551 INTRATUMORAL INFLUENZA VACCINE IN EARLY COLORECTAL CANCER

Mikail Gögenur*, Mustafa Bulut, Senior Resident, Lukas Balsevicius, Anne-Marie Kanstrup Fiehn, Marianne Bøgevang Jensen, Nesibe Özgur Colak, Tobias Freyberg Justesen, Paulo Cesar Martins Urbano, Lasse Bremholm Hansen, Chief Surgeon, Ismail Gögenur. *Zealand University Hospital, Køge, Denmark*

Background Recurrence is the leading cause of increased morbidity and mortality after colorectal cancer surgery, with up to one-third of patients undergoing curatively intended surgery having a recurrence. The degree of tumor-infiltrating immune cells is crucial for the risk of recurrence, which is why interventions targeting the tumor and the local microenvironment are in increased focus. Intratumoral injection of the vaccine has in experimental studies shown to increase the proportion of infiltrating immune cells and lead to tumor shrinkage in both treated and untreated tumors. The purpose of this combined phase 1 and 2 study was to determine the safety of intratumoral influenza vaccine injection and whether it induces local and systemic elicitation of anti-tumor immune response.

Methods All patients with non-metastatic sigmoid and rectal cancer were eligible for inclusion. The intratumoral influenza vaccine was administered by an additional sigmoidoscopy 7-14 days before the scheduled surgery. The primary outcome was safety. The clinical outcome was evaluated as Mandard tumor regression grade (TRG) assessed by two independent pathologists. Translational outcomes included local and systemic immunological changes, analyzed via immunohistochemistry, and local mRNA gene expression.

Results Ten patients were included in the study, four with sigmoid cancer and six with rectum cancer. No serious adverse reactions or events occurred. TRG was rated as five in all patients, except one rated as four by a single pathologist. A significant increase of $CD8^+$ but not $CD3^+$ T cell count was noted based upon immunohistochemical staining. mRNA gene expression showed several differentially expressed genes when comparing pre vs. post vaccination specimens. Functional enrichment analysis showed significant suppression of pro-tumor inflammatory related pathways. Spatial analysis of protein expression revealed an increased expression of PD-1 in areas of $CD8^+$ T cell infiltrated regions of the post-vaccination specimens compared with similar regions in pre-vaccination specimens.

Conclusions Intratumoral influenza vaccine is a safe intervention. The intervention did not lead to tumor regression, while immunohistochemistry and mRNA gene expression analyses revealed a significant increase in $CD8^+$ T cell count and suppression of pro-tumor inflammation, suggesting that intratumoral influenza vaccine induces an anti-tumor response in the tumor microenvironment.

Trial Registration Trial registration on clinicaltrials.gov: NCT04591379

Ethics Approval The study was approved by the regional ethics committee: SJ-834

http://dx.doi.org/10.1136/jitc-2022-SITC2022.0551