Serum Neurofilament Light (sNfL) Levels Indicate Progressive And Sustained Oxaliplatin-Induced Chemotherapy-Induced Peripheral Neurotoxicity (OIPN)

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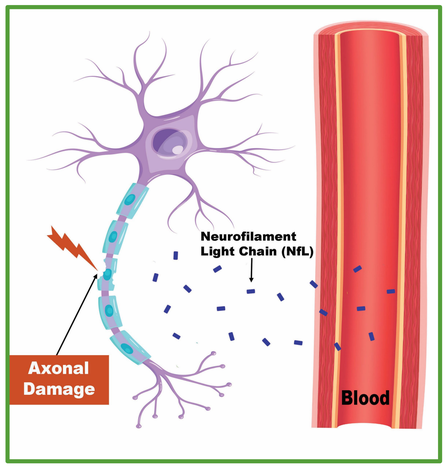
BACKGROUND & SIGNIFICANCE

- Oxaliplatin causes peripheral neurotoxicity: oxaliplatin-induced peripheral neuropathy (OIPN).[1]
- Preliminary data and published research suggest mechanistic connections between OIPN and axonal degeneration.[1-3]
- Axonal degeneration can be quantified with a biomarker: serum neurofilament light (sNfL).[4-6]
- No published longitudinal studies have validated sNfL via comparisons with carefully phenotyped OIPN using patient-reported outcome (PRO) surveys and objective measures of OIPN.
- A validated biomarker can be used to predict and track neurotoxicity at the point-of-care and quantify intervention response in future clinical trials.[4, 7-9]

sNfL Release into the Blood Stream Following Axonal Degeneration



STUDY PURPOSE

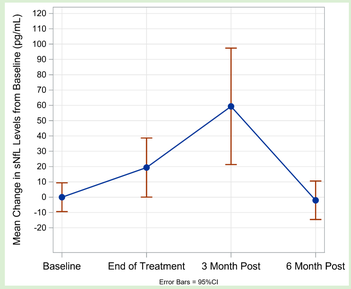
The purpose of this pilot study was to obtain preliminary data to validate neurofilament light chain (sNfL) as a OIPN biomarker.

RESULTS

- **Demographics (*N=17)***
- Mean age = 56.5 years (*SD*=12.8; range=39-75)
- 75% male; 83% Caucasian

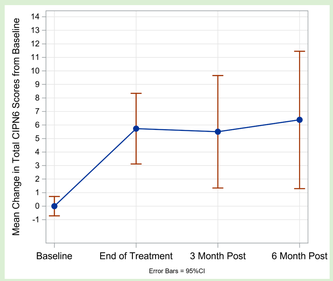
sNfL Change

Mean sNfL change scores increased from Baseline to End of Treatment (19.4 ± 30.4; *p*=.043) and Baseline to 3 Months (59.3 ± 49.5; *p*=.004).



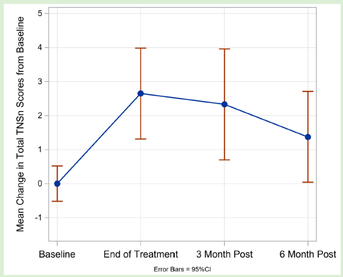
CIPN6 Change

Mean CIPN6 change scores increased from Baseline to End of Treatment (5.0 ± 4.2; *p*=.001*)*.



TNSn Change

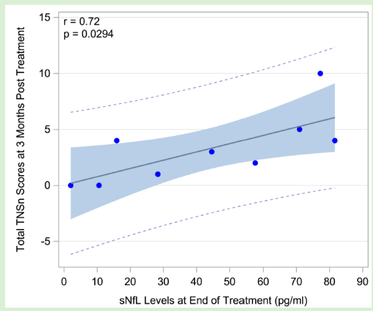
Mean TNSn change scores increased from Baseline to End of Treatment (2.00 ± 2.33; *p*=.004) and 3 Months (2.33 ± 2.12; *p*=.031).



sNfL Correlation with Objective OIPN Measure

sNfL scores at End of Treatment were strongly correlated with TNSn scores at 3 Months (*r=0.72, p=.029)*.

n=9



METHODS

Study Design: Prospective, longitudinal study

Setting: University of Alabama at Birmingham, Birmingham, AL, USA

Eligibility Criteria: colorectal cancer, receiving oxaliplatin, no prior neurotoxic chemotherapy treatment, no baseline peripheral neuropathy, ≥ 18 years

Measures

CIPN6: 6-item PRO survey assessing numbness, tingling, pain in upper & lower extremities (total score range 4-24: higher = worse OIPN) [10]

TNSn: 5-item composite measure assesses pinprick and vibration sensibility, and sensory motor, and autonomic symptoms (total score range 0-16: higher = worse OIPN)[11]

sNfL: A protein found in large myelinated nerve axons that is released into serum[12]

Timepoints

Baseline → End of Treatment → 3 & 6 Months

DISCUSSION

- sNfL may be a valid biomarker of OIPN.
- PRO, objective, and biomarker assessments all increased over time and were the highest 3 months after chemotherapy ended, illustrating OIPN coasting patterns.

LIMITATIONS

- Small sample size compromised statistical validity.
- Findings cannot be generalized to neurotoxicity caused by other chemotherapeutic agents (e.g., taxanes.)

CONCLUSIONS

- sNfL is a promising biomarker of OIPN.
- Future adequately powered studies are needed to confirm and expand upon these findings.

References

https://docs.google.com/document/d/1U6jSWYHcHEU3zgH7gihT_0NimrhmRoTg/edit?usp=sharing&ouid=111583311766501977450&rtpof=true&sd=true

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