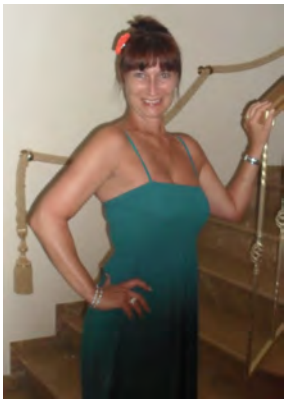
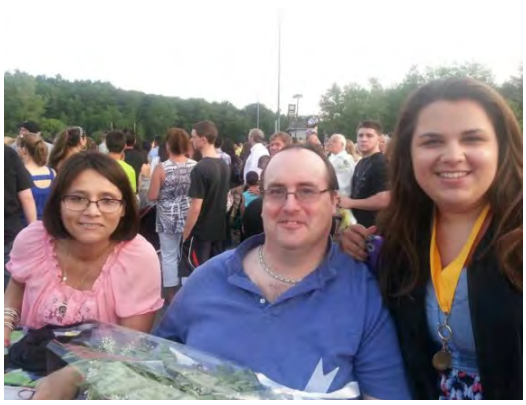
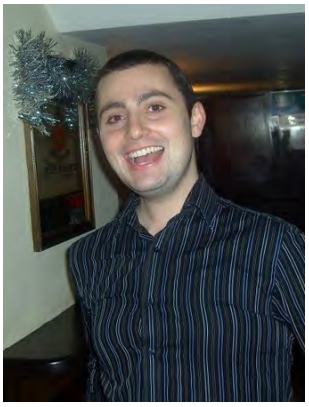
TREAT-NMD Neuromuscular Network

gnemDMP DISEASE MONITORING PROGRAM

ultragenyx pharmaceutical



Welcome to the GNEM-DMP!

Welcome to the fifth GNE Myopathy Disease Monitoring Program (GNEM-DMP) newsletter and thank you for your continued support and participation in the GNEM-DMP. Our newsletter is intended to provide you with regular updates on the GNEM-DMP and scientific updates related to GNE myopathy. We welcome your feedback and suggestions on this newsletter.

In this Edition

To join the GNE Patient Registry please visit: www.gnem-dmp.com
For more information on the GNEM-DMP contact: HIBM@treat-nmd.eu
For more information about Ultragenyx Pharmaceutical Inc. visit: www.ultragenyx.com/patients/gnem
For more information about TREAT-NMD please visit: www.treat-nmd.eu

Announcing the Completion of Enrollment of the Phase 3 Ace-ER (Aceneuramic Acid Extended Release) Clinical Trial.

We are delighted to announce that Ultragenyx Pharmaceutical Inc. has completed enrollment to the Phase 3 Randomized, Double-Blind, Placebo-Controlled Study to Evaluate Aceneuramic Acid in Patients With GNE myopathy (GNEM) or Hereditary Inclusion Body Myopathy (HIBM) (www.clinicaltrials.gov/ct2/show/NCT02377921). This pivotal study in the development of Aceneuramic Acid (Ace-ER) as a possible treatment for GNE myopathy will last for approximately one year. Ultragenyx Pharmaceutical Inc. has successfully enrolled 89 people at trial site locations in USA, Canada, UK, Bulgaria, France, Italy and Israel. These participants are expected to complete in summer 2017.

We would like to take this opportunity to not only thank people who are participating in the trial itself, but also those who are supporting the international patient registry (GNEM-DMP) which has played a pivotal role in raising awareneness and uniting the community.

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Registry Statistics

Fig 1: Worldwide Distribution of GNEM-DMP Participants

As of July 2016 there are now 247 participants (Fig 1) in the GNEM-DMP Registry, from 28 different countries. The map to the left shows the distribution of participants across the continents. There are six countries (spread across four different continents) which make up 81% of all registry participants - USA, UK, Iran, Italy and India.

The average age of the registry participants is 41.3 years old (age range of participants extends from 21 to 72 years old). The majority of participants in the registry fall in the age range between 30-39 years of age (Fig 2), but there is a wide age range of participants to date throughout the registry.

GNE myopathy and its Prevalence in the Families of GNEM-DMP Participants

Within the first questionnaire that is completed by registry participants in the GNEM-DMP, there is a section where we ask you to provide us with a little more information about your family in relation to GNE myopathy. We ask participants "Are there other family members diagnosed?" in order to better understand the frequency of the disease and at the same time give everybody the opportunity to join the GNEM-DMP. We also want to capture the experiences of people from all around the world and learn how the disease affects people from many different cultures.

Of those who answered **Yes** to this question (32.2%, Fig 4), over half informed us that there was one other family member that they were aware of who had also been diagnosed with GNE myopathy and 32% said that they were aware of two other family members. Analysing other responses, one respondent stated that they were aware of seven other family members who had been diagnosed with the disease.

Of the family members diagnosed, 54.1% (Fig 3) of these were identified by participants as their sister and 32.8% as their brother. Furthermore, 6.6% stated that a first cousin had also been diagnosed with GNE myopathy, and 6.6% other family members made up the rest of answers received.

The findings from the data entered by registry confirm our understanding that siblings (brothers/sisters) are the most likely family members to also be affected by GNE myopathy. This is because the disease is autosomal recessive, by which we mean that both parents are usually unaffected (carriers), but can pass on a defect copy of the GNE gene (a mutation) to their affected child.

Fig 2: Breakdown of Male/Female Participants by Age

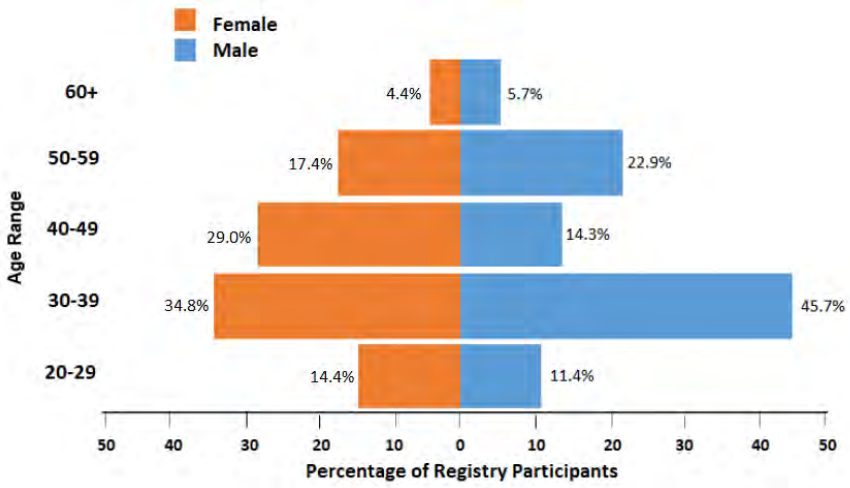


Fig 4: Responses to Registry Question: "Are there other family members diagnosed"

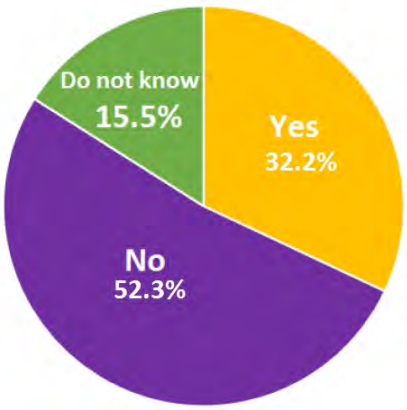
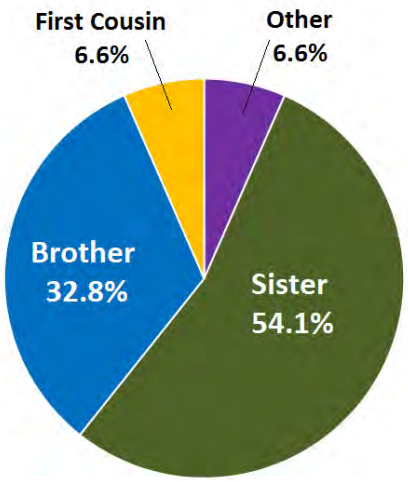


Fig 3: Family Members Identified as bening diagnosed with GNE myopathy



GNE myopathy Patient Advocacy Network Event

On 16 March 2016 during the Myology Conference in Lyon, France, a group of specialist patient advocacy organisations came together to share knowledge and understanding of the needs of GNE myopathy patients, and to help develop networks so that more advocacy groups may become connected and involved with supporting patients and their families.

The day was hosted by Dr. Anthony Behin from the Centre de Reference de Pathologie Neuromusculaire in Paris and was also attended by Dr. Andoni Urtizberea from the Institute of Myology. Representatives from the following patient advocacy organizations were in attendance: AFM Telethon in France, Muscular Dystrophy UK, VSN in The Netherlands, ASEM Federacion and Ana Carolina Diez Mahou Fundacion in Spain. The following people made presentations during the afternoon session:

Dr. Behin presented on the current understanding of the incidence and prevalence of GNE myopathy and the genetic implications, specifically that GNE myopathy remains very rare in many countries with some clusters in Japan, Middle-East, India, Rome, and Bulgaria. He emphasized that better knowledge of the epidemiology and disease history in the different countries is crucial; emphasising the importance of the GNE myopathy registry.

Robert Meadowcroft, the Chief Executive of Muscular Dystophy UK, discussed the importance of a unified service between the clinic and the home for the well-being of every neuromuscular patient. He discussed how the patient groups can provide peer support from those who personally know the challenges to use in combination with the information and advice provided by the clinic.

Maryze Schoneveld van der Linde from Patient Centered Solutions discussed the importance of a good international patient network for rare diseases which often do not have disease specific patient organisations in every country. She gave the example of her experience being part of the country specific neuromuscular organization VSN, as well as forming an International Association for her condition. She sited GNE myopathy International (www.gne-myopathy.org) as being able to provide resources and support for those with GNE myopathy.

Valeria Pace from the Italian GNEM Patient Advocacy Support Group sent a moving video message, which can be viewed at (www://drive.google.com/openid=0B9WbnySs8jnec09iaUpxc2I1NnM) This meeting launched collaborations for those with GNE myopathy into the future, as Valeria explained how families and patients alike can connect to neuromuscular patient advocacy groups.

Patient Advocacy at ultragenyx pharmaceutical

Ultragenyx Pharmaceutical has launched a brand new website [www.ultrarareadvocacy.com] dedicated to everyone affected by rare diseases.

The Patient Advocacy team at Ultragenyx, is passionate about educating and supporting those patients, families and caregivers affected by rare and ultra-rare diseases. Through the new website you can find valuable resources, hear from others who live with rare diseases, and learn more about the commitment from Ultragenyx to the rare disease patient community.

The advocacy team works with patient organisations to understand and represent the views of patients to the company. They strive to provide valuable information, educational materials and resources to the communities they serve. The input also helps guide Ultragenyx's clinical development programs.

Please note that Ultragenyx does not provide healthcare advice. Please consult with your treating physician if you have specific questions about your health status.

Patient Advocacy Summit: "Let's Talk Myopathy" – Barcelona, Spain

On 1 October 2016 in Barcelona, Ultragenyx, ASEM, and Ana Carolina Diez Mahou Fundacion are sponsoring a Patient Advocacy Summit.

This one day panel discussion will bring together independent advocacy groups who support patients with neuromuscular disorders (especially adult onset myopathies) with people who have GNE myopathy to help learn about areas of unmet need within the adult myopathy patient community.

Registration for this event has now closed, however an update on the day's events will be included in the next edition of the GNEM-DMP newsletter.

Fundraising for GNE myopathy

An active member of the GNE community and her friends and family, are currently raising money in support of GNE myopathy by undertaking a number of challenges over the coming months. Find out more about each of these fundraising opportunities and how you can donate, below:
London Duathlon: **www.justgiving.com/crowdfunding/MonaPatel-GNEMyopathy**
London to Paris Bike Ride: **www.justgiving.com/crowdfunding/sat-sanj**

Remudy | 縁取り空胞を伴う遠位型ミオパチー患者さまご登録サイト

Remudy- Registry of Muscular Dystrophies (Japan)

by En Kimura, Manager of Remudy, National Center of Neurology and Psychiatry (NCNP), Japan

The Remudy-GNEM registry (www.remudy.jp) is a Japanese national registry for GNE myopathy that was launched in 2012, run by the National Center of Neurology and Psychiatry, Japan. The registry follows the same format of the TREAT-NMD patient registries for Duchenne Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA), comprising of a patient self-reported registry. Each registry item is certified by their attending physician, and then, double checked by medical and genetic professionals before heading in the Remudy-GNE myopathy registry. By the end of June 2016, 176 GNE myopathy patients were registered, and the number of registrants is still growing. The data collected in this registry has been used so far in a feasibility study (an assessment of the practicality of a proposed project to assess the choice of electronic devices used by GNE myopathy patients) and also in the recruitment for Investigator initiated clinical trials.

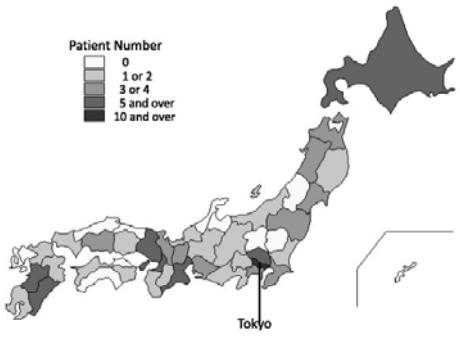
Today, Remudy is led by Dr. Madoka Mori-Yoshimura. The registry team is happy to work in collaboration with the GNEM-DMP so that both of our anonymous data can be combined. The combined anonymized data set will create a powerful data set, that will help us all to push forward the clinical development of treatments for GNE myopathy.

Data collected through the Remudy registry were thoroughly analysed and published in 2014 in a paper titled 'Nationwide Patient Registry for GNE myopathy in Japan'. Below Dr En Kimura, has kindly provided us a brief overview of their findings.

Mori-Yoshimura M, Hayashi YK, Yonemoto N, et al. (2014)
Nationwide patient registry for GNE myopathy in Japan.
Orphanet J Rare Dis 9:150

Abstract

AIMS AND OBJECTIVES: This study aimed to (1) develop a nationwide patient registry for GNE myopathy in order to facilitate the planning of clinical trials and recruitment of candidates, and (2) gain further insight into the disease for the purpose of improving therapy and care.



Participant distribution. *Participants were distributed throughout Japan (38/47 prefectures), and 92 physicians in 73 institutes agreed to contribute to the registry.*

METHODS: Medical records of genetically-confirmed patients with GNE myopathy at the National Center Hospital of the National Center of Neurology and Psychiatry (NCNP) were retrospectively reviewed in order to obtain data reflecting the severity and progression of the disease. We also referred to items in the datasheet of the nationwide registry of dystrophinopathy patients in the Registry of Muscular Dystrophies (Remudy). Items selected for the registration sheet included age, sex, age at onset, past history and complications, family history, body weight and height, pathological findings of muscle biopsy, grip power, walking ability, respiratory function, cardiac function, willingness to join upcoming clinical trials, and participation in patient associations. A copy of the original genetic analysis report was required of each patient.

RESULTS: We successfully established the Remudy-GNE myopathy registry. Currently, 121 patients are registered nationwide (Japan only). Close to 100 physicians from 73 hospitals collaborated with the registry curators to establish the registry. Demographics analysis of the data in the registry showed that the mean age at onset was 27.7 (+/- 9.6 years), and almost 20% of all registry patients (24/121) reported to be able to walk without assistance. On average it takes about 12 years to start using assistive devises after the first symptoms noticed, in 15 years patients start using wheelchairs and in over 20 years the ambulation is lost. Unusual accompanying symptoms were observed in 3 patients who had a past history and/or complication of idiopathic thrombocytopenia (low level of platelets leading to increases chances of hemorrhage). To share the progress of this study with the community, newsletters were published on a regular basis, and included information regarding new phase I clinical trials for GNE myopathy in Japan by Nobel pharma. The newsletters also served as a medium to bring attention to the importance of respiratory evaluation and care for respiratory insufficiency in non-ambulant patients.

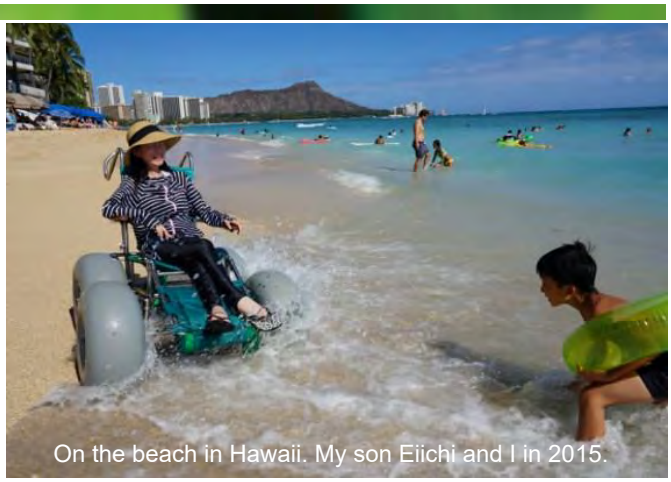
CONCLUSION: The Japanese Remudy-GNE myopathy registry is useful tool for increasing knowledge about the natural history of the disease and recruiting patients GNE myopathy in clinical trials. www.ncbi.nlm.nih.gov/pmc/articles/PMC4203883/

Yuriko Oda - My Journey So Far

Introduction from the editor: Yuriko Oda is the president of the Japanese patient organization 'Patients Association for Distal Myopathies' (PADM) and is also a member of TREAT-NMD Executive Committee. Yuriko is an active member of the YouTube community, hosting her own channel (www.youtube.com/channel/UCHPYy4tcfXzKCa-P0h5u49Q) where she has uploaded a series of videos (with English subtitles). These videos look at a range of day to day issues facing a person with GNE myopathy - activities such as boarding airplanes, traveling by train and also something as simple as picking fruit. Yuriko is a keen traveler and has dedicated much of her free time advocating for the creation of a barrier free and accessible environment to live in, for people with neuromuscular diseases, not only in Japan, but worldwide. Below, Yuriko shares her experiences and wonderful work that she is doing.

When I was around 20 years old I started to feel some abnormal changes in my legs. That was back in 2002 when I was a senior student at University. At that time I was diagnosed with Distal Myopathy with Rimmed Vacuoles (also known today as GNE myopathy). Before the diagnosis was found I always blamed myself for the changes I had felt in my legs. I thought that it was because I was lazy - even though I participated in activities such as swimming, walking my dog and climbing stairs. Honestly, I was so relieved after my diagnosis was confirmed because physicians explained to me that this is a genetic disease.

Just before my 25th birthday in 2005, I visited my primary doctor to discuss family planning and progression of muscle weakness. I was informed that GNE myopathy is a recessive disease and that my children have a very small chance to be affected by the disease as this is an 'autosomal recessive' condition. In other words, it would be an astronomical phenomenon if this were the case. I was informed by my doctor that because of the disease, child birth would become more difficult as the disease progressed in certain parts of my body. So my boyfriend and I decided to marry and have a child, sooner rather than later. The following year, my son Eiichi was born. Although it is challenging to bring up my son, I am really grateful to be able to do it thanks to help from others. I believe that if I do not forget my appreciation to people and be cheerful, I can overcome any hardships.



On the beach in Hawaii. My son Eiichi and I in 2015.

Establishing PADM

PADM (www.npopadm.com) was founded by patients on the 1st April 2008 as a non-profit organization - and now, 9 years later down the line we have 128 members (all of which are patients). PADM was mainly created when we started to hear good news about research in treatment of GNE myopathy, as previously there had been no possible compounds approach to treatment or medicine for my illness. Several Japanese groups decided at this point to come together and form a group who can voice our opinion - PADM. The main objective of PADM is to become a hope for the 'future' – working alongside industry and government across a wide range of issues that affect GNE myopathy patients now, for example (barrier free related actual information to meet the needs of everyday life for disabled people). Also issues that they may face in the future (access to any future medication, creation of rare disease networks). In my home country Japan, leading neurologist Dr. Ichizo Nishino has been leading the research in to GNE myopathy and has been at the forefront of the development of medication related to the disease. Knowing that people are doing something to find a cure for our disease has given me something to look forward to.

Achievement

We have been working hard in the past 9 years and are proud of our achievements. One such result being that on 14th August 2009, the pharmaceutical company Nobelphama Co., Ltd. received a grant from NEDO (New Energy and Industrial Technology Development Organization) to begin work on the development of the DMRV (another name for GNE Myopathy, in Japan) therapeutic agent for practical use. This has led to the current studies that are taking place at Ultragenyx Pharmaceutical Inc. and Nobelphama Co., Ltd. In the midst of these activities, we were also able to make our presence known on a wider and broader scale, thanks to our cause being covered in the media. We were happy that pharmaceutical companies have shown an interest in potentially producing a medicine for GNE myopathy, but this is just the first step of many.

Activity

At present there are 300 patients in Japan diagnosed with GNE myopathy. Our disease is an orphan disease, meaning that there are only a few people in the world affected and research in this are a is very complicated and expensive. As patients, we felt that we had to do something to change the situation, at least about distal myopathy. Aside from collecting signatures from the public to support our cause, we also held symposiums, meetings and round-table conferences. Since April 2008 we have been campaigning and in May 2014, we reached 2.04 million signatures. This signed petition was delivered to several incumbent Ministers of Health, Labour and Welfare Ministry here in Japan. As a result of this, distal myopathy has been registered as a designated rare disease in 2015 in Japan. PADM is supporting clinical research and treatment development. We are working hard to make a difference in the area and welcome collaboration with other groups and organizations because together we are stronger and can find a cure.

Yuriko Oda - My Journey So Far - continued

Google Global Impact Challenge

PADM received the grand prize at the Google Impact Challenge held in 2015, the objective of which is to reward entrepreneurial teams with an idea to change the world and a healthy disregard for the impossible. I also participated at the 6th Global Entrepreneurship Summit in Kenya last year, an event at which President Obama was in attendance.

Progress

4.5 centimeters or 1.8 inches - Do you know what these numbers mean? This is the height of a step that I am unable to go over by myself when I am traveling in my wheelchair. 10 years ago when I was a healthy person, I never imagined that I would someday have to deal with the inconvenience of being in a wheelchair. In Japan alone, there are over 2 million wheelchair users and in many of these cases, these people that are essentially confined to their homes due to a lack of wheelchair accessibility in the outside world. Even within their homes, many are confined to an even smaller living area. A trip to an unknown place requires a great deal of research, careful planning, and above all, courage. One of the ways of dealing with this problem is to create an interactive map that will allow wheelchair user to clearly see accessibility in public spaces. It will allow us to share our experiences and create a virtual guidepost by which we can explore the outside world. It is useful and practical detailed information for the wheelchair users, mothers with babies, walker users and the elderly.

My husband and I, at my University in 2015 for a photoshoot for my second book

Almost all of these people cannot go outside on their own. We wish to collaborate with a diverse group of people all over the world who would like to create the better world. Please support the Barrier Free Map Project (www.b-free.org/english/), It will remove obstacles for us both big and small. We were broadcasted on a series "Women of Vision", of the NHK World. The video is in English. 4.5 centimeters may not sound like a big deal to you, but it means the world to wheelchair users.

With Dr Emil Kakkis, Chief Executive Officer and President of Ultragenyx and PADM members in Tokyo. 2014

Next Steps

We at PADM wish to overcome our difficulties and disabilities not only for GNE myopathy patients, but also for all other kinds of patients. We will continue our activities and are fortunate enough to have already achieved some of our goals. If we (the patients) were able to take the medicine, I think it will be hopeful for not only DMRV, but also for other rare diseases and all people who have disease. Medical specialists are making remarkable advance and researchers will work out the treatment. As we strongly believe that we can change the system for rare disease, we urge implementation of activities that could foster awareness and scientific breakthrough. On our part, we will remain vigilant in our effort to change the medical system and the laws that govern it, in a hope that this movement will last like a flowing river. We strongly expect that scientists will help us have treatment soon, and hopefully it will help us overcome our disease.

With the president of Nobelpharma. Mr Shiomura, his colleagues, Dr. Nishino and some PADM members

Feeling

I was diagnosed with GNE myopathy when I was 22 years old. It was a devastating news but I have learned to have a positive perspective, living my life to the fullest and staying happy because I can do so many activities. It is sometimes hard to live my life in an electric wheelchair. My muscles are becoming weaker and weaker. Now, I can't move without a powered wheelchair. I am determined that I will challenge all things with a conviction that the people who are happy can live a life to contribute oneself to others. I joined the TREAT-NMD Executive Committee because I strongly believe that by working together we can help to promote and support new treatment development that will benefit patients in the neuromuscular community.

Thank you for taking the time to read my story.

Yuriko, Yoichi and Eiichi.

With my family at my friend's wedding party. 2013

If you would like to share your story in the next edition of the GNEM-DMP newsletter, please contact the registry curator at HIBM@treat-nmd.eu