ONCOLYTIC ADENOVIRUS CODING FOR HUMAN MUCIN1 T CELL ENGAGER WITH INTERLEUKIN-2 POTENTIATES ANTI-TUMOR T CELL RESPONSES AGAINST TUMORS

Saru Basnet*, 1Mirte Van der Heijden, Elise Jirovec, 2, James Clubb, 3Susanna AM Grönberg-Vähä-Koskela, 2Victor Arias, 1Santeri A Pakola, 1Anna Kanerva, 2Dafne Alves Quixabeira, 2Iooa Manuel Santos, 2Lyna Haybout, Tatiana Kudling, 2, 3Akseli Hemminki.

1University of Helsinki, Helsinki, Finland; 2Cancer Gene Therapy Group, Translational Immunology Research Program, University of Helsinki, Helsinki, Finland; 3TILT Biotherapeutics, Helsinki, Finland; 4Comprehensive Cancer Center, Helsinki University Hospital, Helsinki, Finland; 5Department of Gynecology and Obstetrics, Helsinki University Hospital, Helsinki, Finland

Background Previously, we demonstrated that 5/3 chimeric oncolytic adenoviruses coding for human mucin1 (MUC1) T cell engager boosted intratumoral T cell activation and proliferation, resulting in effective antitumor efficacy in A549 and patient-derived xenograft (PDX) ovarian cancer mouse models. In this study, we constructed and characterized novel oncolytic adenovirus, Ad5/3-E2F-d24-aMUC1aCD3-IRES-IL2 (TILT-322) built on a backbone of Ad5/3-E2F-d24 carrying a human MUC1 T cell engager transgene. Additionally, human interleukin (IL)-2, which is widely known to stimulate T cell proliferation and differentiation, has been incorporated into the construct design to evaluate the changes in antitumor efficacy and immunomodulatory properties.

Methods Human ovarian cancer ascites samples were received from different patients and centrifuged to obtain a cell pellet. Real time cell killing assays were performed to evaluate cytotoxicity. Immune cell profiling was performed by using flow cytometry in patient samples and a panel of commercially available cell lines followed by virus treatment. In vivo, antitumor efficacy of Ad5/3-E2F-d24-aMUC1aCD3-IL2 was studied using a PDX ovarian cancer murine model.

Results Addition of aMUC1aCD3-IL2 transgenes did not compromise virus replication capacity compared to the backbone virus. When Ad5/3-E2F-d24-aMUC1aCD3-IL2 was combined with T cells, rapid tumor cell lysis and increased T cell activation was observed. The preliminary results indicate activation of effector lymphocytes in the Ad5/3-E2F-d24-aMUC1aCD3-IL2 treated group and that detailed immune studies together with in vivo antitumor efficacy of the virus will be presented at SITC.

Conclusions Ad5/3-E2F-d24-aMUC1aCD3-IL2 virus treatment is a potential immunotherapeutic candidate which combines both direct oncolysis and T cell-mediated killing, resulting in a potent therapeutic outcome that warrants translation into the clinic.

Ethics Approval HUS Regional Committee on Medical Research Ethics has granted the approval for the study of human ovarian ascites samples cancer. The approval number is HUS/3360/2019. The license for the conduction of in vivo experiment was granted by the ESAVI (Regional State Administrative Agencies for Southern Finland) - ESAVI/26562/2022.

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