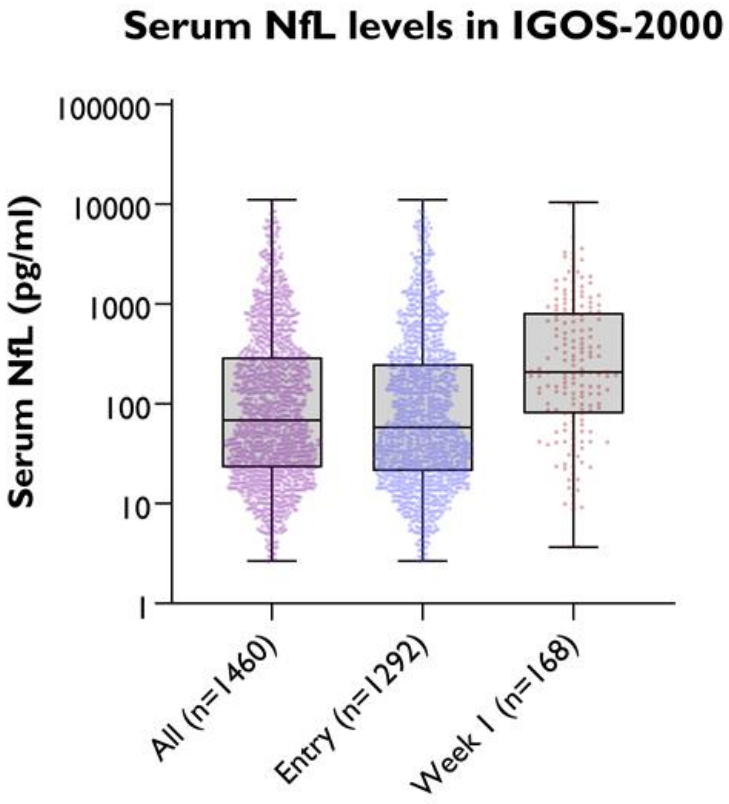
Project title: Neurofilament light chain as biomarker to define the disease dynamics, subtype and prognosis of the Guillain-Barré syndrome.

Progress report of the first year of the study supported by a discovery grant from the GBS-CIDP Foundation International (period from July 2023 to July 2024).

The project has made good progress in the first year as we have been able to finalize the testing of all serum samples for the planned **cross-sectional study** in the International GBS Outcome Study (IGOS). In the first year we have first finalized the study protocol and selected the samples for the study. Eligible were all patients with a confirmed diagnosis of GBS and with sufficient volumes of serum from study entry (or from week 1 when no serum at entry is was available). All serum samples were tested for neurofilament light chain (NfL) levels with ultrasensitive SIMOA technology (SIMOA HD-x analyser) using the NfL light kit (Quanterix) according to the same quality controlled protocol in the same laboratory. In the application we indicate that we expected to be able to test 1200 samples in IGOS, but we were fortunate to be able to test serum NfL in 1460 patients, including from 1292 patients at study entry and from 168 patients at week 1 of study entry.

In the first year we had an initial delay in the testing of the samples because of a technical problem with the NfL test kits by the manufacturer (Quanterix). Because of this about 10% of the samples had to be tested for a second time. The initial problems with the NfL test kits were solved by the manufacturer. The testing was extensively quality controlled, and we confirmed that the second tests showed excellent performance. Therefor we now have high quality data for all patients and these first results are presented in the figure below.



These first results show that that serum NfL is increased already in the early stage of GBS in 93.5% of patients (using a reference value of 9 pg/ml). The medians and IQRs are for all samples combined 68 (23-294) pg/ml, for the entry samples 58 (21-249) pg/ml and for the week 1 samples 207 (80-810) pg/ml. These highly increased levels are compatible with the acute and severe peripheral nerve damage in GBS. Interestingly, there is a considerable variation in NfL levels between patients, ranging from (nearly) normal values op to 10.000 pg/ml. These NfL data are included in the central research database of IGOS and we are currently investigating the relation with preceding infections, anti-ganglioside antibodies, clinical variants and severity and electrophysiological subclassification. Interestingly, these initial findings show that the serum NfL levels are also increased in patients with a demyelinating form of GBS. An important question is if serum NfL can be used to improve the existing clinical prognostic models which will also currently investigated.

We are also preparing for the second part of the project in which an extensive **longitudinal study** of serum NfL levels will be performed to assess the disease dynamics of GBS. For this we are preparing for the selection of a representative subgroup of approximately 300 patients for testing NfL at the various standard follow-up time points in IGOS, including at 2 weeks, 4 weeks, 8 weeks and 3 months. We expect to finale the testing of the serial samples before the end of the year. We are planning to report the NfL results of the cross-sectional and longitudinal study in relation to the clinical course and outcome in a dedicated publication at the end of the project.

As indicated in the project application we are aiming to make the NfL data available for all future projects in IGOS via the Digital Research Environment (DRE) of Erasmus MC. The DRE enables researchers from outside Erasmus MC to have access to IGOS data without violating the strict privacy regulations of the EU. Last year we have been able to develop a procedure for data sharing which worked very well for other projects. Therefore we anticipate that we are also able to share the NfL data (when ready) with the IGOS Consortium for all successive research projects.