Poster P034

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NeofiLos – Rationale, Design, Patient Characteristics (First Interim Data)

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KEY FINDINGS & CONCLUSIONS

- This is the first project making serum NfL (sNfL) available for office-based physicians embedded in a scientific context, showing patient characteristics which will allow insights generation into clinical value in clinical routine setting.
- NfL is a valid biomarker in MS with the ability to detect subclinical disease activity earlier enabling treatment decisions to be made with greater confidence at an individual level.
- A broad range of patients was included in this project (in regard to age, time since first diagnosis of MS and DMT status) indicating the need for disease activity measurement throughout the entire patient journey.
- HCPs confirm high utility of sNfL as a supporting tool for therapy decisions.
- This project is a highly valuable source for defining actual gaps and optimizing future MS patient care

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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 Relapsing Multiple Sclerosis (RMS) disease activity.[1,2,3]
- Elevated NfL levels may reveal "subclinical" disease before lesions appear on MRI or clinical symptoms appear.[4]
- Measuring serum NfL (sNfL) may help elucidate ongoing subclinical disease activity with prognostic value for future disease activity and potentially contribute to optimized decision making.
- NeofiLos is an ongoing program with utility data collection in Germany

OBJECTIVE

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

METHODS

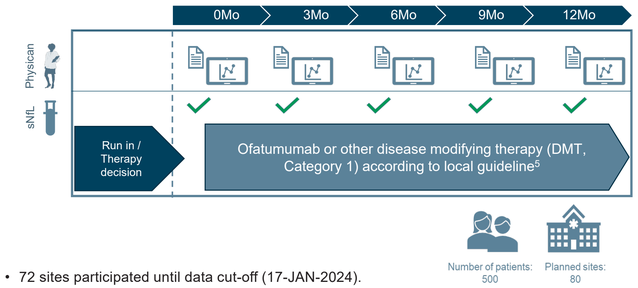
- Project design: NeofiLos is a prospective, multicenter program conducted at 80 sites in Germany, expected to enroll 500 RMS-patients receiving Ofatumumab or other first line disease modifying therapies (DMT) (**Figure 1**)
- This project was reviewed by an independent ethics committee and notified as an observational project to the responsible higher federal authority, the National Association of Statutory Health Insurance Funds, the Association of Private Health Insurance Funds and the National Association of Statutory Health Insurance Physicians in accordance with statutory regulations.
- Assessments
  - sNfL is measured from routine blood draws at program inclusion followed by quarterly intervals up to 5x per patient
  - sNfL is documented in electronic data collection form, visualized using scientific context implementing patient demographics and reported to treating neurologists/ physicians
  - treating neurologists/physicians answer digital questionnaires regarding usability and benefits of sNfL measurements in everyday treatment per patient
- These characteristic data is set into context with sNfL values and demonstrate the opportunities and challenges of sNfL anticipated to be the first blood-based biomarker available for clinical use in MS.
- This first interim analysis includes 622 patients (at timepoint of program inclusion) for which up to 419 questionnaires were completed.
- Results of this interim analysis descriptively depict patient demographics including median age, gender and body-mass-index of the patient collective, as well as diagnosis and therapy decisions made by treating neurologists of those patients at the timepoint of program inclusion.
- Z-Score analysis was used to compare sNFL levels of the project population against a healthy, age-adjusted cohort.

Results

Project overview

- NeofiLos is a multi-center, prospective, program at established neurology specialist centers to assess the benefit and added value of sNfL from a physician's perspective in RMS patients scheduled for ofatumumab or another approved disease modifying therapy (DMT, category 1 according to DGN Sk2 guideline[5]) as routine medical treatment (**Figure 1**).
- Participating physicians will be given the opportunity to gain initial experience with sNfL measurements (up to five measurements per patient within one year) and to test the possible application and integration of sNfL measurement into everyday practice.

Figure 1. NeofiLos project design



- 72 sites participated until data cut-off (17-JAN-2024).
- 622 (99.5%) of 625 enrolled patients were included in this interim analysis. Three patients (0.5%) were excluded from the analysis set as they met not all eligibility criteria for the program
- The primary endpoint of this project is the assessment of usability and benefits of sNfL values for physicians via questionnaires.
- Up to 419 (67.0%) of the possible 622 questionnaires were answered by physicians until data cut-off.

Patient demographics

- Patient demographics of the analyzed population are depicted in **Table 1**.
- The analyzed population was shifted towards female patients (70.1% female compared to 29.9% male patients).
- The mean age was 43±11.5 years.
- On average patients measured 171.6±8.7 cm with a mean weight of 77.0±17.7 kg resulting in an average Body-Mass-Index (BMI) of 26.1±5.3 kg/m^2.

Table 1. Patient Demographics

Patient demographics at the timepoint of program inclusion	Total (N=622)
Sex, n(%)	
Male	185 (29.9)
Female	434 (70.1)
Age [years]	43 (11.5)
Height [cm]	171.6 (8.7)
Weight [kg]	77 (17.7)
BMI [kg /m^2]	26.1 (5.3)

If not otherwise specified, data are presented as mean (±SD)

MS diagnosis

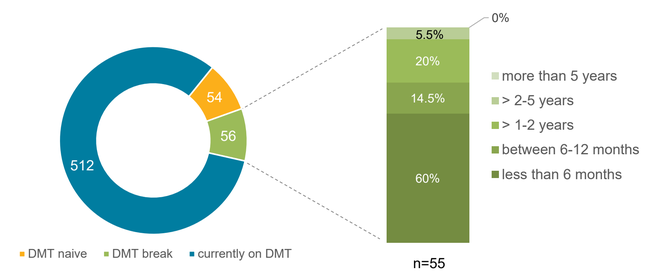
- Information of therapy and treatment status of the analyzed population are depicted in **Table 2** and **Figure 2 and 3**.
- The mean time from first MS diagnosis until program inclusion in the NeofiLos project was 8.7 (±8.4) years. 512 (82.3%) patients received a therapy at timepoint of program inclusion (first blood draw) while 110 (17.7%) received no therapy. The mean time from start of therapy until timepoint of program inclusion in the NeofiLos project was 4.2 (±4.8) months.
- 54 (49.1%) of patients who did not receive therapy were therapy-naïve and 56 (50.9%) patients did receive a therapy in the past but were currently on a break.

Table 2. MS diagnosis

Therapy status, mean (±SD)	Total (N=622)
Time between first diagnosis of MS and program inclusion [years]	8.7 (8.4)
Therapy at blood draw, n(%)	512 (82.3)
No therapy at blood draw, n(%)	110 (17.7)
Time between start of therapy and program inclusion [months] *	4.2 (4.8)

If not otherwise specified, data are presented as mean (±SD)
** Calculated as date (baseline visit) – date (therapy at blood draw). If no month was provided, it was automatically set as „6" unless it would result in a negative value*

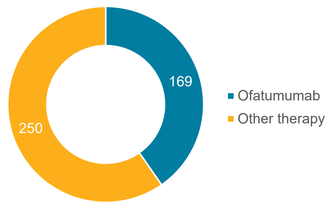
Figure 2. Therapy status at program inclusion (first sample)



Ofatumumab treatment

- 169 (40.3%) of 419 patients had either already received Ofatumumab or started Ofatumumab treatment at program inclusion. 250 (59.7%) patients received another disease modifying therapy (**Figure 4**).

Figure 3. Ofatumumab treatment

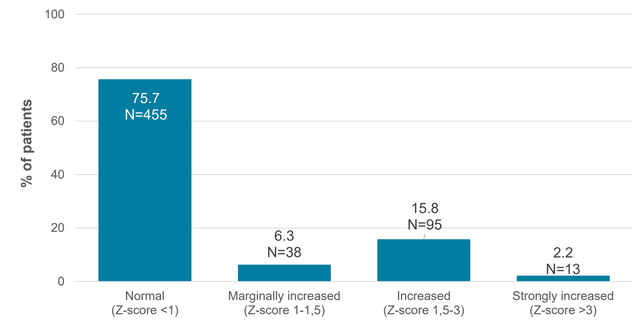


NeofiLos

Aggregated sNfL values

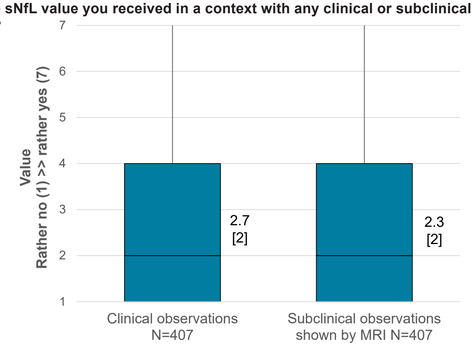
- At the time point of interim analysis, 455 (75.7%) of 622 patients showed at timepoint of program inclusion an sNfL level comparable to a healthy, age-adjusted cohort (Z-score <1 times) despite having RMS.
- 38 (6.3%) of patients showed marginally increased sNfL level (Z-score 1-1.5 times) and 95 (15.8%) showed increased sNfL level (Z-score 1.5-3 times) while 13 (2.2%) showed a strongly increased sNfL level (Z-score >3 times) (**Figure 4**).

Figure 4. sNfL level compared to healthy age-adjusted cohort



- It has been evaluated if received sNfL values of patients are in context with any appearance of clinical (2.7 ±1.9; median=2) or subclinical observations recognized (2.3 ±1.7; median=2). Physicians rated if the sNfL value received is in any context with clinical or subclinical observations for the respective patient on a scale from one (rather no) to seven (rather yes) (**Figure 5**).
- Most sNfL values measured within this program are rather not in a context with any clinical or subclinical observation at timepoint of program inclusion.

Figure 5 Is the sNfL value you received in a context with any clinical or subclinical observations?



Data labels shown as mean [median]

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

References

[1] Thebault S et al. *Mult Scler.* 2022;28(10):1491-1497. [2] Dietmann AS et al. *J Neurol.* 2023;270(3):1416-1429. [3] Kuhle J et al. *Mult Scler.* 2020;26(13):1691-1699. [4] Akgün K et al. *Neurol Neuroimmunol Neuroinflamm.* 2019;6(3):e555 [5] Hemmer B. et al. S2k-Leitlinie. 2023; Deutsche Gesellschaft für Neurologie, Leitlinien für Diagnostik und Therapie in der Neurologie. Online: www.dgn.org/leitlinien (23.01.2024)