clinically

There are many animal models treating the tumor microenvironment. However, there are very few in human studies. For such reason we design using different tumor cell lines and human peripheral blood mononuclear cells (PBMC´s). Afterwards we designed a clinical pilot trial approved by the local ethic committee. We used combinations of local therapy with repurposing drugs. We performed a systematic review of several potential drugs (N=12). For those drugs we decided according with the proof of principle studies use clinically in refractory cancer patients from different tumors the following drugs. Bortezomib, meloxicam, zoledronic acid, gemcitabine and naproxen. The treatment starts over on the inguinal and axillar lymph nodes areas at immunogenic doses. This approach was designed to modulate CD8, ′ δ T cells and Th1. Refractory patients with diverse neoplasia's and Karnofsky > at 80% n=18 were treated with this combination. We started treating first IV and after one week we treated with subcutaneous (SC) injections in the primary tumor site and metastasis areas (2 ml per injection in each site). We selected the SC injection sites in base at the most recent CT scan. Several immunological assays such as peptide ELISA and cytokines IL-6, IL-12, TNF-alpha and IL-10 were measured. The treatment was well tolerated with minor adverse events such as nausea, flu-like symptoms, mild pain in the SC injections and diarrhea. The combination was able to reduce primary tumor, hepatic and lung metastasis in 11/18 patients. Additionally, IL-6 was downregulated in the 11 patients with response (p=0.01) and IL-12 was increased (p=0.005). When the stroma and tumoral microenvironment are treated locally there is genomic, stroma, innate and adaptive immune cells usually associated with immunosuppression. With this approach the tumor cells died mainly by necrosis and several molecules clinically relevant for instance DAMPS, calreticulin and heat shock proteins are able to impact the stop of tumor growth and metastasis. Importantly this combination was able to decrease myeloid derived suppressor cells. This protocol was able to activate the phagocytosis and maturation of dendritic cells after treatment. Treat locally treat systemically is very effective in comparision with systemic myeloablative chemotherapy, because we can develop very important modification of tumoral microenvironment, immunological system reactivation, and we can avoid myeloid suppressor cells, T-regs, neoangiogenesis, with less toxicity.



10x: tumoral microenvironment a lot of stroma and lymphocyte infiltration

Biography

Alejandro Camacho Hernandez is a Hematologist Oncologist with training in Mexico, Mayo Clinic Rochester Minnesota, Massachusetts General Hospital and Arizona Cancer Center, USA. He became an Expert in Solid and Hematological Tumor Microenvironment at the clinical level by manipulating with a cocktail of repurposing drugs the pro-tumors cells of the immune system such as Foxp3 positive cells, Th2, Th17, myeloid derived suppressor cells, etc. He is currently developing in Ciudad Obregon, several clinical pilot protocols to prevent multiple myeloma relapse and has already presented his preliminary data at ESMO 2015 in Vienna. He identified 14 biologically and clinically relevant proteins from multiple myeloma patients and designed 36 peptides containing CD8 and Th1 epitopes and according with his preliminarily data is very promising in combination with repurposing drugs of the tumor microenvironment. He is also treating patients in pilot protocols using subcutaneous treatment to improve the pharmacokinetics and ultimately modify the tumor microenvironment avoiding the systemic toxicity.

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