



European
Reference
Network

for rare or low prevalence
complex diseases

 Network
Paediatric Cancer
(ERN PaedCan)



20.11.2024

Fiona Poyer & Marta Pillon

What to do when toxicity hinders
treatment? A challenging case of T-LBL

Moderation: Andishe Attarbaschi



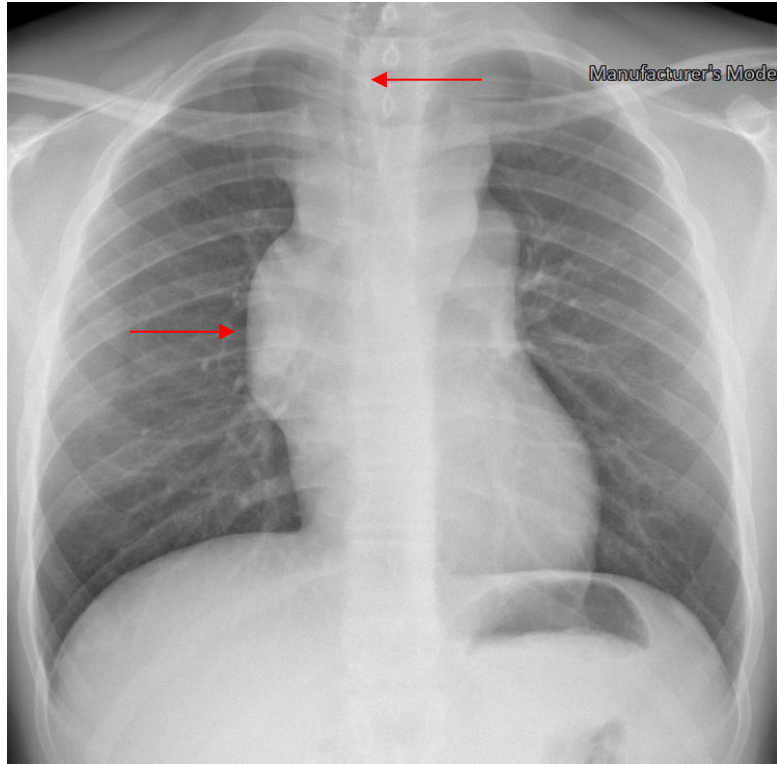
Funded by the European
Union's EU4Health Programme



COI declaration

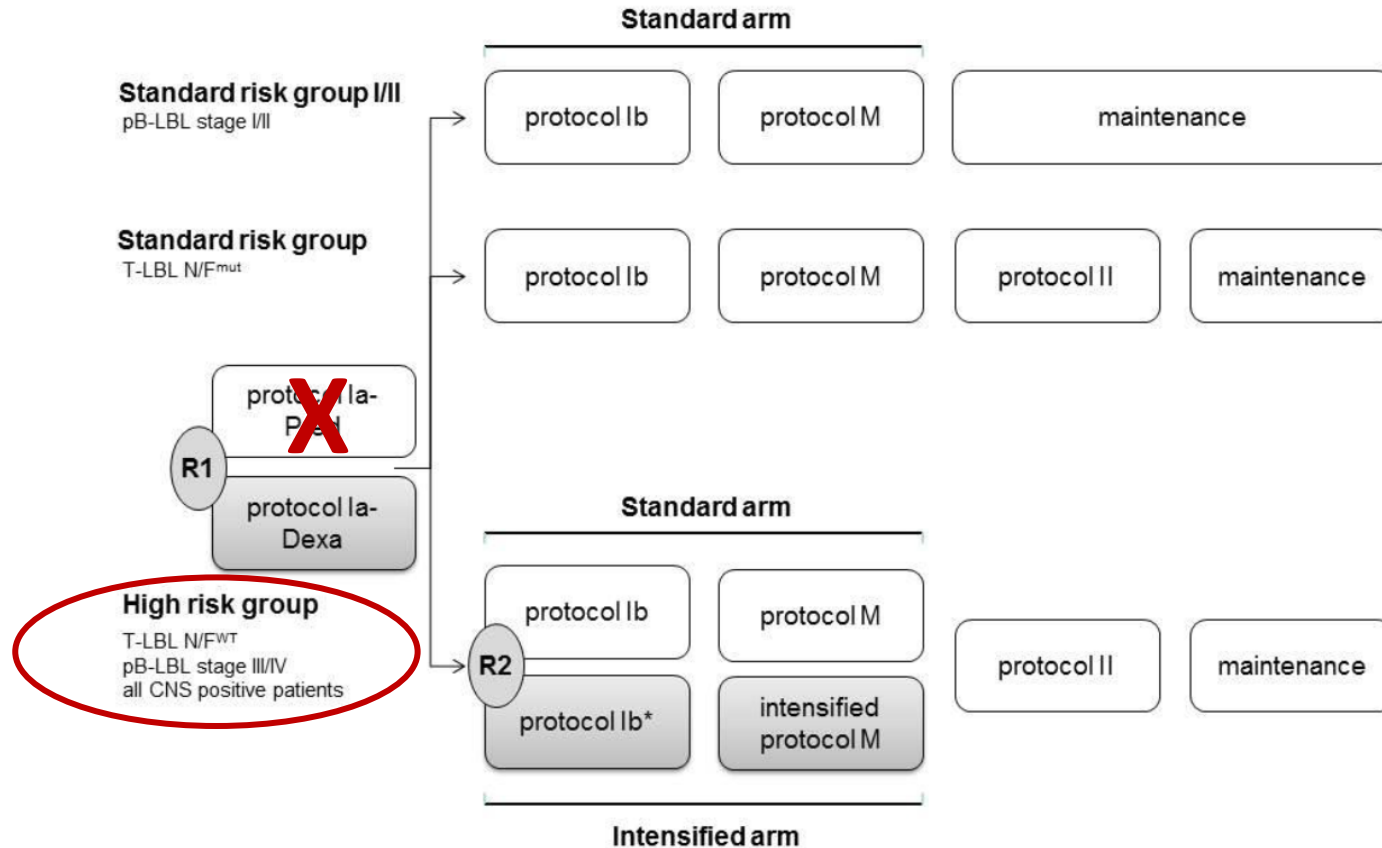
- Fiona Poyer
 - No conflicts of interest
- Marta Pillon
 - Takeda
 - Jazz Pharmaceuticals

Patient Nico K., 16a



- T-lymphoblastic lymphoma
 - MDD PB and BM negative
- Liquor: 212 L/ μ l, 92% Blasts
 - CNS3
- Genetics:
NOTCH1^{WT}/FBXW7^{WT}

LBL 2018 – Treatment plan



Treatment documentation of protocol Ia - dexamethasone

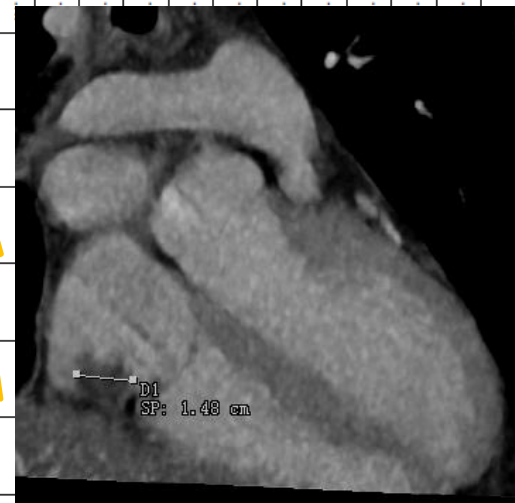
Reg. number: _____

date of birth: |_|_|_|_|. |_|_|_|_|
mm yyyy

weight: |_|_|_|_|. |_|_|_| kg height: |_|_|_| cm body surface: |_|_|. |_|_|_| m²

day	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
date/...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../...../.....
dexamethasone 10 mg/m ² /d iv or po in 3 single doses _ _ mg _ _ mg _ _ mg	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●													
vincristine 1.5 mg/m ² /d (max. 2 mg) iv _ . _ mg	●							●							●													
daunorubicine 30 mg/m ² /d iv (1 h) _ _ mg	●							●							●													
methotrexate intrathecal age-adjusted dose _ _ mg											●																	
cytarabine intrathecal * age-adjusted dose _ _ mg					●						●																	
prednisolone intrathecal * age-adjusted dose _ _ mg					●						●																	

CR?



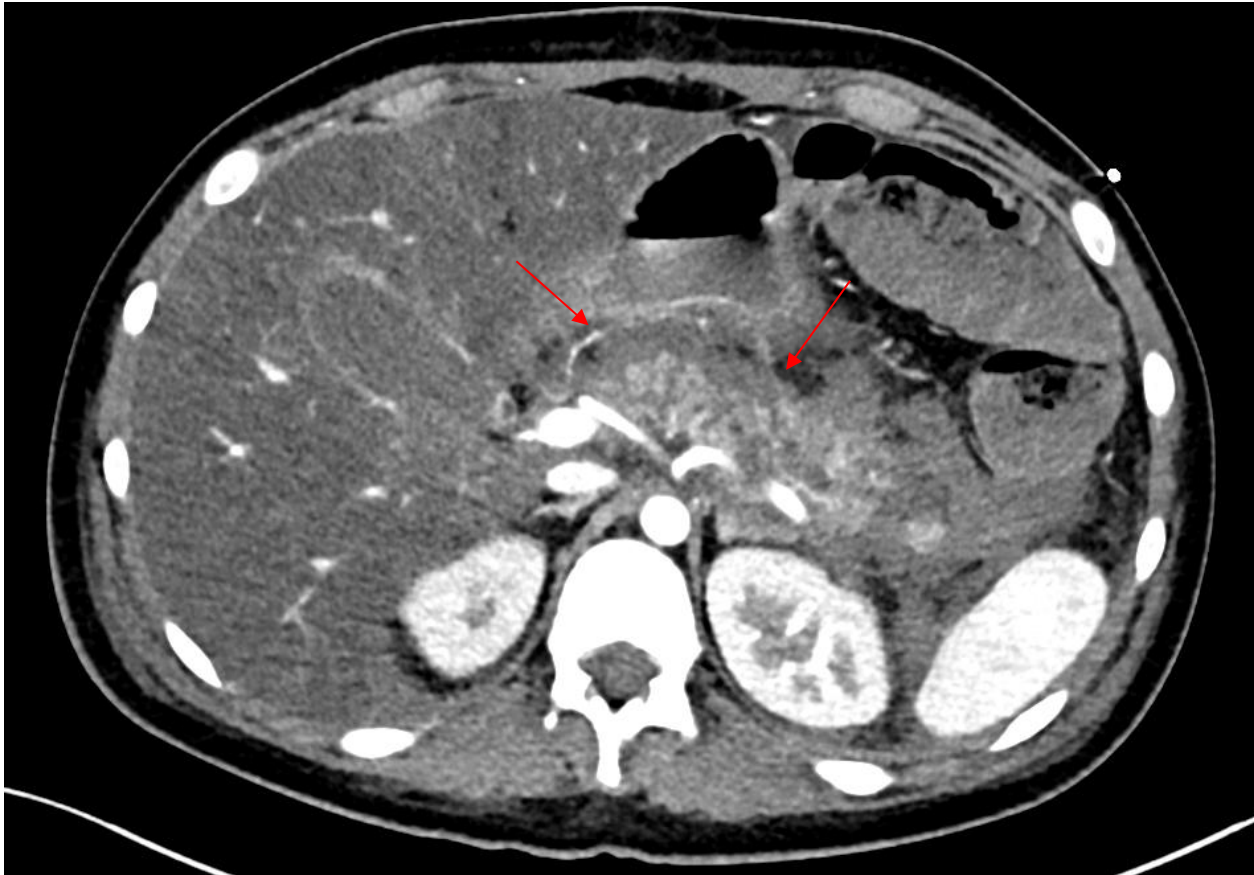
- Sternotomy
- Cardiopulmonary Bypass

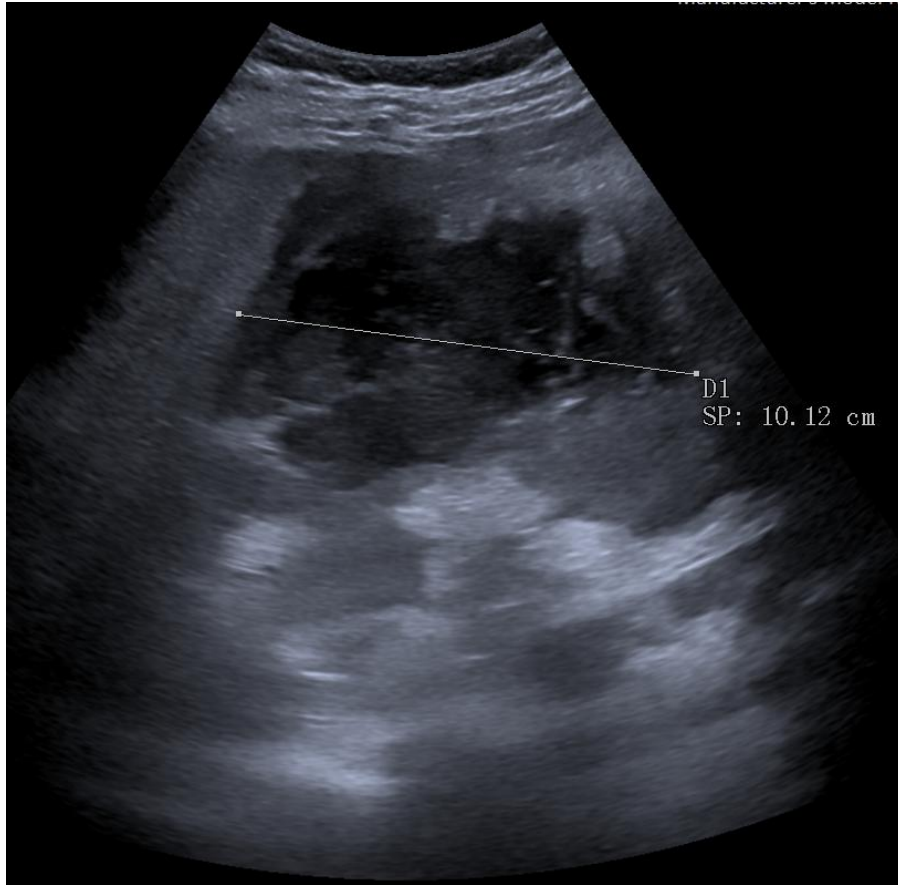
day	12	26
date of PEG asparaginase administration/...../...../...../.....
PEG asparaginase** 2,500 IU/m ² /d (max. 3,750 IU) iv (2 h) _ _ _ _ IU	●	●

* In case of CNS involvement (type 3) twice weekly until clearance of CSF **Please strictly adhere to the 14-day interval

ean
nce
rk
low prevalence
seases
Cancer
n)

SIRS





Prephase
06.-13.08.22

Protocol IA ~~X~~
14.08.-28.08.22



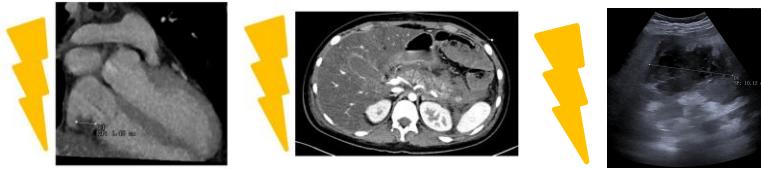
- 2 extracorporeal Drains
- 2 gastrocystostomies
- > 50 endoscopic necrosectomies
- passagery insulin-dependent Diabetes mellitus
- exocrine pancreatic insufficiency
- aneurysm of the V. lienalis (coiling)
- Peritonitis with sepsis

Question 1

- What about the lymphoblastic lymphoma treatment?
 - Pause treatment
 - Dexamethasone only
 - Low-dose chemotherapy?
 - Daratumumab / alternative therapies?

Prephase
 06.-13.08.22

Protocol IA **X**
 14.08.-28.08.22



- 2 extracorporeal Drains
- 2 gastrocystostomies
- > 50 endoscopic necrosectomies
- passagery insulin-dependent Diabetes mellitus
- exocrine pancreatic insufficiency
- aneurysm of the lienalic vein (coiling)
- Peritonitis with sepsis

Dexa 6 mg/m²/d
 21.11.-25.11.22

Dexa 6 mg/m²/d
 28.11.-02.12.22

Dexa 6 mg/m²/d
 12.12.-16.12.22

Dexa 6 mg/m²/d
 19.12.-23.12.22

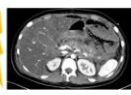
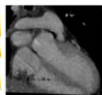
Facial Nerve Palsy
(CNS2, 85% T-lymphoblasts BM)

Prephase

06.-13.08.22

Protocol IA ~~X~~

14.08.-28.08.22



Dexa 6 mg/m²/d

21.11.-25.11.22

Dexa 6 mg/m²/d

28.11.-02.12.22

Dexa 6 mg/m²/d

12.12.-16.12.22

Dexa 6 mg/m²/d

19.12.-23.12.22



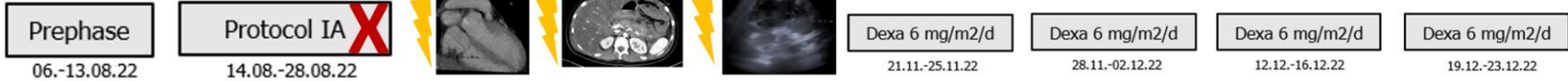
European
Reference
Network

for rare or low prevalence
complex diseases

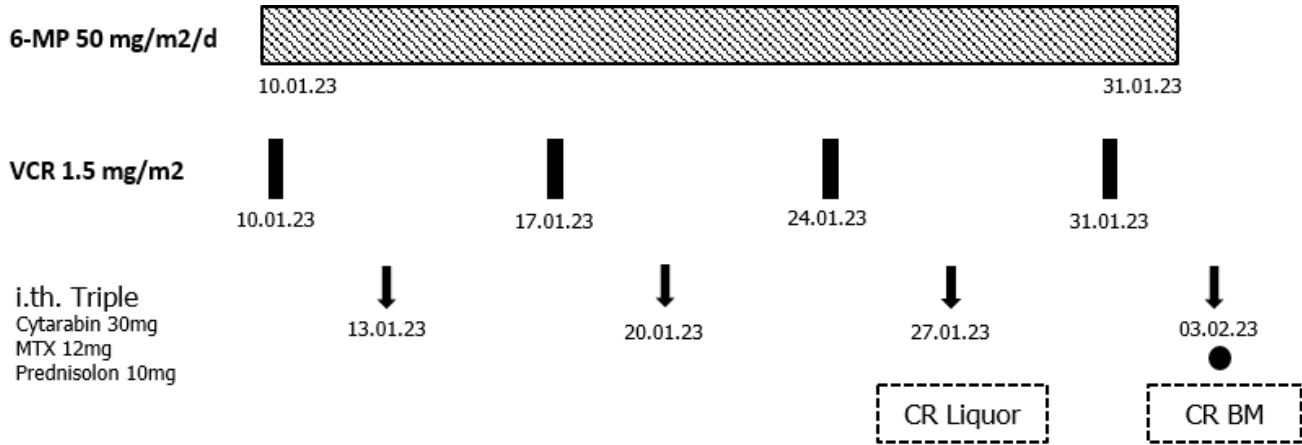
Network
Paediatric Cancer
(ERN PaedCan)

Question 2

- Is it really a relapse, when the disease has never been properly treated?
 - Disease progression?
 - Relapse?

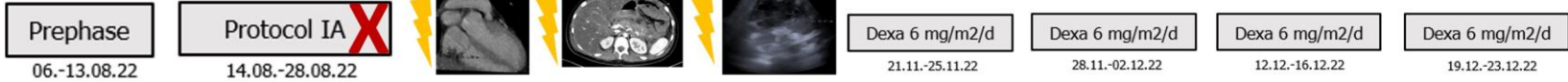


Disease Progression

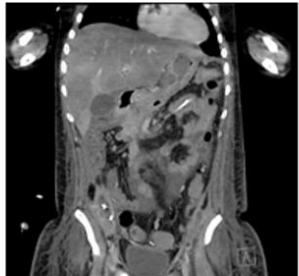
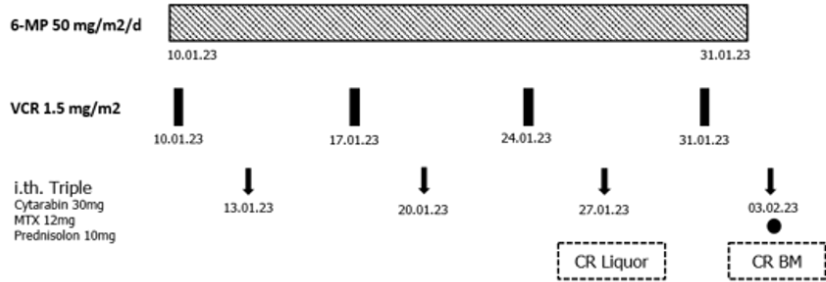




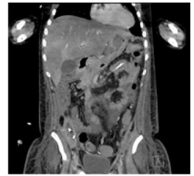
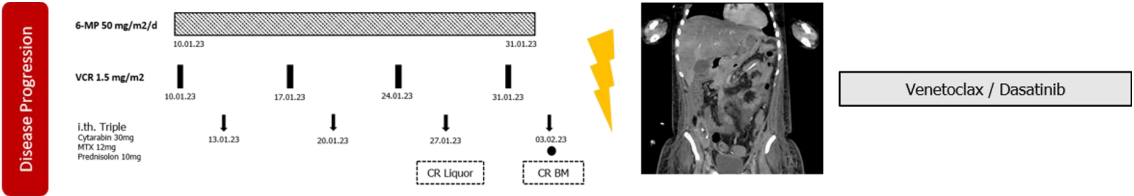
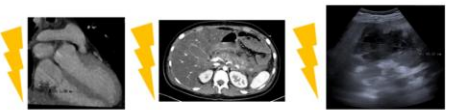
SIRS



Disease Progression



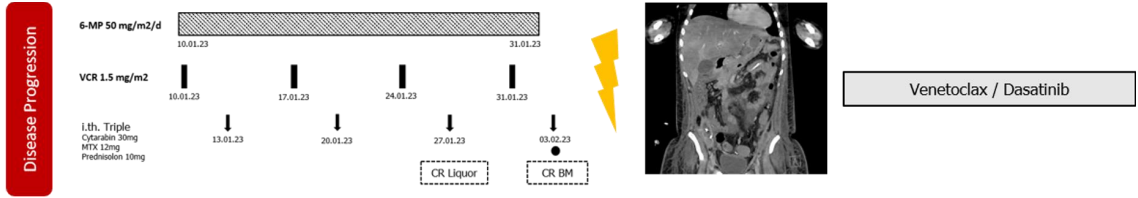
Venetoclax / Dasatinib



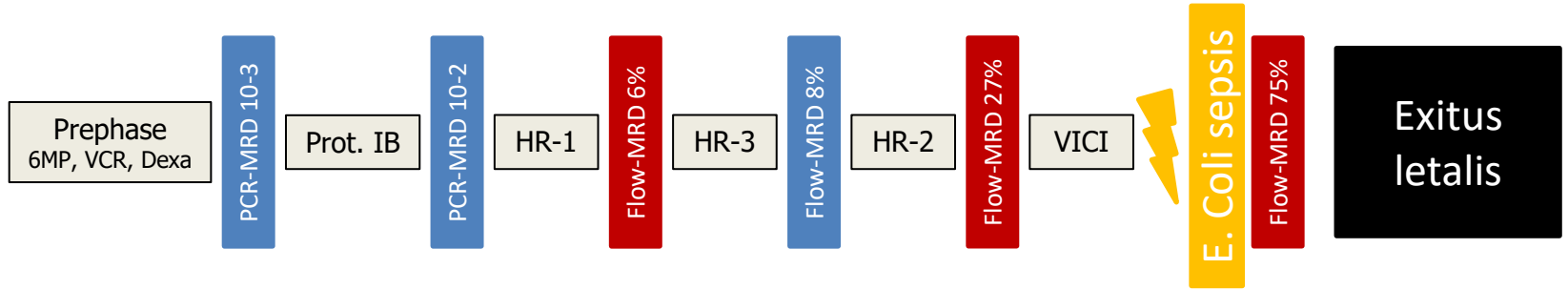
Loss of Vision
 (CNS2, 67% T-lymphoblasts
 BM

Question 3

- What would you offer the patient?
 - Stop treatment?
 - Low dose chemotherapy?
 - High dose Cytarabin / Methotrexate / VICI + Bortezomib?



Loss of Vision
(CNS2, 67% T-lymphoblasts
BM)



Take home messages

- Major ongoing toxicity can compromise the success of the treatment protocol, especially during induction
- Finding the “ideal” therapy should always be a balance between aim to cure, treatment toxicity and the patient’s individual wishes

DISCUSSION

Table 3. Treatment-related mortality.

Treatment phase	TRM (n)	Steroid received at time of death	Age at diagnosis (years)	Immuno-phenotype	Cause of death
Induction Ia	5	Prednisone	2.1	T-LBL	Septic shock
		Prednisone	15.8	early B-LBL	Intracerebral hemorrhage following sinus venous thrombosis
		Dexamethasone	2.2	T-LBL	Sepsis (<i>S. aureus</i> , <i>Acinetobacter</i>)
		Dexamethasone	2.5	T-LBL	Necrotizing adenovirus enteritis and ARDS
		Dexamethasone	9.7	T-LBL	Acute respiratory failure with acute pulmonary edema, coma, and cardiac arrest
Ib	1	*	9.1	pB-LBL	Enterovirus infection, interstitial pneumonia, myocarditis, and pontine myelinolysis
M	2	*	9.3	pB-LBL	Multi-organ failure
		*	0.7	pB-LBL	Septic shock
IIa	3	Dexamethasone*	9.9	T-LBL	Septicemia
		Dexamethasone*	11.0	T-LBL	Pulmonary aspergillosis and ARDS
		Dexamethasone*	11.6	T-LBL	Mycotic infection of the lung and pulmonary hemorrhage
IIb	0				
Maintenance	1	†	7.5	T-LBL	Varicella infection

ARDS: acute respiratory distress syndrome; pB-LBL: precursor B-cell lymphoblastic lymphoma; T-LBL: T-cell lymphoblastic lymphoma; TRM: treatment-related mortality. *Received prednisone during induction phase Ia. †Received dexamethasone during induction phase Ia.

Landmann et al., Haematologica 2017