

## **European Network on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome**

**COST action CA15111**

### **Minutes of the 14.02.2019 Management Committee meeting - Work Group No 2 and No 4**

#### **Participants:**

**MC Chairs:** Modra Murovska, Eliana Lacerda

**Local Meeting Chair:** Carmen Adela Sirbu

**Welcome:** Carmen Adela Sirbu, Local Meeting Chair

#### **Management Committee meeting**

**1. Welcome New Participating Countries:** Austria - Dr Francisco Westermeier, Dr Monika Riederer; Poland - Dr Pawel Zalewski

**2. Modra Murovska:**

- a) Progress Report at 24 months evaluation – conclusions and recommendations of the Action Rapporteur;
- b) Information on GP3 progress - up to February 14, 2019;
- c) GP4 01/05/2019 – 30/04/2020 plan and budget drafting;
- d) Changes in WG leading.

#### **Progress Report at 24 months evaluation**

1. The level of ambition of the MoU objectives was Medium. Overall, most MoU Objectives are progressing appropriately.
2. The level of ambition of the deliverables was low. Overall, some deliverables are progressing appropriately.
3. Publications - Quantity of the Action's co-authored publications is poor.
4. Dissemination and exploitation - The activities undertaken focusing on exploitation were ineffective [Poor].

The final decision is to continue funding the project for the second half-time.

#### **Grant Period 3 progress up to February 14, 2019**

##### ***I. WG tasks of GP3 (01.05.2017 – 30.04.2018)***

**WG 1 Epidemiology:** T2 Synchronisation; T3 Biobanks and protocols; T4 Ethical framework.



**WG 2 Biomarkers:** T4 Data synchronisation; T3 Survey neuro – from the GP1-2

**WG 3 Socio-economics:** T4 Prevention models; T2 Direct loss calculation - from the GP2; T3 Indirect burden – from the GP2;

**WG 4 Clinical research/diagnostic criteria:** T2 Optimal set; T3 Treatment efficacy; T4 Global criteria optimisation; T3 Survey neuro – from the GP1-2 (moved from WG2)

**WG 5 STMS, workshops, conferences:** T1 Training school «Summer school for translational research in ME/CFS»; T2 STSMs; T3 Training panel «Novel methods in potential immunological biomarkers research for ME/CFS».

**WG 6 Dissemination:** T2 Guidelines; T3 Website; T4 Research projects.

## ***II. Deliverables***

- Deliverable 9 (28 month) - Guidelines for usage of immunological biomarkers in ME/CFS diagnosis and therapy evaluation - **submitted**;
- Deliverable 10 (28 month) - Common consensus protocol for economic loss estimation and forecasting due to ME/CFS – **submitted**;
- Deliverable 11 (30 month) - Evaluation scales for assessment of neurological symptoms associated with ME/CFS and usable in diagnostic – **30 November 2018 WG2 → WG4 – not submitted**;
- Deliverable 12 (31 month) - Common strategy protocol for ME/CFS diagnosis: synchronisation between centres, research component integration - **31 December 2018 WG4 - not submitted**;
- Deliverable 13 (36 month) - Protocol and guidelines for ME/CFS subgroups detection (stratification) according to the presence of symptoms and subject to potential biomarkers variation - **30 April 2019 WG4**.

## **To remind: Action plan of WG4 from Paris meeting, April 13, 2018**

- To do draft of Protocol for ME/CFS diagnostic (Includes recommendation for clinical purposes) - Jose Alegre, Ingrid Helland; final draft 1<sup>st</sup> Nov2018; synchronised document 30th Nov 2018; **not done**;
- To do draft of Protocol for ME/CFS diagnostic (Includes recommendation for research purposes) – Luis Nacul, Giorgos Sakkas, Olli Polo; final draft 1st Nov2018; synchronised document 30th Nov 2018; **not done**;
- To do draft of Neurological evaluation and guidance for recommendations – Jerome Authier; final draft 1st Nov2018; synchronised document 30th Nov 2018; **not done**;
- To do draft of Symptom management and relief (non-pharmacological) – Anne Marit Mengshoel, Giorgos Sakkas; final draft 15ns Feb 2019; synchronised document 30th Apr 2019; **draft**;
- To do draft of Symptom management and relief (pharmacological)- Jose Alegre; final draft 1st Nov2018; synchronised document 30th Nov 2018; **not done**;



- Public comments (via website) Lorenzo Lorusso; final draft 15th Apr 2019; synchronised document 30th Apr 2019.

### **III. Publications**

- Estévez-López F., Castro-Marrero J., Wang X., Bakken I.J., Ivanovs A., Nacul L., Sepúlveda N., Strand E.B., Pheby D., Alegre J., Scheibenbogen C., Shikova E., Lorusso L., Capelli E., Sekulic S., Lacerda E., Murovska M. European Network on ME/CFS (EUROMENE) Prevalence and incidence of myalgic encephalomyelitis/chronic fatigue syndrome in Europe-the Euro-epiME study from the European network EUROMENE: a protocol for a systematic review. *BMJ Open*. 2018; 8(9): e020817. Published online 2018 Sep 4. doi: 10.1136/bmjopen-2017-020817
- Rasa S., Nora-Krukle Z., Henning N., Eliassen E., Shikova E., Harrer T., Scheibenbogen C., Murovska M., Prusty B.K. Chronic viral infections in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). European Network on ME/CFS (EUROMENE). *J Transl Med*. 2018 Oct 1; 16(1):268. doi: 10.1186/s12967-018-1644-y.
- Survey of the use of diagnostic criteria and routine clinical assessments in Europe- ?

### **IV. Presentations – ITC Conference Grants**

- Dr Joanna Slomko (Poland). Chronic fatigue as one of the global public health problem: A cross-sectional study of the prevalence of chronic fatigue syndrome in Polish population. 4th World Congress on Public Health & Nutrition, 25-27 February 2019, Berlin, Germany (Plenary speech) - 1230 EUR;
- Maksims Čistjakovs (Latvia). Evaluation of new myalgic encephalomyelitis/chronic fatigue syndrome biomarkers. The International Congress on Controversies in Rheumatology and Autoimmunity (CORA 2019), 14-16 March, 2019, Florence, Italy (Poster presentation) - 1410 EUR.

**Until February 14, 2019 unused – 3/5 grants.**

### **V. STSM**

- Portugal (T.Domingues) 2040 EUR;
- Spain (F. Estevez Lopez) 2400 EUR;
- Romania (S.Diaconu) 2500 EUR

**Until February 14, 2019 unused – 2/5 STSM grants.**

## **GP4 01/05/2019 – 30/04/2020 plan and budget drafting**

### **1. WG tasks:**

WG1 Epidemiology:

- T3 Biobanks and protocols;



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- T4 Ethical framework.
- WG2 Biomarkers:
- T4 Data synchronisation.
- WG3 Socio-economics:
- T4 Prevention models.
- WG4 Clinical research/diagnostic criteria:
- T3 Treatment efficacy;
  - T4 Global criteria optimization.
- WG5 STMS, workshops, conferences
- T2 STSMs;
  - Final conference;
- Dissemination:
- T2 Guidelines;
  - T3 Website;
  - T4 Research projects.

**Objectives for the GP4 should be formulated by the groups' participants and send by WG leader to MC Chair within two weeks.**

### ***Deliverables***

- Deliverable 14, 38<sup>th</sup> month (05.2019) - Collaborative research project on ME/CFS based on synergy with other initiatives and resources integration - WG6;
- Deliverable 15, 45<sup>th</sup> month (12.2019) - Synchronised proposal for guidelines for management/treatment of ME/CFS: accommodating the existing and emerging therapies – WG4;
- Deliverable 16, 47<sup>th</sup> month (02.2020) - Program book/abstract book and overview of final global conference and conclusions - WG6;
- Deliverable 17, 48<sup>th</sup> month (03.2020) - Guidelines for health policy makers on prevention losses due to ME/CFS in health and economy aspects in Europe - WG3.

### ***3. Meetings***

- Title: Core Group meeting, WG3, WG4 meeting on synchronization  
Dates: 27/06/2019 - 27/06/2019, Location: (Poland)  
Participants: 15  
Reimbursed: 15  
Travel costs: 9 000 EUR  
Support grant: 1 000 EUR
- Title: MC/WG (as required) meeting on synchronisation  
Type: MC meeting /WGs (as required)  
Dates: 20/11/2019 - 20/11/2020, Location: Berlin  
Participants: 28  
Reimbursed: 27  
Travel costs: 18 600 EUR  
Support grant: 1 000 EUR

### ***4. Conference***



Dates: 12/03/2020 - 13/03/2020

Location: Riga (Latvia)

### ***Networking tools – 105 000 EUR***

Meetings	2	30 100 EUR
Conference	1	29 500 EUR
STSM	5	12 500 EUR
ITG Conference grants	5	10 000 EUR
Dissemination		
»Webpage maintenance		1 500 EUR
»Publications		1 800 EUR
»Participation in conferences		1 500 EUR
»Dissemination activities		1 557 EUR
FSAC 15%		13 695 EUR
<b>TOTAL</b>		<b>105 000 EUR</b>

### ***WG Leaders presentation:***

- **Carmen Scheibnogen**, Activities of WG2 after London meeting (what is done, results) (see attached presentation);
- **Derek Pheby**, Activities of WG3 after London meeting (what is done, results) (see attached presentation);
- **Jerome Authier** (WG4), draft on symptom management and relief (non-pharmacological) (see attached presentation);
- **Lorenzo Lorusso**, Activities of WG3 after London meeting (what is done, results) (see attached presentation).

### **Changes in WG leading**

Some of our colleagues, who were members of the CG, have changed their working places and positions and can not participate in EUROMENE as actively as before. So Elin B Strand has switched to the Norwegian Ministry of Health, where she is fully loaded with other tasks. In this respect, we need to replace the Leader of WG4. The situation is more than complicated, as the WG4 activities and results are not satisfactory, despite the additionally organised meeting in Paris. In reality, almost nothing of what had been decided in Paris (manuscripts, deliverables etc.) has been completed. WG4 Vice-Leader at present is Prof Jerome Authier and he has agreed to take the leadership of this group. At the London CG meeting, it was decided to nominate Prof Jerome Authier as the WG4 Leader and MC Substitute Dr Luis Nacul as the Vice-Leader of WG4. Dr Elin B Strand will continue to work as the MC Member.

The second question is regarding WG1 leadership. WG1 Leader Dr Jesus Castro Marrero since the beginning of summer last year is on a long-term mission in the United States, so that the real work of the WG1 were headed by Dr Fernando Estévez-López and, under his leadership, many of the planned activities have been successfully carried out and the group's work has been activated. At the London CG meeting it was decided to recommend Dr Fernando Estévez-López



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as the WG1 Leader for the future project period, replacing Dr Jesus Castro Marrero, who will continue to work as the MC Member. Electronic voting was initiated on 21.01.2019 and 28/33 MC Members had:

- 1) approved Dr Fernando Estévez-López (replacing Dr Jesus Castro Marrero, who will continue to act as the MC Member) as WG1 Leader;
- 2) approved Prof Jerome Authier (replacing Dr Elin B Strand, who will continue to act as the MC Member) as the WG4 Leader;
- 3) confirmed MC Substitute Dr Luis Nacul as the WG4 Vice-Leader because he has great experience and expertise in ME/CFS clinic matters.

Unfortunately, also STSM Coordinator Dr Els Tobback has changed her job and cannot continue the STSM supervision therefore I ask you to vote now on Dr Magdalena Efrim-Budisteanu (Romania) who kindly agreed to take this position. All votes are positive and Magdalena Efrim-Budisteanu is responsible for STSM of the project.

### **Conclusion**

1. Conclusions and recommendations on the half period Progress Report and identified gaps discussed in order to find the ways to overcome them.
2. WG2 on biomarkers is the most productive and active one. One paper is planned to published, possibly another together with the WG4.
3. WG3 activity should be increased in terms of preparation of joint publications. One paper is planned for the GP4.
4. WG4 activity should be increased in order to eliminate all identified gaps one of which is preparation of deliverables, manuscripts and protocols for practical use. It is decided to use skype conferences and other possible ways of discussion to increase WG4 activity. 3-4 papers are planned for the GP4.
5. Dr Magdalena Efrim-Budisteanu (Romania) is approved as STSM Coordinator. Two candidates are identified in Romania within to apply for STSM within the GP3.
6. WG5 - Regarding ITC Conference grants – within the GP3 two applications are approved and one is in the approval process. One of the reasons for such low activity is that the grant covers expenses only for the conference days themselves, but not the day before and after the conference required for arrival and departure.
7. WG6 activity should be increased, web page of EUROMENE should be regularly updated and all actual information inserted without delay. Preparation of brochures is planned within GP3. Attention should be payed to involvement of SMS and patients organizations.
8. The WG Leaders should prepare the objectives for GP4 and foreseen the activities in order to recalculated planned financial resources.
9. One of the group meetings could be held in Berlin together with the 1<sup>st</sup> International meeting on CFS and Chronic Fatigue in Cancer and Autoimmunity, Berlin Nov 21/22 2019 (with 100 participants).
10. The second MC and two WG meetings could be held in Poland (dates and WG should be fixed later).
11. Final conference will be organized in Riga during March 2020.
12. MC Chair should inform Science Officer Inga Dadeshidze about the changes in CG.



## **Minutes WG2 on Biomarkers Meeting**

**WG2 leader: Carmen Scheibenbogen**

**Participants:** E.Capelli (Italy), E.Shikova-Lekova (Bulgaria), H.Nielsen (Denmark), S.Rasa (Latvia), M.Murovska (Latvia), Š.Svirskis (Latvia), F.Westermeier (Austria), S.Orlova (Belarus), B.Prusty (Germany), J.Hartwig (Germany), S.Lorenz (Germany)

There is currently no stand-alone diagnostic biomarker in ME/CFS. Recently there were several multiparameter studies claiming that combining markers could reach sufficient sensitivity to be suitable as a diagnostic test.

We reviewed these studies and discussed which of these assays might be suitable to be used as diagnostic assay or to define subgroups of patients and how they should be developed for clinical usage. Topics of interest, which we reviewed, are: metabolomics, autoantibodies/immunosignature, chronic HHV6/7 infection. Further we had a presentation and discussed approaches of multiparameter analyses of clinical and biomarker data.

The second topic we discussed in a joint meeting with WG4 was on functional studies and routine laboratory assays which may aid in the diagnosis and differential diagnosis of ME/CFS. These include lab values, autonomic testing (HRV, POTS testing, COMPASS questionnaire), endothelial dysfunction, and physical fatigue assessment (hand grip).

## **Minutes WG4 on clinical research enablers and diagnostic criteria**

**WG2 leader: Leader Jerome Authier**

**Participants:** L.Nacul (UK), J.Alegre (Spain), O.Polo (Finland), R.Vermeulen (Netherlands), E.Lacerda (UK), L.Lorusso (Italy), M.Budisteanu (Romania),

During the meeting it was small group discussions as well as presentations and discussions in plenary. In WG4 meeting, progress in achieving deliverables was the main topic of the discussions.

1. Concerning D7, the main interest of this work is that it provides a photograph of what is done in European area, even if recommendations are weak. It has proposed to attempt publishing it with the following title: "Myalgic Encephalomyelitis/Chronic fatigue Syndrome (ME/CFS): Investigating care practices pointed out to disparities in diagnosis and treatment across European Union". Targeted journal is PLoS One. A concern arised from the publication of D7 text of in Euromene website. It was proposed to 1) inform editor, and 2) remove D7 text from website. It will be in charge of doing submission, publication fees being endorsed by Euromene.



2. AM.Mengshoel sent us a powerpoint presentation entitled “Scoping review about: Effects of non-pharmacological interventions and patients’ experiences of participating in such interventions” by E.Bolle-Strand, I.Helland and A.M.Mengshoel. J.Authier presented the work. The priority of such study was debated but it relates to our area of intervention. WG also debated the methodology, the level of recommendations and practical commitments. None of present members said he/she was able to contribute to the evaluation of selected papers. So, it was proposed to A.M.Mengshoel, E.Bolle-Strand and I.Helland to continue the work and produce a first draft.
  
3. J.Authier presented updated results of his review about cognitive impairment in ME/CFS. This work was conducted with M.Aoun Sebaiti who is neuropsychologist in J.Authier’s group at Creteil University Hospital. The presentation summarized first data presented in Paris meeting (13th April 2018) and more recent findings. Current analysis included studies evaluating at least 3 of the 6 following groups of functions: attention, short term memory, long term memory, executive functions, processing speed and instrumentals functions. Bibliographical research was performed without restriction for time period, concerned only adults (age>16) and included only studies with objective cognitive tests (self-report measures excluded). The requirements for neuropsychological evaluation include: (1) neuropsychological assessment must be standardized; (2) it must make possible delineating deficits and discriminating functions never altered and therefore screening must be complete and detailed; (3) it must make possible patients' stratification according to the neuropsychological profiles; and (4) it must be short enough to avoid fatigue bias. M.Aoun Sebaiti and J.Authier will produce a draft that will be sent to WG4 members and neurologists in Euromene.
  
4. L.Nacul presented a report of protocol for ME/CFS diagnosis including recommendation for research purposes. The presentation will be sent to WG4 members. His presentation dealt with the following points: (1) A proposal for clinical diagnosis work-out in adults (suspected diagnosis, diagnosis confirmation); (2) Exclusionary conditions and co-morbidities; (3) Different tools used in the context of patients care: symptoms profiling, data collection, routine tests.
  
5. Report on Symptom management and relief for ME/CFS (pharmacological) by J.Alegre and O.Polo was not yet completed

WG4 deliverables include: (I) Common strategy protocol for ME/CFS diagnosis; (II) Protocol and guidelines for ME/CFS subgroups detection according to the presence of symptoms and potential biomarkers variety; and (III) Synchronised guidelines for management/treatment of ME/CFS. Euromene recommendations for the diagnosis, the investigations (specialized clinical



testing such as neuropsychological evaluation, lab tests including biology, electrophysiology, neuroimaging), treatment and care organization will be produced, with writing an article to be published in an international journal.

**Planned tasks:**

Article: ME/CFS: European practices in diagnosis and treatment	J.Authier , E.Bolle-Strand, G.Sakkas, L.Nacul	done	done	Submission March 15th, 2019
Draft: Neuropsychological review	J.Authier, J.D.Korwin, E.Bolle-Strand	March 30 <sup>th</sup> , 2019	April 15 <sup>th</sup> , 2019	Submission for publication May 2019
Protocol for ME/CFS diagnostic (Includes recommendation for clinical purposes)	L.Nacul, I.Helland, G.Sakkas, R.Vermeulen	May 15th 2019	30th June 2019	September 2019
Protocol for ME/CFS diagnostic (Includes recommendation for research purposes)	L.Nacul, O.Polo, J.Authier	May 15th 2019	30th June 2019	September 2019
Symptom management and relief (non-pharmacological)	A.M.Mengshoel , E.Bolle-Strand, I.Helland	30 <sup>th</sup> May 2019	30 <sup>th</sup> June 2019	September 2019
Symptom management and relief (pharmacological)	J.Alegre, O.Polo, P.Grabowski	30 <sup>th</sup> May 2019	30 <sup>th</sup> June 2019	September 2019

	<i>Lunch</i>
14.00 - 17.00	<p><b>Work Group No 1 meeting</b> Leader <b>Jesus Castro-Marrero</b>, Vice-leader <b>Slobodan Sekulic</b></p> <ol style="list-style-type: none"> <li>1. Report on GP1 results.</li> <li>2. Activities of WG1 after Barcelona meeting.</li> <li>3. Problems that need to be addressed to activate the WP1 work.</li> <li>4. How to involve real epidemiologists from participating countries.</li> <li>5. How to collect current epidemiological data on ME/CFS epidemiology.</li> </ol>

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|  | <ol style="list-style-type: none"><li>6. What should be done to increase visibility of ME/CFS epidemiology in Europe.</li><li>7. How professional and non-governmental organizations can help to increase the visibility.</li><li>8. Clarification of the WG1 plan for the next GP2 period (till Sofia meeting).</li><li>9. Biobanking in WP1.</li><li>10. Local projects and support schemes for biobanks.</li></ol> |
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