CENTOGENE
THE RARE DISEASE COMPANY

Lyso-SM-509 is a highly specific and sensitive biomarker for the identification of Niemann-Pick patients: a 30 months study

Claudia Cozma[1], Peter Bauer [1], Gabriela Oprea[1], Jan Lukas[2], Susanne Zielke[2], Arndt Rolfs[1,2]

[1] Centogene AG, Rostock, Germany;
[2]University of Rostock, Rostock, Germany

Introduction: Niemann Pick Type C (NPC) disease is an autosomal recessive disease caused by mutations in NPC1 or NPC2 genes translated in defects of the lysosomes cholesterol transport system leading to abnormal accumulation of cholesterol and glycolipids in the lysosome. Recently developed treatment renders early NPC diagnosis of high most importance. **Material and Methods:** We present data from a 2 year global cohort of Niemann Pick patients using lyso-SM-509 biomarker determination, followed by sequencing of NPC1/2 genes. Determination of lyso-SM-509 is performed by LC/MRM-MS in plasma, serum, EDTA blood and dried blood spots (DBS). We identified in a world-wide study using lyso-SM-509 as primary screening in DBS samples 313 NPC affected patients. The diagnosis was confirmed by sequencing of the NPC1/NPC2 by single gene sequencing, NGS, or MLPA. In NPC1/2 sequencing negative patients with increased lyso-SM-509 concentrations the sequencing of sphingomyelinase (SMPD1) gene was done. We could identify over 807 pathological alleles in 488 different individuals. **Summary:** The levels of lyso-SM-509 in blood has a sensitivity of 100 % and specificity of 99.15 % for NPC1/2 and it reflects the burden of the NP disease and it can be used for the easy diagnosis of NPC patients and for the monitoring of the disease progression.

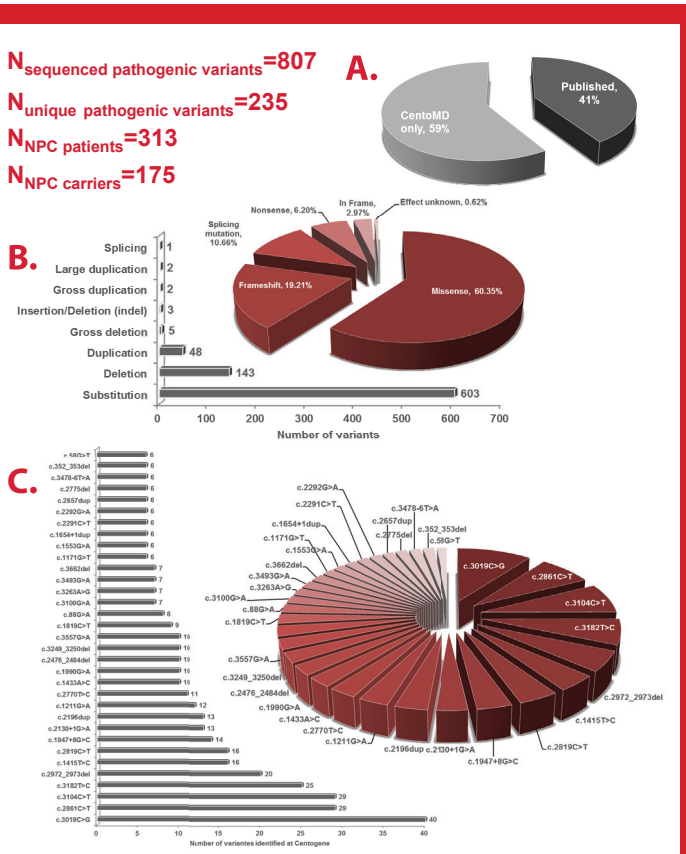

Figure 1: NPC1/2 ´sequenced variants: A. Unpublished unique variants; B. Type of mutation and mutation effect; C. Most abundant variants found in present NPC cohort (> 0.75% of the total variants found)

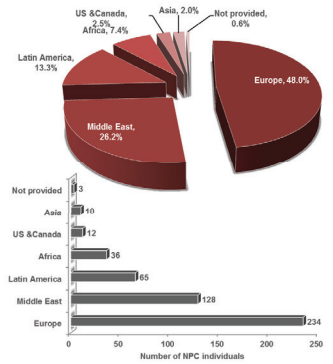

Figure 2: Geographical distribution of NPC1/2 cohort

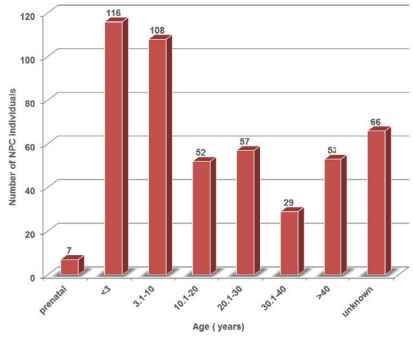

Figure 3: Age of diagnosis for the NPC patients

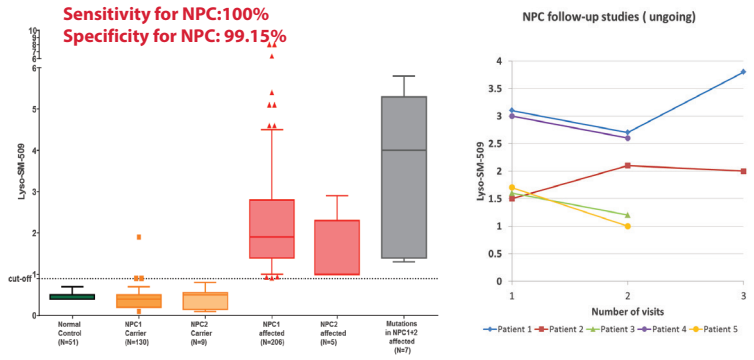

Figure 4: Lyso-SM-509 is a sensitive and specific biomarker for NPC disease A. levels in patients and controls (patients vs controls p<0.00001). B. Ongoing follow-up studies for patients under therapy show lyso-SM responding to the therapies

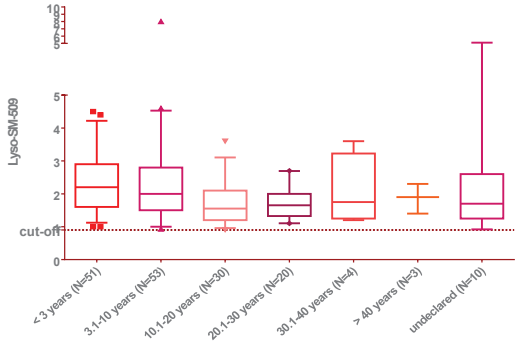

Figure 5: Age of diagnosis vs lyso-SM-509 levels in NPC homozygous patients

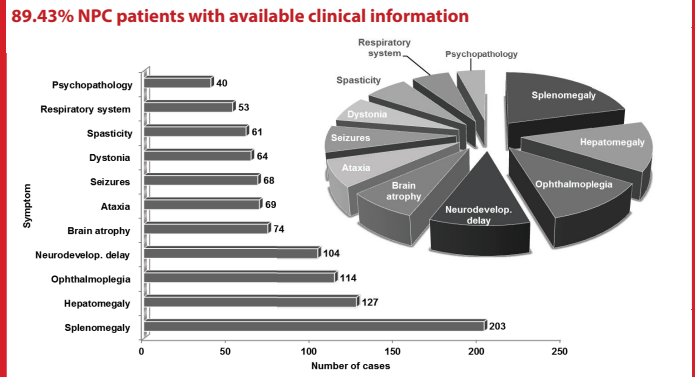

Figure 6: Clinical symptoms presented by the NPC cohort

References

1. Giese et al, 2015
2. Centogene AG, WO2013072060
3. www.centomd.com

Disclosure of conflict of interest:

This study was sustained in part by Centogene AG, Rostock, Author of the presentation, Claudia Cozma, and 2 co-authors are employees of Centogene AG, Rostock, Germany