131

Niclosamide-derived immune modulator to enhance immunotherapy for triple-negative breast cancer

Zhipin Liang[1], Gabrielle Vontz[2], Jun Li[3], Jia Zhou[3] and Qiang Shen[2]
[1]LSU Health Sciences Center New Orleans; [2]LSU Health Sciences Center New Orleans. New Orleans, LA and [3]University of Texas Medical Branch, Galveston, TX

OBJECTIVES/GOALS: Triple-negative breast cancer (TNBC) is a highly aggressive and prevalent breast cancer subtype that lacks targeted therapies. This study aims to investigate whether the niclosamide derivative HJC0152 can modulate tumor-derived PD-L1 expression and enhance the effectiveness of anti-PD-1 immunotherapy in treating TNBC. METHODS/STUDY POPULATION: Niclosamide derivative HJC0152 was developed as a novel cancer therapeutic and immunomodulating agent. Human TNBC cell line (MDA-MB-231) was treated with HJC0152, and activation of the STAT3 signaling pathway was evaluated using Western blotting. RNA-Seq was employed to analyze the expression of protein-coding genes, particularly those related to immune response. To study therapeutic potential in vivo, TNBC mouse models will be treated with single agent treatments as well as a combination therapy of HJC0152 and anti-PD-1. Tumor volume and mass will be measured over time to determine growth inhibition. RESULTS/ANTICIPATED RESULTS: Preliminary studies indicate that HJC0152 exhibits enhanced solubility compared to Niclosamide, along with high anticancer potency both in vitro and in vivo. HJC0152 was found to effectively inhibit the activation of phosphorylated STAT3 (p-STAT3) in MDA-MB-231 cells, a key signaling pathway associated with cancer progression and immune evasion. RNA-Seq analysis of HJC0152-treated MDA-MB-231 cells revealed a decrease in PD-L1 expression, an essential immune checkpoint protein involved in tumor immune suppression. These findings suggest that HJC0152 is a promising immune modulator that may enhance the efficacy of immune checkpoint blockade therapy for TNBC. DISCUSSION/SIGNIFICANCE OF IMPACT: This study explores an innovative immunotherapy for TNBC using the Niclosamide derivative HJC0152, which inhibits STAT3 signaling and downregulates PD-L1. Results from this study will provide a foundation for HJC0152's inclusion in clinical trials and potentially offer a new and promising therapeutic option for TNBC treatment.

132

A novel microsampling measure to evaluate localized inflammation via amniotic fluid

Katherine Kissler[1], Heidi Lennox, Powell[2] and Teri L. Hernandez[1]
[1]University of Colorado Anschutz Medical Campus, College of Nursing and [2]University of Colorado Anschutz Medical Campus, CCTSI Core Lab

OBJECTIVES/GOALS: Intra-amniotic inflammation (IAI) is one of the leading causes of maternal/fetal morbidity globally, yet it is undiagnosed in 90–95% of cases. The purpose of this study was to assess precision and accuracy of a novel microsampling device for measuring cytokines in amniotic fluid (AF) to enable noninvasive evaluation of localized inflammation. METHODS/STUDY POPULATION: AF was obtained from discarded amniocentesis samples from 3 deidentified patients without known inflammation. Samples were spiked to 5 concentrations of interleukin-6 (IL-6) and tumor necrosis factor-a (TNF-a), then sampled using the Neoteryx Mitra volumetric microsampling device (20 μL). Dried/reconstituted samples were analyzed using the Luminex R&D Mag XL multiplex (IL-6, TNF-α) and compared to free-flowing AF. Inter-and intra-assay performances were evaluated across 5-runs in 3 standard cytokine concentrations. Recovery/linearity was assessed by a recovery curve and parameter estimates. Precision was assessed between-run and within-run using coefficients of variance (%CV). Accuracy was evaluated as agreement between microsampled and free-flowing AF using Bland–Altman plots. RESULTS/ANTICIPATED RESULTS: TNF-α results were linear for all 3 patients across 5 concentrations. However, accuracy and recovery consistently failed (mean±SD percent recovery 176±21%). TNF-α results had acceptable precision with %CV within-run of 6.8–12.1% and across-runs of 14.0–15.9%. Microsampled TNF-α agreed with free-flowing sample: 16 of 18 (89%) were within 1SD of the mean difference (-24±36 pg/ml). IL-6 results were linear for 1/3 patients and had unacceptable accuracy and recovery for 13/15 samples (mean±SD percent recovery 764±469%). IL-6 results had acceptable precision (%CV within-run 6.2%, 7.5% and 11.2%; across-run .9–15.2%). Microsampled IL-6 agreed with free-flowing sample; 17 of 18 (94%) were within 1SD of the mean difference (-148±180pg/ml). Free-flowing vs. microsampling methods agreed best at low concentration. DISCUSSION/SIGNIFICANCE OF IMPACT: This study provides preliminary support for noninvasive measurement of cytokines leveraging small amounts of leaking AF providing a promising alternative to amniocentesis and potential for assessing inflammation intrapartum. Clinical application requires development of reference ranges and association between cytokine levels and outcomes.

133

Development of a customized tracking dashboard to enhance support for NIH Funded Investigator-Initiated Clinical Trials

Katie Keenoy, Suresh Vedantham, Emily Lake, Emily Asbury, Chris Sorensen and Sherry Lassa-Claxton
Washington University in St. Louis

OBJECTIVES/GOALS: Early identification and profiling of planned studies is a critical administrative challenge in providing timely support for clinical trials. Here we describe the collaborative design and development of a clinical trial tracking dashboard to enhance support and quality improvement for investigator-initiated clinical trials at our institution. METHODS/STUDY POPULATION: Trial-CARE organized a workgroup with key stakeholders from WashU business units that manage grants, information technology, bioinformatics, data repository stewardship, and clinical trial support. The workgroup strategized next steps in a "proof-of-concept" effort to determine whether NIH investigator-initiated clinical trial metrics would be accessible via the WashU Data Warehouse. The WashU Data Warehouse is a data repository that pulls in pre-award and post-award data from sources such as the WashU Research-Grant Management System (RMS) and the NIH Reporter Tool. The proof-of-concept findings lead to implementing a plan for Phase 1 of the design, development, and piloting of a visual dashboard to track and offer targeted and timely support to NIH investigator-

https://doi.org/10.1017/cts.2024.792 Published online by Cambridge University Press