

DRAFT PROGRAMME OUTLINE

Advancing Trial design in Progressive Multiple Sclerosis

(in association with the Progressive MS Alliance)

Organising Committee

Jeremy Chataway, Robert Fox, David Miller, Xavier Montalban, Maria Pia Sormani

Background

In the last 20 years, and particularly the last five, there has been a welcome profusion of disease modifying treatments (DMTs) for relapsing-remitting MS (RRMS) with reductions in relapse rate compared to placebo and active comparators in the range of 30-75%. Crucial to their development was strong trial design at all levels, but particularly at phase 2 and 3.

Unfortunately this progress has not been mirrored in progressive MS where at present there is no licensed medication with an 'anti-progressive/neuroprotective' disease modifying effect: although there is promise developing at phase 2 (eg, simvastatin) and phase 3 (ocrelizumab) levels.

This workshop will examine trial designs in progressive MS with a wide variety of experts from clinical, methodological, outcome and pharmaceutical backgrounds. Modelling and illustration with examples from real and derived data-sets is encouraged. The planned output is a position paper that will set out what is known, what is under current development and areas to be pursued to take the field forward.

Programme outline

2 day meeting

~50 attendees (32 speakers, ~20 non-speaker participants)

Brief discussion after each talk

Longer roundtable/panel-lead discussions after themed sessions, with facilitators and participation of all workshop attendees that address key themes

Major themes:

- Treatment targets and patient selection
- outcome measures
- trial designs
- statistical analysis models

THURSDAY, 9 MARCH 2017

- 08.30 - 08.45** **Welcome from ECTRIMS**
D. Miller (London, UK)
- 08.45 - 09.45** **Session 1: Progressive MS treatment targets and trials to date**
(talks 15 minutes; discussion 5 minutes)
Chairs: T. Derfuss (Basel, CH), W. Carroll (Nedlands, AU)
- 08.45 Pathogenic mechanisms
H. Lassmann (Vienna, AT)
- 09.05 Overview of progressive MS trials to date
X. Montalban (Barcelona, ES)
- 09.25 Do we need anti-inflammatory and neuroprotective strategies
together or apart?
B. Cree (San Francisco, US)
- 09.45 - 10.30** **Session 2: The human phenotype and trial entry criteria**
(talks 15 mins; discussion 5 mins)
Chairs: P. Soelberg Sørensen (Copenhagen, DK), J. Chataway (London, UK)
- 09.45 Heterogeneity of progressive MS and relevance of the new classification
for trials
A. Thompson (London, UK)
- 10.05 Enrichment: lessons from ORATORIO and other trials
J. Wolinsky (Houston, US)
- 10.30 - 11.00** **Coffee break**
- 11.00 - 11.30** **Roundtable/Panel discussion 1: Progressive MS treatment targets and
patient selection**
*Panel members: A. Thompson (London, UK), P. Soelberg-Sorensen
(Copenhagen, DK), J. Wolinsky (Houston, US), M. Salvetti (Rome, IT),
H. Lassmann (Vienna, AT)*
- 11.30 - 12.50** **Session 3: Clinical outcome measures – their performance and
positioning in progressive MS trials**
(talks 15 minutes; discussion 5 minutes)
Chairs: M. P. Amato (Florence, IT), T. Coetzee (New York, US)
- 12.30 Current role of EDSS
L. Kappos (Basel, CH)
- 12.50 MSFC+ and MSOAC
J. Cohen (Cleveland, US)

- 13.10 Cognition
J. DeLuca (New Orange, US)
- 13.30 Composite scoring
F. Lublin (New York, US)
- 12.50 - 13.50 Lunch break**
- 13.50 - 14.50 Session 3: Clinical outcome measures – their performance and positioning in progressive MS trials (continued)**
(talks 15 minutes; discussion 5 minutes)
Chairs: M. P. Amato (Florence, IT), T. Coetzee (New York, US)
- 13.50 6-minute walk & upper limb scores
K. Zackowski (Baltimore, US)
- 14.30 Patient related outcomes
M.P. Amato (Florence, IT)
- 14.50 - 15.30 Session 4: Interim (phase 2) efficacy outcome measures focused on neuroprotection - their performance and clinical correlation in progressive MS**
(talks 15 minutes; discussion 5 minutes)
Chairs: D. Miller (London, UK), R. Fox (Cleveland, US)
- 14.50 Global and regional brain atrophy measures
N. de Stefano (Siena, IT)
- 15.10 Brain lesions
A. Rovira (Barcelona, ES)
- 15.30 - 16.00 Coffee break**
- 16.00 - 18.00 Session 4: Interim (phase 2) efficacy outcome measures focused on neuroprotection - their performance and clinical correlation in progressive MS (continued)**
(talks 15 minutes; discussion 5 minutes)
Chairs: D. Miller (London, UK), R. Fox (Cleveland, US)
- 16.00 Advanced cranial MRI (MTR, DTI etc)
R. Fox (Cleveland, US)
- 16.20 Spinal cord MRI
O. Ciccarelli (London, US)
- 16.40 OCT
P. Calabresi (Baltimore, US)
- 17.00 Evoked potentials
L. Leocani (Milan, IT)

- 17.20 CSF and blood neurofilaments
J. Kuhle (Basel, CH)
- 17.40 PET
B. Stankoff (Paris, FR)
- 18.00 - 18.30 Roundtable/Panel discussion 2: Outcome measures**
Panel members: M.P. Amato (Florence, IT); chair, D. Miller (London, UK), J. Cohen (Cleveland, US), P. Calabresi (Baltimore, US), P. Zaratin (Genoa, IT)
- 19.30 Workshop Dinner**

FRIDAY, 11 March 2017

- 08.30 - 09.30 Roundtable/Panel discussion 2: Outcome measures (continued)**
- 09.30 - 10.30 Session 5: Progressive MS trial design and statistical analysis**
(talks 15 minutes; discussion 5 minutes)
Chairs: X. Montalban (Barcelona, ES), M. P. Sormani (Genoa, IT)
- 09.30 Validating phase 2 and 3 biomarker outcome measures in progressive MS
M. P. Sormani (Genoa, IT)
- 09.50 Optimisation of pivotal phase 3 trial
G. Cutter (Birmingham, US)
- 10.10 Measurement of brain atrophy in multicentre, phase 3 trials: are some ways better than others?
F. Barkhof (Amsterdam, NL)
- 10.30 - 11.00 Coffee break**
- 11.00 - 12.00 Session 5: Progressive MS trial design and statistical analysis (continued)**
Chairs: X. Montalban (Barcelona, ES), M. P. Sormani (Genoa, IT)
- 11.00 Adaptive trial designs
M. Parmar (London, UK)
- 11.20 Bayesian trial designs
M. Gasparini (Torino, IT)
- 11.40 Lessons from oncology
P. Bruzzi (Genoa, IT)

- 12.00 - 13.00** **Roundtable/Panel discussion 3: Progressive MS trial design and analysis**
Panel members: M.P. Sormani (Genoa, IT); chair, G. Cutter (Birmingham, US), K. Smith (US), M. Parmar (London, UK), F. Barkhof (Amsterdam, NL)
- 13.0 - 14.00** **Lunch break**
- 14.00 - 16.00** **Session 6: Progressive MS - macro views**
(talks 15 minutes; discussion 5 minutes)
Chairs: B. Hemmer (Munich, DE), G. Comi (Milan, IT)
- 14.00 View from the pharmaceutical industry at phase 2/3
P. Chin (San Francisco, US)
- 14.20 Where are the big datasets and what to do with them?
H. Butzkueven (Melbourne, AU)
- 15.10 Regulatory experience and considerations
D. Leppert (Basel, CH)
- 15.30 Lessons from MS-SMART & SPRINT-MS
J. Chataway (London, UK), R. Fox (Cleveland, US)
- 16.00 - 16.15** **Meeting Summary**
J. Chataway (London, UK)