PROGRESS TOGETHER

Inpda

International Niemann-Pick Disease Alliance

# International Niemann Pick Disease Alliance

# 4th Biennial "Face to Face" Meeting

# 23rd – 25th October 2015

FAVORITE Parkhotel, Karl-Weiser Str. 1, 55131 Mainz, Germany

## Meeting Summary

# Friday 23rd October

Following registration over lunch, the introductory session kicked off at 1pm. Delegates were welcomed by our hosts, Ed Fabianski, President of the German patient group Niemann-Pick Selbsthilfegruppe, and Christoph Poincilit, President of Niemann-Pick Suisse.

Jim Green (JG), INPDA President, gave an overview of the meeting's objectives:

- To reduce isolation
- To share information and expertise
- To explore ways of working together
- To maximise the influence of families as partners
- …taken together, to "facilitate progress"

JG outlined who was in attendance:

- 1o INPDA member organisation and clinicians
- 4 new associate organisations
    - Australia
    - Brazil
    - China
    - Norway
- International scientists and clinicians
- Pharmaceutical companies – Actelion, Genzyme, Orphazyme and Vtesse
- Volunteer helpers – Volunteer helpers and spouses
- INPDA Employee

JG also acknowledged and thanked those who made the meeting possible – including the Swiss and German groups; Actelion and Genzyme for their unrestricted grant support; and to Felix Schleuniger and all who supported him on the GDMBR.

Miriam Evans (ME), INPDA Project Coordinator, then introduced each patient organisation. Representative(s) from each group provided a brief overview of their organisation and its activities.

Common themes emerged in these presentations: the need for up to date, accessible information – for families AND healthcare professionals / wider professional network; the desire to reduce isolation felt by NPD families; to offer practical as well as emotional support; the need to work collaboratively to maximise scarce resources.

**Argentina – Marcelo Minotti:**

- NP Argentina established 10 years ago
- 20 patients confirmed (12 NP-C, 8 NP-B), 20 pending confirmation (40% adults, 30% adolescent, 30% children)
- Timely and accurate diagnosis a big challenge
- Large focus on working with healthcare professionals, and wider network (i.e. speech, nutrition, medical students)

**Australia – Mandy Whitechurch and Kellie Adams:**

Newly formed group, families of 5 NP-C patients. Know of around 20 patients in Australia, but challenge of massive geography.

**Brazil – Maria Helena Dourado:**

- Associacou Niemann Pick Brazil (ANPB) established 5 years ago
- Since, has supported 9 NP-B cases, 43 NP-C cases
- Has provided judicial assistance to access Zavesca for 23 patients (2 ongoing)
- Works to increase awareness of NPD, delivered Think NPC campaign

**Canada – Tammy Vaughan**

- Founded in 2005, the CCNNPDF is a sister chapter to the National Niemann-Pick Disease Foundation (NNPDF) (U.S.), working collaboratively, and receives administrative support from the NNPDF
- Challenge of huge geographic territory
- Tremendous relationship with Actelion Canada – collaborative work on Think NPC campaign

**China – Zhang Ai Jun**

- Major diagnostic challenge, as testing only available in a few cities – problems for rural areas
- No official statistics – however the China NPD Association has contact with 79 NP-A/B patients, 27 NP-C patients.
- Treatment for NP-B in China includes splenectomy and liver transplantation
- There is no treatment option available for NP-A or NP-C
- Urgently need clinical care guidelines to be available to Chinese medical professionals (i.e. how to control epilepsy, reduce pain), also to families on how to best manage the conditions
- Keen to join international patient community and participate in clinical trials
- First annual family conference was held in Beijing in December 2011, with 28 patients attending, grown each year since
- Joined the Chinese Organization for Rare Disorders (CORD) in 2014

**France – Zehra Zakiuddin**

- NP group within VML. Held family conference in Lyon. Focus this year on targeting orthoptists regarding VSGP.

**Germany – Sabine Fornfeist**

- Group founded in 1997, current membership includes 40 patients (estimated 150 patients diagnosed in Germany), connected to wider umbrella organisations
- 3 main NPD treatment centres in Germany – Mainz, Münster, Tübingen
- Hold an annual family/professional meeting in Kassel

**Italy - Annalisa Bisconti**

- Italian group founded in 2005

- Works with doctors – NPD training workshops, also promoting early diagnosis
- Provide Educational Holidays – practical training, best practice sharing, holiday, share experiences
- Other projects including "diagnostic ombudsman" (linking services); neurologist mentoring

**Netherlands**

Netherlands VKS were unable to attend the Mainz meeting. ME acknowledged the group's membership of the INPDA and provided a brief introduction – VKS was founded in 1994, an Association for Adults and Children with Metabolic Diseases

**Norway – Siri Skollerud-Blegen**

- 5 million people, but only 4 people diagnosed with NP-C (just one adult), 1 NP-B – under-diagnosis an issue?
- 2 children are on Cyclodextrin – 1 via intra-thecal, 1 with an Ommaye reservoir
- 1 hopes to participate in Orphazyme trial out of Copenhagen

**Spain – Enrique Pilar**

- Founded in 2001
- Membership including 45 families, current patients 4 NP-B, 13 NP-C (aged 4-40 years)
- Hold annual scientific family conference

**Switzerland – Christoph Poincilit**

- Founded 2011
- 13 patients (1 child, 2 juvenile, 10 adult). 4 patients have deceased
- Focus on research – hold bi-annual Loire Valley Meeting
- Swiss specific issues – multiple languages; federal government structure with local delivery; private healthcare. Country-wide campaigns difficult, need to approach individual cantons
- Keen to form an interest group of German speaking countries - Germany, Switzerland, Austria, South Tyrol

**UK – Toni Mathieson and Dave Roberts**

- Founded in 1991. Staff team consists of an Executive Director, Clinical Nurse Specialist, Families Officer, Information Officer, Finance/Admin Officer
- Currently supporting 120 affected families, with emotional and practical advice. Adult NP-C population has increased over recent years.
- Works in collaboration with LSD groups and rare disease umbrella organisations

**USA – Nadine Hill**

- Founded in 1992 by 6 affected families, now with over 450 NP families as members – 43 new families joined this year alone!
- Holds an Annual Family Support and Medical Conference
- October as NP Awareness month

- Met with FDA in April this year to help ensure the patient perspective of living with Niemann-Pick B is better understood.
- Involved in a number of research projects – ASMD PRO tool development, EEG Research Study, Gait testing; and funds a number of research grants and fellowship funding

Following a refreshment break, Will Evans (NP-UK trustee and NP-C dad), chaired a session looking at "**Niemann-Pick diseases, where are we now**?"

1. Professor Marc Patterson began the session, with an overview of **the development of clinical understanding of NP diseases**. Starting in 1914 with Albert Niemann, then Ludwig Pick in the 1920s – where they described progressive neurodegenerative condition with hepatosplenomegaly which was different to Gaucher (first described in 1882).

   Prof Patterson also provided an overview of the clinical trials and natural history studies that have occurred, or are ongoing, for NPD. He also described the phenotypes for both ASMD NP-A and NP-B, and NP-C.

   *"The formation of the INPDA is a landmark for NPD… [we've seen] the mutually powerful interaction between the establishment of patient groups and progress towards understanding and treatment for these diseases"*

   In summary:

   - Original clinical descriptions have stood the test of time
   - Age range has expanded over time – increasing prevalance of adult disease
   - Multiple trials of disease-modifying therapy
   - Understanding of pathophysiology still incomplete
   - Ongoing need for natural history data >> patient owned and professionally managed registry

2. Dr Marie Vanier presented on **the development of laboratory diagnostic testing in the Niemann-Pick Diseases from 1950's-today.** From early diagnostic methods through to current development of the oxysterol assays and the need for a sensitive and specific biochemical test from a blood sample.

   In summary:

   - Delay in diagnosis
     - More lack of awareness from clinicians than slow tests
     - Aggravated by lack of simple, cheap, first screening test
   - Wide use of reliable biomarkers may modify the situation - (still need to confirm with genetics / filipin)
   - Systematic mutation analysis important
     - Prenatal diagnosis, carrier identification

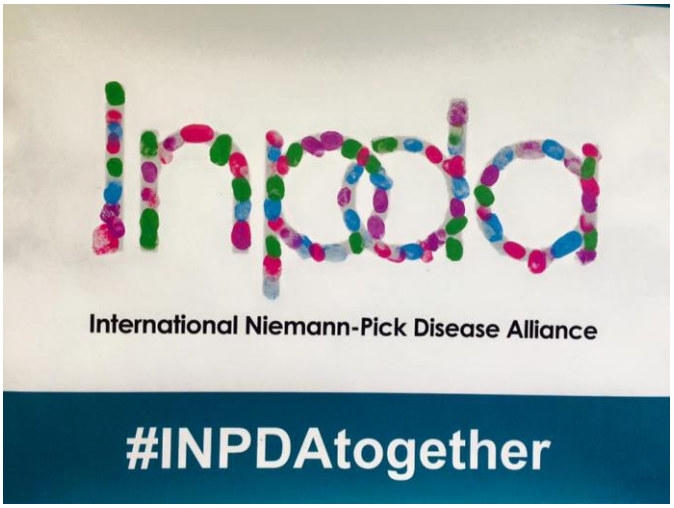
    - To learn more about genetic variants - "genotype/ phenotype correlations" (prognosis?)
- To study results in large cohort of patients is essential - Important role of the INPDR!

3. Professor Frances Platt presented on **the scientific understanding of NPC disease**, emphasising that in order to treat a disease, you must understand it. Prof. Platt provided an excellent overview of NP-C Genes and Proteins, NP-C Biochemistry, and NP-C Cell Biology, in the context of what we know, what we don't know, and what this means for future therapy development.

   Prof. Platt outlined the current pipeline of potential therapies – there has been remarkable progress here – also emphasised that combination therapy is the future. Understanding the disease will help develop therapies, because different therapeutic approaches can target particular aspects in the pathogenic cascade.

*"Success is not final, failure is not fatal: it is the courage to continue that counts"*
Winston Churchill

On Friday evening, we enjoyed dinner together. Delegates used their thumbprints to create the INPDA logo – a symbol of our collaboration:




"*The greatest enemy of knowledge is not ignorance, it is the illusion of knowledge.*"
Stephen Hawking

# Saturday 24th October

The morning session covered current clinical trials:

1. **Clinical Development of Olipudase Alfa for ASMD NP-B: Phase 1 and 1b**

   **Dr. Melissa P. Wasserstein M.D.**

   *Director, Program for Inherited Metabolic Diseases, Associate Professor of Genetics and Genomic Sciences, Mount Sinai School of Medicine, New York, USA*

2. **ASMD Clinical Development Programme Update**

   **Sharon Tan**

   *Global Project Head, Niemann-Pick, Genzyme Corporation, Cambridge, MA, USA*

3. **NIH Clinical Trial Updates for NP-C: HDACi and Cyclodextrin Phase I trial**

   **Forbes D. Porter, MD, PhD**

   *Senior Investigator, PDEGEN, NICHD, NIH, Program Head, PDEGEN, NICHD, NIH; Clinical Director, NICHD, NIH*

4. **Vtesse, Inc.: Clinical Trial Update for VTS-270 for NP-C**

   **Dr. Ben Machielse**

   President and Chief Executive Officer, Vtesse, Inc.

   **Professor Paul Gissen**

   Hon Consultant, Paediatric Metabolic Diseases, Great Ormond Street Hospital and

   Wellcome Trust Senior Research Fellow, Clinical Sciences, UCL Institute of Child Health UK

5. **Orphazyme: Clinical Development of Arimoclomol for NP-C**

   **Thomas Kirkegaard PhD**

   *Chief Scientific Officer, Orphazyme ApS*

   **Dr Eugen Mengel**

   Principal Investigator

In the afternoon, we looked at **INPDA Global Projects**:

1. Miriam Evans provided an **overview of the INPDA** – who we are, our objectives, current members, our projects, possible future focus areas.
2. Toni Mathieson gave an overview of the NP-C awareness campaign "**Think Again. Think NPC**".
3. Christoph Poincilit introduced the **Loire Valley Meeting**, an INPDA research forum held every two years. LVM 2016, to be held at Manoir de Clénord, will continue to span the bridge between fundamental and clinical research.
4. Dr. Tarekegn Hiwot presented the work to date on the **International Niemann-Pick Disease Registry (INPDR)**, a collaborative initiative between patient organisations and clinicians involved in the care of people with NPD.
5. Miriam Evans told delegates about the **Patient Reported** element of the INPDR. This will collect information directly from patients / carers – how the disease first presented, what those first symptoms were, how they progressed, the impact of the disease on their lives, the wider impact on family and employment, schooling, etc. This is in development now, and aim to roll out to patients via the INPDA and its members by the end of the year. Translations will be needed, and Miriam asked for volunteers to assist.

Following a refreshment break, delegates split into two parallel sessions: "INPDR – Working with the Registry", for the INPDA project team, pharmaceutical companies and clinicians; and "Think Again. Think NP-C Workshop" for patient groups.

1. **INPDR – Working with the Registry**
    a. Christiane Denzel from Genzyme gave a presentation on their approach to working with the INPDR, their extensive experience with registries to date, and their view on the issues. Genzyme is keen to collaborate and sees the virtue in a single disease registry.
    b. There was open and constructive debate around the challenges it presents, particularly in the context of clinical trials.
    c. There was an acknowledgement that this would be a new way of working
    d. All agreed that a single, patient owned disease registry 5 years from now is what should be our collective aim – that it was in the patients' best interests, and wanted by regulators
    e. There is some concern from pharma ("who jumps first?")
    f. More work is needed to define requirements from all parties

    ACTION: JG and TH to set up meetings with pharma, EMA, FDA

2. **TATN Workshop**

    A separate slidedeck summarising the workshop is available and will be sent separately.

    Opportunities were identified to further develop the campaign in 2016:

    - Funding is low in some member countries

        - Groups such as Argentina are using social media as a way to continue driving the campaign without funding
        - Look into ways to encourage affiliates and INPDA members to collaborate
    - Further materials could be developed focusing on adults with NP-C
        - Australian group mentioned that there are more adults than children in their country with NP-C and in UK it's 50/50
        - The group agreed that they would like to see more adult-related materials
    - Expand the subsets of healthcare professionals targeted, to reach wider groups who may misdiagnose, including:
        - School psychiatrists
            - See learning difficulties, 'difficult' behaviour
            - Often misdiagnose as autism or attention deficit disorders
        - Ophthalmologists
            - See eye movement disorders
        - Gastroenterologists
            - See hepatosplenomegaly
        - General practitioners
            - Have overview of all symptoms and investigations over time

On Saturday evening delegates enjoyed a sightseeing tour of Mainz, followed by dinner at a local vineyard.

# Sunday 25th October

The first session this morning was an INPDA business meeting.

Executive positions were unanimously elected as follows:

- Jim Green: President
- Sandy Cowie: Vice President
- Toni Mathieson: Secretary
- Peter Henggeler: Treasurer Christoph Poincilit: Information and Development

Jim Green acknowledged and thanked Karen Quandt for her involvement as INPDA Vice President, her commitment and hard work in support of the alliance's formation and development.

Member groups were asked to consider the **role of the INPDA** and what they could do better, and what the priorities are. Discussion fell into four key areas:

| **Share best practice** | **Reach out to other groups** | **Influence and support** | **Process & Share information** |
|---|---|---|---|
| ▪ TATN campaign<br>▪ Communication strategies (social media) | ▪ Share ideas<br>▪ Avoid repetition<br>▪ Engage in other geographies – make truly global | ▪ Pharma/Industry<br>▪ Patient groups (new and established)<br>▪ Leverage INPDR<br>▪ Access to expert clinical & scientific advice | ▪ Ensure relevant and accurate for members/groups<br>▪ Provide information to groups for local distribution<br>▪ Research & Trial info |

The final session on Sunday was an opportunity to look ahead. To capture ideas, delegates were asked to rotate around 4 topics, in a "**café consultation**" style. This created a huge amount of ideas! These are summarised in the table below:

| | |
|---|---|
| Communication | • Improve communication between INPDA member groups<br>• Share email addresses of members<br>• Monthly bulletin/newsletter – assign experts to topic areas, provide trial updates<br>• SEO optimisation for INPDA website<br>• Social media presence for INPDA and member groups<br>• Regular webinars in between f2f meeting<br>• Utilise World Rare Disease Day 2016 to raise profile of NPD (Imagine film, Think NP-C campaign, media templates) |
| Information | • Development of concise, accurate information for dissemination – trials, science, clinical care, diagnostics<br>• INPDA to coordinate translation of such materials<br>• An expert workshop to update NPD clinical guidelines for |

| | |
|---|---|
| | publication should be incorporated in biennial INPDA meeting<br>• Establish Adult NP-C sub-group – how to better address their specific issues, improve diagnosis, better understanding |
| Organisational Development | • Strengthen existing organisational processes – new membership engagement, roles and responsibilities<br>• Raise profile of INPDA among umbrella RD groups, leverage lobbying opportunities – RD plans of different countries<br>• Local member groups to work with local RD groups – raise profile of NPD within RD community<br>• Engage in wider geographies – broaden membership |
| Awareness Raising | • Build on Think NP-C campaign, share best practice<br>• Improve diagnosis of ASMD – similar campaign<br>• Make October a global awareness month for NPD |
| Research | • Drive patient/clinician engagement with registry<br>• Leverage opportunities – i.e. joint funding applications<br>• Connect diagnostic laboratories |

Jim Green ended the meeting by thanking everyone for their involvement and enthusiasm. We look forward to discussing these ideas, identifying project opportunities and resources to take them forward!