

## ALLTogether; Sampling during PEG-asparaginase treatment for patients with Down syndrome (all ages).

Includes:

- Minimal sampling (trough levels on infusions days)
- Recommended extra sampling in NOPHO for prediction of hypersensitivity
- Peak levels and toxicity (A2G substudy); minimum of sampling is indicated, but peak levels may be taken on *all* infusions days. Samples must be taken within one hour after infusion termination (*study only for i.v. administrations*).

No colour = no sampling

Hepatotoxicity (bilirubin, TG, ALT): x=sampling in relation to the study “Peak levels and toxicity”, (x)=recommended extra sampling. It is also recommended to take liver test at the beginning of maintenance as part of this study.

The enzyme activity measurements at the correct time-points after PEG-asparaginase infusion are essential for the recommendations of the subsequent dosing.

|  | Sampling day |    |             |    |              |              |              |     |              |     |              |     |
|--|--------------|----|-------------|----|--------------|--------------|--------------|-----|--------------|-----|--------------|-----|
| <b>ALL PATIENTS WITH DOWN SYNDROME</b> | 4 inf. day   | 11 | 18 inf. day | 22 | 32*          |              |              |     |              |     |              |     |
| Peak levels Hepatotoxicity             | x            |    | x           |    | x            |              |              |     |              |     |              |     |
| <b>SR</b>                              | 71 inf. day  | 78 | 85 inf. day | 92 | 99           | 113          |              |     |              |     |              |     |
| Peak levels Hepatotoxicity             | x            |    | x           |    | x            | x            |              |     |              |     |              |     |
| <b>IR</b>                              | 80 inf. day  | 87 | 94 inf. day | 99 | 108          | 134 inf. day | 141          | 148 | 183          |     |              |     |
| Peak levels Hepatotoxicity             | x            |    | x           |    | x            | x            |              |     | x            |     |              |     |
| <b>HR</b>                              | 51 inf. day  | 58 | 79 inf. day | 86 | 108 inf. day | 117          | 122 inf. day | 134 | 165 inf. day | 169 | 204 inf. day | 211 |
| Peak levels Hepatotoxicity             |              | x  |             | x  |              | x            |              | x   |              | x   |              | x   |

\* If day 32 samples are not possible samples can be done day 29 instead

**In case of treatment delays, samples should be taken  $\leq 14$  days after the last PEG-asparaginase dose in order to make any conclusions for treatment recommendations.**

**In case of allergic reaction:**

**If asparaginase is administered i.v. a sample must be taken immediately after the infusion is stopped, and if possible an additional sample the same day or the day after**

**If asparaginase is administered i.m. a sample must be taken 1 day after the administration of asparaginase, and if possible an additional sample 2 days after administration**

**Both after i.v. and i.m. administration, we recommend an additional sample after 7 days to identify increased clearance.**

Samples:

Register your patient in REDCap (redcap.au.dk) including details of the last dose and actual sample.

**Sampling: 2 ml of plasma: (optimally divided in two tubes)**

4 ml EDTA blood. After centrifugation 10-15 min. at 20°C, 2000 g. Aliquote plasma into two ml tubes - (i.e. 2ml Saerstedt ref. 72.694, or 1.8 ml NUNC cat. No363401). **Tubes must be labeled with date, name and date of birth., and Castor number**

Send samples as soon as possible by standard mail to:  
Aarhus Universitetshospital  
ATT: Dorte Emilie Wulff Tlf +45 51223870  
Børn og Unge Forskning. Indgang G8 –krydspunkt G211  
Palle Juul-Jensens Boulevard 99  
8200 Aarhus N. Denmark.

The treating centers must cover the shipment of samples by standard mail.  
The samples will be analysed for free.

Recommendation for the subsequent treatment (continue PEG-asparaginase/change to Erwinia asparaginase/stop asparaginase treatment) will appear in REDCap before the next planned PEG-asparaginase dose.

Questions regarding REDCap; please contact Dorte Emilie Wulff (biomedical laboratory scientist), e-mail [dorwul@rm.dk](mailto:dorwul@rm.dk) or Karen Ottosen Møller (research nurse), e-mail [karemoel@r.dk](mailto:karemoel@r.dk), mobile 30578723. Questions regarding treatment recommendation; please contact Birgitte Klug Albertsen, e-mail [biralber@rm.dk](mailto:biralber@rm.dk), mobile +45 20224643.