LEUCÉMIE LYMPHOBLASTIQUE AIGUE DE L'ENFANT : PRÉLÈVEMENTS DE SANG ET SUIVI

PRÉLÈVEMENTS DE SANG AU DIAGNOSTIC

- FSC (avec frottis) et après 1x/jour
- Créatinine, urée, glucose, acide urique
- Na, K, Ca, Mg, PO4
- AST, ALT, Bilirubin T/D, PAL
- Protéines totales, albumine, LDH
- Amylase
- Crase
- Groupe ABO-RH
- Sérologies VZV, HIV, CMV, EBV, HAV, HBV, HCV

- **Cytomorphology**
  ☐ 6 frottis de sang (unstained smears of peripheral blood) préparés avec le reste de sang de la formule du jour et envoyés à Zürich

- **PCR-MRD** (seulement si l'analyse n'a pas pu être faite sur la ponction de moelle et si assez de blastes en périphérie)
  ☐ 5-10ml Héparine (si >25% de lymphoblastes dans moelle)

- **Immunophenotyping, FCM-MRD** (seulement si l'analyse n'a pas pu être faite sur la ponction de moelle et si assez de blastes en périphérie)
  ☐ 2ml Héparine pour l'analyse locale à Lausanne
  ☐ 2-5ml Héparine pour l'analyse à Zürich

- **Cytogenetics / molecular genetics** (seulement si l'analyse n'a pas pu être faite sur la ponction de moelle et si assez de blastes en périphérie)
  ☐ 5-10ml Héparine (si >80% de lymphoblastes dans sang périphérique) pour l'analyse locale à Lausanne
  ☐ 5-10ml Héparine (si >80% de lymphoblastes dans sang périphérique) pour l'analyse à Zürich

PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA PHASE D'**INDUCTION** (CYTOREDUCTIVE PREPHASE OU PROTOCOL IA-PRED OU PROTOCOL IA-DEXA OU PROTOCOL IA-CPM)

- Formules sanguines complètes tous les jours jusqu'à la sortie
- Chimie, ASAT/ALAT, BILI T/D 3x/semaine ou selon la clinique
- **Mesure de l'activité de l'asparaginase**
  A faire chez tous les patients avec suspicion de réaction allergique à l'asparaginase, 2 heures après l'arrêt de l'infusion.
  ☐ 0.5-1ml de sang dans tube Sérum, à envoyer à température ambiante à Zürich avec le formulaire « Asparaginase – Monitoring » (en annexe)
- **Génotypage de la TPMT**
  ☐ 1 ml de sang (au moins) dans tube EDTA
  À envoyer à température ambiante à Zürich avec le formulaire « Molekulare and Pränatale Diagnostik » (en annexe)
- **Au jour 8**, prélèvement de sang pour cytomorphology
  ☐ 6 frottis de sang (unstained smears of peripheral blood) préparés avec le reste de sang de la formule du jour et envoyés à Zürich par le laboratoire des moelles
- **Au jour 15 et à tous les timepoints suivants** (TP1, TP2, TP1a, TP HR1, TP HR2, TP HR3, TP HR Blina1 d15, TP HR Blina1 d29, TP HR Blina2 d29, TP MR contr.1, TP MR contr.2, TP MR Blina d1, TP MR Blina d29, TP1b)**,** prélèvement de sang pour PCR-MRD (seulement si l'analyse n'a pas pu être faite sur la ponction de moelle et si assez de blastes en périphérie)
  ☐ 5-10ml Héparine (si >25% de lymphoblastes dans moelle)

- **Conditions pour retour à domicile après J15 et suivi ambulatoire**
  - ✓ Afébrile, pas de signes d'infection, pas d'antibiothérapie en cours
  - ✓ Critères pour un retour à domicile remplis (bonne compréhension de la maladie et du traitement de la part de la famille, situation sociale et psychologique de l'enfant et sa famille permettant un retour à domicile)
  - ✓ Suivi :
    - Examen clinique (EC) et bilan sanguin au minimum 2x/semaine pour < 10 ans & 3x/semaine pour ≥ 10 ans
      - ➢ Laboratoire : FSC, chimie (Na, K, Urée, Créat, ASAT/ALAT, BILI T/D, Amylase et lipase avant PEG-ASP), stix urinaire (exclure glycosurie),

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg Height: _____cm

BSA: _____m^2

AIEOP-BFM ALL 2017: Protocol IA-Pred (IA_P)

for pB-ALL

Version 1.3, 12.03.2019

PRED p.o./i.v. 60 mg/m^2/d |__|__|__| mg/d

*Please enter **cumulative dose of PRED** per phase#:*

VCR i.v. 1.5 mg/m^2/dose |__| . |__|__| mg
max. 2 mg

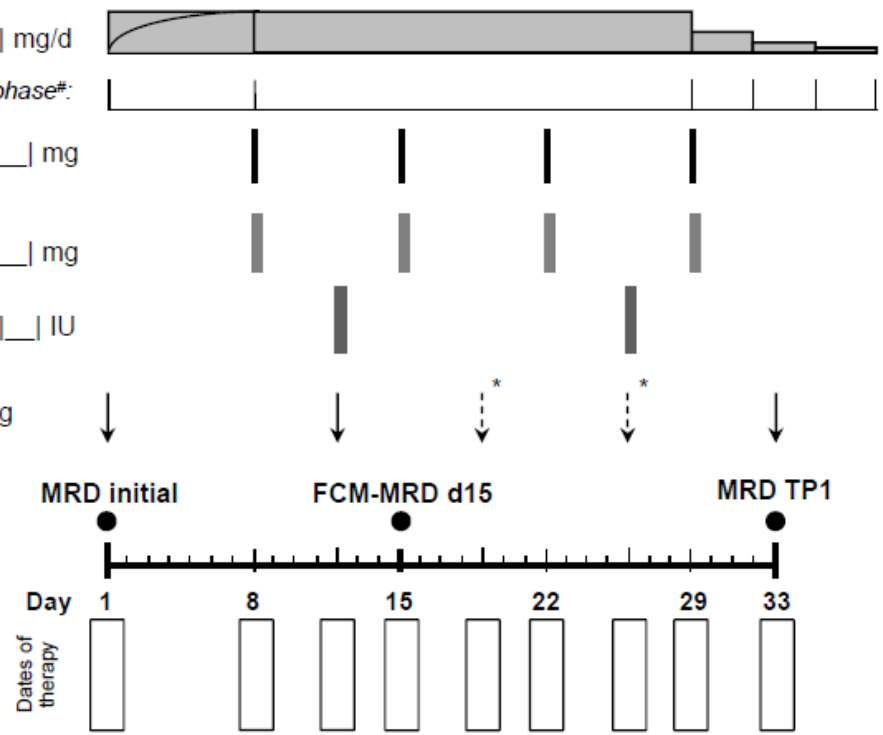
DNR p.i. (1 h) 30 mg/m^2/dose |__|__| . |__| mg

PEG-L-ASP p.i. (2 h) 2500 IU/m^2/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU)

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

*additional i.th. MTX on days 19 and 26 if CNS-positive (CNS 3)



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Please enter actually administered medication with start date (and if applicable end date and other application phases#)!

	Date	
	Start	End
PRED		
Pre-phase		
Main phase (if appl. part 1#)		
if appl., Main phase part 2#		
if appl., Main phase part 3#		
Tapering phase 1		
Tapering phase 2		
Tapering phase 3		
VCR 1		
VCR 2		
VCR 3		
VCR 4		
DNR 1		
DNR 2		
DNR 3		
DNR 4		
PEG-L-ASP 1		
PEG-L-ASP 2		
MTX i.th. day 1		
MTX i.th. day 12		
MTX i.th. day 19* if appl.		
MTX i.th. day 26* if appl.		
MTX i.th. day 33		
MRD initial		
FCM-MRD d15		
MRD TP1		

Hospitalisation: Number of nights with hospitalisation (from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Switch from PEG-L-ASP to Erwinase in this element?

- ❒ no
- ❒ yes, 1st Erwinase administration: |___|___|___| (date)
  last Erwinase administration: |___|___|___| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:

- ❒ allergic reaction, date: |___|___|___|
- ❒ other: _____

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____
Date, name and signature of the investigator

Therapy plan administered as documented

_____
Date, name and signature of the investigator (or documentalist)

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg Height: _____cm

BSA: _____m^2

AIEOP-BFM ALL 2017: Protocol IA-Dexa (IA_D)

for T-ALL PGR

Version 1.3, 12.03.2019

PRED p.o./i.v. 60 mg/m^2/d |__|__|__| mg/d

DEXA p.o./i.v. 10 mg/m^2/d |__|__| . |__| mg/d

*Please enter the **cumulative dose of PRED/DEXA** per phase#:* |

VCR i.v. 1.5 mg/m^2/dose |__| . |__|__| mg
max. 2 mg

DNR p.i. (1 h) 30 mg/m^2/dose |__|__| . |__| mg

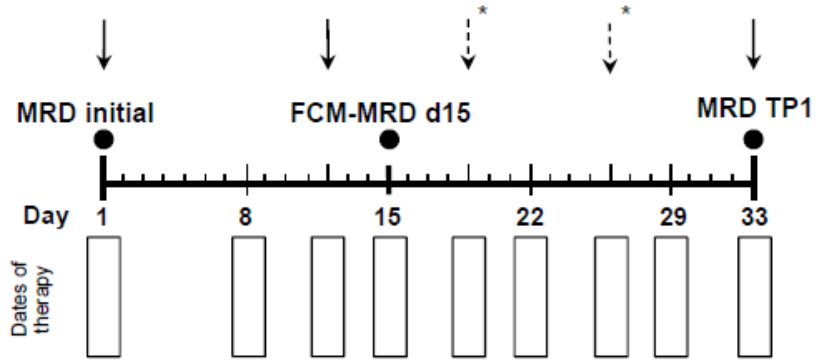
PEG-L-ASP p.i. (2 h) 2500 IU/m^2/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU)

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

* additional i.th. MTX on days 19 and 26 if CNS-positive (CNS 3)

 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases



Hospitalisation: Number of nights with hospitalisation (from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Switch from PEG-L-ASP to Erwinase in this element?

- ❒ no
- ❒ yes, 1st Erwinase administration: |__|__|__| (date)
  last Erwinase administration: |__|__|__| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:

- ❒ allergic reaction, date: |__|__|__|
- ❒ other: _____

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Datte	
	Start	End
PRED Pre-phase		
DEXA		
Main phase (if appl. part 1#)		
if appl., Main phase part 2#		
if appl., Main phase part 3#		
Tapering phase 1		
Tapering phase 2		
Tapering phase 3		
VCR 1		
VCR 2		
VCR 3		
VCR 4		
DNR 1		
DNR 2		
DNR 3		
DNR 4		
PEG-L-ASP 1		
PEG-L-ASP 2		
MTX i.th. day 1		
MTX i.th. day 12		
MTX i.th. day 19* if appl.		
MTX i.th. day 26* if appl.		
MTX i.th. day 33		
MRD initial		
FCM-MRD d15		
MRD TP1		

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg Height: _____cm

BSA: _____m^2

AIEOP-BFM ALL 2017: Protocol IA-CPM (IA_{CPM})

for T-ALL PPR

Version 1.3, 12.03.2019

PRED p.o./i.v. 60 mg/m^2/d |__|__|__| mg/d

*Please enter the **cumulative dose of PRED** per phase#:*

VCR i.v. 1.5 mg/m^2/dose |__| . |__|__| mg
max. 2 mg

DNR p.i. (1 h) 30 mg/m^2/dose |__|__| . |__| mg

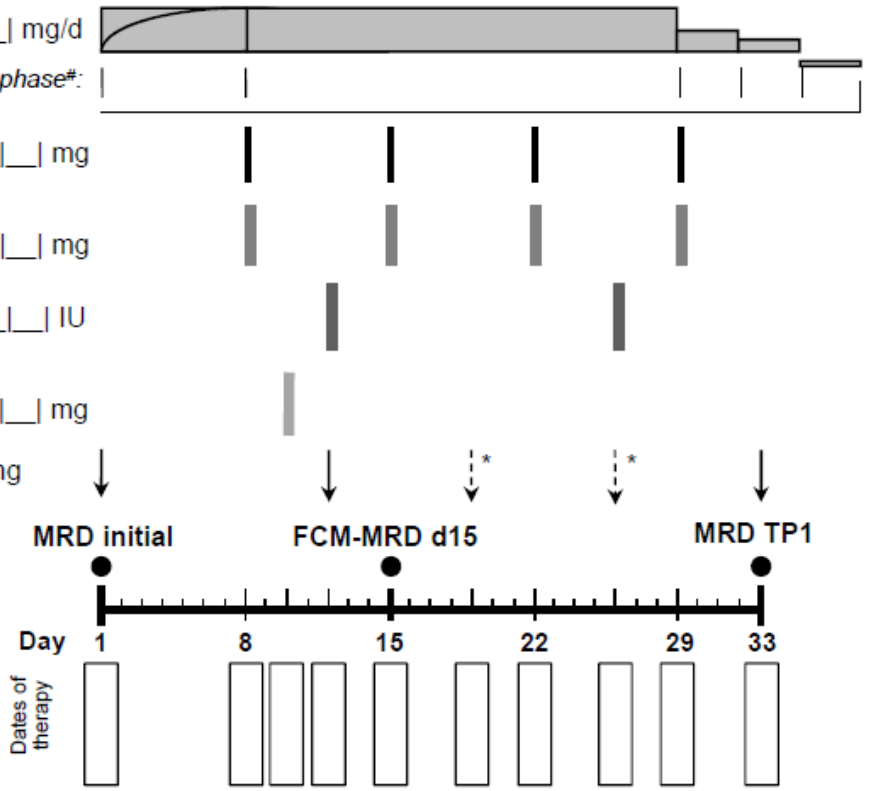
PEG-L-ASP p.i. (2 h) 2500 IU/m^2/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU)

CPM p.i. (1 h) 1000 mg/m^2/dose |__|__| . |__| mg

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

* additional i.th. MTX on days 19 and 26 if CNS-positive (CNS 3)



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
PRED		
Pre-phase		
Main phase (if appl .part 1#)		
if appl., Main phase part 2#		
if appl., Main phase part 3#		
Tapering phase 1		
Tapering phase 2		
Tapering phase 3		
VCR 1		
VCR 2		
VCR 3		
VCR 4		
DNR 1		
DNR 2		
DNR 3		
DNR 4		
PEG-L-ASP 1		
PEG-L-ASP 2		
CPM		
MTX i.th. day 1		
MTX i.th. day 12		
MTX i.th. day 19* if appl.		
MTX i.th. day 26* if appl.		
MTX i.th. day 33		
MRD initial		
FCM-MRD d15		
MRD TP1		

Hospitalisation: Number of nights with hospitalisation (from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Switch from PEG-L-ASP to Erwinase in this element?

- ❒ no
- ❒ yes, 1st Erwinase administration: |___|___|___| (date)
  last Erwinase administration: |___|___|___| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:

- ❒ allergic reaction, date: |___|___|___|
- ❒ other: _____

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

POUR LLA PRE-B: PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA PHASE DE **CONSOLIDATION** (CONSOLIDATION A OU SHORT CONSOLIDATION B OU EXTENDED CONSOLIDATION B OU EXTENDED CONSOLIDATION B + BORTEZOMIB)

- Examen clinique au début du cycle et avant le début de chaque bloc de ARA-C ou VCR

- Formules sanguines complètes au début du cycle et avant chaque bloc d'ARA-C

- Chimie : Na, K, Urée, Créat ASAT/ALAT, BILI T/D au début du cycle et avant chaque bloc d'ARA-C

- **Conditions pour débuter la phase**

Requirements for starting Consol. A

- Adequate clinical condition and no serious infection according to the assessment of the investigator
- Recovering (increasing) blood counts
  - ✓ Granulocytes ≥ 500/µl
  - ✓ Platelets ≥ 50 000/µl

Requirements for starting Consol. B_{short}

- Adequate clinical condition and no serious infection according to the assessment of the investigator
- Normal renal function
- Blood counts
  - ✓ Granulocytes ≥ 500/µl
  - ✓ Platelets ≥ 50 000/µl

There are no specific blood count requirements for the administration of the last Cyclophosphamide dose on day 64.

Requirements for starting Consol. B_{ext} or Consol. B_{ext}+BZM

- Adequate clinical condition and no serious infection according to the assessment of the investigator
- Creatinine clearance ≥ 20 ml/min/1.73 m_2 (only Consol. B_{ext} + BZM)
- Bilirubin <1.5x upper normal limit
- Blood counts
  - ✓ Granulocytes ≥ 500/µl
  - ✓ Platelets ≥ 50 000/µl

Requirements for starting with Cyclophosphamide on day 64 (during Consol. B_{ext} or Consol. B_{ext}+BZM)

- Creatinine clearance ≥ 25 ml/min/1.73 m_2. Dose adjustments of Cyclophosphamide are recommended if Creatinine clearance < 25 ml/min/1.73 m_2
- Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl

There are no specific blood count requirements for the administration of the last Cyclophosphamide dose on day 78

AIEOP-BFM ALL 2017: Consolidation A

for pB-ALL

Version 1.3, 12.03.2019

ARA-C i.v. 75 mg/m²/dose |__|__|__| mg

*Please enter the **cumulative dose given in each ARA-C block**:*

*Please enter the **number of doses given in each ARA-C block**:*

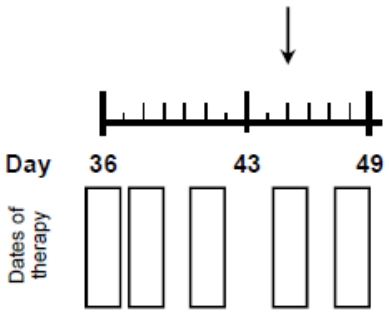
6-MP **p.o. (14 d)** 60 mg/m²/d |__|__|__| . |__| mg/d

*Please enter the **cumulative dose of 6-MP#**:*

MTX **i.th.** dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases



Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg

Height: _____cm

BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
ARA-C block 1 (4 doses)		
ARA-C block 2 (4 doses)		
6-MP (if applicable part 1#)		
if applicable: 6-MP part 2#		
MTX i.th.day 45		

Hospitalisation: Number of nights with hospitalisation (from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

AIEOP-BFM ALL 2017: Short Consolidation B

for early non-HR (pB-ALL)

Version 1.3, 12.03.2019

CPM p.i. (1 h) (+MESNA) 1000 mg/m² /dose |__|__|__|__| mg

ARA-C i.v. 75 mg/m²/dose |__|__|__| mg

*Please enter the **cumulative dose given in each ARA-C block**:* ____ ____

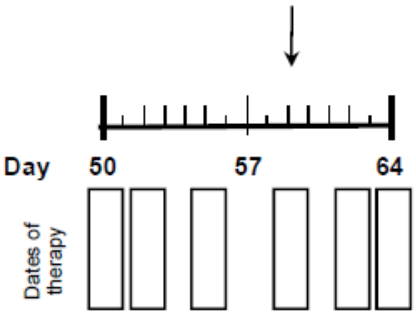
*Please enter the **number of doses given in each ARA-C block**:* ____ ____

6-MP p.o. (14 d) 60 mg/m²/d |__|__|__| . |__| mg/d

*Please enter the **cumulative dose of 6-MP#**:* _____

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg

Height: _____cm

BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
CPM 1		
CPM 2		
ARA-C block 3 (4 doses)		
ARA-C block 4 (4 doses)		
6-MP (if applicable part 1#)		
if applicable: 6-MP part 2#		
MTX i.th. day 59		

Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

AIEOP-BFM ALL 2017: Extended Consolidation B

for early HR (pB-ALL in R-eHR control arm)

Version 1.3, 12.03.2019

DEXA p.o./i.v. 10 mg/m²/d |__|__| , |__| mg/d

*Please enter the **cumulative dose of DEXA#**:*

VCR i.v. 1.5 mg/m²/dose |__| . |__|__| mg
max. 2 mg

PEG-L-ASP p.i. (2 h) 2500 IU/m²/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU)

CPM p.i. (1 h) 1000 mg/m² /dose |__|__|__|__| mg
(+MESNA)

ARA-C i.v. 75 mg/m²/dose |__|__|__| mg

*Please enter the **cumulative dose given in each ARA-C block**:*

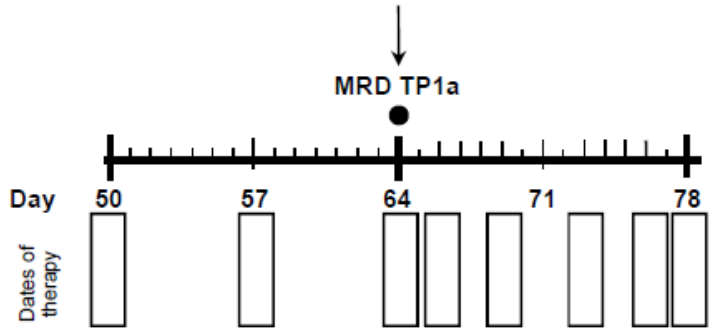
*Please enter the **number of doses given in each ARA-C block**:*

6-MP p.o. (14 d) 60 mg/m²/d |__|__|__| . |__| mg/d

*Please enter the **cumulative dose of 6-MP#**:*

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Switch from PEG-L-ASP to Erwinase in this element?

- ☐ no
- ☐ yes, 1st Erwinase administration: |___|___|___| (date)
  last Erwinase administration: |___|___|___| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:

- ☐ allergic reaction, date: |___|___|___|
- ☐ other: _____

Therapy according to the protocol?

- ☐ yes
- ☐ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ☐ medical reason
  - ☐ psychosocial reason
  - ☐ other reason _____

Were additional antileukemic drugs administered?

- ☐ no
- ☐ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg

Height: _____cm

BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
DEXA (if applicable, part 1#)		
if applicable: DEXA part 2#		
VCR 1		
VCR 2		
PEG-L-ASP		
CPM 1		
CPM 2		
ARA-C block 3 (4 doses)		
ARA-C block 4 (4 doses)		
6-MP (if applicable, part 1#)		
if applicable: 6-MP part 2#		
MTX i.th. day 64		
MRD TP1a		

Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

AIEOP-BFM ALL 2017: Extended Consolidation B + Bortezomib

for early HR (pB-ALL in R-eHR experimental arm)

Version 1.3, 12.03.2019

BZM i.v. 1.3 mg/m²/dose |__| . |__|__| mg

DEXA p.o./i.v. 10 mg/m²/d |__|__| . |__| mg/d

*Please enter the **cumulative dose of DEXA#**:*

VCR i.v. 1.5 mg/m²/dose |__| . |__|__| mg
max. 2 mg

PEG-L-ASP p.i. (2 h) 2500 IU/m²/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU/dose)

CPM p.i. (1 h) 1000 mg/m²/dose |__|__|__|__| mg
(+MESNA)

ARA-C i.v. 75 mg/m²/dose |__|__|__| mg

*Please enter the **cumulative dose given in each ARA-C block**:*

*Please enter the **number of doses given in each ARA-C block**:*

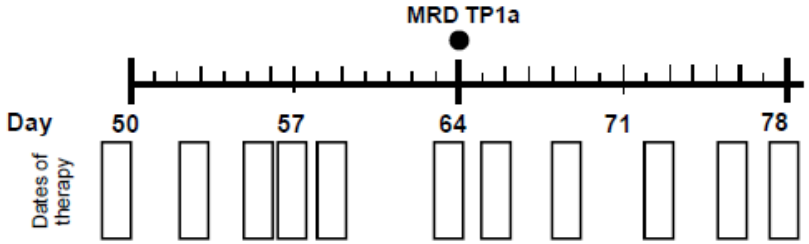
6-MP p.o. (14 d) 60 mg/m²/d |__|__|__| . |__| mg/d

*Please enter the **cumulative dose of 6-MP#**:*

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases



Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Switch from PEG-L-ASP to Erwinase in this element?

- ❒ no
- ❒ yes, 1st Erwinase administration: |__|__|__| (date)
  last Erwinase administration: |__|__|__| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:

- ❒ allergic reaction, date: |__|__|__|
- ❒ other: _____

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg Height: _____cm

BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
BZM 1		
BZM 2		
BZM 3		
BZM 4		
DEXA (if appl. part 1#)		
if applicable: DEXA part 2#		
VCR 1		
VCR 2		
PEG-L-ASP		
CPM 1		
CPM 2		
ARA-C block 3 (4 doses)		
ARA-C block 4 (4 doses)		
6-MP (if applicable part 1#)		
if applicable: 6-MP part 2#		
MTX i.th. day 64		
MRD TP 1a		

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

POUR LLA-T: PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA **PHASE IB** (PROTOCOL IB/PART 1 OU REGULAR PROTOCOL IB/PART 2 OU LONG PROTOCOL IB/2)

- Examen clinique au début du cycle et avant le début de chaque bloc de ARA-C

- Formules sanguines complètes au début du cycle et avant chaque bloc d'ARA-C

- Chimie : Na, K, Urée, Créat ASAT/ALAT, BILI T/D au début du cycle et avant chaque bloc d'ARA-C

- **Conditions pour débuter la phase :**

  Requirements for starting Prot. IB/1
  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Creatinine clearance ≥ 25 ml/min/1.73 m_2. Dose adjustments of Cyclophosphamide if Creatinine clearance < 25 ml/min/1.73 m_2
  - Recovering (increasing) blood counts:
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl

  Requirements for starting Prot. IB/2_{reg}
  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Creatinine clearance ≥ 25 ml/min/1.73 m_2. Dose adjustments of Cyclophosphamide if Creatinine clearance < 25 ml/min/1.73 m_2
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl

  As far as possible, Prot. IB/2_{reg} should not be interrupted. If interruption is nevertheless required, 6-Mercaptopurine should also be withheld for the same period. Omitted 6-Mercaptopurine doses should be made up until the scheduled cumulative dose of 420 mg/m_2 (7x60 mg/m_2) has been reached.
  There are no specific blood count requirements for the administration of the last Cyclophosphamide dose on day 64.

Requirements for starting Prot. IB/2$_{long}$

- Adequate clinical condition and no serious infection according to the assessment of the investigator
- Creatinine clearance ≥ 25 ml/min/1.73 m_2. Dose adjustments of Cyclophosphamide if Creatinine clearance < 25 ml/min/1.73 m_2
- Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl

As far as possible, Prot. IB/2-long should not be interrupted. If nevertheless a Cytarabine block has to be interrupted or postponed, 6-Mercaptopurine should also be withheld for the same period. Omitted 6-Mercaptopurine doses should be made up until the scheduled cumulative dose of 1260 mg/m_2 (21x60 mg/m_2) has been reached.

There are no specific blood count requirements for the administration of the last Cyclophosphamide dose on day 78

AIEOP-BFM ALL 2017: Protocol IB/Part 1 (IB/1)

for T-ALL

Version 1.3, 12.03.2019

CPM p.i. (1 h) 1000 mg/m²/dose |__|__|__|__| mg
(+MESNA)

ARA-C i.v. 75 mg/m²/dose |__|__|__| mg

*Please enter the **cumulative dose given in each ARA-C block**:* |____| |____| |____|

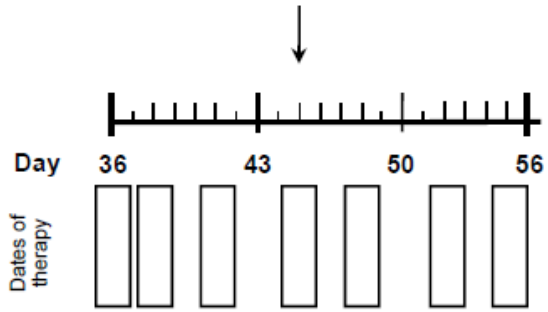
*Please enter the **number of doses given in each ARA-C block**:* |____| |____| |____|

6-MP p.o. (21 d) 60 mg/m²/d |__|__|__| . |__| mg/d

*Please enter the **cumulative dose of 6-MP#**:* |____|

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg

Height: _____cm

BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
CPM 1		
ARA-C block 1 (4 doses)		
ARA-C block 2 (4 doses)		
ARA-C block 3 (4 doses)		
6-MP (if applicable part 1#)		
if applicable 6-MP part 2#		
if applicable 6-MP part 3#		
MTX i.th. day 45		

Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

AIEOP-BFM ALL 2017: Regular Protocol IB/Part 2 ($IB/2_{reg}$)

for early SR T-ALL and early non-SR T-ALL in R-T control arm

Version 1.3, 12.03.2019

CPM p.i. (1 h) (+MESNA) 1000 mg/m²/dose |__|__|__|__| mg

ARA-C i.v. 75 mg/m²/dose |__|__|__| mg

*Please enter the **cumulative dose given in the ARA-C block**:* |____|

*Please enter the **number of doses given in the ARA-C block**:* |____|

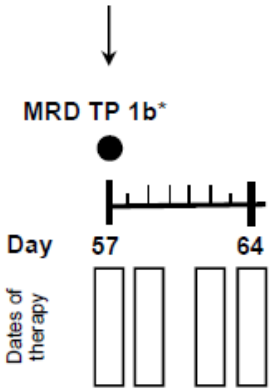
6-MP p.o. (7 d) 60 mg/m²/d |__|__|__| . |__| mg/d

*Please enter the **cumulative dose of** 6-MP#:* |_____|

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

* MRD on TP 1b (d57) only for randomized patients



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg

Height: _____cm

BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
CPM 2		
ARA-C block 4 (4 doses)		
6-MP (if appl. part 1#)		
if appl. 6-MP part 2#		
MTX i. th. day 57		
if appl. MRD TP 1b*		

Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

AIEOP-BFM ALL 2017: Long Protocol IB/2 ($IB/2_{long}$)

for early non-SR T-ALL in R-T experimental arm

Version 1.3, 12.03.2019

CPM p.i. (1 h) (+MESNA) 1000 mg/m²/dose |__|__|__|__| mg

ARA-C i.v. 75 mg/m²/dose |__|__|__| mg

*Please enter the **cumulative dose given in the ARA-C block**:*

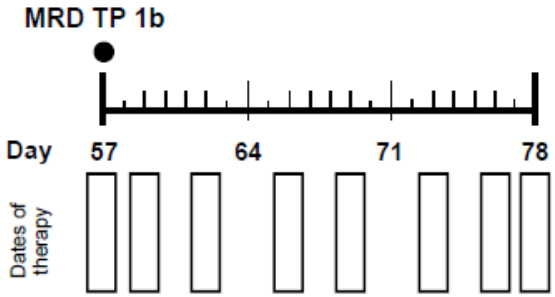
*Please enter the **number of doses given in the ARA-C block**:*

6-MP p.o. (21 d) 60 mg/m²/d |__|__|__| . |__| mg/d

*Please enter the **cumulative dose of** 6-MP#:*

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg

Height: _____cm

BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
CPM 2		
CPM 3		
ARA-C block 4 (4 doses)		
ARA-C block 5 (4 doses)		
ARA-C block 6 (4 doses)		
6-MP (if appl. part 1#)		
if applicable 6-MP part 2#		
if applicable 6-MP part 3#		
MTX i.th. day 57		
MRD TP 1b		

Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA PHASE **PROTOCOL M**

- Formules sanguines complètes au début de la phase M & la veille de chaque HD-Methotrexate

- Chimie, Na, K, Urée, créat, ASAT/ALAT, BILI T/D au début de la phase M & la veille de chaque HD-Methotrexate

- Examen clinique au début de la phase M et à l'admission pour chaque HD-Methotrexate

- **Conditions pour débuter la phase et chaque HD-MTX**

  Requirements for starting Protocol M

  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Normal renal function. **Dose adjustments of HD-MTX are recommended in the case of reduced creatinine clearance**
  - No urinary obstruction
  - No pleural effusion, no ascitis
  - Recovering (increasing) blood counts:
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl
  - GOT/GPT <10 x upper normal limit
  - Bilirubin <3 x upper normal limit with normal direct bilirubin

  Requirements for start of a HD-MTX block

  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Normal renal function. Dose adjustments of HD-MTX are recommended in the case of reduced creatinine clearance.
  - No urinary obstruction
  - Stable blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl
  - GOT/GPT <10 x upper normal limit
  - Bilirubin <3 x upper normal limit with normal direct bilirubin

  If transaminases are between 10 and 20 times of the upper normal limit, wait 36 to 48 hours and check to ensure that the levels are decreasing. If GOT and/or GPT are ≥ 20 times of normal upper limits, contact the national study coordinator for further recommendations.

AIEOP-BFM ALL 2017: Protocol M

for non-HR patients (pB and T-ALL)

Version 1.3, 12.03.2019

6-MP p.o. (56 d) 25 mg/m²/d |__|__| . |__| mg/d
(in the evening)

*Please enter the **cumulative dose of 6-MP#**:* |_____|

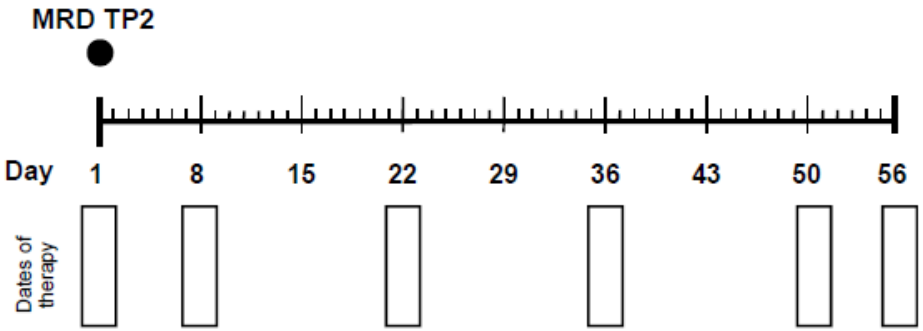
HD-MTX p.i. (24 h) 5000 mg/m²/dose
(10% over 0.5 h, 90% over 23.5 h)

|__|__|__|__| mg |__|__|__|__| mg |__|__|__|__| mg |__|__|__|__| mg

LCV-Rescue i.v. 15 mg/m²/dose
42, 48, and 54 h after start HD-MTX

MTX i.th. dose age-adjusted |__|__| mg
(during MTX infusion)

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Stud.-No. (Pat.-ID): _____
DOB: _____
Weight: _____kg
Height: _____cm
BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
6-MP Protocol M		
6-MP (if appl. part 1#)		
if applicable part 2#		
if applicable part 3#		
if applicable part 4#		
if applicable part 5#		
HD-MTX p.i. dose 1		
HD-MTX p.i. dose 2		
HD-MTX p.i. dose 3		
HD-MTX p.i. dose 4		
MTX i.th. day 8		
MTX i.th. day 22		
MTX i.th. day 36		
MTX i.th. day 50		
MRD TP2		

Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Therapy according to the protocol?
- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?
- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____
Date, name and signature of the investigator

Therapy plan administered as documented

_____
Date, name and signature of the investigator (or documentalist)

PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA PHASE **PROTOCOL II**

- Formules sanguines complètes 1x/semaine
- Chimie, Na, K, Urée, créat, ASAT/ALAT, BILI T/D 1x/semaine
- Stix urinaire (exclure glycosurie) 2x/semaine sous stéroïdes
- Examen clinique au début du cycle et 2x/semaine pendant le traitement par Dexamethasone et avant chaque bloc de ARA-C iv
- **Echo-ECG is mandatory prior to the 1st Doxorubicin**
- **Mesure de l'activité de l'asparaginase**
  A faire chez tous les patients avec suspicion de réaction allergique à l'asparaginase, 2 heures après l'arrêt de l'infusion.
  ☐ 0.5-1ml de sang dans tube Sérum, à envoyer à température ambiante à Zürich avec le formulaire « Asparaginase – Monitoring » (en annexe).
- **Conditions pour débuter la phase IIA & IIB :**
  Requirements for starting Protocol IIA
  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl

  If symptoms/signs of cardiac insufficiency are present and/or if the LV-SF is repeatedly below 30% or the EF below 50%, contact the national study coordinator for consideration of procedure.

  Requirements for starting Protocol IIB
  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Creatinine clearance ≥ 25 ml/min/1.73 m2. Dose adjustments of Cyclophosphamide are recommended if Creatinine clearance < 25 ml/min/1.73 m2
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl

Stud.-No. (Pat.-ID): _____
DOB: _____
Weight: _____kg Height: _____cm
BSA: _____m^2

AIEOP-BFM ALL 2017: Protocol II

for non-HR patients (pB and T-ALL)

Version 1.3, 12.03.2019

DEXA p.o./i.v. (21 d) 10 mg/m^2/d |__|__|. |__|mg/d

*Please enter the **cumulative dose of DEXA** per phase#:*

VCR i.v. 1.5 mg/m^2/dose max. 2 mg |__| . |__|__| mg

DOX p.i. (1 h) 30 mg/m^2/dose |__|__| . |__| mg

PEG-L-ASP p.i. (2 h) 2500 IU/m^2/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU)

CPM p.i. (1 h) 1000 mg/m^2/dose (+MESNA) |__|__|__|__| mg

ARA-C i.v. 75 mg/m^2/dose |__|__|__| mg

*Please enter the **cumulative dose given in each ARA-C block**:*

*Please enter the **number of doses given in each ARA-C block**:*

TG p.o. (14 d) 60 mg/m^2/d |__|__|__| . |__| mg/d

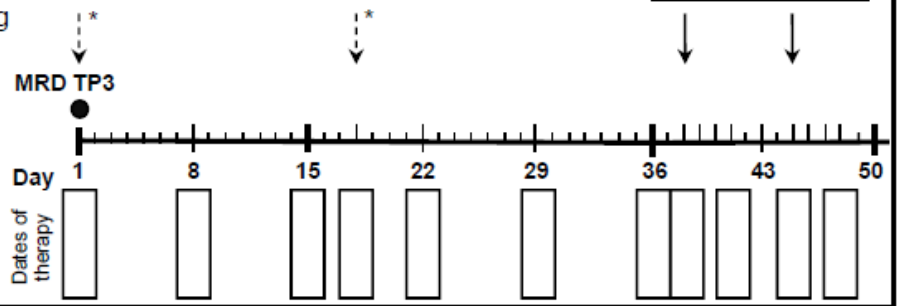
*Please enter the **cumulative dose of TG#**:*

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

*additional i.th. MTX on day 1 and 18 in CNS-positive (CNS 3) patients

Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
DEXA		
Main phase (if appl. part 1#)		
if appl., Main phase part 2#		
if appl., Main phase part 3#		
Tapering phase 1		
Tapering phase 2		
Tapering phase 3		
VCR 1		
VCR 2		
VCR 3		
VCR 4		
DOX 1		
DOX 2		
DOX 3		
DOX 4		
PEG-L-ASP		
CPM		
ARA-C block 1		
ARA-C block 2		
TG (if applicable part 1#)		
if applicable TG part 2#		
if applicable TG part 3#		
if appl. MTX i.th. day 1*		
if appl. MTX i.th. day 18*		
MTX i.th. day 38		
MTX i.th. day 45		
MRD TP3		

Switch from PEG-L-ASP to Erwinase in this element?
- ❒ no
- ❒ yes, 1st Erwinase administration: |___|___|___| (date)
  last Erwinase administration: |___|___|___| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:
- ❒ allergic reaction, date: |___|___|___|
- ❒ other: _____

Therapy according to the protocol?
- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?
- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____
Date, name and signature of the investigator

Therapy plan administered as documented

_____
Date, name and signature of the investigator (or documentalist)

PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LES **CYCLES HR** (BLOCK HR-1' OU BLOCK HR-2' OU BLOCK HR-3')

- Formules sanguines complètes avant chaque bloc

- Chimie, Na, K, Urée, créat, ASAT/ALAT, BILI T/D avant chaque cycle et après selon indication

- Patient hospitalisé pendant le cycle et jusqu'à récupération des valeurs sanguines

- **Mesure de l'activité de l'asparaginase**
  A faire chez tous les patients avec suspicion de réaction allergique à l'asparaginase, 2 heures après l'arrêt de l'infusion.
  ☐ 0.5-1ml de sang dans tube Sérum, à envoyer à température ambiante à Zürich avec le formulaire « Asparaginase – Monitoring » (en annexe)

- **Prophylaxie antifongique et antibiotique dès la fin du cycle**

- **Conditions pour débuter chaque HR bloc :**
  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - No urinary obstruction
  - Intact mucous membranes
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl
  - No essential organ dysfunction: Normal renal function. Dose adjustments of HD-Methotrexate and High-dose Cytarabine are recommended in the case of reduced creatinine clearance.
  Dose adjustment of Cyclophosphamide is recommended if creatinine clearance < 25 ml/min/1.73 m²
    - ✓ GOT/GPT <10 x upper normal limit
    - ✓ Bilirubin <3 x upper normal limit with normal direct bilirubin

AIEOP-BFM ALL 2017: Block HR-1'

Version 1.3, 12.03.2019

DEXA p.o./i.v. (5d) 20 mg/m²/d |__|__| . |__| mg/d

*Please enter the **cumulative dose of DEXA** per phase#:* |_____|

VCR i.v. 1.5 mg/m²/dose |__| . |__|__| mg
max. 2 mg

HD-ARA-C p.i. (3 h) 2000 mg/m²/dose |__|__|__|__| mg

HD-MTX p.i. (24 h) 5000 mg/m²/dose |__|__|__|__| mg
(10% over 0,5 h., 90% over 23.5 h)

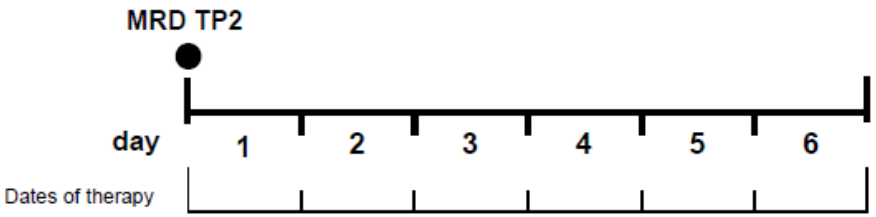
LCV-Rescue i.v. 15 mg/m²/dose |__|__| mg
42, 48, and 54 h after start HD-MTX

CPM p.i. (1 h) 200 mg/m²/dose |__|__|__| mg
with MESNA: 70 mg/m²/dose 0, 4, and 8 h of CPM

PEG-L-ASP p.i. (2 h) 2500 IU/m²/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU)

MTX i.th. dose age-adjusted |__|__| mg
(during MTX infusion)

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Hospitalisation: Number of nights with hospitalisation (from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Switch from PEG-L-ASP to Erwinase in this element?
- ❒ no
- ❒ yes, 1st Erwinase administration: |___|___|___| (date)
  last Erwinase administration: |___|___|___| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:
- ❒ allergic reaction, date: |___|___|___|
- ❒ other: _____

Therapy according to the protocol?
- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?
- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Stud.-No. (Pat.-ID): _____
DOB: _____
Weight: _____kg Height: _____cm
BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
DEXA (if appl. part 1#)		
if appl. DEXA part 2#		
VCR 1		
VCR 2		
HD-ARA-C 1		
HD-ARA-C 2		
HD-MTX		
CPM 1		
CPM 2		
CPM 3		
CPM 4		
CPM 5		
PEG-L-ASP		
MTX i.th. day 1		
MRD TP 2		
Was G-CSF administered? ❒ yes (enter date) ❒ no		

Therapy plan calculated and prepared

_____
Date, name and signature of the investigator

Therapy plan administered as documented

_____
Date, name and signature of the investigator (or documentalist)

AIEOP-BFM ALL 2017: Block HR-2'

Version 1.3, 12.03.2019

DEXA p.o./i.v. (5d) 20 mg/m²/d |__|__|.|__| mg/d

*Please enter the **cumulative dose of DEXA** per phase#:* |_____|

VDS i.v. 3 mg/m²/dose |__|.|__|__| mg
max. 5 mg

DNR p.i. (24 h) 30 mg/m²/dose |__|__|__|__| mg

HD-MTX p.i. (24 h) 5000 mg/m²/dose |__|__|__|__| mg
(10% over 0.5 h, 90% over 23.5 h)

LCV-Rescue i.v. 15 mg/m²/dose |__|__| mg
42, 48, and 54 h after start HD-MTX

IFO p.i. (1 h) 800 mg/m²/dose |__|__|__| mg
with MESNA: 300 mg/m²/dose 0, 4, and 8 h of IFO

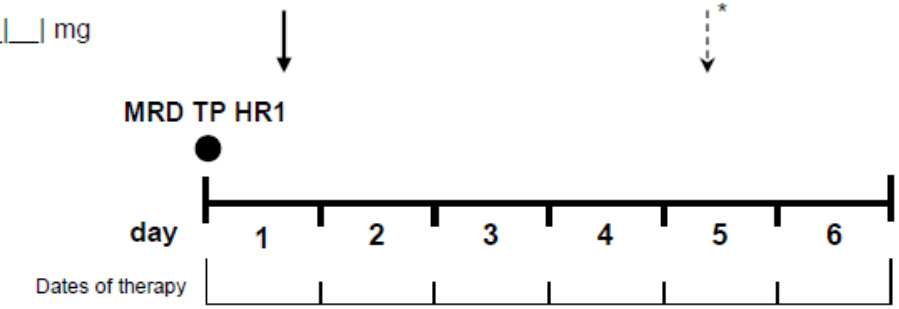
PEG-L-ASP p.i. (2 h) 2500 IU/m²/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU)

MTX i.th. dose age-adjusted |__|__| mg
(during MTX infusion)

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

* additional i.th. MTX on day 5 if CNS-positive (CNS 3)

 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases



Hospitalisation: Number of nights with hospitalisation (from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Switch from PEG-L-ASP to Erwinase in this element?

- ❒ no
- ❒ yes, 1st Erwinase administration: |__|__|__| (date)
  last Erwinase administration: |__|__|__| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:

- ❒ allergic reaction, date: |__|__|__|
- ❒ other: _____

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg Height: _____cm

BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
DEXA (if appl. part 1#)		
if appl. DEXA part 2#		
VDS 1		
VDS 2		
DNR		
HD-MTX		
IFO 1		
IFO 2		
IFO 3		
IFO 4		
IFO 5		
PEG-L-ASP		
MTX i.th. day 1		
if appl. MTX i.th. day 5*		
MRD TP HR1		
Was G-CSF administered? ❒ yes (enter date) ❒ no		

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist

AIEOP-BFM ALL 2017: Block HR-3'

Version 1.3, 12.03.2019

DEXA p.o./i.v. (5d) 20 mg/m²/d |__|__| . |__| mg/d

*Please enter the **cumulative dose of DEXA** per phase#:* _____

HD-ARA-C p.i. (3 h) 2000 mg/m²/dose |__|__|__|__| mg

VP-16 p.i. (1 h) 100 mg/m²/dose |__|__|__| mg

PEG-L-ASP p.i. (2 h) 2500 IU/m²/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU)

MTX i.th. dose age-adjusted |__|__| mg
(during MTX infusion)

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

MRD TP HR2

Day 1 2 3 4 5 6

Dates of therapy

Hospitalisation: Number of nights with hospitalisation (from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Switch from PEG-L-ASP to Erwinase in this element?
- ❒ no
- ❒ yes, 1st Erwinase administration: |___|___|___| (date)
  last Erwinase administration: |___|___|___| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:
- ❒ allergic reaction, date: |___|___|___|
- ❒ other: _____

Therapy according to the protocol?
- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?
- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Stud.-No. (Pat.-ID): _____
DOB: _____
Weight: _____kg
Height: _____cm
BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
DEXA (if appl. part 1#)		
if applicable DEXA Teil 2#		
HD-ARA-C 1		
HD-ARA-C 2		
HD-ARA-C 3		
HD-ARA-C 4		
VP-16 dose 1		
VP-16 dose 2		
VP-16 dose 3		
VP-16 dose 4		
VP-16 dose 5		
PEG-L-ASP		
MTX i.th. day 1		
MRD TP HR2		
Was G-CSF administered? ❒ yes (enter date) ❒ no		

Therapy plan calculated and prepared

_____
Date, name and signature of the investigator

Therapy plan administered as documented

_____
Date, name and signature of the investigator (or documentalist)

PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA PHASE **BLINATUMOMAB** (IN MR OR IN HR)

- Formules sanguines complètes 1x/semaine
- Chimie, Na, K, Urée, créat, ASAT/ALAT, BILI T/D 2x/semaine au changement de la casette (voir SOP Blinatunomab)
- Examen clinique 2x/semaine au changement de la cassette (voir SOP Blinatunomab)
- A la fin de l'administration du Blinatumomab, doser IgG, IgA et IgM
- Détails de la préparation et de l'administration du Blinatumomab dans le SOP Blinatunomab
- **Conditions pour débuter le Blinatunomab :**
  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Intact mucous membranes
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl
  - No essential organ dysfunction:
    - ✓ No renal dysfunction
    - ✓ GOT/GPT <10 x upper normal limit
    - ✓ Bilirubin <3 x upper normal limit with normal direct bilirubin

Stud.-No. (Pat.-ID): _____
DOB: _____
Weight: _____kg
Height: _____cm
BSA: _____m²

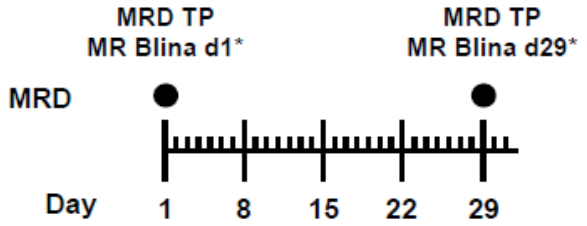
AIEOP-BFM ALL 2017: Blinatumomab in MR

for MR pB-ALL in R-MR experimental arm

Version 1.3, 12.03.2019

BLINATUMOMAB p.i. (28 d) 15 µg/m²/d |__|__|__| . |__| µg/d

*only if PCR-MRD was positive at TP2



Please enter date of MRD!

	Date
MRD TP MR Blina d1*	
MRD TP MR Blina d29*	

Please enter actually administered glucocorticoids!

Drug name	Dose (absolute)	Date

Was Tocilizumab administered during this cycle?
❒ no
❒ yes, on :_____ (date)
Dose (absolute)_____

Please enter actually administered Blinatumomab with start and end date!
For interruptions > 1 h and/or dose changes > 10 %, please start a new application phase within this cycle and document weight, height and body surface for each application phase.
Please document the reason for interruption(s) or (premature) discontinuation of the cycle (=end of application phase) (see legend on the right).
For a cycle that was restarted from the beginning after previous interruption, please use a new CRF.

Application phase	Blinatumomab cumulative dose	Start		End		Reason for end of application phase	Body measurements		
		Date	Time	Date	Time		Weight (kg)	Height (cm)	BSA (m²)
1									
2									
3									
4									
5									

Is this a restarted cycle after previous discontinuation of a cycle?
❒ yes ❒ no

Therapy plan calculated and prepared

_____
Date, name and signature of the investigator

Therapy plan administered as documented

_____
Date, name and signature of the investigator (or documentalist)

Hospitalisation: Number of nights with hospitalisation (from start of the cycle until beginning of the next therapy element): _____

Possible reasons for (premature) discontinuation or interruption of the cycle (→ reason for the end of a application phase):

a) Cycle completed

b) Interruption > 1 h:
- b1) (S)AE
- b2) Non-Compliance
- b3) Request of the patient or the patient's guardian(s)
- b4) Delayed restart after bag change
- b5) Malfunction of infusion pump
- b6) Infusion bag emptied prematurely
- b7) Other

c) Dose change > 10 %:
- c1)) Dose reduction or re-escalation due to (previous) (S)AE
- c2) Non-Compliance
- c3) Adjustment to weight change
- c4) Dose administration error
- c5) Other

d) Premature discontinuation of this cycle:
- d1) (S)AE
- d2) Non-Compliance
- d3) Request of the patient or the patient's guardian(s)
- d4) Other

e) Permanent withdrawal of Blinatumomab treatment:
- e1) (S)AE
- e2) Non-Compliance
- e3) Request of the patient or the patient's guardian(s)
- e4) ALL relapse or progression
- e5) Death
- e6) Retrospectively ineligible
- e7) Other

Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg Height: _____cm

BSA: _____m²

AIEOP-BFM ALL 2017: Blinatumomab in HR:
1. Cycle for HR pB-ALL in R-HR experimental arm

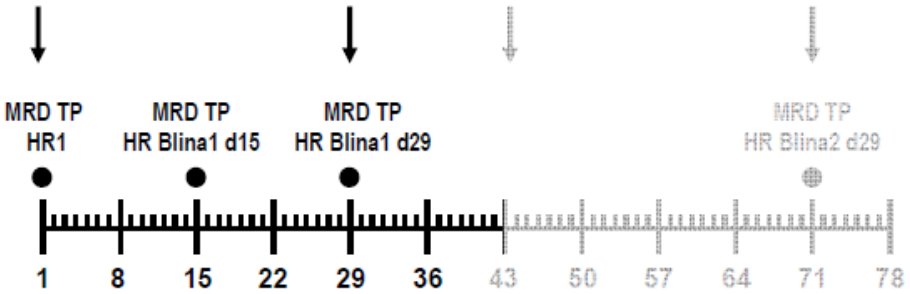
Version 1.3, 12.03.2019

BLINATUMOMAB |__|__|__| . |__| µg
p.i. (2x28 d) 15 µg/m²/d

MTX i.th. dose age-adapted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

1. Cycle | 2. Cycle



Please enter date for actually administered MTX and MRD!

	Date
MTX i.th. day 1	
MTX i.th. day 29	
MRD TP HR1	
MRD TP HR Blina1 d15	
MRD TP HR Blina1 d29	

Please enter actually administered glucocorticoids!

Drug name	Dose (absolute)	Date

Was Tocilizumab administered during this cycle?
❒ no
❒ yes, on :_____ (date)
Dose (absolute)_____

Please enter actually administered Blinatumomab with start and end date!
For interruptions > 1 h and/or dose changes > 10%, please start a new application phase within this cycle and document weight, height and body surface for each application phase.
Please document the reason for interruption(s) or (premature) discontinuation of the cycle (=end of application phase) (see legend on the right).
For a cycle that was restarted from the beginning after previous interruption, please use a new CRF.

Application phase	Blinatumomab cumulative dose	Start		End		Reason for end of application phase	Body measurements		
		Date	Time	Date	Time		Weight (kg)	Height (cm)	BSA (m²)
1									
2									
3									
4									
5									

Is this a restarted cycle after previous discontinuation of a cycle?
❒ yes ❒ no

Therapy plan calculated and prepared

_____
Date, name and signature of the investigator

Therapy plan administered as documented

_____
Date, name and signature of the investigator (or documentalist)

Hospitalisation: Number of nights with hospitalisation (from start of the cycle until beginning of the next therapy element): _____

Possible reasons for (premature) discontinuation or interruption of the cycle (→ reason for the end of a application phase):

a) Cycle completed

b) Interruption > 1 h:
- b1) (S)AE
- b2) Non-Compliance
- b3) Request of the patient or the patient's guardian(s)
- b4) Delayed restart after bag change
- b5) Malfunction of infusion pump
- b6) Infusion bag emptied prematurely
- b7) Other

c) Dose change > 10 %:
- c1)) Dose reduction or re-escalation due to (previous) (S)AE
- c2) Non-Compliance
- c3) Adjustment to weight change
- c4) Dose administration error
- c5) Other

d) Premature discontinuation of this cycle:
- d1) (S)AE
- d2) Non-Compliance
- d3) Request of the patient or the patient's guardian(s)
- d4) Other

e) Permanent withdrawal of Blinatumomab treatment:
- e1) (S)AE
- e2) Non-Compliance
- e3) Request of the patient or the patient's guardian(s)
- e4) ALL relapse or progression
- e5) Death
- e6) Retrospectively ineligible
- e7) Other

Stud.-No. (Pat.-ID): _____
DOB: _____
Weight: _____kg Height: _____cm
BSA: _____m²

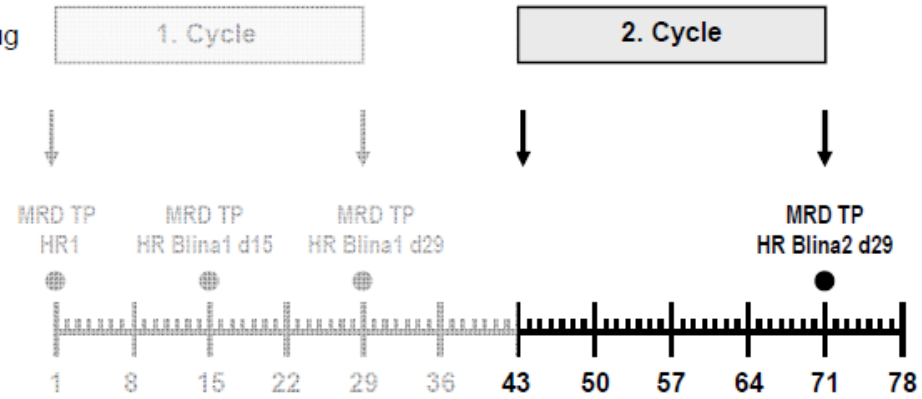
AIEOP-BFM ALL 2017: Blinatumomab in HR:
2. Cycle for HR pB-ALL in R-HR experimental arm

Version 1.3, 12.03.2019

BLINATUMOMAB |__|__|__| . |__| µg
p.i. (2x28 d) 15 µg/m²/d

MTX i.th. dose age-adapted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg



Please enter date for actually entered MTX and MRD!

	Date
MTX i.th. day 43	
MTX i.th. day 71	
MRD TP HR Blina2 d29	

Please enter actually administered glucocorticoids!

Drug name	Dose (absolute)	Date

Was Tocilizumab administered during this cycle?
❒ no
❒ yes, on :_____ (date)
Dose (absolute)_____

Please enter actually administered Blinatumomab with start and end date!
For interruptions > 1 h and/or dose changes > 10%, please start a new application phase within this cycle and document weight, height and body surface for each application phase.
Please document the reason for interruption(s) or (premature) discontinuation of the cycle (=end of application phase) (see legend on the right).
For a cycle that was restarted from the beginning after previous interruption, please use a new CRF.

Application phase	Blinatumomab cumulative dose	Start		End		Reason for end of application phase	Body measurements		
		Date	Time	Date	Time		Weight (kg)	Height (cm)	BSA (m²)
1									
2									
3									
4									
5									

Is this a restarted cycle after previous discontinuation of a cycle?
❒ yes ❒ no

Therapy plan calculated and prepared

_____
Date, name and signature of the investigator

Therapy plan administered as documented

_____
Date, name and signature of the investigator (or documentalist)

Hospitalisation: Number of nights with hospitalisation (from start of the cycle until beginning of the next therapy element): _____

Possible reasons for (premature) discontinuation or interruption of the cycle (→ reason for the end of a application phase):

a) Cycle completed

b) Interruption > 1 h:
- b1) (S)AE
- b2) Non-Compliance
- b3) Request of the patient or the patient's guardian(s)
- b4) Delayed restart after bag change
- b5) Malfunction of infusion pump
- b6) Infusion bag emptied prematurely
- b7) Other

c) Dose change > 10 %:
- c1) Dose reduction or re-escalation due to (previous) (S)AE
- c2) Non-Compliance
- c3) Adjustment to weight change
- c4) Dose administration error
- c5) Other

d) Premature discontinuation of this cycle:
- d1) (S)AE
- d2) Non-Compliance
- d3) Request of the patient or the patient's guardian(s)
- d4) Other

e) Permanent withdrawal of Blinatumomab treatment:
- e1) (S)AE
- e2) Non-Compliance
- e3) Request of the patient or the patient's guardian(s)
- e4) ALL relapse or progression
- e5) Death
- e6) Retrospectively ineligible
- e7) Other

PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA PHASE **PROTOCOL III**

- Formules sanguines complètes avant le cycle et après 1x/semaine
- Chimie, Na, K, Urée, créat, ASAT/ALAT, BILI T/D avant le cycle et après 1x/semaine
- Examen clinique avant le cycle et après 2x/semaine pendant le TTT par Dexamethasone, après 1x/semaine
- Stix Urinaire 2x/semaine sous Dexamethasone (exclure une glycosurie)
- **Mesure de l'activité de l'asparaginase**
  A faire chez tous les patients avec suspicion de réaction allergique à l'asparaginase, 2 heures après l'arrêt de l'infusion.
  ☐ 0.5-1ml de sang dans tube Sérum, à envoyer à température ambiante à Zürich avec le formulaire « Asparaginase – Monitoring » (en annexe)
- **Echo-ECG is mandatory prior to the 1st Doxorubicin of each Protocol III**
- **Conditions pour débuter le protocol IIIA & B :**
  Requirements for starting Protocol IIIA
  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl

  If symptoms/signs of cardiac insufficiency are present and/or if the LV-SF is repeatedly below 30% or the EF below 50%, contact the national study coordinator for consideration of procedure.

  Requirements for starting Protocol IIIB
  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Creatinine clearance ≥ 25 ml/min/1.73 m_2. Dose adjustments of Cyclophosphamide are recommended if Creatinine clearance < 25 ml/min/1.73 m_2
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl

Stud.-No. (Pat.-ID): _____
DOB: _____
Weight: _____kg Height: _____cm
BSA: _____m^2

AIEOP-BFM ALL 2017: Protocol III

for HR patients (pB and T-ALL)

Version 1.3, 12.03.2019

DEXA p.o./i.v. (14d+) 10 mg/m^2/d |__|__| . |__| mg/d

*Please enter the **cumulative dose of DEXA** per phase#:*

VCR i.v. 1.5 mg/m^2/dose |__| . |__|__| mg
max. 2 mg

DOX p.i. (1 h) 30 mg/m^2/dose |__|__| . |__| mg

PEG-L-ASP p.i. (2 h) 2500 IU/m^2/dose |__|__|__|__| IU
ONCASPAR® (max. 3750 IU)

CPM p.i. (1 h) 500 mg/m^2/dose |__|__|__|__| mg
(+MESNA)

ARA-C i.v. 75 mg/m^2/dose |__|__|__| mg

*Please enter the **cumulative dose given in each ARA-C block**:*

*Please enter the **number of doses given in each ARA-C block**:*

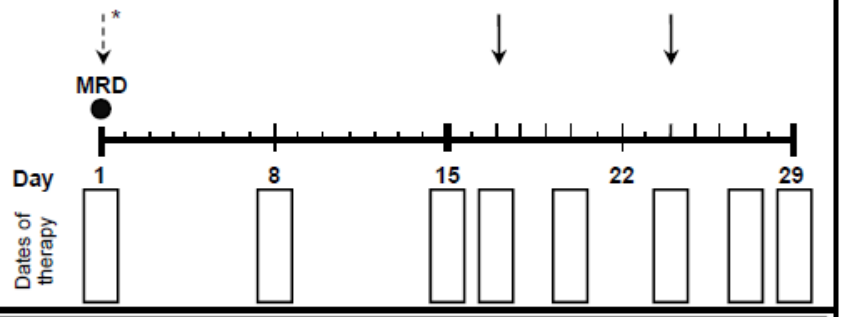
TG p.o. (14 d) 60 mg/m^2/d |__|__|__| , |__| mg/d

*Please enter the **cumulative dose of TG#**:*

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg

* additional i.th. MTX on day 1 in CNS-positive (CNS 3) patients



 # Please mark therapy interruptions with a vertical line and enter the cumulative dose for the resulting application phases

Please enter actually administered medication with start date (and if applicable end date and other application phases #)!

	Date	
	Start	End
DEXA		
Main phase (if appl. part 1#)		
if appl. Main phase part 2#		
if appl. Main phase part 3#		
Tapering phase 1		
Tapering phase 2		
Tapering phase 3		
VCR 1		
VCR 2		
DOX 1		
DOX 2		
PEG-L-ASP		
CPM		
ARA-C block 1		
ARA-C block 2		
TG (if applicable part 1#)		
if applicable TG part 2#		
if applicable TG part 3#		
if appl. MTX i.th. day 1*		
MTX i.th. day 17		
MTX i.th. day 24		
MRD day 1 Prot. III		

Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Switch from PEG-L-ASP to Erwinase in this element?

- ☐ no
- ☐ yes, 1st Erwinase administration: |___|___|___| (date)
  last Erwinase administration: |___|___|___| (date)
  number of Erwinase doses: |____|
  administered dosage/administration: |__|__|__|__|__| IU

Reason for switch to Erwinase:

- ☐ allergic reaction, date: |___|___|___|
- ☐ other: _____

Therapy according to the protocol?

- ☐ yes
- ☐ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ☐ medical reason
  - ☐ psychosocial reason
  - ☐ other reason _____

Were additional antileukemic drugs administered?

- ☐ no
- ☐ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____
Date, name and signature of the investigator

Therapy plan administered as documented

_____
Date, name and signature of the investigator (or documentalist)

PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA PHASE **DNX-FLA**

- Formules sanguines complètes avant DNX-FLA

- Chimie, Na, K, Urée, créat, ASAT/ALAT, BILI T/D avant DNX-FLA et après selon indication

- Patient hospitalisé pendant le cycle et jusqu'à récupération des valeurs sanguines

- **Prophylaxie antifongique et antibiotique dès la fin du cycle**

- **Conditions pour débuter DNX-FLA**

  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl
  - No essential organ dysfunction: o Normal renal function. Dose adjustment of High-dose Cytarabine and Fludarabine should be considered in the case of reduced creatinine clearance.
    - ✓ GOT/GPT <10 x upper normal limit
    - ✓ Bilirubin <3 x upper normal limit with normal direct bilirubin

AIEOP-BFM ALL 2017: DNX-FLA

Version 1.3, 12.03.2019

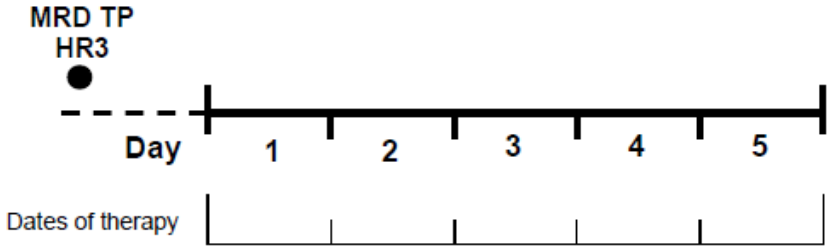
Fludarabine **p.i. (30 min)** 30 mg/m²/dose |__|__| mg

HD-ARA-C **p.i. (3 h)** 2000 mg/m²/dose |__|__|__|__| mg
starting 4 hours after end of Fludarabine infusion

Daunoxome **p.i. (1 h)** 60 mg/m²/dose |__|__|__| mg

MTX i.th. dose age-adjusted |__|__| mg

Age	<1 y	1-<2 y	2-<3 y	≥ 3 y
MTX dose i.th.	6 mg	8 mg	10 mg	12 mg



Stud.-No. (Pat.-ID): _____

DOB: _____

Weight: _____kg

Height: _____cm

BSA: _____m²

Please enter actually administered medication with start date (and if applicable end date and other application phases#)!

	Date	
	Start	End
Fludarabine dose 1		
Fludarabine dose 2		
Fludarabine dose 3		
Fludarabine dose 4		
Fludarabine dose 5		
HD-ARA-C dose 1		
HD-ARA-C dose 2		
HD-ARA-C dose 3		
HD-ARA-C dose 4		
HD-ARA-C dose 5		
Daunoxome dose 1		
Daunoxome dose 2		
Daunoxome dose 3		
MTX i.th. day 1		
MRD TP HR3		

Hospitalisation: Number of nights with hospitalisation from start of this treatment phase until beginning of the next therapy element): |__|__|__|

Therapy according to the protocol?

- ❒ yes
- ❒ no (deviations of cumulative dose for a drug by >10% in this therapy phase, or additional antileukemic drugs given)
  - ❒ medical reason
  - ❒ psychosocial reason
  - ❒ other reason _____

Were additional antileukemic drugs administered?

- ❒ no
- ❒ yes (please document on CRF „Documentation of cytotoxic/antileukemic drugs or treatment phases deviating from the treatment protocol")

Therapy plan calculated and prepared

_____

Date, name and signature of the investigator

Therapy plan administered as documented

_____

Date, name and signature of the investigator (or documentalist)

PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA PHASE **INTERIM MAINTENANCE**

- Formules sanguines complètes au début du cycle et après 2x/semaine

- Chimie, Na, K, Urée, créat, ASAT/ALAT, BILI T/D au début du cycle et après 2x/semaine

- Examen clinique au début du cycle et après 2x/semaine

- **Conditions pour débuter la phase de interim Maintenance :**
  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl
  - GOT/GPT <10 x upper normal limit
  - Bilirubin <3 x upper normal limit with normal direct bilirubin

PRÉLÈVEMENTS DE SANG ET SUIVI PENDANT LA PHASE DE **MAINTENANCE**

- **Examen clinique (EC) et labo** :

  Avant le début de la maintenance : EC, labo : FSC, Na, K, urée, créat., ASAT/ALAT, BILI T/D

  Sem 2 : EC, labo : FSC, Na, K, urée, créat., ASAT/ALAT, BILI T/D

  Sem 4 : EC, labo : FSC, Na, K, urée, créat., ASAT/ALAT, BILI T/D, premier dosage des métabolites (TG, MPP)

  Sem 8 et chaque 4 semaines pour la suite de la Maintenance et jusqu'à la fin : EC, labo : FSC, Na, K, urée, créat., ASAT/ALAT, BILI T/D

- Métabolites (TG, MPP) d'office 4 semaines post début de la maintenance, 1x/mois jusqu'à dose stable de 6-Mercaptopurine et après 1x chaque 3 mois (cf. SOP Métabolites 6-Mercaptopurine)

- **Conditions pour débuter la phase de maintenance :**

  - Adequate clinical condition and no serious infection according to the assessment of the investigator
  - Recovering (increasing) blood counts
    - ✓ Granulocytes ≥ 500/µl
    - ✓ Platelets ≥ 50 000/µl
  - GOT/GPT <10 x upper normal limit
  - Bilirubin <3 x upper normal limit with normal direct bilirubin

AIEOP-BFM ALL 2017: Documentation of Maintenance therapy for patients of randomization R-MR

(Version 1.3, 12.03.2019)

Please document the first 8 weeks of Maintenance therapy for both treatment arms (control arm or experimental arm)!

Patient: Study No. (Pat.-ID): _____ Date of birth: _____

Date of examination*:	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|
Blood counts:						
WBC ☐ /µl ☐ Gpt/l	_____	_____	_____	_____	_____	_____
Neutrophils (%)	__| __	__| __	__| __	__| __	__| __	__| __
Lymphocytes (%)	__| __	__| __	__| __	__| __	__| __	__| __
Haemoglobin ☐ g/dl ☐ mmol/l	__|__,__	__|__,__	__|__,__	__|__,__	__|__,__	__|__,__
Platelets ☐ /µl ☐ Gpt/l	_____	_____	_____	_____	_____	_____
Body measurements:						
Weight (kg)	__|__|__,__	__|__|__,__	__|__|__,__	__|__|__,__	__|__|__,__	__|__|__,__
Height (cm)	__|__|__	__|__|__	__|__|__	__|__|__	__|__|__	__|__|__
Therapy documentation:						
in the period§ from (date)	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|
to (date)	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|	__|__|__|__|__|__|
Cumulative dose (in the above period):						
6-MP (mg)	__|__|__	__|__|__	__|__|__	__|__|__	__|__|__	__|__|__
MTX (mg)	__|__|__	__|__|__	__|__|__	__|__|__	__|__|__	__|__|__
Therapy break(s) (in the above period):						
Number of days	__| __	__| __	__| __	__| __	__| __	__| __
Nights of hospitalization (in the above period):	__| __	__| __	__| __	__| __	__| __	__| __
Comments (e.g. infections, reasons for treatment breaks...)						

Sheet No. ____ *(use additional sheets if needed)*

Documented by (Investigator or Documentalist):

_____ _____ _____

Name (in block letters) **Date** **Signature**

*Please document each medical visit.

§Period from the day of the last examination until the day preceding the current examination with the aim of a complete documentation of the first 8 weeks of Maintenance

UNIVERSITÄTS-
KINDERSPITAL ZÜRICH
Das Spital der Eleonorenstiftung
STS 0286

Abteilung für Klinische Chemie und Biochemie
Steinwiesstrasse 75, 8032 Zürich
OP.U9 Tel. 044 266 77 37 Fax 044 266 81 55

Auftraggeber (Stempel):

Patientendaten oder Patientenetikette

Name: _____
Vorname: _____
Geschlecht: _____
Geburtsdatum: _____
Strasse: _____
PLZ/Ort: _____

Stud-Nr.: ALL17CH _____

Körpergrösse: ..... cm Gewicht: .....kg

Benötigtes Material:	0.5-1 ml Serum (1-2 m Vollblut)
Probenentnahme:	Bei jedem Verdacht auf allergische Reaktion auf Asparaginase 2 Std. nach Stop der Infusion, bei der Gabe von Oncaspar™ am Tag 7 nach Gabe. Im Protokoll IIA bei Non-HR, bzw. 7 Tage nach jeder Asparaginase Gabe in den HR-Blöcken und in den Protokollen IIIA.
Lagerung:	Bis zum Versand bei -20°C (Gefrierschrank, Gefrierfach) lagern.
Versand:	Per Post bei Raumtemperatur

Asparaginase - Monitoring

Zuordnung der Probenentnahme zu den PEG-L-Asparaginase Gaben

Probenentnahme nach PEG-L-ASP-Gabe:

Non-HR
☐Protokoll II, Tag 8

HR-Patienten
☐HR-1'-Block, Tag 8
☐HR-2'-Block, Tag 8
☐HR-3'-Block, Tag 8
☐1. Protokoll III, Tag 8
☐2. Protokoll III, Tag 8
☐3. Protokoll III, Tag 8

☐Anderer Zeitpunkt:

_____

Medikament:
☐Oncaspar™ (pegylierte E.coli Asparaginase)
☐Erwinase (Erwinia-Asparaginase)
☐Andere: _____

☐i.v.-Infusion ☐ i.m.

Dosierung :
Dosis/m^2 _____ U/m^2
Dosis/absolut _____ U

Letzte Asparaginase Gabe:

Datum: _____ Uhrzeit: _____

Probenentnahme (ogligat):

Datum:_____ Uhrzeit: _____

Material:
☐Serum ☐Liquor
Infektiös? ☐ ja ☐ nein

☐Nicht zutreffend: Bei letzter Asparaginase-Gabe wurde Erwinase verabreicht.

Ergänzende Informationen zur letzten Asparaginase-Gabe:
☐Klinisch gesicherte allergische Reaktion
☐Verdacht auf allergische Reaktion
☐Kein Hinweis auf allergische Reaktion

Cave: Diese Analyse ist nicht Bestandteil der eidgenössischen Analysenliste. Eine obligatorische Leistungspflicht der Kostenträger ist deshalb nicht gegeben. Die Analyse wird dem Auftraggeber in Form eines Preisäquivalents direkt in Rechnung gestellt. Wir empfehlen eine Kostengutsprache bei der Krankenkasse einzuholen.

Weitere Informationen und Abkürzungen finden Sie unter https://kispiportal.uzh.ch/analyseauskunft/ und im Vademecum auf der Website.

061120LEHPE

IKC 6 UniversitätsSpital Zürich
Institut für Klinische Chemie
Akkreditiert nach ISO 17025, STS 0206
Rämistrasse 100, 8091 Zürich Tel: 044 255 22 68 Fax: 044 255 45 90

Molekulare und Pränatale Diagnostik

externe Referenznummer

Patienten-Etikette oder Patienten-Angaben

Name:
Vorname:
Geschlecht:
Geburtsdatum:
Strasse:
PLZ/Ort:

Abnahme-Datum T T M M J J J J

Abnahme-Zeit H H M M

Nachbestellung von Auftragsformularen
☐ 10 Stück ☐ 50 Stück
☐ 30 Stück ☐ 100 Stück

Arzt-Suchernr.

Tel. Station

Rechnung an:
☐ Patient
☐ Auftraggeber
☐ Drittzahler

☐ Befundkopie an:

Vacutainer **violett** (EDTA)

Für molekulargenetische Untersuchungen benötigen wir EDTA-Vollblut.
Das Röhrchen darf zum Schutz vor Kontamination nicht geöffnet werden.
Einverständniserklärung zu allen genetischen Untersuchungen erforderlich (siehe unten).

Markierung
Richtig
Falsch

Einsendercode Auftraggeber

Kardiovaskuläre Risikofaktoren

☐ MTHFR Gen C677T
☐ Apo E Gen (ε2,ε3,ε4)

Stoffwechsel

☐ HFE Gen (C282Y,H63D,S65C)
☐ LCT Gen T-13910C

Pharmakogenetik

☐ BCHE Gen A-/ K- Var. ①
☐ CYP 2C9 Gen (*2,*3) ①
☐ CYP 2C19 Gen (*2,*3,*17) ①
☐ CYP 2D6 Gen (*3,*4,*5,*6, 2x2) ①
☐ NAT2 Gen ①
☐ VKORC1 Gen (G-1639A) ①
☐ HLA-B*5701 ②
☐ TPMT-Aktivität ③
☐ TPMT Gen (*1,*2,*3A,*3B,*3C) ②
☐ DPYD Gen (Exon 14-skipping mut.) ②
☐ UGT1A1 Gen (TA) 6/7 ②
☐ UGT1A6 Gen T181A ①
☐ IL-28B Gen ①
☐ MTHFR Gen C677T

☐ DNA-Extraktion

Bitte jedes Röhrchen nach Blutentnahme 5 mal sorgfältig kippen!

① Kostenübernahme durch die Krankenversicherung gemäss KVG bei Verordnung durch einen Arzt/eine Ärztin mit eidg. Weiterbildungstitel in Klin. Pharmakologie und Toxikologie. Bitte wenden Sie sich ggf. an die Klinik für Klinische Pharmakologie und Toxikologie des USZ:
Tel: 044 255 27 70 oder e-mail: pharmakologie@usz.ch
Limitationen: Analyseliste des BAG "Pharmakogenetische Analyse".

② Kostenübernahme durch die Krankenversicherung gemäss KVG durch alle Ärzte/Ärztinnen unabhängig von Weiterbildungstitel.
Limitationen: Analyseliste des BAG "Pharmakogenetische Analyse".

③ Separates EDTA Röhrchen

Einwilligung zur genetischen Untersuchung

Ich bestätige hiermit, dass ich den oben genannten Patienten über die genetische Untersuchung gemäss dem Gesetz über genetische Untersuchungen beim Menschen (GUMG) hinreichend aufgeklärt habe, und dass der Patient dieser Untersuchung zugestimmt hat.

Das Probenmaterial darf für Qualitätssicherungsmassnahmen und zur Entwicklung und Evaluation neuer Tests am Institut für Klinische Chemie verwendet werden. ☐ Ja ☐ Nein

Zuweisender Arzt: Name und Adresse (vollständig + Stempel):

Ort und Datum:

Unterschrift:

Labornummer

Bemerkungen:

Bitte in Blockschrift ausfüllen

010050270063

Pränataldiagnostik

Perinataldiagnostik (Fruchtwasser) — Nativ-Röhrchen

PRÄNATALE EINZELPARAMETER — Vacutainer **rot** (Serum)

- ☐ AFP im Fruchtwasser ④
- ☐ freies β-HCG (ohne Risikobewertung) ⑤
- ☐ PAPP-A (ohne Risikobewertung) ⑤
- ☐ AFP (ohne Risikobewertung) ④
- ☐ 1. Trimester Screening (freies β-HCG + PAPP-A) ohne Risikobewertung ⑤

Schwangerschaftsdauer:

Wochen: ☐☐

Tage: ☐

Diagnose:

Bitte in Blockschrift ausfüllen

Therapie:

Bitte in Blockschrift ausfüllen

☐ 1. Trimester Screening

Zeitpunkt: 45-84 mm SSL. Schliesst Messung des freien b-HCG und PAPP-A ein ⑤

Gewicht der Frau in kg:

100 200
10 20 30 40 50 60 70 80 90
1 2 3 4 5 6 7 8 9

Ethnische Herkunft

- ☐ Europäisch und Nordafrika
- ☐ Ostasiatisch
- ☐ Afro-Karibisch
- ☐ Südasiatisch
- ☐ Südostasiatisch
- ☐ Gemischt
- ☐ Andere

Anzahl Feten:

☐ 1 ☐ 2 ☐ 3 ☐ >3

Chorionizität bei Zwillingsschwangerschaft

☐ dichorial ☐ monochorial

IVF-Schwangerschaften

Datum der Befruchtung _____

Ggf. Geburtsdatum der Eizellspenderin _____

Vorangegangene Fehlgeburt(en)

☐ Ja ☐ Nein

Vorangegangene SS mit Trisomie

- Trisomie 21 ☐ Ja ☐ Nein
- Trisomie 18 ☐ Ja ☐ Nein
- Trisomie 13 ☐ Ja ☐ Nein

Name des/der Ultraschallers/in: *Blockschrift*

Name anfordernder Arzt/in: *Blockschrift*

Datum des Ultraschalls:

Tag 10 20 30 / 1 2 3 4 5 6 7 8 9

Monat Jan Feb März April Mai Juni Juli Aug Sept Okt Nov Dez

SSL (CRL) in mm:

40 50 60 70 80
1 2 3 4 5 6 7 8 9

Gestationsalter gemäss SSL:

Wochen 10 20 30 40 / 1 2 3 4 5 6 7 8 9

Tage 1 2 3 4 5 6

Nackentransparenz in mm:

10
1 2 3 4 5 6 7 8 9
0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9

Insulinpflichtiger Diabetes mellitus der Schwangeren

☐ Ja ☐ Nein

Nikotin

☐ Ja ☐ Nein

☐ AFP Plus Test

Zeitpunkt: 14 + 0 bis 18 + 6 SSW. Schliesst Messung des freien b-HCG und AFP ein. Risikobewertung für Trisomie 21 und Neuralrohrdefekte. ⑤

oder

☐ AFP-Test:

Zeitpunkt: 14 + 0 bis 18 + 6 SSW. Schliesst Messung von AFP ein. Nur Risikobewertung für Neuralrohrdefekte ④

Datum der letzten Periode:

Tag 10 20 30 / 1 2 3 4 5 6 7 8 9

Monat Jan Feb März April Mai Juni Juli Aug Sept Okt Nov Dez

Gewicht der Frau in kg:

100 200
10 20 30 40 50 60 70 80 90
1 2 3 4 5 6 7 8 9

Ethnische Herkunft

- ☐ Europäisch und Nordafrika
- ☐ Ostasiatisch
- ☐ Afro-Karibisch
- ☐ Südasiatisch
- ☐ Südostasiatisch
- ☐ Gemischt
- ☐ Andere

Anzahl Feten:

☐ 1 ☐ 2 ☐ 3 ☐ >3

Datum des ersten Ultraschalls:

Tag 10 20 30 / 1 2 3 4 5 6 7 8 9

Monat Jan Feb März April Mai Juni Juli Aug Sept Okt Nov Dez

Dies entsprach damals:

Wochen 10 20 30 40 / 1 2 3 4 5 6 7 8 9

Tage 1 2 3 4 5 6

Muss auf Grund des US der Termin korrigiert werden

☐ Ja ☐ Nein

Vorangegangener Neuralrohrdefekt

☐ Ja ☐ Nein

Vorangegangene SS mit Trisomie 21

☐ Ja ☐ Nein

Insulinpflichtiger Diabetes mellitus der Schwangeren

☐ Ja ☐ Nein

Nikotin

☐ Ja ☐ Nein

Bemerkungen:

Bitte in Blockschrift ausfüllen

④ USZ Extern: Bei Versand bei Raumtemperatur, Probe innerhalb von 24h im Labor, sonst gekühlt schicken.

⑤ USZ Extern: Probe gekühlt schicken

000000000001

HISTORIQUE DES RÉVISIONS

Version	Raison de la révision	Auteur	Validité	Diffusion
V01	Première version	27.11.2020 Dr Ceppi	15.03.2021	16.03.2021