Swiss-Reg-NMD

UNIVERSITÄT BERN

Swiss Registry for Neuromuscular Disorders

Annual report for 2022

Swiss-Reg-NMD

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For the Swiss Registry for Neuromuscular Disorders:
Dominique Baumann
Anne Tscherter
Nadine Lötscher
Susanne Hofer
Claudia Kühni
Andrea Klein

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Swiss Registry for Neuromuscular Disorders

Institute of Social and Preventive Medicine
University of Bern
Mittelstrasse 43
CH-3012 Bern
Switzerland

Tel. +41 (0)31 684 33 95
E-mail: swiss-reg-nmd@ispm.unibe.ch

Bern, 06 March 2022, Swiss Registry for Neuromuscular Disorders

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1. Executive Summary

The 'Swiss Registry for Neuromuscular Disorders' (Swiss-Reg-NMD) collects medical information from people with neuromuscular disorders. It is led by specialized physicians from all over Switzerland and located at the Institute of Social and Preventive Medicine in Bern. The registry includes children and adults living in Switzerland who are diagnosed with Duchenne-Becker Muscular Dystrophy (DMD/BMD/IMD), Spinal Muscular Atrophy (SMA), LAMA2-related muscular dystrophy (LAMA2-RMD) or Collagen-VI-related dystrophies (COL6-RD). The registry operates according to the ethics approval #2018-00289.
The Swiss-Reg-NMD pursues the following objectives:

- to register and to collect relevant health data of any patient affected by a neuromuscular disorder living or treated in Switzerland
- to facilitate the participation of patients in national and international therapeutic trials
- to facilitate the establishment of study centers in Switzerland
- to harmonize diagnosis and care on a national level (standards of care)
- to establish a national platform for Post-Marketing Follow-up

On 31.12.2022, a total of 375 patients with neuromuscular disorders were registered in the Swiss-Reg-NMD (not reported as deceased): about 200 patients with DMD/BMD/IMD, 157 patients with SMA, about 15 patients with LAMA2-RMD and 5 patients with COL6-RD. Compared to the previous year, 43 additional patients are included in the registry thanks to the active recruitment of the participating centres. Accordingly, this represents a significant increase in the workload for data collection. In 2022, some patients with DMD participated in the Ciffreo or in the Lelantos study in Switzerland. Some patients with SMA continued to participate in the Jewelfish or Sunfish trial or in an observational study at the University Hospital Zürich investigating cardiac and muscle involvement in SMA.

As in previous years, the registry answered requests from multiple stakeholders. In particular, we answered several questions from TREAT-NMD, researchers at Swiss University Hospitals and from pharmaceutical companies about the feasibility of clinical studies.

The registry collects medical data to learn more on the health, care and needs of people with a neuromuscular disease in Switzerland. Our specific SMA dataset allows us to investigate the effectiveness and side effects of all three currently approved SMA therapies. In 2022, we also started with the collection of defined medical data from patients with LAMA2-RMD.

The collected data were used for several research projects. For example, two articles were submitted in 2022 and accepted in the beginning of 2023, one on the effects of the Covid-19 pandemic on access to education and participation in children and adolescents with DMD and one on the treatment of SMA with Onasemnogene Abeparvovec.

Also, we support the Swiss pediatric neuromuscular centers to implement a nationwide newborn screening for SMA.

In 2022, the Swiss-Reg-NMD received funding from ‘Schweizerische Muskelgesellschaft’, ‘Association Suisse Romande Intervenant contre les Maladies neuro-Musculaires’, ‘Associazione malattie genetiche rare della svizzera italiana’,‘SMA Schweiz’, ‘Duchenne Schweiz’ and the ‘Schweizerische Stiftung für die Erforschung der Muskelkrankheiten’, from Biogen Switzerland, Novartis Gene Therapies, Pfizer Switzerland, PTC Therapeutics Switzerland and Roche Pharma Switzerland. We thank these organisations and companies for their support.

Zusammenfassung

Das 'Schweizer Register für neuromuskuläre Erkrankungen' (Swiss-Reg-NMD) sammelt medizinische Informationen von Menschen mit neuromuskulären Erkrankungen. Es wird von Fachärzten aus der ganzen Schweiz geführt und befindet sich am Institut für Sozial- und Präventivmedizin in Bern. Das Register erfasst in der Schweiz lebende Kinder und Erwachsene, bei denen Duchenne-Becker-Muskeldystrophie (DMD/BMD/IMD), Spinale Muskelatrophie (SMA), LAMA2-assoziierte Muskeldystrophie (LAMA2-MD) oder Collagen VI-assoziierte Dystrophie (COL6-RD) diagnostiziert wurde. Das Register arbeitet gemäss der Ethik-Genehmigung #2018-00289.
Das Swiss-Reg-NMD verfolgt die folgenden Ziele:

- die Registrierung und Erfassung relevanter Gesundheitsdaten aller in der Schweiz lebenden Patienten mit neuromuskulären Erkrankungen
- die erleichterte Teilnahme von Patienten an nationalen und internationalen therapeutischen Studien
- die erleichterte Einrichtung von Studienzentren in der Schweiz
- die Harmonisierung von Diagnose und Versorgung auf nationaler Ebene (Versorgungsstandards)
- die Einrichtung einer nationalen Plattform für das Post-Marketing Follow-up

Am 31.12.2022 waren insgesamt 375 Patient*innen mit neuromuskulären Erkrankungen im Swiss-Reg-NMD registriert (und nicht als verstorben gemeldet): etwa 200 Patient*innen mit DMD/BMD/IMD, 157 Patient*innen mit SMA, etwa 15 Patient*innen mit LAMA2-MD und 5 Patient*innen mit COL6-RD. Im Vergleich zum Vorjahr sind dank der aktiven Rekrutierung der teilnehmenden Zentren 43 zusätzliche Patienten in das Register aufgenommen worden. Dies bedeutet einen erheblichen Anstieg des Arbeitsaufwands für die Datenerfassung. Im Jahr 2022 nahmen einige Patient*innen mit DMD an der Ciffreo- oder an der Lelantos-Studie in der Schweiz teil. Einige Patient*innen mit SMA nahmen weiterhin an der Jewelfish- oder Sunfish-Studie teil, andere an einer Beobachtungsstudie am Universitätsspital Zürich, in der die Beteiligung des Herzens und der Muskeln bei SMA untersucht wurde.

Wie in den Vorjahren beantwortete das Register Anfragen von verschiedenen Interessengruppen. Insbesondere beantworteten wir mehrere Anfragen von TREAT-NMD, von Forschenden an Schweizer Universitätsspitälern und von Pharmaunternehmen zur Durchführbarkeit klinischer Studien.

Das Register sammelt medizinische Daten, um mehr über die Gesundheit, die Versorgung und die Bedürfnisse von Menschen mit einer neuromuskulären Erkrankung in der Schweiz zu erfahren. Unser spezifischer SMA-Datensatz ermöglicht es uns, die Wirksamkeit und die Nebenwirkungen aller drei derzeit zugelassenen SMA-Therapien zu untersuchen. Im Jahr 2022 begannen wir auch mit der Sammlung von definierten medizinischen Daten von Patienten mit einer LAMA2-MD.

Die gesammelten Daten wurden für mehrere Forschungsprojekte verwendet. So wurden zum Beispiel zwei Artikel eingereicht und anfangs 2023 angenommen, einer über die Auswirkungen der Covid-19-Pandemie auf den Zugang zu Bildung und Teilhabe bei Kindern und Jugendlichen mit DMD und einer über die Behandlung von SMA mit Onasemnogene Abeparvovec. Ausserdem unterstützen wir die Schweizer neuromuskulären Kinderzentren bei der Durchführung eines landesweiten Neugeborenen-Screenings auf SMA.

Im Jahr 2022 erhielt das Swiss-Reg-NMD finanzielle Unterstützung von der ‘Schweizerischen Muskelgesellschaft’, der ‘Association Suisse Romande Intervenant contre les Maladies neuro-Musculaires’, der ‘Associazione malattie genetiche rare della svizzera italiana’, von ‘SMA Schweiz’, von ‘Duchenne Schweiz’ und der ‘Schweizerischen Stiftung für die Erforschung der Muskelkrankheiten’, von Biogen Schweiz, Novartis Gene Therapies Inc, Pfizer AG Schweiz, PTC Therapeutics International, Roche Pharma AG Schweiz und Sarepta International. Wir danken diesen Organisationen und Unternehmen für ihre Unterstützung

Sommaire

Le 'Registre suisse des maladies neuromusculaires' (Swiss-Reg-NMD) recueille des informations médicales de personnes atteintes d'une maladie neuromusculaire. Il est dirigé par des médecins spécialistes de toute la Suisse et se trouve à l'Institut de médecine sociale et préventive à Berne. Le registre inclut des enfants et des adultes vivant en Suisse avec un diagnostic de dystrophie musculaire de Duchenne-Becker (DMD/BMD/IMD), d'amyotrophie spinale (SMA), de dystrophie musculaire liée à LAMA2 (LAMA2-MD) ou de dystrophie liée au collagène VI (COL6-RD). Le registre fonctionne conformément à l'approbation éthique #2018-00289.

Le Swiss-Reg-NMD poursuit les objectifs suivants :

- enregistrer et collecter les données médicales essentielles de tout patient·e atteint·e d'une maladie neuromusculaire vivant en Suisse
- faciliter la participation des patient·es dans des études cliniques nationales et internationales
- faciliter la création de sites d'étude clinique en Suisse
- harmoniser le diagnostic et les soins au niveau national (standards de soins)
- mise en place d'une plate-forme nationale pour le suivi post-commercialisation

Au 31.12.2022, un total de 375 patient·es atteint·es de maladies neuromusculaires étaient enregistrés dans le Swiss-Reg-NMD (et n'étaient pas déclarés comme décédés) : environ 200 patient·es atteint·es de DMD/BMD/IMD, 157 patient·es atteint·es de SMA, environ 15 patient·es atteint·es de LAMA2-MD et 5 patient·es atteint·es de COL6-RD. Par rapport à l'année précédente, 43 patient·es supplémentaires sont inclus dans le registre grâce, notamment au recrutement actif des centres participants. Par conséquent, cela représente une forte augmentation de la charge de travail pour la collecte des données. En 2022, quelques patient·es atteint·es de DMD ont participé à l'étude Ciffreo ou Lelantos en Suisse. Quelques patient·es atteint·es de SMA ont continué à participer à l'étude Jewelfish ou Sunfish ou à une étude observationnelle à l'hôpital universitaire de Zurich sur l'implication cardiaque et musculaire dans la SMA.

Comme les années précédentes, le registre a répondu aux demandes de multiples partenaires. En particulier, nous avons répondu à plusieurs questions de TREAT-NMD, de chercheurs d'hôpitaux universitaires suisses et d'entreprises pharmaceutiques concernant la faisabilité d'études cliniques.

Le registre recueille des données médicales afin d'en savoir plus sur la santé, les soins et les besoins des personnes atteintes d'une maladie neuromusculaire en Suisse. Nos données sur la SMA nous permettent d'étudier l'efficacité et les effets secondaires des trois thérapies de la SMA actuellement approuvées. En 2022, nous avons également commencé à collecter des données médicales de patient·es atteint·es de LAMA2-MD.

Les données collectées ont été utilisées pour plusieurs projets de recherche. Par exemple, deux articles ont été soumis en 2022 et acceptés début 2023, l'un sur les effets de la pandémie de Covid-19 sur l'accès à l'éducation et la participation des enfants et adolescent·es atteint·es de DMD et l'autre sur le traitement de la SMA avec l'Onasemnogene Abeparvovec. De plus, nous soutenons les centres neuromusculaires pédiatriques suisses pour mettre en place le dépistage néonatal de la SMA à l'échelle nationale.

En 2022, le Swiss-Reg-NMD a reçu un financement de 'Schweizerische Muskelgesellschaft', de l'Association Suisse Romande Intervenant contre les Maladies neuro-Musculaires', de l'Associazione malattie genetiche rare della svizzera italiana', de 'SMA Suisse', de 'Duchenne Suisse' et de la 'Fondation suisse pour la recherche sur les maladies musculaires', de Biogen Suisse, de Novartis Gene Therapies Inc, de Pfizer Suisse, de PTC Therapeutics International, de Roche Pharma Suisse et de Sarepta International. Nous remercions ces organisations et entreprises pour leur soutien.

2. Introduction

Neuromuscular disorders (NMDs) are diseases that affect the functioning of the first motoneuron (CNS) and of the peripheral nervous system (motor neurons, nerves, neuromuscular transmission and muscle). Most have a genetic origin and all NMDs are rare diseases with few patients scattered across the country. Symptoms vary depending on the disease but commonly include muscle weakness, delayed motor development and/or functional impairment. In addition, patients may also suffer from chronic pain, intellectual impairment, problems with eating or communication. Hence they require multi-disciplinary care. Symptoms often begin in childhood but can occur throughout life.

In 2008, a national registry for NMD was launched at the Centre hospitalier universitaire vaudois (CHUV) in Lausanne to give patients access to new therapies and to facilitate the identification of patients for clinical trials in Switzerland. In 2017, the registry moved to the Institute of Social and Preventive Medicine (ISPM) in Bern and was modernized to meet current and future data quality and security standards and satisfy the needs of patient organisations, health authorities and research organisations. Its long-term goal is to improve the care and well-being of people with neuromuscular diseases in Switzerland.

This report provides an overview of the Swiss-Reg-NMD and its activities in 2022.

3. Description of the Swiss-Reg-NMD

3.1. Organisational structure

On a daily basis, the Swiss-Reg-NMD is run by a clinical lead and an executive office. The registry has a steering board which meets a few times per year. This board consists of paediatric neurologists, neurologists and since 2021 also of a pulmonologist working across different neuromuscular centres in Switzerland. The overall lead of the registry is shared between the clinical lead and a legal representative at the ISPM. Nine neuromuscular centres report regularly to the registry. The organisational structure of the Swiss-Reg-NMD is displayed in Table 1.

Table 1. People involved in the registry

Lead		
Andrea Klein, Prof. MD	Clinical Lead	Inselspital, Bern; UKBB, Basel
Claudia Kuehni, Prof. MD	Legal representative	ISPM, Bern
Steering Board		
Andrea Klein, Prof. MD	Clinical Lead, Pediatric Neurologist	Inselspital, Bern; UKBB, Basel
David Jacquier, MD	Vice Clinical Lead, Pediatrician	CHUV, Lausanne; Inselspital, Bern
Paolo Ripellino, MD	Neurologist	EOC, Lugano
Georg Stettner, PD MD	Pediatric Neurologist	Kinderspital, Zürich
Olivier Scheidegger, PD MD	Neurologist	Inselspital, Bern
Bettina Schreiner, PD MD	Neurologist	Universitätsspital Zürich
Esther Irene Schwarz, PD MD	Pulmonologist	Universitätsspital Zürich
Executive Office		
Claudia Kuehni, Prof. MD	Legal representative	ISPM, University of Bern
Dominique Baumann, PhD	Project manager	ISPM, University of Bern
Anne Tscherter, PD PhD	Project manager	ISPM, University of Bern
Nadine Lötscher, BA and Nrs	Data manager and research assistant	ISPM, University of Bern
Susanne Hofer, M.Sc.	Data manager	ISPM, University of Bern
Advisors		
F. Joncourt, PhD	Genetic curator	Previously Genetic Laboratory University Hospital Bern
Participating centres		
Aarau, Basel, Bern, Geneva, Lausanne, Luzern, St. Gallen, Ticino, Zürich, and private practices.		

3.2. Objectives

The main objective of the Swiss-Reg-NMD is to facilitate the inclusion of Swiss patients in therapeutic trials and to improve, on the basis of a better knowledge, the current and future care and well-being of individuals with NMDs. In addition, it offers a platform to observe the overall outcome of patients receiving new drugs and to improve communication and collaboration.

The specific aims of the registry are therefore:

1. Provide epidemiological data:
    - Incidence
    - Prevalence
    - Clinical spectrum at diagnosis
    - Disease progression / prognosis
    - Survival rates and mortality

2. Provide a platform for clinical research and Post-Marketing Follow-up:
    - Recruitment of patients into therapeutic trials
    - Collection of outcome data during treatment
    - Facilitation of observational studies e.g. on healthcare, education and quality of life
3. Provide a platform for communication:
    - Promotion of the exchange of knowledge between clinics, researchers, therapists and health authorities
    - Facilitation of national and international collaborations

3.3. Inclusion criteria

The Swiss-Reg-NMD includes children, adolescents and adults living or treated in Switzerland who are diagnosed with a NMD. The diagnosis needs to be confirmed, whenever possible, by genetic testing, or at least by biopsy and/or electroneuromyography, according to international standards for the diagnosis of the given NMD. Once the diagnosis is established, there are no specific exclusion criteria.

Currently, patients with DMD/BMD/IMD, SMA and patients with a congenital muscular dystrophy (CMD) due to mutations in the laminin-α-2 gene (LAMA2-RMD) or collagen VI (COL6-RD) genes are included in the registry. In the future, patients with other NMDs may also be included.

Duchenne Muscular Dystrophy (DMD) is an X-linked progressive muscular dystrophy affecting one in every 3’600-10'000 live male births (Mah et al. 2014). Becker Muscular Dystrophy (BMD) is the less severe form affecting about one in every 18’000 live male births (Emery et al. 1991). Patients with a less severe form than DMD but more severe than BMD are classified as intermediate form (IMD). These disorders are caused by mutations in the dystrophin gene. Boys present delayed motor development and muscle weakness and progress to loss of ambulation, and, in the more severe cases, respiratory and heart failure.

Spinal Muscular Atrophy (SMA) is a disease affecting motor neurons in the spinal cord and the brain stem. It is an autosomal recessive disease affecting about one in every 10'000 live births (Faravelli et al. 2015). It is caused by mutations in the ‘survival motor neuron 1’ gene (*SMN1*). Patients with SMA present with progressive motor weakness and weakness of bulbar and respiratory muscles. Conventionally, SMA is divided into four clinical subtypes, from type I with onset before 6 months and, if untreated, death before the second birthday to type IV with adult onset, weakness and a slowly progressing course. In recent years, three treatments for SMA have been developed and approved by Swissmedic. The first was Nusinersen (Spinraza®), followed by Risdiplam (Evrysdi®) and Onasemnogene abeparvovec-xioi (Zolgensma®).

Congenital muscular dystrophies (CMD) are a group of diseases that are mostly inherited in an autosomal recessive manner. The prevalence has been estimated at 7×10^{-6} (Mostacciuolo et al. 1996). LAMA2-related muscular dystrophy and COL6-related muscular dystrophy are the two most frequent forms of CMD. Both forms lead to marked weakness of skeletal muscles, the tendency to develop contractures and rigidity of the spine as well as respiratory muscle weakness. Therapeutic compounds showing promising results in preclinical studies are in development for LAMA2- related myopathies (Smeets et al. 2021). It is therefore important to include these forms with more detail for natural history data and trial readiness (Sarkozy et al. 2020).

3.4. Registration of patients and collection of medical data

In general, a paediatric or adult neurologist diagnoses an individual with a NMD. The physician then informs the patient and/or their parents (or other legal representative) about the Swiss-Reg-NMD during a routine medical consultation. The physician also gives them printed information about the registry and a form that they can sign if they want to participate in the registry (informed consent form). This information can be taken home so that a decision can be made after careful deliberation.

If consent is given, the physician reports the patient to the Swiss-Reg-NMD, and provides data on the clinical status of the patient at regular intervals (once per year or, for SMA, 2-3 times per year for Post-Marketing Follow-up). At the ISPM (the Institute of Social and Preventive Medicine of the University of Bern where the registry is hosted), this information is then entered into a secured database.

If consent is not given, the patient can still be reported, but with very minimal non-identifying data (diagnosis, gender, birth year, date and cause of death) to allow a proper estimate of the incidence and prevalence of the diseases in Switzerland to be made. No further information is collected.

3.5. Data protection / Ethics approval

The Human Research Act (HFG) sets the framework conditions for medical research. The Swiss-Reg-NMD is subject to this Act. In 2008, the old registry for DMD/BMD and SMA received ethics approval in the different cantons. In 2018 approval for the new, improved Swiss-Reg-NMD was obtained from the Cantonal Ethics Committee of Bern (#2018-00289). This approval allows the collection of data all over Switzerland.

If consent is given, the Swiss-Reg-NMD is authorised to collect the medical data as long as these data are collected routinely in the course of the treatment and follow-up of the patient. It is permitted to use these data for reports and in-depth research studies. In addition, the registry is allowed to initiate questionnaire studies on quality of life, development, health and health care use. Finally, the registry can inform patients directly about clinical trials.

Study information and consent forms are available in four different languages (French, German, Italian and English). All data made available to the Swiss-Reg-NMD is stored in a secure IT environment at the University of Bern. This data is kept strictly in accordance with the requirements of the Data Protection Acts. All staff members of the Swiss-Reg-NMD are bound to professional secrecy. Only coded data (without names or identifying data) is used for research purposes.

3.6. Funding

In 2022, the Swiss-Reg-NMD has received unconditional funding from the ‘Schweizerische Muskelgesellschaft’, the ‘Association Suisse Romande Intervenant contre les Maladies neuro-Musculaires’, the ‘Associazione malattie genetiche rare della svizzera italiana’, from ‘SMA Schweiz’, from ‘Duchenne Schweiz’ and from the ‘Schweizerische Stiftung für die Erforschung der Muskelkrankheiten’.

Furthermore, Biogen Switzerland AG, Novartis Gene Therapies Inc., Pfizer AG, PTC Therapeutics Switzerland GmbH and Roche Pharma AG Switzerland have supported the work of the Swiss-Reg-NMD financially.

We want to thank all these organisations and companies for their support.

4. Registered patients and data collection

On 31.12.2022, a total of 375 patients with neuromuscular disorders were registered in the Swiss-Reg-NMD (not reported as deceased, Table 2 and Table 3): about 200 patients with dystrophin associated muscular dystrophy (DMD/BMD/IMD), 157 patients with SMA, about 15 patients with LAMA2-RMD and 5 patients with COL6-RD. In 2022, ≤3 patients with DMD included in the Swiss-Reg-NMD were reported as deceased.

To ensure patient confidentiality we mask small numbers with "≤3" in our annual report.

Not all patients with a NMD living or treated in Switzerland are registered in the Swiss-Reg-NMD. The participation is voluntary. Since the new ethics approval of 2018, 6 people have declined to participate in the registry (not included in Table 2 and 3).

Table 2. Total number of patients alive[a] by neuromuscular disorder and age (status as at 31.12.2022).

	Age 0-20	Age 20-65	Total
DMD-Duchenne	107	50	**157**
BMD-Becker	19	18	**37**
IMD-Intermediate	≤3	≤3	**4** [b]
SMA type 1	27	≤3	**29** [b]
SMA type 2	34	30	**64**
SMA type 3	13	48	**61**
SMA unspecified[c]	≤3	0	**3** [b]
LAMA2-RMD	12	≤3	**15** [b]
COL6-RD	5	0	**5**
Total	**222**	**153**	**375**

DMD: Duchenne Muscular Dystrophy; BMD: Becker Muscular Dystrophy; IMD: Intermediate form; SMA1-3: Spinal Muscular Atrophy type 1-3; LAMA2-RMD: LAMA2-related Muscular Dystrophy, COL6-RD: Collagen-VI-related dystrophy.

[a] Not reported as deceased; [b] Approximate value to ensure patient confidentiality; [c] unspecified SMA type, e.g. patient currently pre-symptomatic.

Table 3. Total number of patients alive[a] by centers (status as at 31.12.2022).

Center	DMD/BMD/IMD	SMA	LAMA2-RMD	COL6-RD	Total
Aarau	8	0	0	0	**8**
Basel	15	7	6	≤3	**29** [b]
Bern	22	44	5	≤3	**72** [b]
Geneva	7	4	≤3	0	**12** [b]
Lausanne	43	31	≤3	0	**75** [b]
Luzern	6	≤3	0	0	**9** [b]
St. Gallen	≤3	26	0	0	**29** [b]
Ticino	11	6	≤3	≤3	**20**
Zürich	65	36	≤3	0	**102** [b]
Other	18	7	0	0	**25**

We have included patients treated in private practices among 'other'. Note that some patients with SMA are seen and therefore listed in two centres. DMD: Duchenne Muscular Dystrophy; BMD: Becker Muscular Dystrophy; IMD: Intermediate form; SMA: Spinal Muscular Atrophy; LAMA2-RMD: LAMA2-related Muscular Dystrophy; COL6-RD: Collagen-VI-related dystrophy. [a] Not reported as deceased; [b] Approximate value to ensure patient confidentiality.

Compared to the previous year, 43 (13%) more patients are included in the registry. This increase primarily reflects the active work of the participating centres to recruit patients diagnosed with a neuromuscular disease in earlier years. Accordingly, in 2022 the workload for data collection has significantly increased for both the centres and the registry team at ISPM. In fact, we have collected medical data from 123 patients with DMD/BMD/IMD and 133 patients with SMA, with the data collection for 2022 not yet completed. The workload for the neuromuscular centres is even higher, as data are collected 3 (2 in a minority) times a year for patients with SMA treated with a disease modifying therapy (almost 80% of the patients).

Clinical Trials

In 2022, two trials involving **patients with DMD** were conducted in Switzerland:

- The Ciffreo study (NCT04281485) is an international placebo controlled trial investigating the safety and efficacy of gene therapy in boys with DMD. In 2022, 4 patients were included in this study.
- The Lelantos study (NCT04371666) evaluates the efficacy and safety of pamrevlumab versus placebo in participants with DMD. In 2022, ≤3 patients were included in this study.

In 2022, some **patients with SMA** were participating in trials conducted in Switzerland:

- The Jewelfish trial (NCT03032172) conducted by Roche investigates the effect of Risdiplam, a small molecule that enhances the functioning of the SMN2 gene, in different groups of patients with SMA. Currently, ≤3 Swiss patients are participating in this trial (UKBB, principle investigator Prof. Dirk Fischer).
- The Sunfish trial (NCT02908685) conducted by Roche investigates the effect of Risdiplam in comparison with a placebo group in patients with SMA 2 and 3. Currently, ≤3 Swiss patients are included.
- ≤3 patients with SMA are currently enrolled in an observational study at the University Hospital Zürich investigating cardiac and muscle involvement in SMA (NCT03660969).

Note: the above mentioned numbers include only the patients registered in Swiss-Reg-NMD.

5. Achievements of the Swiss-Reg-NMD in 2022

5.1. Requests to the registry

The registry always replies to requests in a way that no identifying information is disclosed. Conclusions about individual persons are not possible under any circumstances. The identity of the enquirer is confidential and is not disclosed either.

Requests on the feasibility for studies and clinical trials

- We answered three consecutive requests from a Swiss research group (University Hospitals) concerning the same feasibility study by providing information on the incidence of SMA in Switzerland and on the genetic background of SMA diagnosis.
- We answered a request from a Swiss University Hospital and identified patients with DMD eligible for a clinical trial in Switzerland. We asked the treating physicians to inform these patients on the planned study.

Further requests and collaborations

- We provided various researchers from Swiss Universities with non-identifying medical data of all registered patients for a cohort profile study, for a LAMA2-RMD cross-sectional cohort, and an SMA observational cohort study on a specific SMA treatment.
- To determine the use of a particular drug in Switzerland, we provided a Swiss university hospital with information on the number of patients with DMD who were receiving this drug at the given time.
- We provided aggregated data to answer three large research requests from TREAT-NMD
    - on the role of gender in SMA pathology
    - on the distribution of the many mutations that make up DMD as a disease
    - for a high-level overview of the data within the Global Registry Network
- We answered two small industry requests needed for FOPH.
- We responded to another small industry request to provide the proportion of registered patients with DMD per predefined disease stages.

5.2. Collaboration with TREAT-NMD (treat-nmd.org)

TREAT-NMD is a network for the neuromuscular field that provides an infrastructure to ensure that the most promising new therapies reach patients as quickly as possible. Since its launch in January 2007 the network's focus has been on the development of tools that industry, clinicians and scientists need to bring novel therapeutic approaches through preclinical development and into the clinic, and on establishing best-practice care for neuromuscular patients worldwide.
Dr. Andrea Klein is an elected member of the TREAT-NMD Global Database Oversight Committee (TGDOC) for the international registry for SMA and DMD. The TGDOC is responsible for reviewing all requests for data from the global database.

Collaboration with TREAT-NMD in 2022

TREAT-NMD works with the European Medicines Agency (EMA) regarding a real-world evidence, longitudinal research study in patients with SMA across Europe. This research study aims to investigate SMA patients' course of disease and standards of care delivery over time in European countries, using data routinely collected by existing SMA registries.

Additionally, TREAT-NMD supports a post-authorisation efficacy study of disease modifying treatments (DMTs) by collaborating with the SMA Global Registry Network. This study is a long-term, observational study to further evaluate disease progression in patients with SMA who are being treated with DMTs and to compare the data collected with natural history data collected from untreated patients.
As a Core Member Registry for SMA, the Swiss-Reg-NMD was invited by TREAT-NMD to participate in both these studies. The Steering Board of the registry will decide on the final participation in these international studies.

5.3. Development of the registry

Main steps in 2022

- In 2022, we continued our efforts to improve data collection especially for adult patients. We intensified on-site data collection at the clinics and introduced interested medical staff to direct data entry into our databases.
- In early summer 2022, we slightly revised the dataset for the collection of LAMA2-RMD medical data and set up the corresponding database. Data collection was standardized.
- Dr. Franziska Joncourt, genetic curator of the registry, has updated the genetic data of DMD/BMD/IMD patients according to the latest international HGVS rules. We thank Ms Joncourt for her valuable contribution.

5.4. Dissemination and Networking

On our website *www.swiss-reg-nmd.ch*, we provide the information leaflets and consent forms as downloads and news on the work of the registry. Further information can also be found on the clinicaltrials.gov website (NCT05102916).

Members of the Steering Board and/or of the executive office represented the registry at the following meetings in 2022:

- 254th European Neuromuscular Center (ENMC) International Virtual Workshop: “Formation of a European network to initiate a European data collection, along with development and sharing of treatment guidelines for adult SMA patients”, ‘The Swiss experience’, 28.-30.01.2022
- European Paediatric Neurology Society (EPNS), Virtual Training Course, 30.-31.03.2022
- Half-year session of Swiss patient organisations for people affected by neuromuscular disorders, Bern, 05.04.2022
- Jahrestagung pädiatrie Schweiz, Luzern, 02.-03.06.2022
- 17th International Congress on Neuromuscular Diseases (ICNMD), ‘Treatment of SMA with Onasemnogene Abeparvovec in Switzerland’, Brussels, 05.-09.07.2022
- Jahrestreffen des fachlichen Beirats Myosuisse, Bern, 25.08.2022
- 3. Duchenne Konferenz Schweiz, Nottwil, 09.-10.09.2022
- Swiss Research Network of Clinical Pediatric Hubs (SwissPedNet), Field trip at SwissPedReg, ISPM, “Pediatric medical registries”, Bern, 26.10.2022
- 14. Neuromuskuläres Symposium, Universitätsspital Zürich, ‘SMA-Gentherapien – Erfahrungen in der Schweiz’, 24.11.2022
- Jahrestagung der Schweizerischen Gesellschaft für Neuropädiatrie, St. Gallen, 12.-13.12.2022

5.5. Research and Post-Marketing Follow-up

- In collaboration with researchers from the University Children's Hospital Basel (UKBB), we analysed the data of the DMD survey "Neurocognitive functions, education, participation and quality of life in children and adolescents with Duchenne muscular dystrophy in Switzerland". A first manuscript entitled "Effects of the Covid-19 Pandemic on Access to Education and Participation in Children and Adolescents with Duchenne Muscular Dystrophy in Switzerland" was submitted to the journal Neuropediatrics. It was accepted in January 2023 and will be published soon.
- Another article with further results from the above-mentioned questionnaire study on education and participation among children and adolescents with DMD in Switzerland is in preparation.
- In collaboration with the treating clinicians and data providers, an article entitled "Treatment of Spinal Muscular Atrophy with Onasemnogene Abeparvovec in Switzerland: A prospective observational case series study" was published in BMC Neurology in February 2023.
- In collaboration with researchers from Inselspital Bern, we analysed the relevant registry data and, together with the data providers, we plan to submit an article on real-world outcomes of treatment with nusinersen and risdiplam in adult patients with SMA in Switzerland.
- The Swiss-Reg-NMD has started a collaboration with Swiss Newborn screening laboratory and the Swiss pediatric neuromuscular centers. This joint work is dedicated to the implementation of a nationwide newborn screening for SMA, the application is currently under review at the Federal Office for Public Health.
- A cross sectional study to describe the cohort of Swiss patients with LAMA2-related myopathies is ongoing and is followed by a natural history study.
- We prepared a manuscript describing the Swiss Registry for Neuromuscular Disorders cohort study and we plan to submit it together with the data providers.
- We supported a master thesis project from the University Hospital of Lausanne investigating the access to dental care for children and adolescents with a motor disability. The findings will be described in a scientific publication and will soon be submitted to a scientific journal.
- We collaborated to a study involving different researchers from Swiss and British Universities, University Hospitals and representatives of a Swiss patient organisation resulting in an article entitled "Mental health challenges and digital platform opportunities in patients and families affected by pediatric neuromuscular diseases". The manuscript was submitted to the journal Swiss Medical Weekly in January 2023.
- To investigate the safety and effectiveness of all three currently approved SMA therapies even after their market introduction, we continued to collect data regarding therapy administration, motor function, motor assessments, nutrition, respiration and side effects and analyse these data. This work with real-world medical data from people diagnosed with SMA is crucial for patients and treating physicians to optimize future care.

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