744 MULTI-ARMED MYXOMA VIRUS HAS THERAPEUTIC POTENTIAL FOR TREATMENT OF MULTIPLE MYELOMA

Lina Franco, Christopher Fraser, Lino Torres-Dominguez, Nicole Grigaitis, Jack St. Peter, Mario Abrantes, Zachary Tacner, Heather Hrach, Ana de Matos, Leslie Sharp*. *OncoMyx Therapeutics, Phoenix, AZ, United States*

Background Despite improvements with new therapeutics, multiple myeloma (MM) patients still relapse and become refractory. Myxoma virus (MYXV) selectively replicates in human tumor cells and stimulates the immune system. MYXV selectively kills human patient MM cells and spares normal progenitors. MYXV also eradicates growth of a disseminated mouse MM in vivo. MYXV is a large, double stranded DNA poxvirus, and has a genome size amenable to insertion of multiple transgenes. We generated MYXV carrying IL-12 and decorin. IL-12 is an immune modulator that activates T- and NK-cells. Cellular responses to decorin include tumor cell intrinsic signaling effects, tumor matrix modulation, and inhibition of the TGF-beta pathway. This represents a promising therapeutic option for MM patients that do not respond well to immunotherapy. The current work suggests MYXV armed with IL-12 and decorin could be an effective anti-MM therapy.

Methods Cytotoxicity assays were performed using a cell viability assay. Transgene expression levels were analyzed by microscopy, flow cytometry, and ELISA.

Results Human MM cell line U266 infected with MYXV (vMYX-hIL-12/Dec) carrying human IL-12, decorin, and green fluorescent protein (GFP) produced transgenes in a dose and time responsive manner. A panel of human MM cell lines was infected with vMYX-hIL-12/Dec and transgene expression in supernatant, cell killing EC50, and GFP levels were evaluated. Sensitive and resistant human MM cell lines were identified. The comparison of replication, cell killing capacity, and transgene expression highlighted the independent importance of these mechanisms in overall activity.

Conclusions The current work describes the oncolytic activity and transgene expression following exposure to vMYX-hIL-12/Dec in human MM cell lines in vitro. Our initial studies suggest there is significant value in pursuing vMYX-hIL-12/Dec and other armed MYXV as a new approach towards MM therapy.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.744