E-IMD Scientific Board: 2018 spokesman's report

Carlo Dionisi-Vici

Bambino Gesù Childrens Research Hospital

Rome - Italy

E-IMD scientific board: current status (2015-2018)

Name	First name	Country	City
Baumgartner	Matthias	Switzerland	Zürich
Schiff*	Manuel	France	Paris
Burlina	Alberto	Italy	Padova
Chakrapani	Anupam	United Kingdom	London
Chapman	Kimberly	USA	Washington DC
Dionisi-Vici**	Carlo	Italy	Rome
Dobbelaere	Dries	France	Lille
Garcia Cazorla	Angeles	Spain	Barcelona
Häberle	Johannes	Switzerland	Zürich
Kölker	Stefan	Germany	Heidelberg
Lund	Allan Meldgaard	Denmark	Copenhagen
Williams	Monique	The Netherlands	Rotterdam

* replaced Peter Burgard; **spokesman's

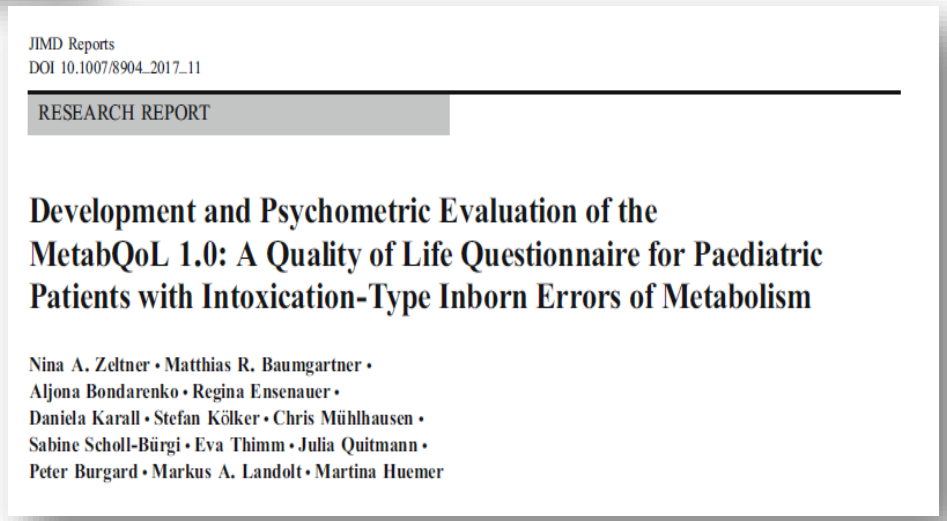
Publications 2017-2018

Journal of Inherited Metabolic Disease
https://doi.org/10.1007/s10545-018-0222-z

ORIGINAL ARTICLE

Transatlantic combined and comparative data analysis of 1095 patients with urea cycle disorders—a successful strategy for clinical research of rare diseases

Roland Posset[1] · Sven F. Garbade[1] · Nikolas Boy[1] · Alberto B. Burlina[2] · Carlo Dionisi-Vici[3] · Dries Dobbelaere[4] · Angeles Garcia-Cazorla[5] · Pascale de Lonlay[6] · Elisa Leão Teles[7] · Roshni Vara[8] · Nicholas Ah Mew[9] · Mark L. Batshaw[9] · Matthias R. Baumgartner[10] · Shawn McCandless[11] · Jennifer Seminara[9] · Marshall Summar[12] · Georg F. Hoffmann[1] · Stefan Kölker[1] · Peter Burgard[1] · Additional individual contributors of the UCDC and the E-IMD consortium



JIMD Reports
DOI 10.1007/8904_2017_11

RESEARCH REPORT

Development and Psychometric Evaluation of the MetabQoL 1.0: A Quality of Life Questionnaire for Paediatric Patients with Intoxication-Type Inborn Errors of Metabolism

Nina A. Zeltner · Matthias R. Baumgartner · Aljona Bondarenko · Regina Ensenauer · Daniela Karall · Stefan Kölker · Chris Mühlhausen · Sabine Scholl-Bürgi · Eva Thimm · Julia Quitmann · Peter Burgard · Markus A. Landolt · Martina Huemer

Publications 2017-2018

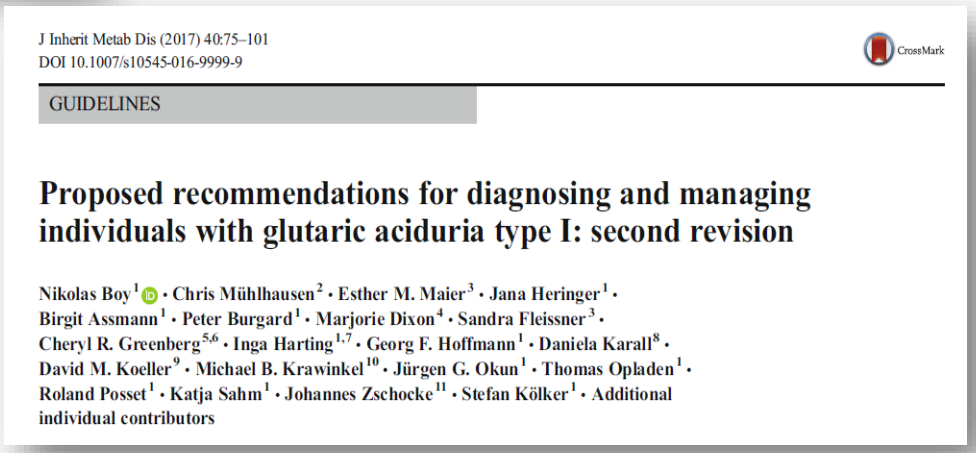
Nettesheim *et al. Orphanet Journal of Rare Diseases* (2017) 12:111
DOI 10.1186/s13023-017-0661-x

Orphanet Journal of Rare Diseases

RESEARCH Open Access

Incidence, disease onset and short-term outcome in urea cycle disorders –cross-border surveillance in Germany, Austria and Switzerland

Susanne Nettesheim[1†], Stefan Kölker[1†], Daniela Karall[2], Johannes Häberle[3], Roland Posset[1], Georg F. Hoffmann[1], Beate Heinrich[4], Florian Gleich[1], Sven F. Garbade[1*], On behalf of Arbeitsgemeinschaft für Pädiatrische Stoffwechselstörungen (APS); European registry and network for Intoxication type Metabolic Diseases (E-IMD); Erhebungseinheit für Seltene Pädiatrische Erkrankungen in Deutschland (ESPED); Austrian Metabolic Group; Swiss Paediatric Surveillance Unit (SPSU)



J Inherit Metab Dis (2017) 40:75–101
DOI 10.1007/s10545-016-9999-9

GUIDELINES

Proposed recommendations for diagnosing and managing individuals with glutaric aciduria type I: second revision

Nikolas Boy[1] · Chris Mühlhausen[2] · Esther M. Maier[3] · Jana Heringer[1] · Birgit Assmann[1] · Peter Burgard[1] · Marjorie Dixon[4] · Sandra Fleissner[3] · Cheryl R. Greenberg[5,6] · Inga Harting[1,7] · Georg F. Hoffmann[1] · Daniela Karall[8] · David M. Koeller[9] · Michael B. Krawinkel[10] · Jürgen G. Okun[1] · Thomas Opladen[1] · Roland Posset[1] · Katja Sahm[1] · Johannes Zschocke[11] · Stefan Kölker[1] · Additional individual contributors

Errata corrige

Correction to: Age at disease onset and peak ammonium level rather than interventional variables predict the neurological outcome in urea cycle disorders.
Posset R, Garcia-Cazorla A, Valayannopoulos V, Leão Teles E, Dionisi-Vici C, Brassier A, Burlina AB, Burgard P, Cortès-Saladelafont E, Dobbelaere D, Couce ML, Sykut-Cegielska J, Häberle J, Lund AM, Chakrapani A, Schiff M, Walter JH, Zeman J, Vara R, Kölker S; Additional individual contributors of the E-IMD consortium. J Inherit Metab Dis. 2018 Jul;41(4):743-744. doi: 10.1007/s10545-017-0117-4. PubMed PMID: 29330779.

Correction to: Impact of age at onset and newborn screening on outcome in organic acidurias.
Heringer J, Valayannopoulos V, Lund AM, Wijburg FA, Freisinger P, Barić I, Baumgartner MR, Burgard P, Burlina AB, Chapman KA, I Saladelafont EC, Karall D, Mühlhausen C, Riches V, Schiff M, Sykut-Cegielska J, Walter JH, Zeman J, Chabrol B, Kölker S; Additional individual contributors of the E-IMD consortium. J Inherit Metab Dis. 2018 Jul;41(4):741-742. doi: 10.1007/s10545-017-0116-5. PubMed PMID: 29234995.

Ongoing projects

“Impact of arginine and BCAA on growth in UCD and classic OAD”
(Lead by F. Molema and M. Williams)

Decreased plasma L-arginine levels in classic organic acidurias (MMA and PA) and decreased plasma branched-chain amino acid levels in urea-cycle disorders as a potential cause of growth retardation: *options for treatment.*

Authors: Femke Molema[1], Florian Gleich[2], Peter Burgard[2], Ans van der Ploeg[1], Marshall L. Summar[3], Kimberly A. Chapman[3], Allan M Lund[4], Dimitris Rizopoulos[5], Stefan Kölker[3], Monique Williams[1]; additional individual contributors from E-IMD.

Submitted to Mol Genet Metab, under review

Ongoing projects

“Impact of arginine and BCAA on growth in UCD and classic OAD”
(Lead by F. Molema and M. Williams)

Evaluation of dietary treatment and amino acid supplementation in classic organic acidurias and urea-cycle disorders. *On the basis of information from a European multicenter database (E-IMD).*

F. Molema, F. Gleich, P. Burgard, AT. van der Ploeg, M.L. Summar, K.A. Chapman, I. Barić, A.M. Lund, S. Kölker, Monique Williams; additional individual contributors from E-IMD

(A. M. Jelsig, P. de Lonlay, F.A.Wijburg, A. Bosch, P. Freisinger, K. Jeltsch, R. Posset, N. Boy, K. Mengler, P. Augoustides-Savvopoulou, P. Avram1, M. R. Baumgartner, J. Häberl, J. Blasco-Alonso, A. B. Burlina, L. Rubert, A. Garcia Cazorl, E. Cortes i Saladelafont, C. Dionisi-Vici, D. Martinelli, D. Dobbelaere, K. Mention, S. Grünewald, A. Chakrapani, Wuh-Liang Hwu, Yin-Hsiu Chien, Ni-Chung Lee, D. Karall, S. Scholl-Bürgi, R. Lachmann, C. De Laet, S. Matsumoto, L. de Meirleir, C.Mühlhausen, M. Schiff, L. Peña-Quintana, M. Djordjevic, A. Sarajlija, A. Wisniewska, J. Sykut-Cegielska, E. Leao-Teles, S. Alves, R. Vara, I. V. Pinera, A. Morris, J. Zeman, B. Chabrol, N. Thompson, F. Eyskens, M. Lindner, N. Luesebrink, A. Jalan, E. Sokal, V. Legros and M.C. Nassogne)

<u>submitted to JIMD, major revision requested</u>

This work was accepted for presentation on

- **2017 ESN congress in Leuven**
- **2017 EMG congress in Zagreb**
- **2018 SSIEM Athens poster**

Ongoing projects

Revision UCD guidelines (Lead J. Haeberle)

- *217 citation in Scopus*
- *324 citation in Google scholar*

manuscript under revision by Authors (27 October 2018)
to be submitted to JIMD by the end of November 2018

Suggested guidelines for the diagnosis and management of urea cycle disorders: first revision

Johannes Häberle[1], Alberto Burlina[2], Anupam Chakrapani[3], Marjorie Dixon[4], Daniela Karall[5], Martin Lindner[6], Hanna Mandel[7], Diego Martinelli[8], Guillem Pintos-Morell[9], René Santer[10], Anastasia Skouma[11], Aude Servais[12], Galit Tal[13], Vicente Rubio[14,*], Martina Huemer[1,15,*], Carlo Dionisi-Vici[8,*]

Ongoing projects

Part II. 13:00 – 15:45

- **Long-term outcome in individuals with cblA vs. mut0 deficiency (Hörster)**
- **Severity score for methylmalonic and propionic aciduria (Chapman)**
- **Organ transplantation in individuals with urea cycle disorders and classic organic acidurias (Williams, Molema, Dionisi Vici)**
- **Genotype phenotype correlation in citrullinemia type I (Zielonka)**
- **Evidence-based recommendations for isovaleric aciduria (Thimm, Dobbelaere)**

Election of E-IMD scientific board 2019-2021

List of candidates: election @11:40

Name	First name	Country	City
Baumgartner	Matthias	Switzerland	Zürich
Schiff	Manuel	France	Paris
Burlina	Alberto	Italy	Padova
Chakrapani	Anupam	United Kingdom	London
Chapman	Kimberly	USA	Washington DC
Dionisi-Vici	Carlo	Italy	Rome
Dobbelaere	Dries	France	Lille
Garcia Cazorla	Angeles	Spain	Barcelona
Häberle	Johannes	Switzerland	Zürich
Kölker	Stefan	Germany	Heidelberg
Lund	Allan Meldgaard	Denmark	Copenhagen
Williams	Monique	The Netherlands	Rotterdam

Organ transplantation in MMA

Luca dello Strologo
OPBG

CERTAIN Central EuropeanPaediatric Renal Transpl-Ant INitiative

Tönshoff, Burkhard
Krupka Kai
Hörster, Friederike
Heidelberg University

Study Title	Clinical outcomes of MMA patients undergoing renal, liver or simultaneous transplant: a descriptive study
Objectives & Hypotheses	The objective of this study is to describe the clinical outcomes of MMA patients who underwent kidney, liver or combined liver-kidney transplantation in the period **2006-2017** The clinical outcomes that will be investigated include survival probability, short and long-term morbidity including neurological status, and graft survival.
Study Design	**Since MMA is a rare disorder, clear evidences about the best strategy could only be achieved on a European basis using multinational platforms (registries, consortia, network) as** • **European transplant registry (CERTAIN)** • **E-IMD consortium** • **MetabERN** • **Rare Renal Disease (EuRenNet)** • **ERN Transplant Child**

Organ transplantation in MMA

Outcome after isolated or combined liver or kidney transplantation in patients with methylmalonic acidemia: A multicenter registry analysis New abstract created on Sunday November 4, 2018

Luca Dello Strologo[1], Marco Spada[1], Carlo Dionisi Vici[1], Noel Knops[3], Elena Levtchenko[3], Lars Wennberg[4], James Squires[5], George Mazariegos[5], Mohan Shenoy[6], Sangeet Sidhu[6], Lorenzo D'Antiga[7], Laura Martelli[7], Anna Kristina Bjerre [8], Trine Tangeras[8], Lyndsay Harshman[9], Stephen Marks[10], Pierluigi Calvo[11], Marco Spada[11], Waldo Conception[12], Friederike Horster[2], Burkhard Tönshoff[2].

[1]Pediatric, Bambino Gesu Children's Hospital, Rome, Italy; [2]Department of Pediatrics I, University Children's Hospital, Heidelberg, Germany; [3]Department of Pediatric Nephrology, University of Leuven, Leuven, Belgium; [4]Departement of Transplantation Surgery, Karolinska University Hospital , Stockholm, Sweden; [5]Pediatric Hepatogy and Transplant Surgery, UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, United States; [6]Pediatric Nephrology, Royal Manchester Children's Hospital, , Manchester, United Kingdom; [7]Paediatric Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy; [8]Dep of Paediatric and Adoles Med, Oslo University Hospital, Oslo, Norway; [9]University of Iowa, University of Iowa, Iowa, IA, United States; [10]University College London, Great Ormond Street Institute of Child Health, London, United Kingdom; [11]Department of Pediatrics, University of Torino, Turin, Italy; [12]Division of Transplantation, Stanford University School of Medicine , Stanford, CA, United States

Introduction

Methylmalonic acidemia (MMA) is a rare inherited metabolic disorder characterized by the accumulation of methylmalonic acid, leading to recurrent metabolic decompensation episodes and to chronic organ injury. Recently, there has been a growing interest in organ transplantation approaches: kidney transplantation (KTx) corrects renal failure but only partially restores the enzyme activity which is better obtained by liver (LTx) or combined liver/kidney transplant (LKTx). A consensus on the optimal transplant strategy is lacking. Our aim was to compare in a large multicenter study the results of different transplant approaches in patients affected by MMA.

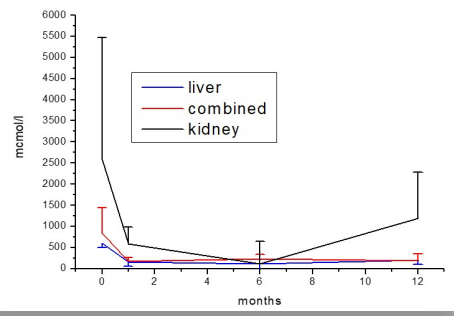
Material and methods

Within centers of the Cooperative European Paediatric Renal Transplant Initiative (CERTAIN) Registry and additional centers both in the US and in Europe (thanks to the joint effort of ESPN and MidWest consortium) we collected retrospective clinical and biochemical outcome data from transplanted patients with MMA from the year 2000 to present.

Results

So far, 58 patients were registered. Currently, data are available for 34 patients: 19 with KTx, 7 with LTx and 8 with LKTx. Median age (years) at transplant was 13.6 for KTx, 2.5 for LTx and 8.2 for LKTx. Median pre-transplant plasma MMA was higher in patients with KTx (2572 µmol/L) than in LTx (599 µmol/L) or LKTx (836 µmol/L). Post-transplant MMA was evaluated at 1, 6 and 12 months (Figure). At 1 and 6 months, all patients had a clear reduction of plasma MMA, whereas at 12 months only KTx patients showed a negative trend with a return plasma MMA increase. LTx and LKTx patients maintained significantly lower MMA plasma levels.

MMA plasma level pre and post-transplant



These data show a more pronounced and persistent post-transplant reduction of plasma MMA levels following LTx or LKTx compared to KTx alone. Graft and possibly patient survival is suboptimal following isolated KTx, where impaired graft function likely leads to reduction in renal filtration of MMA and lower intrarenal enzymatic activity, both of which increase MMA plasma levels driving further decline of renal function.