Fludarabine administration and blood sampling for TDM

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Please note:

- Email farmalab@umcutrecht.nl to submit a request for fludarabine TDM. If Farmalab is not cc'd, the request will not be scheduled.
- We cannot perform TDM without a completed form (see below).
- The standard schedule includes a fixed dose on days 1 and 2, followed by TDM-guided doses on Days 3 and 4. Due to frequent sample delays, this is the only feasible schedule.
- We can only process fludarabine samples on weekdays. Therefore, the day 1 dose (first dose) should be administered Saturday through Wednesday to ensure processing.
- If the package arrives later than 10:00 CET (10 am) on Friday, we won't be able to process it before the weekend and will analyze it on Monday.

TDM request

Email farmalab@umcutrecht.nl to submit a request for fludarabine TDM. If Farmalab is not cc'd, the request will not be scheduled. Please include the patient's DOB, initials, and the planned date of the first dose in the request.

Samples

The samples need to be centrifuged (plasma) and send us on dry ice. For more information on sampling times and the blood tubes see our website (link: <u>Fludarabine - UMC Utrecht</u>). Samples can be kept refrigerated as whole blood during the sampling process, then spun to separate plasma, which then can be frozen (do not freeze the whole blood samples!).

Link: https://www.umcutrecht.nl/bepalingenwijzer/fludarabine-english

Sampling schedule (FLU TDM)

- 5 min after infusion
- 1 hour after infusion
- 3 hours after infusion
- 6 hours after infusion

Please inform us if you'd like to also arrange busulfan TDM, as it will impact the sampling schedule. Additionally, the schedule will be affected if the patient is undergoing intermittent hemodialysis or CRRT.

Dosing schedule

Due to frequent delays and the typical full-day transit time even with express delivery, we propose the following schedule.

- Day 1: fixed fludarabine dose + sampling (Mo-Wed)
- Day 2: fixed fludarabine dose
- Day 3: TDM-guided fludarabine dose (processing of the samples by laboratory)
- Day 4: TDM-quided fludarabine dose

We can only process fludarabine samples on weekdays. Therefore, the day 1 dose should be administered Saturday through Wednesday to ensure processing on a weekday.

Target exposure

Allogeneic HCT

The cumulative target area under the concentration curve (AUC) for allo-HCT that we recommend for both adults and children is 20 mg*h/L (range 17.5-22.5 mg*h/L) (Blood Adv. 2019 Jul 23;3(14):2179-2187).

CAR-T

For children who receive fludarabine prior to CAR T-cell infusion, we recommend a cumulative target AUC of 14-18 mg*h/L (Blood Adv. 2022;6(7):1969-1976.)

Please let us know which target you prefer and if you want to deviate from these targets.

Additional information

We kindly ask you to always fill in the following information on our standardized form, <u>link</u>: Link: https://www.umcutrecht.nl/nl/form-fludarabine

- Contact information of the treating physician
- Email address for reporting dosing advise
- Patient ID (hospital identification number)
- Patient name and date of birth
- Planned dates of fludarabine dosing
- Length and weight of the patient
- Fludarabine dose administered
- Start time of the fludarabine infusion, stop time of the infusion
- Sampling times
- Most recent creatinine concentration
- Target fludarabine AUC (cumulative AUC in mg*h/L)

We cannot perform TDM without a completed form.

Forms:

- Form Fludarabine UMC Utrecht (form)
- <u>Divisie Lab: Bepalingenwijzer Fludarabine (English) UMC Utrecht (additional information with link to form)</u>

Shipping

Given frequent delays and the typical full-day transit time, please send the package with express delivery by Wednesday evening at the latest. We can only process fludarabine samples on weekdays. Therefore, the day 1 dose should be administered Saturday through Wednesday to ensure processing by Friday at the latest. If we receive package later then Friday 10:00 CET (10 am) or over the weekend, we will process the samples on the following Monday.

Please sent the samples to the following address:

UMC Utrecht
Centraal Diagnostisch Laboratorium
Centrale Balie, loket Externe Monsterontvangst
HP G.03.330
Heidelberglaan 100
3584CX Utrecht, the Netherlands

Contact information

farmalab@umcutrecht.nl