The European Lambert-Eaton Myasthenic Syndrome Registry: Long-Term Outcomes Following Symptomatic Treatment

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Supplementary Figure S1. Patient disposition
### Supplementary Table S1. Ethical approvals

| Principal Investigator | Affiliation/study site | EC Committee name | Ref # and decision date |
|------------------------|------------------------|-------------------|------------------------|
| Dr. Sabrina Sacconi, Prof. Claude Desnuelle (former PI) | Centre Hospitalier Universitaire de Nice, Hôpital Pasteur 2, Pôle Neuroscience Clinique, Nice, France | Ministère de l’Enseignement Supérieur et de la Recherche, Comity Consultatif sur le Traitement de l’Information en matière de Recherche dans le Domaine de la Santé Ministère de l’Enseignement supérieur et de la Recherche (CCTRIS), Paris | DGRI CCTIRS MG/CPO10.868 21/10/2010 |
| Dr. Arnaud Lacour | Hôpital Roger Salengro, Service de Neurologie D, rue Emile Laine 59037 Lille France | | |
| Dr. Giovanni Castelnovo | Centre Hospitalier Universitaire de Nîmes, Hôpital Caremeau, département de Neurologie, Nîmes, France | | |
| Dr. Jean Francois Lemaire | Centre Hospitalier Régional La Source, Service de Neurologie, 14 avenue de l’Hôpital 45067 Orléans France | | |
| Dr. Mohamed Beghdadi, Dr. Laurent Martini (former PI) | Cabinet de Neurologie 76, Allé d'Iéna 11000 Carcassonne, France | Commission Nationale de l'Informatique et des Libertés (CNIL), Paris | |
| Dr. Faycal Derouiche | Centre Hospitalier Emile Muller, Mulhouse, France | | |
| Dr. Jerome Lapras | Cabinet de Neurologie 4, rue Mic’arème 42000 St Etienne, France | | 910495 07/02/2011 |
| Dr. Françoise Le Bras | Cabinet de Neurologie 3 RUE ERNEST PEROCHON 79000 Niort, France | | |
| Dr. Jean Michel Croguennec | Cabinet de Neurologie Saint Adrian 19000 Tulle, France | | |
| Dr. Amar Smail | Centre Hospitalier Universitaire d’Amiens, Hôpital Nord, Amiens, France | | |
| Dr. Vivien Pautot | Centre Hospitalier Universitaires d’Angers, Département de Neurologie et Explorations Fonctionnelles, France | | |
| Prof. Gwendal Le Masson | Centre Hospitalier Universitaire de Bordeaux, Hôpital Pellegrin, Service de Neurologie, Bordeaux, France | | |
| Dr. Perrine Devic, Dr. Adrien Didelot (former PI) | Centre Hospitalier Lyon Sud, Service d’Explorations Fonctionnelles Neurologiques, Pierre Bénite, France | | |
| Prof. Andreas Meisel | Charité Universitätsmedizin Berlin, Germany | Ethikausschuss 1 am Campus Charité Mitte, Berlin | EA1/048/10 |
| Dr. Alexander Emmer, Dr. Berit Jordan (former PI), Dr. Susanne Schilling (former PI) Prof. Dr. med. Frank Hanisch (former PI) | Martin-Luther-Universität Halle-Wittenberg, Germany | Medizinische Facultät Ethik-Kommission, Martin-Luther-Universität Halle-Wittenberg | hm – di 17/06/2011 |
| Prof. Dr. med. Thomas Emskötter | Neurologikum Hamburg, Germany | Ethik-kommission der Ätztekammer Hamburg | MC-278/10 27/05/2011 |
| Name                                | Institution                                                                 | Ethics Committee                                                                 | Code | Date         |
|-------------------------------------|-----------------------------------------------------------------------------|----------------------------------------------------------------------------------|------|--------------|
| **Prof. Dr. med. Wilhelm Schulte-Mattler** | Neurologische Klinik und Poliklinik, Universität Regensburg, Germany       | Ethikkommission, universitätsklinikum, Regensburg                                | 11-103-0181 | 10/08/2011  |
| **Prof. Joern-Peter Sieb**          | Hanse-Klinikum Stralsund Abt Neurologie, Germany                           | Ethikkommission, Universität Greifswald, Greifswald                               | BB 113/10 | 29/09/2010  |
| **Dr. Andreas Schröter**            | Klinikum Bremen Ost, Klinik für Neurologie, Germany                        | Ethikkommission, Ärztekammer Bremen, Bremen                                      | Nr. 284 | 18/01/2011  |
| **Dr. Peter Trillenberg**           | UNIVERSITÄTSKLINIKUM Schleswig-Holstein, Campus Lübeck Klinik für Neurologie, Germany | Ethik-Kommission, Universität zu Lübeck, Lübeck                                    | 11-135 | 14/07/2011  |
| **Dr. Thorsten Rosenkranz**         | ASKLEPIOS proresearch, Germany                                              | Ethik-kommission der Ärztekammer Hamburg                                          | MC-278/10 | 27/05/2011  |
| **Dr. Karl Christian Knop**         | NEUROLOGIE NEUER WALL, Germany                                              | Ethik-kommission der Ärztekammer Hamburg                                          | MC-278/10 | 21/12/2011  |
| **Dr. Jörn Schattschneider**        | Neurologie Ev.-Luth. Diakonissenanstalt zu Flensburg Zentrum für Gesundheit und Diakonie, Germany | Ethik-kommission Medizinische Fakultät der Christian-Albrechts-Universität zu Kiel | B328/11 | 04/10/2010  |
| **Dr. Renato Mantegazza**           | Istituto Neurologico Carlo Besta, Italy                                     | Comitato Etico della Fondazione IRCCS Instituto Neurologico “Carlo Besta”, Milano | Comitato Etico, Verbale n. 11 | 12/01/2011  |
| **Prof. Amelia Evoli**              | Universita Cattolica del Sacro Cuore. Dipartimento di Neuroscienze Policlinico Universitario ‘Agostino Gemelli’, Italy | Comitato Etico, Università Cattolica del Sacro Cuore Facoltà. di Medicina e Chirurgia “Agostino Gemelli”, Roma | (A.199)/C.E./2011 | 12/10/2011  |
| **Dr. Alfredo Romani**              | Istituto Neurologico Nazionale C. Mondino, Italy                           | Ethics Committee, “Casimiro Mondino National Neurological Institute” Foundation, Pavia | LEMS-01 | 28/09/2010  |
| **Dr. Joseph Rodolico**             | Policlinico Universitario G. Martino, Italy                                | Comitato Etico Scientifico, Azienda Ospedaliera Universitaria Policlinico “G. Martino”, Messina | Prot. E 32/11 | 11/05/2011  |
| **Dr. Vichez Padilla**              | Servicio Neurologia Experimental Hospital Universitari i Politécnic La Fe, Spain | Comité Ético de Investigación Clínica del Hospital Universitario y Politécnico La Fe, Valencia | BIO-AMI-2010-01 | 24/07/2012  |
| **Dr. Muñoz Blanco**                | Unidad ELA-Neuromuscular Hospital G.U. Gregorio Marañón, Spain             | Comité Ético de Investigación Clínica Hospital General Universitario Gregorio Marañón, Madrid | LEMS-01 | 12/09/2011  |
| **Dr. Gomez Vicenti**               | Hospital Universitario Quiron Madrid C/Diego de Velazquez 1, Spain         | EC submission made and approved, see attached BioMarin note to file dated 4/4/2012 1. This site did not recruit any patients and was closed prior to database lock 2. | R1697 | 08/10/2014  |
| **Dr. Thekkootu Nandakumar**        | HULL AND EAST YORKSHIRE HOSPITALS NHS TRUST Neurology department, UK       | Research Ethics Committee, Hull and East Yorkshire Hospitals NHS Trust, Research & Development Department, Cottingham | R1697 | 08/10/2014  |

*Site closed prior to database lock.

Sites not recruiting any patient are highlighted with a grey fill in the table.
Supplementary Table S2. History of malignancy among patients participating in the European LEMS Registry

| Malignancy                                   | Ongoing at the time of study entry | Prior to study entry | Unknown |
|----------------------------------------------|------------------------------------|----------------------|---------|
| SCLC                                         | 8                                  | 3                    | –       |
| Prostate                                     | 2                                  | 1                    | –       |
| Lung                                         | 2\(^a\)                            | –                    | –       |
| Merkel carcinoma                             | 1                                  | –                    | –       |
| Thymus                                       | 1                                  | 1                    | –       |
| Breast                                       | 1                                  | –                    | –       |
| Colon                                        | 1                                  | –                    | –       |
| Squamous cell carcinoma of the right cheek   | 1                                  | –                    | –       |
| Thyroid\(^b\)                                | 1                                  | –                    | –       |
| Acoustic neuroma                             | –                                  | 1                    | –       |
| Epidermoid cancer of the lower lip           | –                                  | 1                    | –       |
| Caecum                                       | –                                  | 1                    | –       |
| Cervix                                       | –                                  | 1                    | –       |
| Cystadenolymphoma                            | –                                  | 1                    | –       |
| Epidermoid cancer of the vocal cords         | –                                  | 1                    | –       |
| Hodgkin lymphoma                             | –                                  | 1                    | –       |
| Kidney                                       | –                                  | 1                    | –       |
| Lower esophagus                              | –                                  | 1                    | –       |
| Multiple myeloma                             | –                                  | 1                    | –       |
| Pancreatic neuroendocrine                    | –                                  | 1                    | –       |
| Uterus                                       | –                                  | –                    | 1       |

\(^a\)Oncologic follow-up was negative for one patient; \(^b\)One additional participant had two thyroid lumps discovered during ultrasounds in follow-up; no data is available about the final diagnosis.

LEMS, Lambert-Eaton myasthenic syndrome; SCLC, small cell lung cancer.
**Supplementary Table S3.** LEMS-specific treatments administered at any time, by drug class and registry treatment group.

| n (%)                          | Treatment group (LEMS-specific treatment received at time of enrollment) |
|-------------------------------|-------------------------------------------------------------------------|
|                              | 3,4-DAPP (N=50) | 3,4-DAP (N=21) | Other (n=25) | Total (N=96) |
| 3,4-DAPP                     | 50 (100)        | 7 (33)          | 13 (52)      | 70 (73)       |
| 3,4-DAP                      | 8 (16)          | 21 (100)        | 3 (12)       | 32 (33)       |
| Pyridostigmine                | 25 (50)         | 14 (67)         | 9 (36)       | 48 (50)       |
| Prednisone                    | 17 (34)         | 3 (14)          | 10 (40)      | 30 (31)       |
| IVIg                          | 13 (26)         | 6 (29)          | 8 (32)       | 27 (28)       |
| Azathioprine                  | 17 (34)         | 4 (19)          | 5 (20)       | 26 (27)       |
| Rituximab                     | 6 (12)          | 3 (14)          | 2 (8)        | 11 (11)       |
| Pyridostigmine                | 8 (16)          | 21 (100)        | 3 (12)       | 32 (33)       |
| Prednisone                    | 17 (34)         | 4 (19)          | 5 (20)       | 26 (27)       |
| Azathioprine                  | 17 (34)         | 4 (19)          | 5 (20)       | 26 (27)       |
| Prednisolone                  | 6 (12)          | 2 (10)          | 2 (8)        | 10 (10)       |
| Methylprednisolone            | 6 (12)          | 2 (10)          | 2 (8)        | 9 (9)         |
| Plasma exchange               | 3 (6)           | 2 (10)          | 2 (8)        | 7 (7)         |
| Cyclosporin                   | 4 (8)           | –               | –            | 4 (4)         |
| Neostigmine                   | 2 (4)           | –               | –            | 2 (2)         |
| Pregabalin                    | 2 (4)           | –               | –            | 2 (2)         |
| 4-Diaminopyridine             | 1 (2)           | –               | –            | 1 (1)         |
| Methotrexate                  | 1 (2)           | –               | –            | 1 (1)         |
| Cyclophosphamide              | –               | –               | 1 (4)        | 1 (1)         |

*Administered ≥30 days before or ≥30 days after enrollment.

3,4-DAP, 3,4-diaminopyridine; 3,4-DAPP, 3,4-diaminopyridine phosphate; IVIg, intravenous immunoglobulin; LEMS, Lambert-Eaton myasthenic syndrome.