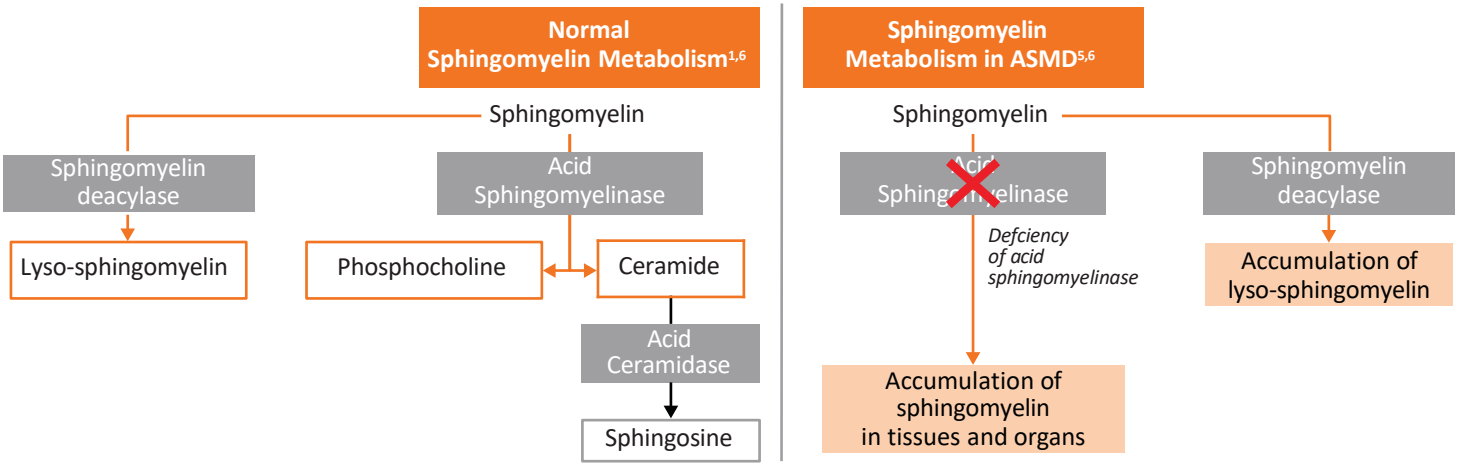
Acid Sphingomyelinase Deficiency Biomarker: Lyso-Sphingomyelin

Disease Overview

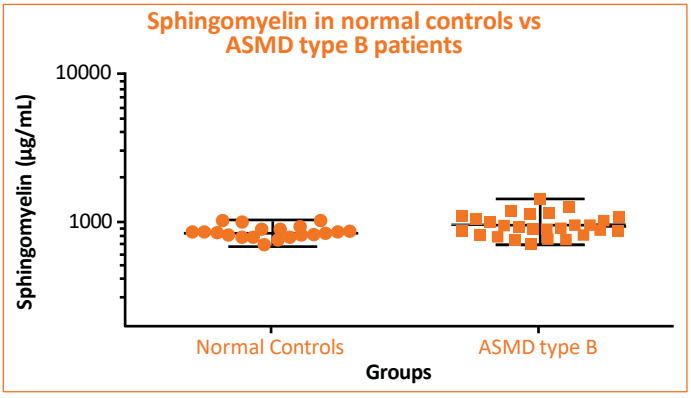
- Acid Sphingomyelinase Deficiency (ASMD) is a rare lysosomal storage disease caused by deficient enzyme activity in the lysosomal hydrolase acid sphingomyelinase (ASM).[1,2,3]
- ASM is encoded by the sphingomyelin phosphodiesterase 1 *(SMPD1)* gene. Bi-allelic pathogenic variants in *SMPD1* lead to reduced ASM enzymatic activity and subsequent accumulation of its lipid substrate, sphingomyelin (SPM), and the de-acylated form, lyso-sphingomyelin (LSM).[2]
- These lipids can accumulate in multiple cell types and organs throughout the body, resulting in multi-systemic disease manifestations such as hepatosplenomegaly, thrombocytopenia, interstitial lung disease, and dyslipidemia.[1,4]
- SPM accumulation is not elevated in plasma, whole blood, or urine in ASMD patients, highlighting the need for a specific body fluid biomarker for ASMD.[4]

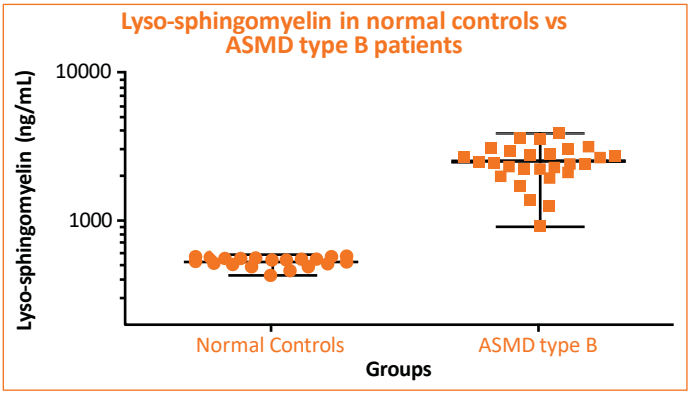


Lyso-sphingomyelin as a biomarker in ASMD

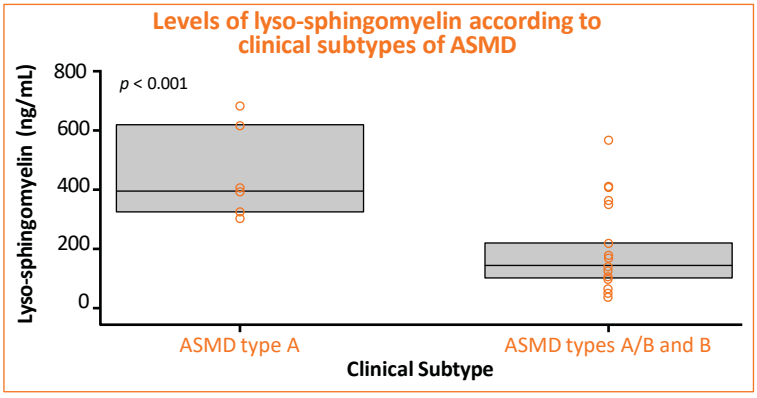
- LSM is a specific biomarker for ASMD.[2]
- LSM is detectable at elevated levels in ASMD patient blood samples compared to controls.[4]

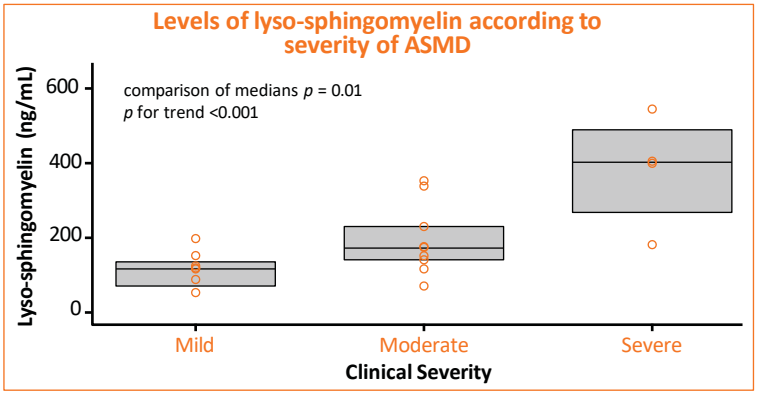
LSM levels, and not SPM levels, are elevated in dried blood spots (DBS) in ASMD type B.[4]





Plasma LSM levels are positively associated with clinical severity of ASMD.[2]





Testing Options for Lyso-sphingomyelin

Some of the laboratories offering testing for lyso-sphingomyelin are listed below. There may be other testing appropriate for your patient, and this is not an endorsement of any specific laboratory. Other testing options can be found at www.concertgenetics.com or www.ncbi.nlm.nih.gov/gtr. Consult each laboratory for a full range of options. Content is current at time of publication, and tests may not be available in all states; please call laboratory to confirm test availability, sample shipping information, and all other logistics. Sanofi does not review or control the content of non-Sanofi websites. This listing does not constitute an endorsement by Sanofi of information provided by any other organizations.

Laboratory	Test Name and Code	Sample Requirements
ArchimedLife	Lyso-SPM	DBS card: 5 circles (minimum 3) *Note: this European lab does not yet have CLIA certification. Therefore, all results are reported on a research basis.*
Centogene	LSM-509** with reflex to LSM	WB: 1 mL EDTA (lavender) tube; DBS card: 10 circles
Mayo Clinic Laboratories	Oxysterols (includes quantitative LSM and qualitative LSM-509**)	WB: 1 mL EDTA (lavender) or ACD (yellow) or sodium heparin (green) tubes; Frozen Plasma: min 0.25 mL; DBS card: 2 circles
Rare Disease Specialty Testing Program (performed at Labcorp)	Lyso-SM	Plasma: 1 ml (from EDTA/lavender tube)

Laboratory	Kits	Avg TAT	Mobile Blood	Billing	Contact
ArchimedLife	DBS	10 d	No	No Charge*	E: eumedicalservices@sanofi.com W: http://webportal.archimedlife.com (account required)
Centogene	Blood, DBS	7 d	No	Inst, Self-pay, Ins	P: 617-580-2102 E: customer.supportUS@centogene.com W: www.centogene.com
Mayo Clinic Laboratories	DBS	2-8 d	No	Inst, Ins&	P: 800-533-1710 E: mcl@mayo.edu W: www.mayocliniclabs.com
Rare Disease Specialty Testing Program (performed at Labcorp)	Blood#	12 d	No~	No charge* (account required)	P: 888-681-1701 E: RareDiseaseProgram@labcorp.com

Note: LSM may be bundled with a panel of biomarkers (oxysterols) or LSM-509, to allow for evaluation for both ASMD and other disorders of sphingolipid metabolism.**

***This testing is performed at no charge; local charges may apply for sample collection, processing, or shipping. **LSM-509 is an analog of LSM and is elevated in both ASMD and Niemann-Pick disease type C. #Individual testing supplies can be ordered. ~Phlebotomy is covered if performed at a Patient Service Center. &Insurance can be billed in some cases, but an account is required.**

Avg = Average; CLIA = Clinical Laboratory Improvement Amendments; d = days; DBS = dried blood spot; Ins = Insurance; Inst = Institution; LSM = Lyso-sphingomyelin; TAT = turnaround time; WB = whole blood

References: 1. Schuchman EH, et al. Mol Genet Metab. 2017;120 (1-2):27–33; **2**. Breilyn MS, et al. Mol Genet Metab Rep. 2021;28:100780; **3**. Wasserstein M, et al. Mol Genet Metab. 2019;126(2):98-105; **4**. Chuang WL, et al. Mol Genet Metab. 2014;111:209-11; **5**. McGovern MM et al. Orphanet J Rare Dis 2017;12(1):41; **6**. Heringdorf D, et al. Biochim Biophys Acta. 2002;1582(1-3):178-89.

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