7th ERN EURO-NMD

ANNUAL MEETING

NBS for SMA
Experience from Poland

21st – 23rd February 2024

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European Reference Network
for rare or low prevalence complex diseases

Network Neuromuscular Diseases (ERN EURO-NMD)

Funded by the European Union

The ERN EURO-NMD is funded by the European Commission under the EU4Health programme (EURO-NMD 23-27 — 101156434 — EU4H-2023-ERN2-IBA)

Speaker Disclosures

- Participation at scientific advisory boards for Biogen and Novartis Gene Therapies
- Received honoraria for lectures from Novartis Gene Therapies, Biogen, and Roche
- Travel support from Biogen and Roche
- Acting as a sub-investigator for Roche (for olesoxime and risdiplam trials for SMA)

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Poland

Current population: 37,600,000
272,000 live births/year (decreasing)

Current number of patients with SMA:
approx. 1300 patients
~40 new SMA cases/year

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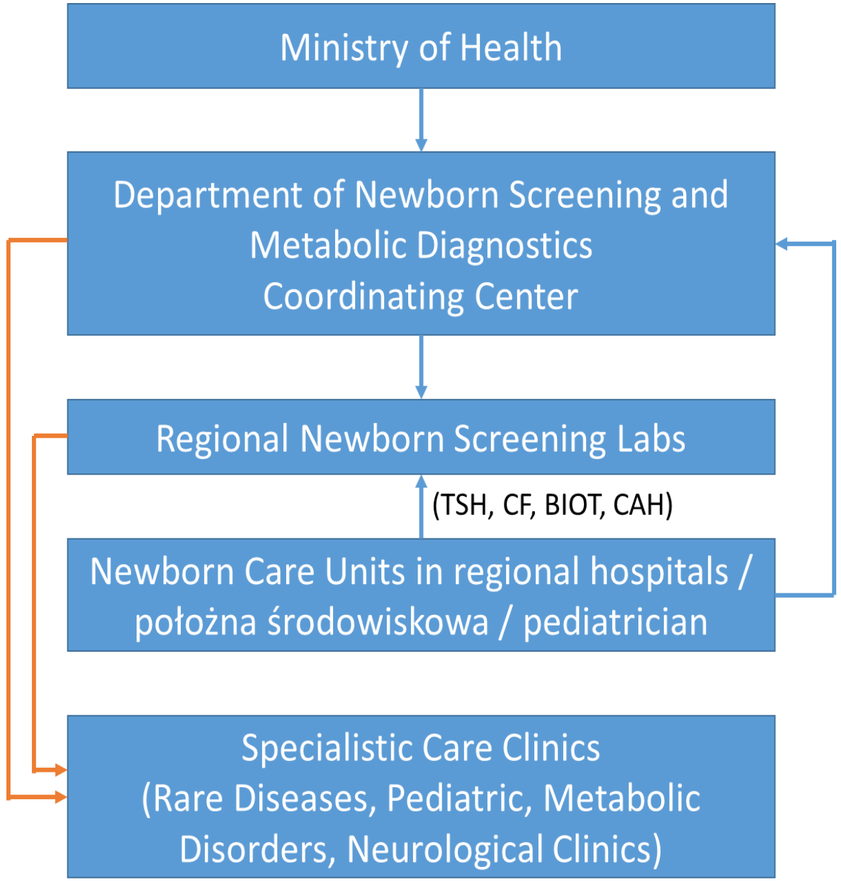
NBS in Poland



- NBS in Poland is carried out under the 4-year health policy programs of the Ministry of Health
- The Department of Newborn Screening and Metabolic Diagnostics of the Institute of Mother and Child in Warsaw organizes and coordinates all tasks within the NBS program in Poland
- Currently NBS in Poland covers 30 diseases: hypothyroidism, phenylketonuria, congenital adrenal hyperplasia, cystic fibrosis, congenital biotinidase deficiency and congenital metabolism defects (including 23 diseases), and SMA
- SMA has been included in the existing NBS program
- Approximately 450 patients are diagnosed annually

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01.2019	• Nusinersen accepted for financing from goverment funds for all SMA types • First efforts for SMA NBS (medical specialists and SMA patient care organization - Fundacja SMA)
2020	• Application to Ministry of Health to include SMA NBS into the current NBS Programme in Poland (2017-2021); • Need of evaluation by the Agency for Health Technology Assessment and Tariff System • First negative decision (lack of assessment of financial effectiveness of the treatment; appeal → positive decision
02.2021	• Final decision about the implementation of SMA to NBS Programme for 2017-2021
04.2021	• Tender and purchase of reagents and laboratory equipment • Official start of SMA NBS
04.2022	• All newborns are tested for SMA (opt-in for genetic testing)
09.2022	• Onasemnogen abeparvovec and Risdiplam accepted for financing from goverment funds

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NBS for SMA

- Implemented since April 2021
- NBS for SMA is currently underway in the whole country (since 04.2022)
- Molecular tests performed in the Institute of Mother and Child in Warsaw

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Diagnostic and therapeutic algorithm

Maternity hospital	**Dried blood samples (DBS)** are collected from the heel of the newborn on Guthrie paper **(48 – 72 h after birth)**
Screening center	**Positive screening result** (**up to 7 working days** from the receipt of the Guthrie paper to the screening center), **two** tests performed: PCR-HRM and MLPA (initially known **number of *SMN2* gene** copies); results sent to the treatment center
Treatment center (by place of residence)	**First hospitalization (up to 2 days)** • *discussion on preliminary results of genetic tests / possible clinical course (SMN2)* • *clinical evaluation of the patient* • *collecting blood for genetic tests to verify the screening result* • *discussion on treatment options* • *decision on management: treatment vs monitoring* • *in the case of a decision to undertake treatment: initial qualification for the treatment program or* • *in the case of a symptomatic patient - immediate initiation of therapy* • *planning of hospitalization after obtaining the verification result*
Genetic center	**Verification of the screening result** (MLPA, final estimation of *SMN2* copy number, result **up to 4 working** days)- the **third** genetic test
Treatment center	**Second hospitalization** • *in patients with 2 and 3 copies - therapy no later than 2 weeks after the screening result, discussion on the multidisciplinary care plan* • *in patients with ≥4 copies, theraphy or plan of follow-up visits, discussion on the multidisciplinary care plan*

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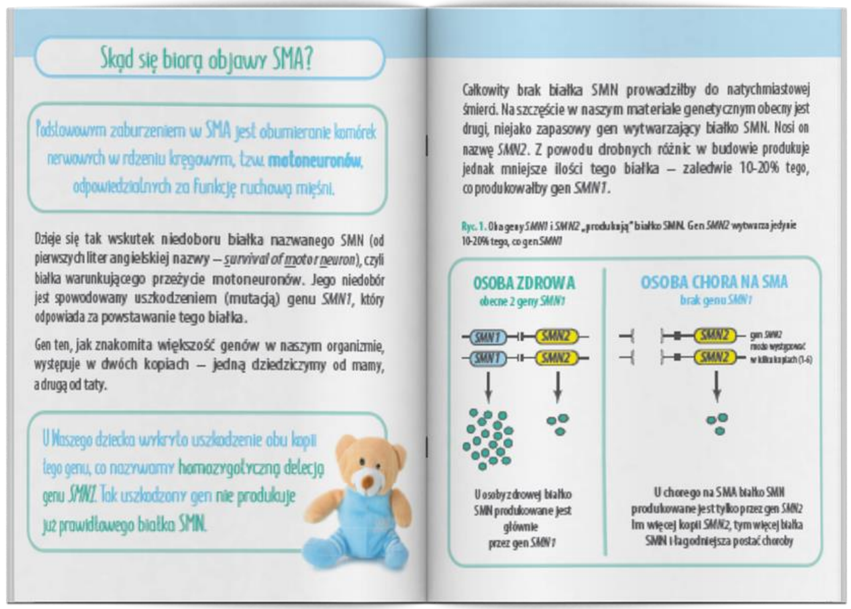
Training/guides

- Guide for Parents of Children Diagnosed With SMA via NBS



Skąd się biorą objawy SMA?

Podstawowym zaburzeniem w SMA jest obumieranie komórek nerwowych w rdzeniu kręgowym, tzw. **motoneuronów**, odpowiedzialnych za funkcję ruchową mięśni.

Dzieje się tak wskutek niedoboru białka nazwanego SMN (od pierwszych liter angielskiej nazwy – *survival of motor neuron*), czyli białka warunkującego przeżycie motoneuronów. Jego niedobór jest spowodowany uszkodzeniem (mutacją) genu *SMN1*, który odpowiada za powstawanie tego białka.

Gen ten, jak znakomita większość genów w naszym organizmie, występuje w dwóch kopiach – jedną dziedziczymy od mamy, a drugą od taty.

U Waszego dziecka wykryto uszkodzenie obu kopii tego genu, co nazywamy homozygotyczną delecją genu *SMN1*. Tak uszkodzony gen nie produkuje już prawidłowego białka SMN.

Całkowity brak białka SMN prowadziłby do natychmiastowej śmierci. Na szczęście w naszym materiale genetycznym obecny jest drugi, niejako zapasowy gen wytwarzający białko SMN. Nosi on nazwę *SMN2*. Z powodu drobnych różnic w budowie produkuje jednak mniejsze ilości tego białka – zaledwie 10-20% tego, co produkowałby gen *SMN1*.

Ryc. 1. Oba geny *SMN1* i *SMN2* „produkują" białko SMN. Gen *SMN2* wytwarza jedynie 10-20% tego, co gen *SMN1*

OSOBA ZDROWA
obecne 2 geny *SMN1*

OSOBA CHORA NA SMA
brak genu *SMN1*

SMN1 SMN2 SMN1 SMN2

SMN2 SMN2
gen *SMN2* może występować w kilku kopiach (1-4)

U osoby zdrowej białko SMN produkowane jest głównie przez gen *SMN1*

U chorego na SMA białko SMN produkowane jest tylko przez gen *SMN2*. Im więcej kopii *SMN2*, tym więcej białka SMN i łagodniejsza postać choroby

- Educational Training for HCPs

"Dealing with crises during communication with parents of a child suffering from SMA allows shared responsibility"

HCPs face challenges in communicating with parents of patients with SMA regarding

- Results of screening tests
- Positive diagnosis of SMA
- Initiating treatment

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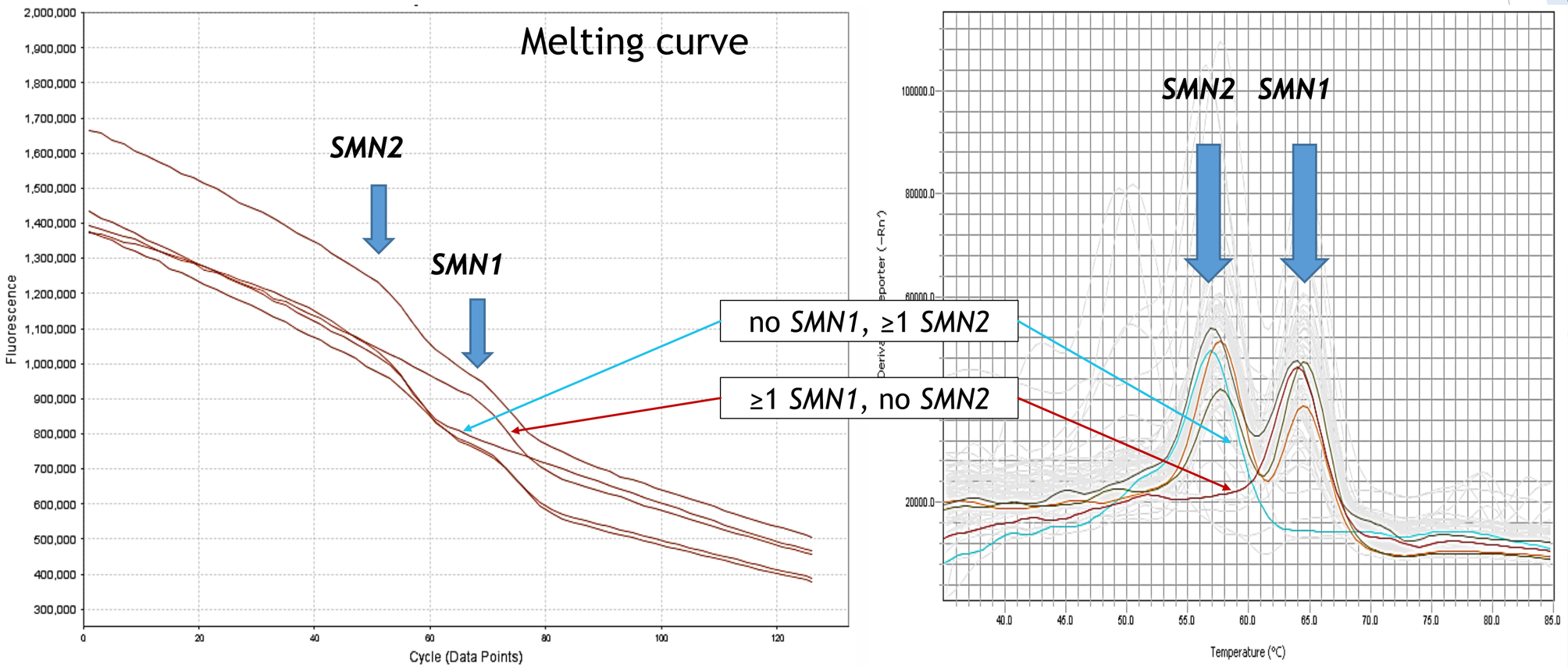
SMA NBS testing method – PCR-HRM (MC002 MRC Holland)



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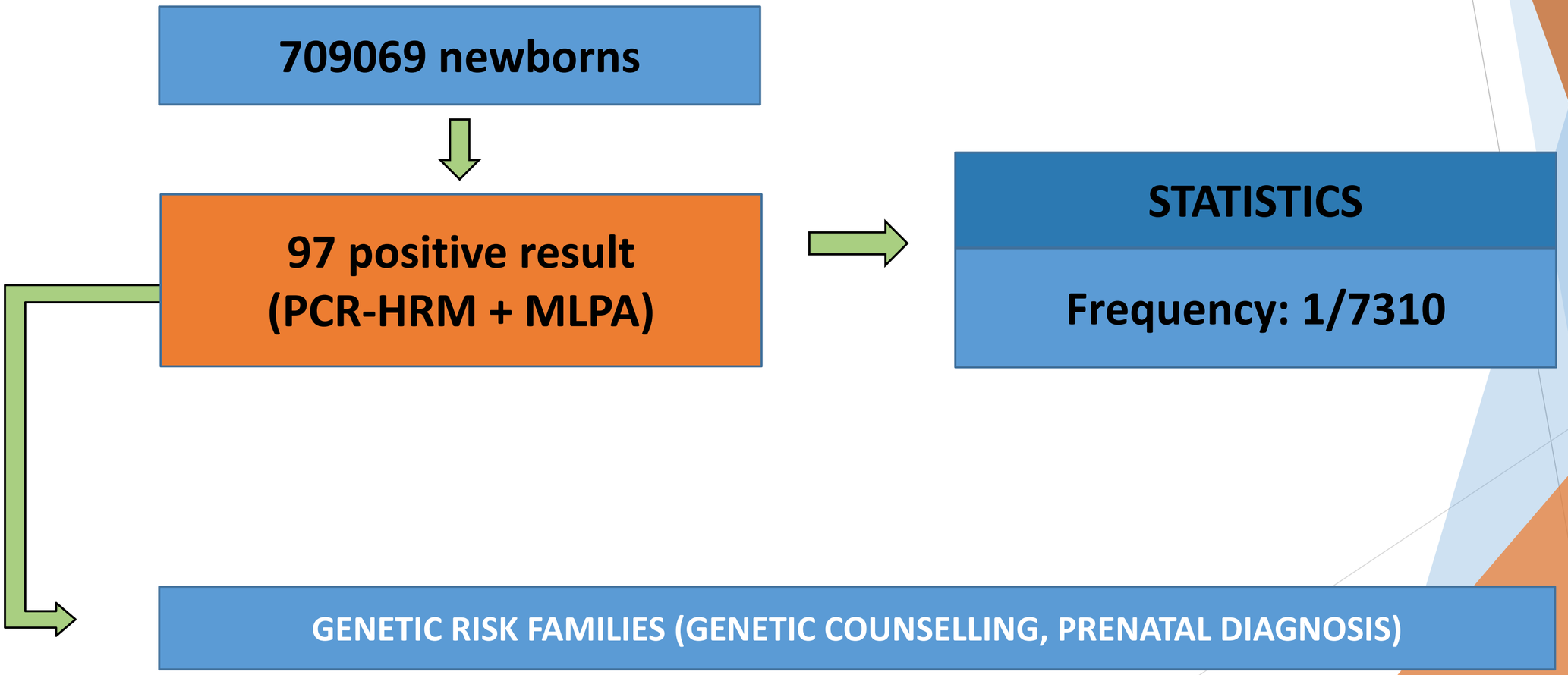
NBS-SMA (16.02.2024)



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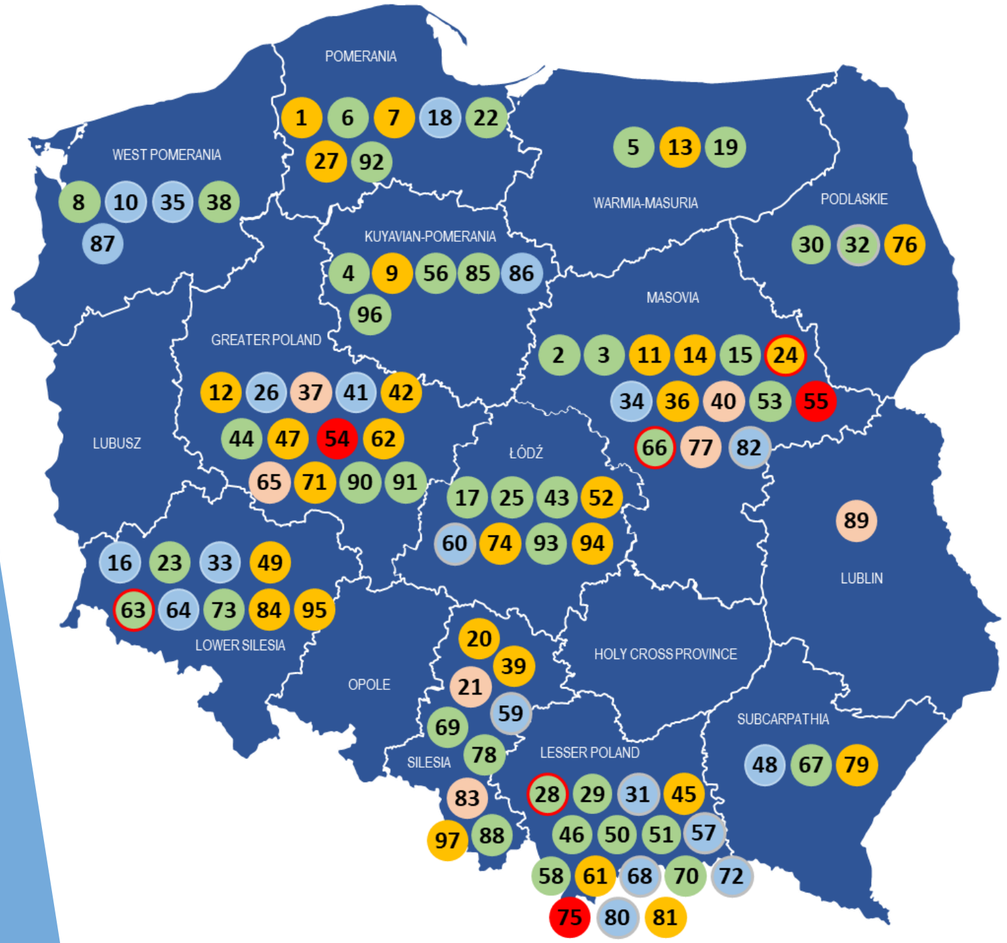
NBS-SMA –results

(16.02.2024)



District	Starting date	Number of cases
Masovia	01/02/2021	14
Podlaskie	04/05/2021	3
Warmia-Masuria	17/05/2021	3
Lublin	01/06/2021	1
Łódź	07/06/2021	8
Pomerania	12/07/2021	7
Kuyavian-Pomerania	26/07/2021	6
West Pomerania	16/08/2021	5
Lubusz	23/09/2021	0
Greater Poland	23/09/2021	13
Lower Silesia	22/11/2021	9
Opole	22/11/2021	0
Silesia	03/01/2022	9
Lesser Poland	07/03/2022	16
Subcarpathia	28/03/2022	3
Hole Cross Province	28/03/2022	0
TOTAL		**97**

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SMN2 copy number

SMN2	N	%
1	3	3.09%
2	28	28.87%
3	39	40.21%
4	20	20.62%
≥5	7	7.22%

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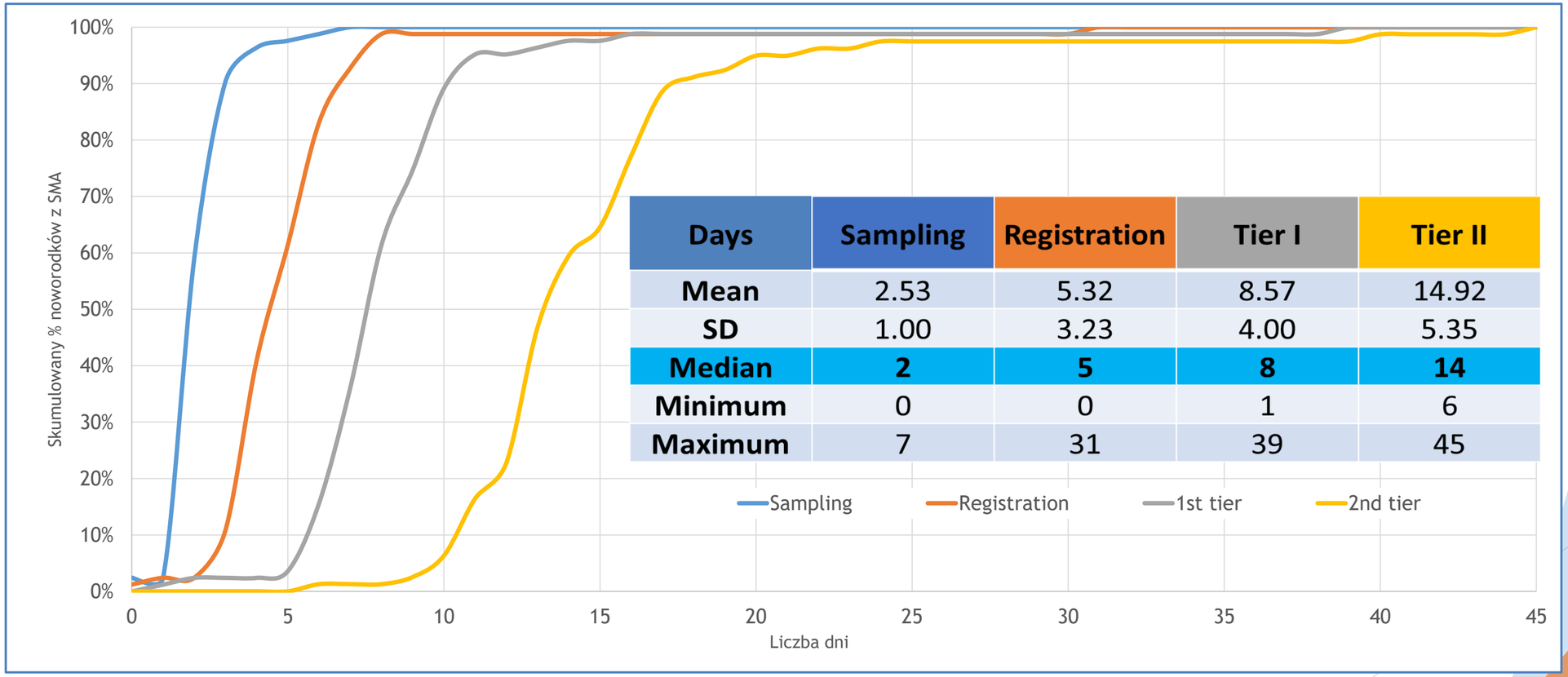
Time of screening/diagnostic result



Days	Sampling	Registration	Tier I	Tier II
Mean	2.53	5.32	8.57	14.92
SD	1.00	3.23	4.00	5.35
Median	**2**	**5**	**8**	**14**
Minimum	0	0	1	6
Maximum	7	31	39	45

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Treatment of patients from NBS

- only with info available

	All	Nusinersen	Onasemnogen abeparvovek	Risdiplam
No	53	29	22	2
Mean	25.6	18.4	35.4	22.0
SD	15.4	7.2	18.6	0
Median	**22**	**18**	**29**	**22**
Minimum	5	5	8	22
Maximum	70	45	70	22

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NBS for SMA in Poland- summary

- Implemented **since April 2021**
- **709 069** of newborns screened; **97** positive results for SMA
- On average, the initial screening result was obtained at **8** days after birth
- On average, diagnostic result was obtained at **14** days after birth
- Diagnosis of SMA is reliable – in summary three genetic tests are performed (two from DBS and one from independent blood collection)
- Treatment can be started in the third/fourth week of newborn's life (mediana **22** days after birth)

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Thank you!

Thanks to:

Monika Gos, PhD, Mariusz Ołtarzewski PhD, Jerzy Bal Prof

Joanna Wasiluk MSc, Magdalena Frączyk PhD,
Aleksandra Landowska MSc, Mariola Jurzyk MSc,
Katarzyna Durda MSc, Wioletta Wawer MSc,
Joanna Gzowska MSc, Paulina Kubiszyn MSc,
Jessica Wieczorek MSc, Liliia Nosarieva MSc

Department of Newborn Screening and Metabolic Diagnostic

Department of Medical Genetics

Institute of Mother and Child

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