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THE CLINICAL IMPORTANCE AND IMMUNOMODULATION OF THE TUMOR MICROENVIRONMENT

Alejandro Camacho Hernandez

Sonora Cancer Research Center (CICS Sonora), Mexico

Background: The tumor microenvironment has been studied for many years and there are a few clinical studies and usually using one drug. We study four potential drugs able to modulate the microenvironment clinically by applying the treatment between intravenous (IV) and subcutaneous (SC) close to the primary tumor and their metastasis. We used bortezomib, gemcitabine, zoledronic acid and cyclophosphamide one week IV and one-week SC. We were able to demonstrate that this quadruple combination was able to modulate several pro-tumoral mechanisms such as cytokines, platelets and pro-tumor immune cells and ultimate the tumor stroma with clinical significance of the modulation of tumor microenvironment.

Methods: Refractory patients with diverse neoplasias and Karnofsky > at 80% n=18 were treated with this combination after the local IRB ethics committee approval. We started treating IV with the four drugs and after one week we treated with subcutaneous injections in the primary tumor site and metastasis (2 ml per injection in each site). We selected the SC injection sites in base at the most recent CT scan. ELISA such as IL-6, IL-12, TNF-alpha and IL-10 measured cytokines.

Results: 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 down regulated in the 11 patients with response (p=0.01) and IL-12 was increased (p=0.005).

Discussion: Refractory patients are a challenge as unfortunately even the patients are in that clinical condition some of them are still well preserved to try therapies that potentially may impact the tumor and improve the chances to have less palliative care especially in patients with good clinical conditions. The quadruple combination so far decreased bad prognosis cytokines such as IL-6 and increase cytokines such as IL-12 that improve the polarization of dendritic cells to activate the cells to Th1 cells to have a better tumor microenvironment. Treat systemically is a feasible approach that we will prepare for a phase I/II clinical trial.

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 clinically speaking in expert in solid and hematological tumors microenvironment by manipulating with a cocktail of repurposing drugs the pro-tumors cells of the immune system such as Foxp3 positive cells, Th2, Th17, myeloid suppressor cells, etc. He is currently developing in Ciudad Obregon, several clinical pilot protocols to prevent multiple myeloma relapse and he already presented his preliminary data at ESMO 2015 in Vienna. He identified 14 biologically and clinically relevant proteins from multiple myeloma patients and now he 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 works at the alliance in ImmunoOncology from Seattle and Sonora. He is also studying the potential role in prospective studies of patients with different types of tumors of the role of the platelets, coagulation factors and acute phase proteins in order to try at least five different drugs to combine with the standard of care treatment and look for clinical benefits either in PFS or OS

alejandro.hematologo.camacho@gmail.com