FRACTIONATED IRRADIATION ACTIVATES GLIOMA IMMUNE MICROENVIRONMENT AND BOOSTS ANTIGEN-SPECIFIC T CELL RESPONSE IN EXPERIMENTAL GLIOMAS

1,2,3Nirmeen Elmadany*, 2,3Julius Michel, 3Jana Sonner, 4Svetlana Ovchinnikova, 2,3Khwab Sanghvi, 2,3,4Isabelle Bernhardt, 3,4Xin-Wen Zhang, 3Kristine Jähne, 3Arvita Satl, 4Simon Anders, 3Michael Bredowoldt, 2,3,4,5Michael Platten, 2,3Katharina Sahm. 1UMM/ DKFZ, Heidelberg, Germany; 2Mannheim Center for Translation Neuroscience (MCTN), Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany; 3DKTK (German Cancer Consortium) Clinical Cooperation Unit (CCU) Neuroimmunology and Brain Tumor Immunology, German Cancer Research Center (DKFZ), Heidelberg, Germany; 4Center for Molecular Biology of Heidelberg University (ZMBH), Heidelberg, Germany; 5German Cancer Research Center, Heidelberg, Germany; 4Department of Neuroradiology, Heidelberg University Hospital, University of Heidelberg, Heidelberg, Germany; 1DKFZ Hector Cancer Institute at the University Medical Center Mannheim, Mannheim, Germany; 4Immune Monitoring Unit, National Center for Tumor Diseases (NCT), Heidelberg, Germany; 1Helmholtz Institute of Translational Oncology (HI-TRON), Mainz, Germany

Background Glioblastoma (GBM) is the most aggressive primary brain tumor with a survival rate of 14–16 months. Several ongoing clinical trials employ vaccine, immune checkpoint inhibitors and/or adoptive T cell therapy to treat GBM. However, the impact of irradiation as part of the standard of care on the immune microenvironment and response to immunotherapy is ill-defined.

Methods In the present study, we employed clinically relevant fractionated irradiation (FIR) at a dose of 4x 2 Gy to investigate the response of experimental orthotopic glioma expressing the tumor-associated antigen glycoprotein (gp)100 in immunocompetent syngeneic mice to a gp100 peptide vaccine as well as to adoptively transferred T cells. We employed single cell RNA sequencing to decipher the post-irradiation changes in the GBM immune microenvironment and elucidate the impact FIR on the efficacy of T cell-mediated immunotherapies.

Results FIR boosted the response of orthotopically-implanted GL261 tumors to a gp100 vaccine. Furthermore, FIR enhanced the infiltration of GL261-gp100 gliomas by adoptively-transferred gp100 T cell receptor-transgenic T cells, which also displayed a more activated and less exhausted phenotype post-irradiation. Single cell transcriptomic studies of tumor-infiltrating CD45+ leukocytes revealed that FIR promotes the expression of leukocyte-endothelial adhesion molecules in T cells, and transcripts encoding proinflammatory M1-like genes in tumor-associated microglia and macrophages.

Conclusions Our preclinical findings support the use of FIR with to increase response to T cell-based immunotherapies.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0861

A960

J Immunother Cancer 2023;11(Suppl 1):A1–A1686