883 AN ANTI-CARCINOMA MONOCLONAL ANTIBODY (MAB) NEO-201 CAN ALSO TARGET HUMAN ACUTE MYELOID LEUKEMIA (AML) CELL LINES IN VITRO

[1]Alessandra Romano*, [1]Nunziatina Parrinello, [1]Sara Marino, Enrico La Spina[1], [2]Massimo Fantini, [3]Philip Arlen, [2]Kwong Tsang, [1]Francesco Di Raimondo. *[1]Universita di Catania, Catania, Italy; [2]Precision Biologics, Inc., Bethesda, MD, USA; [3]Precision Biolgics, Inc., Bethesda, MD, USA*

Background NEO-201 is an IgG1 mAb targeting variants of CEACAM5/6 and has demonstrated tumor sensitivity and specificity in epithelial cells. Functional analysis has revealed that NEO-201 can engage innate immune effector mechanisms including ADCC and CDC to directly kill tumor cells expressing its target. A recent Phase 1 clinical trial at the NCI has determined both safety and recommended Phase 2 dosing. We have also seen the expression of the NEO-201 target on hematologic cells, specifically Tregs and neutrophils. Due to epitope being expressed both on malignant epithelial cells as well as several hematologic cells, we designed this study to explore the reactivity of NEO-201 against hematological neoplastic cells in vitro.

Methods Phenotypic analysis was conducted by flow cytometry. Cell lines used were six AML (HL60, U937, MOLM13, AML2, IMS-M2 and OCL-AML3), two multiple myelomas (MM) (OPM2, MM1.S), two acute lymphoblastic leukemia (ALL) (SUP-B15, RPMI8402) and four mantle cell lymphoma (MCL) (Jeko-1, Z138, JVM2 and JVM13). Markers used for flow cytometry analysis were CD15, CD45, CD38, CD138, CD14, CD19 and NEO-201. Functional analysis was performed by evaluating the ability of NEO-201 to mediate ADCC activity against AML cell lines using human NK cells as effector cells.

Results 5 of 6 AML cell lines tested bind to NEO-201 and the% of positive cells were 47%, 99.5%,100%,100% and 97.8% for HL60, U937, MOLM13, AML3 and IMS-M2, respectively. The% of positive cells in the two MM cell line were 99% and 18% for OPM2 and MM1.S, respectively. NEO-201 binding was not detected in the two ALL and the four MCL cell lines tested. Functional analysis has demonstrated that NEO-201 can mediate ADCC activity against the AML cell line (HL60) tested.

Conclusions This study demonstrates that NEO-201 mAb's target is expressed in most of the AML cell lines tested in vitro. In addition, we have shown it can mediate ADCC activity against HL60 cells (AML). Together, these findings provide a rationale for further investigation of the role of NEO-201 in AML as well as MM, further exploring patient PBMCs and bone marrow samples.

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