Big MS Data Network

Minutes

Lyon 13 February, 2020

Big MS Data Network: Jan Hillert, Anna Glaser, Melinda Magyari, Sandra Vuksic, Maria Trojano, Helmut Butzkueven, Dana Horakova, Orla Gray, Lars Forsberg, Hanne Joensen, Patrick Grivot, Romain Casey, Pietro Iaffaldano, Giuseppe Lucisano, Tim Spelman, Jiri Drahota

Other: Veronique Millot, Flore Ballaud

8.30 – 10.30

Coordination Centre update

Anna and Jan presented current state of affairs.

Helmut suggested that we could benefit from medical writing support from pharma if we'd chose.

It was raised that pharma sometimes misunderstand what access to data they will get from supporting BMSD and that this should be clarified to avoid possible misunderstanding.

Suggested that our openness to new registries joining BMSD should be expressed by describing the principles for joining and that we should actively approach those registries we think could/should join.

Scientific coordination for BMSD could be better emphasized.

Update on BMSD PASS

CLARIOMS/Merck: Den, Swe and MSBase (separate agreement with Merck for specific aspects) up and running. Italy close to agreement, OFSEP may join if/when cladribine becomes available in France.

Ocrelizumab/(Roche): Their approach appears more coordinated. Has a good developed analysis model.

Sandra and Helmut emphasized that we should work towards a joint analysis model for all BMSD PASS, which could build on the one from the ocrelizumab PASS. Unified exposure and event definitions will be central. Tim proposes that data managers should be involved.

Discussion on patient level data analysis in BMSD PASS

So far not part of started PASS, unfinanced.
We discussed options and distinctions between merged and federated analyses.
EMA and FDA are likely to ask questions to pharma which would benefit from a joint analysis. We could consider making a catalogue of such potential questions.
Discussion on who can still share data, mostly optimism if within BMSD.

Points of view expressed:
Merging of data should be performed for specific questions.
Mission for patient safety would need merging of data. This should be offered by BMSD. Not general safety questions.
Are there concerns of patient consent?
Merged data kept or destroyed? "Rapid" merging and analysis.
Many levels of approvals and registry governance.
Is umbrella agreement possible? For fast approval in exceptional conditions? Although sense of urgency may be exaggerated (6 months perhaps normal)
Fra – not possible. Specific merge needed for specific question.
Italy – specific question. Collaboration on specific project. Not general data provider.
Den – Danish data protection is very regulated. Usually specific question.

CR – maybe possibilities

Suggested that BMSD could have an annual calendar, when specific questions could be filed (e.g. in January and September). Specific safety studies suggested and discussed in BMSD.
Basic data counts projects could be faster and could be provided by the individual registries.
Periodic data extraction needs to be on request.
Specific questions are what the database is for.

PASS could be an important source of income for BMSD. Analysis of safety for specific questions. Additional contracts. CC could do analysis as part additional agreements.

Helmut stated that if EMA chooses different reviewers for new MS drugs, this may increase the need of standards set by BMSD. Core protocol could be extended with details on analyses, definitions, standards etc.

Homepage

Work is initiated and some early aspects were reported.
ECTRIMS presentation? Ask ECTRIMS for link to the ECTRIMS library. Internal login for BMSD.
Hire communicator? Presence on social media e.g. Twitter, LinkedIn. Weekly postings would be good.

SUMMARY:

A. Some projects are suitable for MS registries and some for BMSD (especially when data is sparse, rare events). Encouragement of new MS registries need to be carefully phrased.
B. Homepage has been started. The homepage should show what are the conditions of BMSD. ECTRIMS presentation? Ask ECTRIMS for link. Internal login for BMSD. Hire communicator? Presence on social media e.g. Twitter, LinkedIn. Weekly postings would be good.
C. EMA application for qualification of BMSD and the included MS registries has been initiated.
D. Important to have a coordinated approach to report SAs and facilitate how to improve and agree on analysis. Level of reporting should be coordinated. Need for a joint analysis plan will be proposed to pharma on 14 Feb

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11 - 13

H2020

We had an intense and creative discussion concluding with a decision to have a go for the call focussing on MS and co-morbidities.

From the discussion:
Flore will help with administration of application.
Important with a pharma independent focus.
ECF also interested in applying. Two MS projects may be problematic? ECF focussed on PROs and we concluded that they aimed for another call (Note: it was revealed after the meeting that the ECF proposal was for the same call, so there will be no BMSD paricpation if the ECF proposal if they decide to go on).

Demonstrate potential of RWD as opposed to clinical trials. MS community should be behind. Another program after H2020 could be a possibility for BMSD so proposal could be recycled if we failed this time.

It was decided that we'd go for co-morbidities, DMTs, disease progression, co-morbidities consequence of DMTs, treatment outcomes in pats with comorbidities. Obesity, smoking, diabetes influence outcome. Treatment in patients with comorbidities quite different. Multidisciplinary visits do not include co morbidities.

Title? **External determinants of prognosis in MS: role of comorbidities, social depravation and DMTs.** Proposal 70 pages! The proposed access to data needs to be defended

Focus on BMSD and the access to data, tools for the project
Objectives and tasks should be described. CDM and harmonisation. Emphasis on digital technology.
Multidisciplinary is important. Data access and legal aspects partner? Claude Bernard? Tight deadline 7 April

Hypotheses:
1) Comorbidities affect MS outcome
2) How is effectiveness of DMs affected by comorbidities
3) Comorbidities associated with DMTs
4) Comorbidities and association of comorbidities
5) The special case of primary progressive MS

Statistical analysis should be described. Study approach needs carefully explained.
People working will need to be justified and described to motivate. Statistical team.
Description of the partners for expertise. WP project management. WP communication and dissemination (patients, patient associations, health care authorities). ECTRIMS?
Differences in health care systems between countries should be addressed. Own WP?
Leader of WPs to collect info needed

1.Excellence. Science. How to answer objectives
2. Methods. How the project will be done. Gender aspects
3. Impact section. How the project will be addressed. Relate health care organisations. Communication with public.
4. Implementation. Describe the tasks of WPs.

Milestones defined in WPs. Realistic deliverables. Spread over period.

SUMMARY:
Tight deadline 7 April! BMSD will work on a H2020 application independently of ECF.

The application will be focussed on MS and comorbidities.
WP1 project management (Lyon)
WP2 definition of cohorts and methods (KI)
WP 3 sharing data (Bernard?)
WP 4 comorbidities and MS outcome (Denmark)
WP 5 effectiveness of DMTs affected by comorbidities (MSBase)
WP6 comorbidities and treatment choice (Lyon)
WP7 comorbidities associated with DMTs (KI and all)
WP8 PP (Italy)
WP 8 communication and dissemination (Denmark and Lyon)

Flore will coordinate the application and will contact the WP leaders for their contributions.

14-16 Steering Committee. Data managers had their own break-out session

<u>Organisation of BMSD</u>
Pros and cons of legal entity were discussed,

BMSD has been invited to join ECF by Giancarlo Comi
ECF builds on pharma support and their Annual meeting is a main event (500 participants) but also other educational events.
BMSD could join fully (like MSDA) or become one of several “MS Initiatives” around ECF’s table.

Pros in joining: Support, visibility, alignment MSDA, ECF board members in BMSD
Cons to joining: Independence unclear, align with ECF principles, credibility, acceptance by MS registries, ECF board members in BMSD

How do we view ECF? BMSD should avoid reduction of BMSD.
Independence? BMSD independence is very valuable
MSDA needs BMSD more than the reverse.
ECTRIMS more important than ECF

We decided after due consideration to stay independent from ECF and from MSDA.

Response to prof Comi:
"Thanks for offer
BMSD has good organisation and wishes to remain independent
Offer ECF participate in pharma meeting
ECF can support BMSD projects
ECF can perhaps be mentioned on BMSD homepage"

Scientific credibility is key. New MS registries should be encouraged
"Independence and credibility"

But there would be evident advantages for BMSD to become its own legal body.

SUMMARY:

A. The offer from ECF will be politely declined at this point. Maybe rather relation with ECTRIMS than ECF. If ECF has research question this could be analysed by BMSD.
B. To create a non for profit legal organisation could be the best option for BMSD. This will be explored and attempted. Although this may include more staff needed for BMSD

MSDA

Liesbet Peeters is, in her researcher's role, doing two MSBase projects. Soon also Swedish ones.
MSIF is now leading the PROMs project we previously proposed EMSP/MSDA to take charge of.

We reviewed the MSDA toolbox with its components the MSDA dictionary, the MSDA switchbox including a common data model definition, and the MSDA cohort explorer. We concluded that we have the competence and ability to complete the parts of this structure that we need.

Jan informed on his impression that MSDA speaks "with the voice of MS registries" for instance on the big MSDA Stakeholder conference in Baveno in November with 100+ participants. Liesbet has stated is unintentional.

Maria and Jan have been invited to serve on an advisory MSDA board. (Note: after the meeting Maria and Jan decided to decline this invitation).

Jan has been invited to participate in planning of a MSDA workshop for emerging registries (Note: after the meeting, Jan decided to decline being an organizer but would consider an invitation to speak)

We concluded that there is a competitive aspect between BMSD and MSDA in getting funding from pharma and in aspiring a leadership in the MS RWE field, which causes confusion in the community and within pharma.

Therefore it was agreed that BMSD will be clear in its communication of what BMSD is, by communication and by not contributing to MSDA efforts.

It was concluded, though, that Liesbet Peeters is an appreciated person whose place in the MS community should be supported, but in other ways. An interest was expressed to include Liesbet as a person in BMSD activities if possible.

Was agreed that BMSD should contact other MS registries regarding interest for BMSD. Especially regarding PASS. Invite leaders for MS registries to describe how we see the future. Invite observers and have a qualification procedure.
The following registries seem to be the best candidates:
Swiss, Norway, Finland, Germany and possibly Belgium and Austria

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SUMMARY:

A. BMSD feels that MSDA has little to offer at this point. BMSD should contact other MS registries to describe to inform about BMSD and avoid the concept of not being open to more qualified registries joining the network.
B. BMSD will not join MSDA efforts as an active member.

RCN

France can now participate since Novartis has signed an agreement to support OFSEP.
RCN projects will need to apply for access. May need direct contract with Novartis. Italy may have problems participating in the project with UK as PI (as part of BMSD).
It was emphasized that BMSD will work as a united as BMSD within RCN as much as possible.

There is some concern for the UK data quality

16-18:30: Data managers joined the Steering committee

Report from DM committee break-out:

CDM – Common data model:
Variable metadata standardisation has been done within the Danish Registry
Johannes Lorscheider and team close to finalize an R-script for Extraction / compilation of BMSD data format. This is a great start of a CDM effort.

Aim of a first CDM effort: Identify minimal data set - Patient data; Visits; Relapse; Treatments. We could build this around the MSBase format.

Common tools standardisation, resource sharing
Important to be applicable to new registries
Standardized scripts
Federated analysis may be useful (may require continuous outcome)
MSDA cohort explorer – automated federated data, if multiple requests you could collect entire dataset

Login to website possible with pw

Other possible projects for BMSD:
RW PALYs (productivity adjusted life-years.
RW cost effectiveness / linkage more broadly where possible

Prognostic tools. Was discussed that current efficacious DMTs make this difficult - what was prognostically poor before is now beneficial because of DMTs, like MRI activity or early attack rate.
Trends in Outcomes could be done better than before.
Trends over time in phase III recently published, approx. 15 outcomes per study. Use RWD instead would have many pros.

Publication core protocol (ideally together with the Roche analysis plan)

Pregnancy studies
Kerstin Hellwig is very active and may perhaps be interested in collaborating; Could be interesting to BMSD; There will be possibilities to do these studies.
Danish reg has 120 pregnancies recorded, OFSEP has 200 per year (50 % of estimated 400).

SUMMARY:
The data managers have a number of different issues and agreed on some common approaches. The suggested BMSD publications include the BMSD core protocol, Prognostic tools and Trends in outcomes

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Lyon 14 February, 2020, 8.30-10.30 am

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Other: Liesbet Peeters

8.30 – 10.30
Meeting between Steering Committee and Liesbet Peeters

We informed that BMSD would not join ECF
We informed BMSD will not join the work with the MSDA Toolbox
BMSD's own DMs have sufficient competence.
Collaborations in data science with LP would be welcome.
The "gap" argued for by MSDA is not there for the well-developed MS registries.

LP – "Similar mission with different initiatives BMSD and MSDA. Possible collaborations"
LP join BMSD? "win-win" as a data scientist. Finland, Malta, Kosovo ..? What happens to them?
BMSD needs to be more proactive to other MS registries! Should be an open invitation!

From data collection in clinical care to a registry is a process that will take time and care
Workshop on good practise? Sharing experiences on how to create regs. Data collection, harmonisation, legal matters. One day or online course? LP suggests
MSBase provides infrastructure already to registries how to run
Passion is good but it is a daily effort!
Charcot fellowships possible?
Encourage MS registries to join MSBase? Structure, organisation, all is there already
Many people show interest but fail to complete the process.
Perhaps with a new generation MS registry data collection will improve?
Toolbox no Academia probably no. Workshops could include reps of individual MS registries.

Liesbet leaves

Discussion:
Maybe not even sensible to have individual registries in all countries? (min 10 milllion population?)
How to work with BMSD needs to be clearer? PR machine would be useful

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SUMMARY (MSDA and Liesbet Peeters):
BMSD does not need MSDA but collaborations with scientist Liesbet Peeters would be welcome. There is a need to be clearer regarding how to join and how to collaborate with BMSD.

Sanofi PASS
Sanofi has asked us if BMSD can be the basis for PASS projects related to new requirements on Sanofi from EMA on alemtuzumab (Lemtrada), one Mortality study and one Drug Utilization Study (DUS) to follow adherence to contraindications and proper monitoring.

Sanofiu is now investigating registries that could participate. Project plan needs to be completed in June for approval in July, so there is a time constraint.

It was concluded that mortality can be studied by participating registries, retro- and prospectively.
It was believed that few new patients will be put on Lemtrada. But a retrospective mortality is feasible.

DUS harder to know if we can deliver high enough quality data.
Indications can be monitored.
Contra-indications more variable between registries.
Treatment monitoring is a challenge (regular laboratory data over many years,

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SUMMARY (Sanofi PASS):
It is feasible for the at least some of the BMSD registries to participate in the Sanofi safety study. Mortality more feasible than DUS. The registries should be approached individually be Sanofi.