

Standard operating procedure

MLD Treatment Eligibility Panel

The MLD initiative
ERN-RND

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Purpose of this document	Describe the standard operating procedure for the panel discussing and advising on HSCT/GT eligibility in metachromatic leukodystrophy on individual case base.

Version control

Version number	Revision date	Summary of major changes

SOP MLD Treatment Eligibility Panel

Table of contents

Treatment eligibility panel	3
Rationale and purpose	3
Composition of the panel.....	3
Work flow.....	3
When is discussion and advise by this panel recommended?	3
Convene a meeting.....	3
During the meeting.....	4
After the meeting	5

Treatment eligibility panel

Rationale and purpose

Treatment with hematopoietic stem cell transplantation or gene therapy is only beneficial in early disease stages. Determining which patients might benefit from treatment and which do not, can be difficult. Therefore, an international MLD treatment eligibility expert panel can be consulted. When there is a need to discuss a case, the panel is convened on an ad hoc basis.

Composition of the panel

MLD experts affiliated to the European Reference Network on Rare Neurological Diseases (ERN-RND) or European Reference Network on Hereditary Metabolic Diseases (Metab-ERN) and/or the MLD initiative can be invited to join the panel.

A number of agreements have been made:

- a minimum number of 5 experts attend the meeting (in urgent/exceptional cases a number of 3 is acceptable);
- those experts should have a medical specialist/consultant position;
- the referring physician attends the meeting;
- preferably all relevant medical fields (neurological, metabolic, transplant) are represented;
- at least one neurologist experienced with the relevant age group attends the meeting.

Work flow

When is discussion and advice by this panel recommended?

- Cases eligible for discussion include patients with a confirmed diagnosis of MLD for whom possible benefits of treatment with hematopoietic stem cell transplantation or gene therapy are not straightforward. Also presymptomatic cases can be discussed, e.g. regarding timing of HSCT/GT.
- All physicians in Europe are advised to discuss these cases with this panel.
- Also physicians from other geographical areas are invited to share and discuss their cases.

Convene a meeting

- Referring physician contacts CPMS team and/or the MLD initiative: cpms-helpdesk_ern-rnd@med.uni-tuebingen.de or MLDinitiative@amsterdamumc.nl

SOP MLD Treatment Eligibility Panel

- Internal routing:
 - Make sure that both the CPMS and MLDi team are informed.
 - Check whether case is eligible for discussion. In case of doubt, discuss with MLDi team. If the referring physician is involved in the MLDi and based in the EU, the case can be considered eligible for panel discussion without checking with MLDi team.
 - If referring physician is based in EU: CPMS system is used for uploading information.
- If referring physician is from non-EU country: MLDi team collects the information. CPMS consent form as well as the MLDi information letter and consent form are shared with the referring physician to ask permission for inclusion in the MLDi registry and data sharing. The referring physician is responsible for appropriate consent from the patient/guardian and responsible for complying to local/national regulations.
 - In case the referring physician is an MLDi Partner (according to the Joint Data Registry Agreement): the referring physician completes the informed consent procedure and inclusion in the MLDi registry.
 - In case the referring physician is not an MLDi Partner (according to the Joint Data Registry Agreement): the MLDi team completes the informed consent procedure and inclusion in the MLDi registry.
- The CPMS team of ERN-RND arranges date and time for a video call using Zoom if the local regulations allow.
 - Standard time slots will be used: Monday 16:30/Tuesday 16:30 /Friday 16:30
- The referring physician completes the MLDi 'Questions for Referring Physician' send by the MLDi team
 - In case of EU-referring physician with CPMS account: referring physician uploads this document in the CPMS. In addition, MRI pictures can be uploaded in the CPMS. The CPMS team (cpms-helpdesk_ern-rnd@med.uni-tuebingen.de) provides user guides and technical support. The CPMS team shares this information with the panel.
 - In case of non-EU-referring physician without a CPMS account: the MLDi team uploads the document in the CPMS system or shares the document with the panelists.

During the meeting

- The referring physician presents the case.
- This presentation is followed by a discussion.

SOP MLD Treatment Eligibility Panel

- All experts give their opinion and advice, based on their experience and comparison with similar cases.
- Minutes are taken by CPMS team or the MLDi team.
- Final conclusion and advice is formulated.

After the meeting

- Minutes are shared with the referring physician.
- The minutes are archived.
 - In case of EU-referring physician with CPMS account: The CPMS team ensures that the minutes are uploaded and archived in the CPMS system. The CPMS team posts the minutes in the CPMS system as 'Outcome Document'. The referring physician has to sign off/close the panel in the CPMS system.
 - In case the referring physician is non-EU and has no CPMS account: the MLDi team archives the minutes.
- Inclusion of the patient in the MLDi registry is completed by the MLDi team to ensure longtime follow-up.
- 6 months after meeting MLDi team asks the referring physician about the decision made.