ECTRIMS
EUROPEAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS

ECTRIMS Focused Workshop 2024

7-8 March 2024 | Nice, France

Expectations, outcomes and study designs for regenerative studies in MS

THURSDAY, 7 MARCH 2024

08.45	**Welcome and Introduction** B. Stankoff (Paris, FR), M. P. Sormani (Genoa, IT)
09.00 - 10.00	**Session 1: Selecting promyelinating strategies: diversity and redundancy of targeted mechanisms, a comprehensive overview** Chairs: K. Akassoglou (San Francisco, US), D. Adams (Cleveland, US), B. Nait Oumesmar (Paris, FR)
09.00	Basic mechanisms of repair: An overview *A. Williams (Edinburgh, UK)* A lot has been achieved to improve the understanding of myelination and remyelination during the last decades. This overview will summarize the key mechanisms underlying myelin regeneration in various experimental models, and to which extent they can be applied (or not) to the human CNS in the context of MS.
09.20	Pathways to be targeted: Can we prioritize? *L. Lairson (La Jolla, US)* Screening strategies and experimental pipelines have succeeded to identify signalling pathways and pharmacological targets that now hold promises for remyelinating strategies in MS. To which extent candidate drugs share similar or diverse mechanisms of action, and what is the respective level of evidence supporting their translation towards clinical trials will be reviewed, tempting to prioritize these translational steps.
09.40	Dealing with the inflammatory environment of MS: Should this guide compound selection? *T. Kuhlmann (Münster, DE)*

MS is inseparable from its inflammatory environment that involves adaptative and innate immune cells, as well as activated glial cells. How this inflammatory environment may impact endogenous remyelination or the efficacy of promyelinating drugs will be discussed, trying to highlight what are the underlying mechanisms and how this may influence the choice for compounds for trials.

10.00 - 11.00 **Round table discussion**

The discussion will be initiated by a 5 min comment from each chair. Chairs will then animate a general discussion and propose for the end of the symposium 5-10 statements summarizing the session and discussion.

11.00 - 11.20 **Coffee Break**

11.20 - 12.20 **Session 2: What can we expect from remyelinating therapies in subjects with MS?**

Chairs: F. Di Pauli (Innsbruck, AT), B. Stankoff (Paris, FR), G. Martino (Milan, IT)

11.20 Remyelination a strategy to promote recovery, neuroprotection, or both? From models to humans

R. Franklin (Cambridge, UK)

The design of a remyelination trial may vary depending whether the ultimate goal is to promote recovery of existing symptoms (assuming they are a consequence of demyelination), or to prevent neurodegeneration over disease course, (assuming that remyelination can protect neurons). Whereas there is no unique answer to this question, this talk will review the evidence supporting the benefits of remyelination, both in experimentation and in subjects with MS.

11.40 Are longitudinal cohorts informative about remyelination in MS?

M. Tintoré (Barcelona, SP)

Over past decades, well defined longitudinal cohort have enabled to improve our knowledge regarding the natural history of the disease, the clinical descriptors, and some biological processes underlying the heterogeneity in disease evolution. Whether these cohorts could also bring insight into repair over the disease course (consequences of demyelination, heterogeneity of recovery … according to patients, demographics, lesion location…) will be discussed.

12.00 Remyelination along the MS disease course. What could be the optimal therapeutic window (age, disease stage and form)?
R. Franklin (Cambridge, UK)
Phase II trials should attempt to include homogeneous groups of patients. Up to now we lack recommendation for the selection of the optimal groups of subjects who could best benefit from remyetinating strategies, a topic that will overviewed in this talk.

12.20 Round table discussion
The discussion will be initiated by a 5 min comment from each chair. Chairs will then animate a general discussion, and propose for the end of the symposium 5-10 statements summarizing the session and discussion.

13.00 - 14.00 Lunch Break

14.00 - 15.00 Session 3: Remyelination in MS: Functional outcomes
Chairs: M. Inglese (Genoa, IT), A. Coles (Cambridge, UK), D. Kos (Leuven, BE)

14.00 Remyelination in the optic pathway: How to measure it? Functional benefit?
A. Green (San Francisco, US)
Several pilot remyelination trials have selected the visual system for the assessment of repair. The proxies that can be used to evaluate remyelination, the potential relationship between their evolution and clinical benefit, as well as the advantages and limitations of focusing on this system will be reviewed.

14.20 Remyelination in other functional systems: Sensori-motor, oculo-motor, cognition. How to measure it? Functional benefit?
G. Boffa (Genoa, IT)
Beside the visual system, repair might be assessed in other systems involved in sensori-motor functions, eyes movements, cognition… What could be the outcomes to assess repair in these systems and to which extent their remyelination result in clinical changes will be reviewed and discussed

14.40 Neurophysiological tools to assess remyelination (evoked potentials, MEG and others)
L. Leocani (Milan, IT)

Neurophysiological tools have the potential to assess repair and its consequence on neuronal systems. Advantages, applicability, technical pitfalls, and limitation of each of these metrics will be discussed.

15.00 **Round table discussion**
The discussion will be initiated by a 5 min comment from each chair. Chairs will then animate a general discussion and propose for the end of the symposium 5-10 statements summarizing the session and discussion.

16.00 - 16.20 **Coffee Break**

16.20 - 17.20 **Session 4: Imaging and non-imaging biomarkers to assess remyelination**
Chairs: J. Oh (Toronto, CN), D. Reich (Bethesda, US),
B. Bodini (Paris, FR)
The various imaging techniques proposed to evaluate remyelination will be overviewed and discussed regarding their sensitivity, specificity, accessibility, and previous achievements for assessing remyelination in vivo in subjects with MS.

16.20 Imaging microstructure (MTR, iMTR, myelin water fraction, QSM and others)
C. Granziera (Basel, CH)

16.40 Molecular imaging and novel algorithms
T. Soulier (Paris, FR)

17.00 Biomarkers of remyelination
A. Abdelhak (San Francisco, US)
How existing or developing fluid biomarkers could help to assess remyelination in trials will discussed.

17.20 - 18.20 **Round table discussion**
The discussion will be initiated by a 5 min comment from each chair. Chairs will then animate a general discussion and propose for the end of the symposium 5-10 statements summarizing the session and discussion.

19.30 **Focused Workshop Dinner**

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FRIDAY, 8 MARCH 2024

08.30 - 09.30 **Session 5: Lessons from previous trials: What should we keep? What should we avoid?**
O. Ciccarelli (London, UK), X. Montalban (Barcelona, SP)

08.30 Lessons from Lingo-1, bexarotene, clemastine and H3 blockers trials
W. Brown (Cambridge, UK)
A critical review of the main published pharmacological phase 2 remyelinating trials (outcomes used, patients' profiles, key results, limitations…)

08.50 Promoting repair by modulating electrical activity or exercise
C. Louapre (Paris, FR)
An overview of basic and clinical evidence supporting a role of neuromodulation or exercise on remyelination, and how this may influence study design

09.10 Overview of the design of other ongoing repair trials
E. Hernandez Martinez (Barcelona, SP)
Description of ongoing repair trials (drugs/device, subjects, outcomes, general design…)

09.30 **Round table discussion**
The discussion will be initiated by a 5 min comment from each chair. Chairs will then animate a general discussion and propose for the end of the symposium 5-10 statements summarizing the session and discussion.

10.15 - 10.45 **Coffee Break**

10.45 - 12.20 **Working Groups: Repair trials: Unmet needs and possible designs**
Group 1: Why and how to integrate exercise and rehabilitation in the trials?
C. Louapre (Paris, FR); P. Feys (Diepenbeek, BE)
Group 2: Can we prioritize paraclinical outcomes?
B. Stankoff (Paris, FR), J. Oh (Toronto, CA)
Group 3: Can we include and prioritize clinical outcomes?
M. Inglese (Genoa, IT), M. P. Sormani (Genoa, IT)

	Group 4: Is it time to include patients' reported outcomes and/or wearable devices? *G. Brichetto (Genoa, IT), O. Ciccarelli (London, UK)* **Group 5: Recommendations for the selection of subjects** *A. Coles (Cambridge, UK), B. Willekens (Edegem, BE)*
12.20	Feedback from working group chairs (10 min each group), concluding remarks and future directions (20 min Chairs)
As of 13.30	**Lunch and individual departure**