Poster P033

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A Prospective Data Collection to Evaluate Utility and Added Value of Serum NfL in Multiple Sclerosis - First Interim Insights from NeofiLos

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KEY FINDINGS & CONCLUSIONS

- **This is the 1st physician reported data on implementation of sNfL in routine medical care setting highlighting the importance and added benefit of sNfL as additional assessment in MS patient management.**
- Results show that **sNfL measurements** will mainly be used to
  - **determine disease activity** (complementing clinical and MRI assessments)
  - monitor therapy effectiveness
- Although none of the participating physicians had experience with sNfL testing before start of this project, the majority indicated that they would act on or be **alerted by elevated sNfL level**.

INTRODUCTION

- Neuroaxonal damage results in release of neurofilaments such as neurofilament light chain (NfL) into cerebrospinal fluid (CSF) and blood with elevated NfL potentially indicating disease activity in RMS patients. [1,2,3]
- Elevated NfL levels may reveal "subclinical" disease before lesions on MRI or clinical symptoms appear.[4]
- Measuring serum NfL (sNfL) levels may help to reflect ongoing disease activity, uncover “subclinical” disease and be of prognostic value for future disease activity, with the potential to contribute to allowing for optimized treatment decision making.

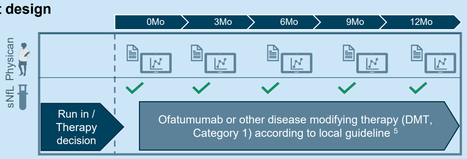
OBJECTIVE

- NeofiLos enables office-based physicians to access sNfL testing aiming to assess utility of sNfL measurements in clinical routine

METHODS

- Project design: NeofiLos is a prospective, multicenter program conducted at 80 sites in Germany, expected to enroll 500 RMS-patients receiving Ofatumumab or other disease modifying therapy (DMT).
- NeofiLos enables office-based centers to access sNfL testing aiming to assess utility of sNfL measurements in clinical routine.
- sNfL is measured from routine blood draws at program inclusion followed by quarterly intervals up to 5x per patient (**Figure 1**).
- Treating neurologists assess the implementation of sNfL into clinical routine regarding aspects like therapy choice and switch or suitability of NfL as a biomarker by completing questionnaires.
- Answers are given on a scale from 1 (no influence) to 7 (high influence).
- Mean values were calculated as mean of all evaluations for patients treated by the same neurologist.
- This first interim analysis includes 622 patients for which up to 419 questionnaires were completed.
- The data will provide insights on general perception of sNfL at program inclusion including benefits and gaps based on current knowledge and experience with sNfL.

Figure 1. NeofiLos project design

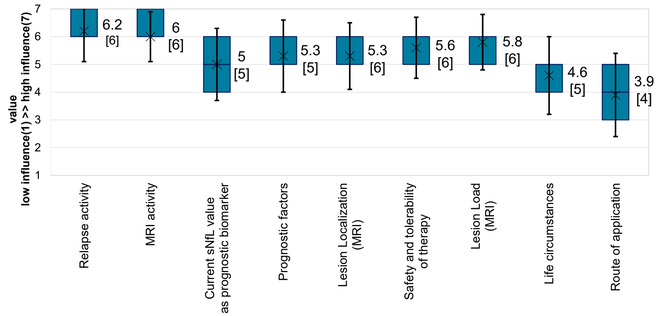


RESULTS

Factors influencing neurologists‘ choice of therapy

- Factors influencing neurologists’ therapy choice are depicted in **Figure 2**.
- Although none of the physicians had experience with sNfL testing before project start, at least half of all participating physicians rated the prognostic value of NfL as intermediate (mean=5.0±1.3; median=5)

Figure 2: Factors influencing neurologists‘ therapy choice.

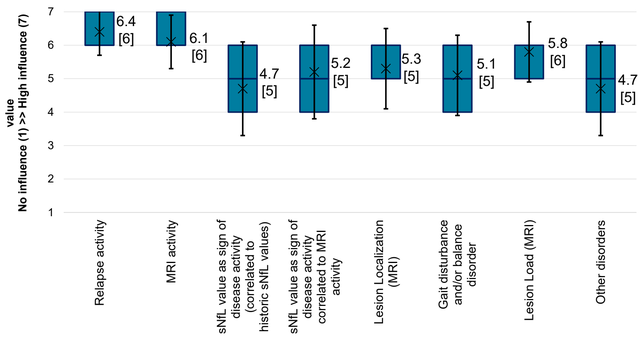


X: mean with SD | Datapoints are labeled as mean [median] | N=63 Neurologists

Factors influencing neurologists‘ decision to change therapy

- Factors influencing neurologists’ decision to change therapy in general are depicted in **Figure 3**.
- Relapse activity (mean=6.4±0.6; median=6) and general MRI activity (mean=6±0.7; median=6) were found to have the **greatest** influence on neurologists’ choice for switching MS therapy.
- Lesion load (mean=5.8±0.8; median=6) and location (mean=5.2±1.1; median=5) determined by MRI have an intermediate to high influence to change a therapy.
- sNfL values have a lower influence on neurologists’ choice for switching a therapy (in correlation to historic sNfL values, mean=4.5±1.2; median=5; in correlation with MRI activity mean=5.1±1.2; median=5). Other factors like gait disturbance and/or balance disorder (mean=4.9±1.1; median=5), cognition impairment or increased fatigue were also rated with lower influence on therapy change (depicted as “other disorders”, mean=4.4±1.3; median=5).

Figure 3: Factors influencing neurologists‘ decision to change therapy.

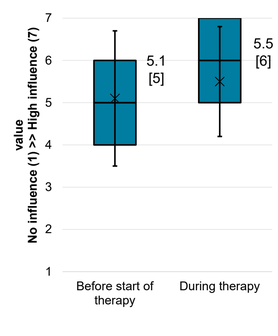


X: mean with SD | Datapoints are labeled as mean [median] | N=63 Neurologists

sNfL as an easily accessible biomarker regarding disease activity

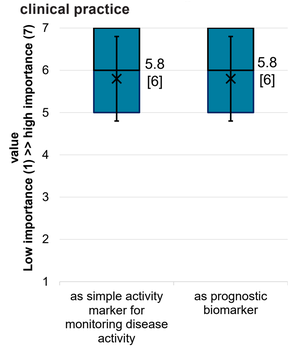
- Comparing their opinion „before start of therapy“ (mean=5±1.4; median=5) and „during therapy“ (mean=5.5±1.1; median=5.9), neurologists considered sNfL measurements as more valuable during therapy and monitoring/ follow up of MS disease than at therapy start (**Figure 4**).
- Overall, participating neurologists would appreciate an easily accessible biomarker for measuring disease activity in their daily clinical routine (**Figure 5**).

Figure 4: Perception of sNfL as a biomarker regarding MS disease activity assessment



X: mean with SD
Datapoints are labeled as mean [median]
N=61 Neurologists

Figure 5: importance of an easily accessible biomarker for measuring disease activity for clinical practice



X: mean with SD
Datapoints are labeled as mean [median]
N=63 Neurologists

- Most neurologists consider sNfL values in their decision to switch or modify the current MS therapy (79.7%) while 20.3% base their decision solely on other factors (**Table 1**).
- 56.5% of all neurologists think that sNfL levels can be used as a first hint of need of treatment optimization. 6.8% of neurologists base this decision on single sNfL levels and 16.4% of neurologists on a trend of increasing sNfL levels.
- 92.9% of neurologists expect that sNfL levels can be used to assess therapy stability (**Table 2**).

Table 1. Perception of sNfL as a biomarker regarding therapy modification

Would you optimize MS treatment based on the sNfL level? n (%)	Total (N=410)
Yes	28 (6.8)
Yes, based on increasing sNfL levels over time	67 (16.4)
It gives me a first hint	231 (56.5)
No	83 (20.3)

Table 2. Perception of sNfL as a biomarker to assess therapy response

sNfL as a biomarker to assess treatment response, n (%)	Total (N=409)
Would sNfL help to assess if a patient is stable / responding to therapy?	
Yes	380 (92.9)
No	29 (7.1)

Neurologists‘ opinion on early use of high effective MS therapies (HET)

- Physicians support the early use of HET as very high (mean=6.5±0.7) and also adopted this in daily clinical practice (mean=6.1±0.9).
- 49.9% of neurologists state that they changed their treatment algo-rhythm based on data supporting early usage of HET while 38.7% negate this statement and 11.5% are unsure if their treatment behavior has changed (**Table 3**).

Table 3. Evaluation of early use of HET

Evaluation of early highly effective MS therapies, mean (±SD)	Total (N=419)
Support of early use of high effective therapy	6.5 (0.7)
Use of HET in daily clinical practice	6.1 (0.9)
Change in treatment behavior based on the data, n (%)	**Total (N=419)**
Yes	209 (49.9)
No	162 (38.7)
Unsure	48 (11.5)

If not otherwise specified, data are presented as mean (±SD) on a scale from one (no at all) to seven (high).

Future benefits, implementation and usage of routine sNfL testing

- Neurologists would use sNfL testing in daily clinical routine for multiple reasons (**Figure 6**). Most neurologists (90.7%) would use sNfL measurements to complement existing disease activity assessments, followed by its use as an additional prognostic factor.
- Neurologists would measure sNfL levels at various timepoints (**Figure 7**) with a frequency of around two times per year (**Figure 9**).
- To implement sNfL testing into daily clinical routine, most neurologists would like to have more evidence of benefits and a recommendation from clinical guidelines (each 66.3%) or from professional society and MS competence network (59.7%) as well as more own experience with sNfL testing (54.8%) (**Figure 8**).
- If a licensed sNfL test would be available and a certain sNfL level would be exceeded, 75.6% of neurologists would immediately act on this result and advise further disease activity assessments like MRI (**Figure 10**).

Figure 6: Usage of sNfL in daily clinical routine

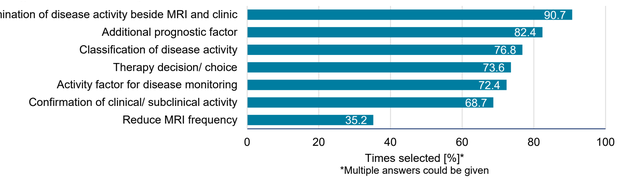


Figure 7: Timepoint of sNfL testing

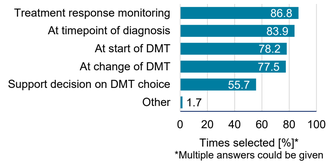


Figure 8: Conditions for implementation in daily routine

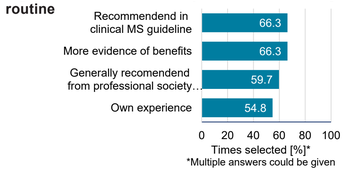


Figure 9: Frequency of sNfL testing

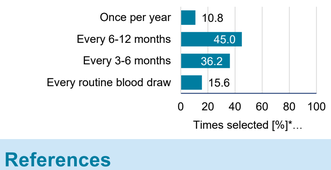
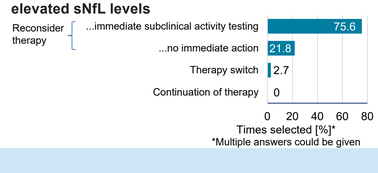


Figure 10: Consequences in daily routine after elevated sNfL levels



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U Schulze-Topphoff, K Schuh and I Schwab Sauerbeck are employees of Novartis.

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