Progress Report

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Title of Project: Measuring Nerve Damage after Chemotherapy Treatment

Summary:

Chemotherapy-induced nerve damage or peripheral neuropathy (CIPN) is a major side effect of cancer treatment, leading to early cessation of treatment and long-lasting disability. Despite successful treatment, up to 40% of cancer survivors may be left with long-term disability and reduced quality of life due to CIPN following treatment with neurotoxic chemotherapies. This project will measure the trajectory of nerve degeneration in patients with CIPN through innovative methods of assessing nerve dysfunction, including specialised nerve testing methods and analysis of protein markers of axon degeneration in blood. A key emerging marker of nerve damage is called neurofilament light chain (NfL), which is a key structural protein of nerves, released during injury. This marker NfL has been identified as a marker of axonal damage in animal models of CIPN, but it has not been assessed in large-scale clinical studies. Further it has never been compared with sensitive neurophysiological measures of CIPN.

Accordingly, this project aims to use clinical phenotyping, longitudinal assessment, functional outcomes coupled with these specialised neurophysiological and protein biomarker approaches, to determine key mechanisms underlying the development of nerve damage following chemotherapy treatment, enabling quantification of markers of toxicity and optimisation of risk prediction for neurotoxicity. Aim 1 is to determine association between neurophysiological and serum markers of axonal degeneration in chemotherapy-induced neurotoxicity. Aim 2 is to define the trajectory of axonal degeneration and neurotoxicity in this cohort over time. Achieving these aims requires collection of a longitudinal cohort of patients, to assess the development of neurotoxicity during chemotherapy as well as monitoring lasting nerve damage following chemotherapy completion.

Our team has made good progress towards these aims in 2022. The project has collected longitudinal serum samples and matched clinical and neurological data from 61 patients treated with platinum-based chemotherapies (45 patients treated with oxaliplatin and 16 patients treated with cisplatin). We have extracted and analysed neurophysiological data,

including nerve excitability studies which can provide more detailed information regarding axonal function and membrane properties than conventional nerve testing.

Ultimately, this will enable development of neuroprotective strategies to prevent nerve damage following chemotherapy. Further, this information will be valuable towards understanding how to measure and monitor progression of axonal degeneration across multiple disorders.