7th ICORD/ICORD2012

(International Conference for Rare Diseases and Orphan Drugs)

- C3 : Connection and Collaboration, for Creation-

Report

7th ICORD International Conference for Rare and Intractable Diseases and Orphan Drugs - C3 : Connection and Collaboration, for Creation-
Report

Summary

Name of Academic Conference:	ICORD (International Conference for Rare Diseases and Orphan Drugs)
Date and time:	February 4 (Saturday), 5 (Sunday) and 6 (Monday), 2012 (Pre-meeting on February 3) (Postponed from the originally scheduled May 21-23, 2012 due to the earthquake)
Venue:	Convention Hall, Komaba Research Campus, University of Tokyo 4-6-1 Komaba, Meguro-ku, Tokyo
Hosts:	ICORD (International Conference for Rare Diseases and Orphan Drugs) Promotion of Research on IP (PRIP Tokyo, non-profit organization)
Conference Chair:	Ichiro Kanazawa (Former Chair of the Science Council of Japan, President of the Graduate School of International University of Health and Welfare)
Cosponsor:	Tokyo University Research Center for Advance Science and Technology
Sponsors:	Ministry of Health, Labour and Welfare, National Institute of Public Health, Pharmaceuticals and Medical Devices Agency (Incorporated Administrative Agency), Nationwide Network to Support Children with Intractable Diseases, Japan Pharmaceutical Manufacturers Association, Japan Patients Association
Cosponsors:	GlaxoSmithKline, KK, Genzyme Corporation, Shire Pharmaceuticals, BioMarin Pharmaceutical Inc., Pfizer Japan Inc.
Donations:	Astellas Pharma Inc., Eisai Co., Ltd., Takeda Pharmaceutical Company Limited

Assistance (in order of the Japanese syllabary):	Uehara Memorial Life Science Foundation (Public Interest Corporation), Kato Memorial Bioscience Foundation(Public Interest Corporation), Takeshi Nagao Intractable Diseases Research Foundation (charitable trust), Terumo Life Science Foundation (charitable foundation), Naito Foundation
Cooperation:	Congress Corporation, JR East Building Co., Ltd.

About ICORD

ICORD is an international forum held to improve health conditions of patients of rare and intractable diseases and their families internationally and regionally. This improvement is accomplished by enhanced knowledge, research, treatment, information, education, and awareness. In the field of rare and intractable diseases, which is the subject of this forum, very few patients have these diseases; therefore, research and drug discovery has tended to be marginalized by society. However, if the total number of these patients with rare and intractable diseases is considered, it is found that they constitute several percent of the population. Therefore, it is now thought that their presence absolutely cannot be ignored. Furthermore, because of progress in basic research of diseases, rare and intractable diseases are being further subdivided into disease categories that contain even fewer patients. This is because these rare and intractable diseases share a common pathophysiology with so-called “common diseases” that affect many patients, and because a new, pathogenesis-based concept of common diseases themselves is being advocated. More than ever, it is has become necessary to regard rare and intractable diseases as a global medical problem. Amidst these changes in circumstances, the current situation is that in various countries there is more demand than ever for cooperation and sharing of information about conditions, research, and policies.

In this international forum, relevant parties from all points of view related to rare and intractable diseases participate not only in forum venues, but also globally. These parties include basic and clinical researchers, physicians, people involved in clinical studies and development, patients, people involved with patients, and people involved in legislation and public offices. Thus, comprehensive, international information-sharing, and discussion in this field can also be simultaneously implemented. In the past, this symposium has promoted research, ethics, policy, and action plans related to patients with rare and intractable diseases and to orphan drugs. It has also promoted smooth communication and discussion among all relevant parties

involved with rare and intractable diseases and with orphan drugs and has resulted in formation of consensus opinions on these issues. This international forum promotes international discussions on orphan drugs and rare intractable diseases, and also promotes collaboration and coordination related to research-linked discovery of therapeutic drugs and connected to policy choices. Furthermore, by sharing of best practices related to rare diseases and orphan drugs, the forum is developing international approaches and tools connected to common problems in this field.

History of ICORD 2012

In the past, the forum has been held in Stockholm, Madrid, Brussels, Washington, Rome, and Buenos Aires, but this time it will be held in Asia for the first time. International cooperation in this area so far has occurred almost entirely in Europe and North America. Until now, hardly any information has been shared about conditions in Asia, including in Japan. However, in previous forums it became clear that the forum participants wanted to collaborate and share information about conditions in Asia, including Japan. Furthermore, the relevant parties in Japan also understood the necessity of collaboration and understanding of current international affairs related to rare and intractable diseases at ICORD, and they understood the significance of sharing information about the situation in Japan with the world. Therefore, in response to the ICORD council, ICORD 2012 will be held in Japan to more widely share information about these issues in Asia and Japan and to significantly change course toward international collaboration. By holding the next symposium in Japan, it will be possible to begin international cooperation in the true sense, with Asia added to the present stage. Although the forum was scheduled to be held in May 2011, it was postponed due to the consequences of the Great East Japan Earthquake that occurred on March 11.

Achievements of ICORD 2012

A total of 268 participants, the largest number in history, from 21 countries (China, Taiwan, Korea, Hong Kong, Singapore, America, Canada, Australia, New Zealand, Argentina, Brazil, Belgium, Sweden, Bulgaria, the United Kingdom, Spain, France, Russia, Italy, and Nigeria) participated in ICORD2012. About 143 of the participants were Japanese, and about half were foreign participants. It was a lineup that could truly be called an international conference. In terms of applicant affiliations as well, all of the “relevant parties of all points of view related to rare and intractable diseases” anticipated by ICORD were present: businesses (pharmaceutical), universities, research institutes, patients' associations, governments, hospitals, foundations, NPOs,

and businesses (other).

All lectures were given by invited speakers, and the content of all of these lectures was of high quality. The forum aimed to address all topics related to rare and intractable diseases. Therefore, it covered a wide range of topics related to support of drug discovery, from presentations of basic research to presentations on national policies on regulations. In particular, in the sessions by patients' associations, 11 leaders of patients' associations from various countries around the world gathered and contributed significantly to international collaboration by describing their own experiences and the histories of their associations. Not only was this a very valuable opportunity to have discussions with various relevant parties from abroad while in Japan, but it also revealed once again the high level of interest in Japan. For example, personnel involved in Japanese patients' associations received a barrage of questions from foreign participants.

A total of 53 posters were collected from Japan and abroad. Many of these posters were announcements from university personnel, and enthusiastic exchanges of opinions occurred at the poster session. A total of 5 "selected posters" were introduced at the forum.

Below, the contents of the forum are reported for each session.

Pre meeting:

On the day before the forum, several meetings were established as Pre-Meetings. First, with the title "How Patient Advocacy Groups Promote Rare Disease Research and Development in a Proactive Way," the venue for opinion exchange was decided under the leadership of researchers. A Professional Meeting was also held for 1) regulatory authorities and 2) leaders of patients' associations. In both meetings, substantial exchanges of opinion occurred that were truly expert in nature. Finally, in the Asian meeting, participants from China, Korea, Taiwan and Japan gathered, gave presentations and exchanged opinions about Asian affairs.

Welcome Address :

The first information session of ICORD 2012 included greetings by organizer and PRIP Tokyo President Junji Annen, Chair Ichiro Kanazawa, and ICORD Chair Domenica Taruscio. Chair Kanazawa described the history of Japanese measures against intractable diseases and described current problems and future prospects. Chair Taruscio described the history of past ICORD forums and expressed his expectations for future forums.

Session 1:

Successful example of clinical research in Rare Diseases

In this session, to share experience and know-how of past clinical successes for specific diseases and apply them to other diseases, 4 speakers introduced examples of successful development of therapeutic drugs, diagnosis approaches for rare diseases.

Using a case of a disease called familial hemophagocytic lymphohistiocytosis (FHL) as an example, Jan-Inge Henter (Professor, Dept of Women's and Children's Health, Karolinska Institute, Sweden) described an example of a success related to an international cooperative clinical study that was tied to everything from creation of diagnostic guidelines to establishment of treatment protocols for FHL, for which there had been no clear diagnostic approaches or treatment methods. Furthermore, Jan-Inge Henter mentioned that clinical research on rare diseases is also tied to other diseases which affect many patients, and he mentioned the importance of international clinical studies and patient-organized research conferences. Eiichi Ishii (Professor, Department of Pediatrics, Ehime University Graduate School of Medicine, Japan) described a specific example of the establishment of diagnostic approaches and methods for judging pathological conditions of HLH (EBV-HLH), which is caused by the EB virus. He also mentioned that the relationship between physicians, patients and researchers is an essential element for promotion of clinical research. Emilio Roldán (Geiser Foundation and Gador SA, Argentina) described re-profiling of existing drugs that have already been approved, citing osteogenesis imperfecta as an example. He also stated that collaboration between industry, government, academia and patients is essential for development of therapeutic drugs for rare diseases, and that it is important to build a win-win strategy from the perspective of each of these stakeholders. He also emphasized the efficacy of re-profiling existing drugs as one such strategy. Furthermore, he stated that for development of drugs for rare diseases it is necessary for patients to stay actively and vigorously involved in clinical trials. The last speaker, Stefaan van Gool (Professor, Pediatric Hemato-Oncology and Neuro-Oncology, University Hospital Gasthuisberg, Belgium) described the development of immunotherapy using dendritic cells for malignant glioma, which affects a small number of patients. He emphasized that behind the development of this immunotherapy lay advances in basic biology in academia, from the discovery of dendritic cells to the elucidation of the body's immune system. Furthermore, he stated that all rare disease with no effective treatment should be subjects of research in academia.

In this session, the importance of active involvement of the patients themselves in

clinical research was mentioned repeatedly. Furthermore, throughout the entire session, the key words “importance of clinical research and basic research” left a lasting impression. Even research that seems irrelevant to treatment contributes to the progress of biology and may potentially benefit patients in the future. Furthermore, ICORD seemed to play a significant role as a venue that connected patients, physicians and researchers.

Session 2

Access to and Reimbursement for Diagnosis and Therapy

In this session, access (medical systems) to diagnosis and treatment and reimbursement (social security systems) in each country were introduced, and problems facing patients of rare and intractable diseases and their families were addressed.

Jack Goldblatt (Director Genetic Services & Familial Cancer Program of Western Australia, Clinical Professor, School of Paediatrics and Child Health, University of Western Australia, Australia) described the past history, conditions, and problems with national programs for orphan drug therapy for Gaucher's disease in Australia. An advisory committee has reviewed implementation of enzyme replacement therapy and treatment using this therapy for Gaucher's disease in accordance with a unified program. Furthermore, a patient registry is being developed. Harrie Seeverens (Ministry of Health-The Netherlands, Netherland) described the current state of access to orphan drugs and treatment and reimbursement in the Netherlands. In the Netherlands, reimbursement for orphan drugs has been limited to university hospitals since January 2012 to maintain quality of medical care while aiming for shared and equal access. Howard Yuwen (Senior Director Regulatory Affairs, Shire, USA) described the current state of early access to treatment of rare and intractable diseases in the United States. Out of 7,000 rare diseases, orphan drugs have been developed for only 370 diseases, or 5%. Under these circumstances, many patients need early access to treatment. As long as the safety of patients and ongoing clinical trials is not compromised, the FDA supports early access. Stefaan Van Gool (Professor, Pediatric Hemato-oncology and Neuro-oncology, University Hospital Gasthuisberg, Belgium) described the obstacles, problems, threats and challenges of vaccine therapy for brain tumors. Development of advanced-therapy medicinal products for rare diseases has progressed, mainly in academia, but regulatory and administrative barriers have inhibited its development. He complained that it is difficult to develop new drugs because regulations are strict, and even when approval is obtained from patients, permission is not obtained from the concerned authorities. Tomoko Kodama described

access (medical system) to diagnosis and treatment and reimbursement (social security system) in Japan. Measures for intractable diseases as administrative policies of Japan began as the Outline for Measures against Intractable Diseases, established in 1972. Today, clinical research is being conducted for 130 diseases and encouraged for 214 diseases (since 2010), and 10.4 billion yen in research funding has been contributed. In accordance with the Research Project for the Treatment of Special Chronic Diseases, state, prefectural and city government are subsidizing part of the self-pay cost of health-insurance treatment for patients with 56 of these 130 diseases as a public expense.

Throughout the entire session, access (medical systems) to diagnosis and treatment and reimbursement (social security system) in each country were described, and problems facing patients of rare and intractable diseases and their families were highlighted. Furthermore, a panel discussion was held on systems of patient registration for clinical trials, and it was concluded that the problems of rare diseases are not only problems of rare diseases.

Session 3:

Regulatory Aspects of Orphan Drugs

In this session, initiatives by each regulatory authority (Japan, the U.S. and Europe) regarding measures for promotion of research and development of orphan drugs were discussed, and then awareness of the current situation and expectations for the future for businesses were described.

Kenichi Tamiya (Deputy Director, Research and Development Division, Health Policy Bureau, MHLW, Japan) gave a lecture on initiatives related to orphan drugs in Japan. To promote development, the Ministry of Health, Labour and Welfare Pharmaceutical and Food Safety Bureau Evaluation and Licensing Division (in collaboration with the pharmaceuticals and Medical Devices Agency) plays a major role in “review and approval,” the Health Policy Bureau Research and Development Division of the same ministry (in collaboration with the National Institute of Biomedical Innovation) plays a major role in “research and development promotion and grants,” and the Health Service Bureau Disease Control Division of the same ministry plays a major role in “measures against rare diseases.” For a drug to be designated as an orphan drug under the Pharmaceutical Affairs Law, it must treat a disease that affects fewer than 50,000 patients, there must be a strong need for medical treatment, and the drug must have a high probability of being developed. Incentives for advancing research and development include pre-application consultations, funding for research and development, tax

deductions for research and development, priority reviews, cost reduction of application and consultation, and extensions of re-examination periods. Since 1993, 261 products have been designated as orphan, and 165 products have been approved. As examples of recent endeavors to contribute to promotion of research and development, a meeting was held to address unapproved drugs and drugs for off-label use that were necessary for medical treatment (374 development needs were evaluated), and development of new drugs was accelerated by a premium to promote the development of new drugs and eliminate off-label use. In the future, the focus will be on bridging the gap between basic research and clinical development, including promotion of development of "ultra" orphan drugs. Saint Raymond Agnes (Head of Human Medicines Special Areas, European Medicines Agency, UK) spoke about initiatives for orphan drugs in the EU. Evaluation and monitoring of drugs are carried out at the European Medicines Agency (EMA), and when drugs are designated as orphan drugs, recommendations are made by the Committee for Orphan Medicinal Products (COMP), which consists of representatives from 27 countries. The criteria for orphan designation is that the disease has an incidence rate of less than 5 per 10,000 people, is severe and does not have effective treatment. Incentives for promoting research and development include cost reduction or exemption and 10 years of market exclusivity (and a 2 year extension if pediatric applications are added). About 6,000,000 Euros in grants were awarded in the EU in one year (2011), and a large percent (66%) of these consisted of support for creation of protocols. The rate of successful orphan designations was about 70%, and cancer was the largest therapeutic area (39%), followed by musculoskeletal and nerve disorders (17%) (2011). Various initiatives are being implemented to improve the transparency of orphan designation and to make operations for orphan designation more efficient. In Europe and North America, the same application forms can be used in all countries, and information is exchanged closely in post-approval safety monitoring. Debra Lewis (Acting Director, Office of Orphan Products Development, Food Drug Administration, USA) spoke about initiatives for orphan drugs in the U.S. The Orphan Drug Act was put into effect in 1983, and the OOPD of the FDA plays an important role in orphan designation. The definition of "rare" is that there are fewer than 200,000 patients, and it is estimated that there are about 7,000 diseases and about 30,000,000 patients. Incentives for promoting research and development include 7 years of market exclusivity, tax deductions for clinical research, and exemption from the Prescription Drug User Fee Act (PDUFA). Since the legislation of the Orphan Drug Act, applications for orphan designation have been submitted for at least 3660 products, at least 2550 of these products have been designated as orphan drugs, and at least 396 of these products

have been approved. In addition, about 1/3 of novel compounds are orphan drugs, with cancer being the largest therapeutic area (36%), followed by metabolic disorders (11%). A new 10 to 15-year grant has been implemented that covers HUDs, which are used by less than 40,000 patients per year in the US. Many workshops are held for coalition-building. Patient Advocacy Day is scheduled to be held this year in March, and Natural History of Rare Diseases is scheduled to be held in May. Lewis mentioned that ongoing collaboration always encourages aggressive action. Marc Dunoyer (Global head, GSK Rare Disease, UK) talked about awareness of the problems of development of orphan drugs from the perspective of businesses. The current situation is that the environment has changed greatly due to the introduction of regulations related to orphan drugs, but the number of approvals is not increasing. To accelerate approval, 1) harmonization of international regulations, 2) an advanced approval system, and 3) increased mutual dialog will be important in the future. As an international examination system, a collaborative approach is more desirable than a parallel approach, and mutual authentication and consistency of requests are desired. Furthermore, to achieve early access to new drugs, a risk-based approach is necessary, and patient advocacy groups and physicians play an important role in this approach. Dialog between sponsors, regulatory authorities and patient advocacy groups are also indispensable in the search for the best approaches for clinical development and patient access. Improvement of political support for government regulation and improvement of reimbursement systems leads to promotion of patient access. Marc Dunoyer mentioned that harmonization of new regulations should be developed such that patients with rare diseases can receive more effective and earlier treatment.

Session 4:

Regional Pan-Pacific session - providing access to knowledge and collaboration-

In this session, examples such as support systems for patients with rare diseases in Asian countries were described. Wang Cheng-guang (Professor, Tsinghua University, China) described the differences between developing and developed countries regarding measures against rare diseases, and presented 5 principles of legislation. Furthermore, as an actual example, he described how these endeavors are already making progress in regions of Shanghai. Naoko Yamamoto (Director, Disease Control Division, Ministry of Health, Labour and Welfare, Japan) described problems that are being recognized regarding measures against intractable diseases in Japan, and she described research-support projects that are now being implemented. Furthermore, she said that in view of the current situation in which it is difficult to designate new intractable

diseases, a new framework is being considered. She also explained specific problems such as the gap between basic and clinical research in Japan. Cherng-Tay James Hsueh explained that Taiwan's system was the first system to consider prevention, and he explained its role in the insurance system. He also described a database for intractable diseases and a drug logistics center. Hyun-Young Park described an example in which information was translated and entered into a database so that it would be available to the English-speaking world.. Park also described a project to create a database of genetic mutations so that new knowledge can be shared by many people. During a question-and-answer session, in response to the question "What incentives do governments have to support measures against intractable diseases?" it was recognized that such measures should be regarded as a form of social security. Furthermore, in response to the question "Should intractable diseases and genetic diseases be treated as synonymous?" it was reported that this was essentially the case in a specific example in China. Although knowledge tends to advance in Europe and North America, in this session the sharing of information among Asian countries with similar genetic backgrounds is valuable and important for determining whether this advanced knowledge can also be applied to Asia.

Session 5

Patient groups - their connection and needs

In this session, efforts by overseas patient advocacy groups to address rare and intractable diseases were described.

Citing examples, John Forman (Executive Director, NZORD (New Zealand Organization for Rare Disorders), New Zealand) asserted that to solve various problems caused by the conditions surrounding patients and their families, it is first important to focus on these patients and their families. He emphasized the importance of building good relationships with the environments surrounding patient advocacy groups and patients. Tim Cote (Chief Medical Officer, National Organization for Rare Disorders, USA) described enterprising actions to solve problems related to regulatory authorities, research fields, and patient registries in order to promote development of drugs for rare diseases. He emphasized that the most important thing is to build relationships between patient advocacy groups and each organization. As a patient, Tateo Ito (President, Japan Patients Association, Japan) introduced the activities of patient advocacy groups in Japan. This was the first time that a patient gave a presentation at ICORD. Further, Ito mentioned that to promote research and development in the fields of rare diseases, patients were actively involved not only within patients' associations

but also in national projects for the establishment of registries of medical staff, researchers, and patients. Yann Le Camm (President, EURORDIS, France) described how the voices of patients have been brought forward through various actions by EURORDIS. He explained that as a result, intractable diseases have become the top priority of EU measures against rare diseases, and 2 important policies related to intractable diseases have been formulated in recent years. He mentioned that a future aim is to increase awareness of rare and intractable diseases as an international issue and to make them a priority for public health. Showing a 15-minute video, Min−Chen Tseng (President, Taiwan Foundation for Rare Disorders, Taiwan) described TFRD, a group of associations of patients with intractable diseases that was founded in 2000, and described the group's efforts to tackle a wide range of rare and intractable diseases.

Tania Levy (representative, former President, Brazilian Gaucher patient association, Brazil) described how methods for Disease Control and Prevention were developed through the activities of a Gaucher's disease patient advocacy group that she founded. She also gave examples of coalitions among Gaucher's disease patient advocacy groups in various regions throughout her country and emphasized the importance of solidarity among patients with rare diseases. Svetlana Karimova (National Association of Organization of Patients with Rare Diseases Genetics, Russia) reported that councils in Russia are carrying out various educational activities about rare and genetic diseases. In particular, she mentioned the importance of active promotion of cooperation among the media, the government, the EU, and Asia in Rare Disease Day activities, and the importance of spreading these activities abroad. Sharon Terry (President, Genetic Alliance, USA) pointed out problems facing coalitions of patient advocacy groups and recommended measures to solve them. She also stressed that it is important for patient advocacy groups to have access to government and information about disease research. Vladimir Tomov (National Alliance of People with Rare Diseases, Bulgaria) described vigorous activities carried out by the groups shortly after they were formed. He emphasized the importance of government-affiliated assistance, legislation, and support for patients. Hyon J. Kim (Chairman, Korean Foundation for Rare Disease, Korea) talked about domestic patient advocacy groups and described real examples of assistance for patient advocacy groups from a physician's perspective.

Throughout the entire session, many of the histories of national patient advocacy groups were about how they were formed because patients' families plead for assistance. These stories about the experiences of these groups from the time of their founding were beneficial information for many patient advocacy groups and supporters. Furthermore, overseas exchange of disease information and support information on a global scale as

seen in this session is sure to further accelerate support for patients with rare and intractable diseases. On the other hand, if appropriate information is not exchanged and organized among patients, governments, researchers and pharmaceutical companies, there is a danger that differences in information and access to information about patient support may arise.

Many participants held the opinion that building multiple networks (from lines to networks) from various perspectives, actively building good relationships between patient advocacy groups and governments, research institutes, businesses and local societies, and collaborating on a global scale lead to promotion of development of orphan drugs.

Session 6:
Supporting Product Development and Venture Capital

In this session, efforts and opinions were described from the perspectives of the players and supporters involved in how to promote action, from research to the market, in order to satisfy unmet medical needs.

Segolene Ayme (Emeritus director of research, Orphanet, France) introduced Orphanet. Orphanet is a database that enables reference and retrieval of a wide variety of information about rare and intractable diseases. Information for patients can be searched by drug generic name, drug trade names, the Anatomical Therapeutic Chemical Classification System (ATC categories), disease name, and (drug) marketing authorization holder. Clinical trial information can also be searched by disease name, gene name, drug information, research institute, authority name, or clinical-trial category. For researchers and pharmaceutical companies, naturally, information from dissertations can o be searched, as well as information about market size, morbidity prevalence rates, pathogenesis, and the like. Mechanism-based annotations, symptoms states, regional information and the like have also been added to the database. Soon Japanese and Chinese languages will be supported, and cooperation is needed for further language diversification. Jin Shiomura (CEO, Nobelpharma Company Ltd., Japan) described the portfolio of Nobelpharma and described challenges from the perspective of representatives from pharmaceutical companies. Drugs in the Nobelpharma portfolio include drugs for which development was promoted by support from patients' associations, drugs for which development depended on financial support from government-funded organizations (NIBIO), and drugs that had been pulled from the development process of a leading company (Pfizer) for some reason and for which a license was purchased. Drug discovery for rare and intractable diseases can be

promoted not only by research and development by independent companies, but also by involvement of various stakeholders such as patients and other businesses. In Japan, the inadequacy of budgets for conducting clinical trials for rare diseases (about 1/10 to 1/100 of the budget in America) is a problem. There is a public opinion that government support of specific businesses is malicious. However, for drug development for diseases affecting few patients and having an unknown market after being launched, development is difficult without government support. Shiomura concluded by saying that public understanding is necessary for this reason as well. Charles Cho (Palo Alto investors, USA) explained the perspectives of investors in the market of orphan drugs. Orphan drugs are now an attractive market for investors in various ways: their pricing can be set, there are no similar products, they are truly valuable to patients and are beneficial to society, exclusive marketing rights can be obtained by patenting them, there is no competition, and their unmet needs are large. Orphan drugs are also attracting attention from major pharmaceutical companies as a source of future revenue after blockbuster-drug patents expire. There are now many diseases for which only symptomatic treatment is available, but diagnostics and therapeutic drugs will probably become focus areas in the future. Charles Cho said that early detection and treatment for patients has great social significance, and that an exclusivity period of 7 years is sufficient even for recovery of investment in development. (Companies that obtain approval from the FDA for the first time for drugs for intractable diseases obtain exclusive marketing rights for 7 years.) Ron Bartek (President, Friedreich's Ataxia Research Foundation, USA) described Friedreich's Ataxia (FA) and described know-how that was gained over a period of 13 years at a foundation for research on FA. Mitochondrial dysfunction is an important cause of FA. Because many other diseases involve mitochondrial dysfunction, FA therapeutic drugs that have entered a late clinical stage of the development process are also being tested for other diseases. FARA not only collects patient information and provides infrastructure development and research funding, but also provides cells, including iPS cells. FARA also plans to develop biomarkers. To vitalize the market for orphan drugs, it is also necessary to focus on diseases for which results can easily be obtained relative to investment, and if this goal is achieved, pharmaceutical companies will also be interested. For development of basic drug-discovery research, drugs that are close to being marketed are focused on. FARA has been successful because it has opportunely matched researchers, governmental organizations and patient advocacy groups. Bartek also emphasized that cooperation with FARA can save time and money for pharmaceutical companies.

Session 7:

International Health Policies for Rare Diseases and Orphan Drugs

International Health Policy Related to Rare Diseases and Orphan Drugs

In this session, national circumstances surrounding rare diseases were described from the perspectives of organizations that carry out policies in the EU, the US, China, South America, Italy, and Australia.

Stefan Schreck (Head of the Health Information Unit in DG SANCO, European Commission) described policy recommendations and organizations for rare diseases in the EU, which comprises 27 member states. He stressed the importance of eliminating boundaries between member states, protecting the rights of patients to choose the country where they will receive treatment, and forming networks among research centers. Marcelo Cheresky (Vice President, Rare Diseases JAPAC & LATAM Regions, Genzyme Corp., USA) described the change in the number of approvals of orphan drugs from the past to the present (from fewer than 10 before 2000 to almost 400 in America and almost 70 in the EU in 2011). He also emphasized the importance of early diagnosis, delaying onset, and proper treatment of the diseases. Steve Groft (Director, Office of Rare Diseases, NIH, USA) described examples of efforts by the NIH to promote research on rare diseases, and described a goal to establish 200 treatment methods and diagnostic approaches for many rare diseases by 2020. He also talked about a growing interest in rare diseases and orphan drugs and stressed the importance of collaborative research, including among countries. Duan Ma (Professor, Shanghai Medical College, Fudan University, China) described examples of pioneering activities carried out in Shanghai to tackle rare diseases. He also talked about the growing interest in rare diseases, about China's own definition of rare disease, and about the "Rare, But Fare!" movement related to rare diseases and human rights. His lecture suggested that Shanghai is important for rare diseases in China. Virgina Llera (President, GEISER Foundation, Argentina) explained her conclusions about collaboration among organizations for rare diseases. She described examples of changes in the structures of organizations (at international, national and local levels) before and after ICORD in South America and the how these changes relate to results. Because advantages vary depending on the structure of each organization, a lasting effect can be expected by combining international efforts with activities at the local level. Domenica Taruscio (President of ICORD / Director National Centre for Rare Diseases, Istituto Superiore di Sanità, Italy) described the circumstances surrounding rare diseases in Italy, gave examples of international collaborative activities of the National Centre for Rare Diseases (*Centro Nazionale Malattie Rare,* CNMR), and emphasized their importance.

He also touched on EUROPLAN and talked about the importance of building resources and networks in clinical and research fields as well as sustainable planning and improving patient status. Hugh Dawkins (A/Director, Office of Population Health Genomics Public Health Division, Health Department of Western Australia) described examples of awareness and policies regarding the actual situation of rare diseases in his country. He emphasized that much support has been received from the community, including from ICORD, and he stressed the importance of human networks.

Session 8:

The value of and promotion of basic research in RD -The future for international research collaboration-

In this session, expert opinions were expressed about international cooperation in basic research that is necessary for promotion of research. Yoshikatsu Eto (Professor and Director, Department of Genetics & Genome Science,, Tokyo Jikei University School of Medicine, Japan) presented an overview of lysosomal storage diseases. Lysosomal storage diseases are caused by accumulation of sugar in the body, and among these diseases, Fabry's disease affects the largest number of patients, followed by Pompe disease and Gaucher's disease. He also described mechanisms, symptoms, and treatment methods, and focused particularly on enzyme replacement therapy for Fabry's disease. He described the advantages and disadvantages of enzyme replacement therapy and compared it to new treatment methods. In particular, he emphasized that international cooperation is necessary for treatments using iPS cells, which have been the focus of attention in recent years. Kenji Hayashi (President, National Institute of Public Health, Japan) focused on rare diseases and grant subsidies. He said that subsidies have been granted for 56 rare diseases that affect 700,000 patients. He said that the challenge is to increase awareness about treatment policies for ulcerative colitis, systemic lupus erythematosus, and Parkinson's disease, all of which affect many patients. On the other hand, he mentioned the necessity of clinical studies for diseases that affect few patients, and he emphasized the need for international cooperation. Steve Groft (Director, Office of Rare Diseases, NIH, USA) spoke about the initiative of the NIH in supporting translational science (hereafter referred to as TS). He said that the NIH established the National Center for Advancing Translational Sciences, cooperated with businesses, and is working on ways to quickly take new drugs to the phase-2 stage of clinical trials. In addition, he mentioned that the NIH has launched a program for treatment of rare and neglected diseases and is working on increasing the speed of development of new drugs. Yann le Com (Executive Director, EURORDIS,

France) provided an overview of EURORDIS and described its mission. He explained that over the past 10 years, EURORDIS has consolidated various regulatory environments and is aiming to consolidate policy environments, and that research will be directed toward treatment for the next 10 years. He also mentioned that EURORDIS has established an international consortium for research on rare diseases that is tying development of treatment methods for rare diseases to researchers, investors, and other stakeholders. The session gave a keen sense that government-led, new drug development projects focusing on rare diseases are necessary in Japan as well.

Session 9:

It's All about the Patients

All for the benefit of patients, this entire session was about activities by families of patients with cystic fibrosis, establishment of advocacy groups for patients with rare and intractable diseases, activities of patient's associations, and global development of therapeutic drugs for patients with rare diseases.

Yann Le Cam (Executive Director, EURORDIS, France) spoke about his 20 years with his family and daughter who developed cystic fibrosis. She was diagnosed with cystic fibrosis at a children's hospital in Paris, received treatment at the CF clinic at John Hopkins University Hospital, and development of an orphan drug was started with the help of NORD and Genetic Alliance. A center for medical specialists was formed for treatment of cystic fibrosis. Physicians and then patients need to take action. Because there were few patients, international cooperation was also promoted. Depending on the case, diagnosis can sometimes be made earlier when the patient was examined overseas. Le Cam's daughter is now 21 years old and is studying law. A major theme for the future will be how patients can live independently. Mark Krueger (Mark Krueger and Associates, USA) described the establishment of an advocacy group for patients with rare and intractable diseases. He said that the patient advocacy groups carry out 1) patient support, 2) education and information-sharing, and 3) political activities, and he talked about the life cycles and advocacy of patient advocacy groups. Patients with rare diseases must work hand-in-hand, and therefore they need to share information. To this end, patient advocacy groups must first be established. However, he said that patient advocacy groups must also form treatment policy through lobbying and the like. Regarding patient's associations, Barbara Wuebbels（Director Global Patient Advocacy Programs, BioMarin Pharmaceuticals, USA）posed the questions "Who are patient's associations? What are patient advocacy groups? Where are these patient advocacy groups? When do these patient advocacy groups carry out activities? Patients should be

involved in orphan drug development from the beginning. She argued for the need to improve advocacy skills among patient's societies, and she described a summer program offered by EURRODIS. Ginny Beakes Read (Executive Director, Global Regulatory Policy and Intelligence, Eisai, Inc, USA/Japan) spoke about global development of therapeutic drugs for rare diseases. A program for the Orphan Drug Act initiated in America in 1980 was a success. Subsequent to this success, the orphan drug development program spread to various countries and became global. Read described the orphan drug development programs of the following countries: America, Japan, Europe, Australia, Thailand, Taiwan, Korea, Columbia, Mexico, Argentina, Ecuador, Peru, Panama, Brazil and Russia.

Throughout the entire session, the focus was on "all for the benefit of patients": activities of the patients, their families, and patient advocacy groups, and about global development of drugs to treat rare and intractable diseases. In a panel discussion, opinions were exchanged about new technologies for development and clinical trials of therapeutic drugs for rare diseases, for genome sequencing, and for social networking.

Final Discussion:

Discussion / Workshop Summary / ICORD Position statement / Closing

In this closing session, the discussions of each group during the workshops were summarized, the entire conference was summarized, the participants were thanked, and preparations for the next conference were discussed.

John Forman (Board of ICORD, New Zealand) delivered a position statement for ICORD. The purpose of creating ICORD's Position Statement is to describe not what is happening, but what is not happening with regard to rare diseases, and to make this statement be the framework for legislation on rare diseases. Some people will ask, "If achieving this objective is difficult in developed countries, won't it be even more so in poor countries?" and "Why should patients of rare diseases get special treatment?" However, we believe that the government has obligations regarding human rights and that all people need to receive proper medical care. The Position Statement lists 6 principles and 12 guidance points and explains what governments should consider when legislating. The name of the statement is "The Yukiwariso Declaration," in honor of a rare and precious flower in Japan.

During the summary of the working groups, each one reported on what it had discussed. The "Research Collaboration" group concluded with a statement that more researchers need to participate in the planning of ICORD and that toward this end they

will need to participate in research meetings and hold symposiums. The “Obtaining the Diagnosis of Rare Diseases” group thinks that diagnostic accuracy has a great impact on prognosis. It is important to use algorithms and software and also to build a common platform and a network of experts. The group concluded by saying that they thought the most important factor is motivation of physicians. The “Access to Therapy in Countries with or without Orphan Drug Legislation” group mentioned that the issue of reimbursement of insurance premiums is a problem in most countries. The group said that when thinking about reimbursement, it is important to consider whether the insurance is worth the cost. The group also said that although many governments are spending money on rare diseases, they need to reconsider their approach. The group concluded by saying that it is important for policy to be created with consideration of all interests, including government budgets, and that models will be created that will lead to solving problems in the future. The “Bioethics in Rare Diseases” group focused their discussion on informed consent (IF). The group concluded by saying that although IF is necessary when patients are used as subjects for research, implementation of IF can differ among countries, and therefore guidelines need to include standardized IF. The “Diet, Environment and Rare Diseases” group summarized the importance of the patient’s environments, including drug adverse effects, diet, and mother-to-child transmission. The group also mentioned the importance of advanced research.

Next, key members of ICORD, including the current president and the president-elect, delivered messages that summarized the conference and addressed preparation for the next conference. There was also an announcement that the next ICORD will be held next year in Shanghai.

Next, on behalf of the hosts of this conference, Yukiko Nishimura (Chief secretariat of ICORD2012, Japan) described the development of this conference and gave acknowledgements to those involved. She reported that there were 268 participants from 21 countries and that there were 53 posters. She also explained again the slogan of this conference, C^3 (C^3:Connection + Collaboration = Creation). She declared that participants are now at the stage of making connections and that they must work toward the goals of collaboration and creation in the near future.

Finally, on behalf of the hosts of this conference, Li Dingguo (Chair of ICORD2013) delivered a message that, on behalf of the organizers of the next ICORD conference, he would like to cooperate with Japan, Taiwan, and other countries representing Asia and do his best in Shanghai.

After ICORD ended, a town meeting was held as an extra session.

Dealing with the Natural Disasters "Earthquake

In this meeting, panelists were invited from among patients and their support groups who were affected by the Great East Japan Earthquake experienced by Japan on March 11, 2011.

Among the panelists, Akemi Suzuki of the Multiple Sclerosis (MS) Rainbow Association (Miyagi) emphasized that it is necessary for supporters and government to understand the differences among patient needs (assistance after the earthquake, and assistance and preparation for life in temporary housing), which have changed moment to moment from immediately after the earthquake. In response, Koj*i* Mizutani of *the Japan Patient's Association (JPA)* reported from the standpoint of patient support on the difficulties of providing assistance in disaster-stricken areas (the Act on the Protection of Personal Information obstructs confirmation of patient safety, and it is difficult to obtain information about needed supplies*)*, and emphasized the necessity of ties among patient advocacy groups and support groups during normal times. Kenichi Chiba of the Iwate Prefectural Association of Patient Advocacy Groups for Rare Diseases repeatedly emphasized the need for not only physical but also psychological care of patients affected by disasters, and stressed that the earthquake disaster has not ended but is continuing. Yukiko Nishimura of PRIP-Tokyo/University of Tokyo reported that it was difficult to match assistance to the needs of patients in disaster-stricken areas and emphasized the need to continually strive to understand disease and share medical information.

At the venue, about 80 participants from various countries gathered and requested stories about experiences of patient support during the earthquake—stories of which past examples have been few—and called for authentic voices of people who have actually helped patients at the disaster sites. From the venue, after the announcements from the speakers, Segolene Ayme of Orphanet (France) reported that a patient-information card carried by patients with intractable diseases and a national centralized patient information management system are effective. She expressed the opinion that there may need to be legislation that enables such information management and its immediate use during emergencies.

At the end of the meeting, the following consensus opinions were summarized with the agreement of the participants:

- The great earthquake disaster made it clear for the first time that it is necessary to be prepared to assist patients during emergencies.
- Patient support needs have been changing moment by moment since the time of the earthquake disaster.

- To provide assistance that addresses these changes, there needs to be groups that carefully collect information from patients about their needs, such as patient support groups that link patients and supporters (government and business).
- In the future, assistance will be needed that includes not only physical but also psychological care.

Conclusion of ICORD

A subtheme of this conference is "C^3 (C cubed): Connection + Collaboration = Creation" At ICORD 2012, a balanced lineup of officials from around the world gathered and gave high-quality presentations that provided us with knowledge about their situations. There were also many direct meetings, exchanges of opinion, and discussions for the purpose of cooperation. The greatest achievements of this conference were in terms of the "connection" portion mentioned above. To reach the "collaboration" and "creation" stages in the future, in addition to continuing to hold this conference and participate in it, it will be important for all parties (organizations) to collaborate and for there to be a system to support them. In particular, to eliminate feelings of unfairness among patients, it is hoped that cooperative relationships will be developed at the national level.

Finally, we would like to extend our deep gratitude to the officials and staff who have provided generous support to help make this conference possible. Preparation for this conference took about 2 years, partly due to the earthquake, but we assert that the conference would have been impossible without those who made preparations and coordinated without abate in the midst of those hardships.

We sincerely hope that as a result of this conference, research and development in the field of rare and intractable diseases will become increasingly active, and that understanding and cooperation among officials will be promoted domestically and abroad.

ICORD 2012 is not our goal, it is our beginning.

Yukiko Nishimura (*Chief Secretariat, ICORD 2012) is responsible for the content of this report.*