Appendix for BLD-2020-008825R1

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Supplemental Table 1: Inclusion criteria and exclusion criteria

Inclusion criteria

1. Age: 18 to 60 years
2. Gender: Male and female patients will be included.
3. Risk group: Poor prognosis patients (patients with stage I and aaIPI 0 are excluded)
4. Histology:

Diagnosis of mature (peripheral) T-cell lymphoma, confirmed by an excisional biopsy of a lymph node or by a sufficiently extensive biopsy of an extranodal manifestation if there is no lymph node involvement. For anaplastic large cell lymphoma (ALCL) the ALK (anaplastic lymphoma kinase) status must be known.

The following entities will be treated:

peripheral T-cell lymphoma, (PTCL) NOS

Lennert's lymphoma

T-zone lymphoma

T-immunoblastic variant

Perifollicular/Follicular variant

angioimmunoblastic T-cell lymphoma (AITL)

anaplastic large cell lymphoma, ALK negative

extranodal NK/T-cell lymphoma, nasal type

intestinal T-/NK-cell lymphoma (± enteropathy)

hepatosplenic gamma-delta lymphoma

subcutaneous panniculitis-like PTCL

5. Performance status:

Performance status ECOG 0-3 (Karnofsky 40-100%) at time of randomization (definitions see appendix). Patients will be accepted if they reach the required performance state after prephase treatment.

6. Registration as study center

The center must be registered as study center before initiation of study, meaning a contract has been made between sponsor and center and the center has to be initiated by the Trial Office.

7. Written consent of the patient

Exclusion criteria

1. Stage I with aaIPI 0
2. Any lymphoma specific pre-treatment with two exceptions:

a. prephase treatment with vincristine and prednisone/prednisolone

b. one course of (R)-CHO(E)P given before final diagnosis

3. Serious accompanying disorder or impaired organ function as indicated by:

ASAT and ALAT 2 x > N*

Serum bilirubin 2 x > N*

Alkaline phosphatase 2 x > N*

Creatinine 1.5 > N*

Severe cardiac dysfunction or arrhythmias

Pulmonary diffusion capacity < 40 % N

(*If these abnormalities are due to lymphoma, patients may still be included into the study, please contact the Trial Office/Clinical Counselors)

4. Known hypersensitivity to the medication to be used
5. Known HIV-positivity
6. Active hepatitis

7. Suspected poor patient compliance
8. Simultaneous participation in another study protocol
9. Prior chemo- or radiotherapy for previous disorder
10. Other concomitant malignant disease or history of active cancer in the past 5 years, except carcinoma of the skin or stage 0 cervical carcinoma
11. Pregnancy and lactation
12. Inability to give informed consent due to mental or language problems
13. B-cell lymphomas and the following T-cell lymphomas cannot be included: precursor T-cell lymphomas, anaplastic large cell lymphoma ALK+, primary cutaneous lymphoma, leukemic/disseminated forms of mature T-cell lymphoma, T-CLL, primary CNS lymphoma.
14. CNS involvement of lymphoma (intracerebral, intraspinal or meningeal)

Supplemental Table 2: Number of infused CD34+ cells and recovery after transplantation.

	BEAM/ AutoSCT[#] n=41				FBC/ AlloSCT n=26			
	n	Median	Quartiles	Range	n	Median	Quartiles	Range
Number of infused CD34+ cells (10^6/ kg body weight)	41	5.0	(4.0; 7.3)	(2.3; 25.8)	26	6.6	(4.6; 8.0)	(2.0; 13.6)
Days to ANC > $0.5x10^9$/l	38	10	(9; 13)	(0; >20)	24	15	(12; 17)	(8; >50)
Days to leukocytes > $1x10^9$/l	39	10	(9; 12)	(0; >20)	26	13	(12; 16)	(10; >50)
Days to platelets > $20x10^9$/l	40	11	(7; 13)	(0; >20)	26	12	(9; 14)	(0; >50)

[#] seven patients randomized to AlloSCT are included

Supplemental Table 3: Causes of death according to treatment arm for randomized patients and transplanted patients only.

	Randomized patients		Transplanted patients	
	AutoSCT	**AlloSCT**	**AutoSCT[#]**	**AlloSCT**
	n=54	**n=49**	**n=41**	**n=26**
Lymphoma related	13/18 (72%)	11/21 (52%)	7/9 (78%)	1/9 (11%)
Study treatment related	0/18 (0%)	8/21 (38%)	0/9 (0%)	8/9 (89%)
Salvage treatment related	4/18 (22%)	2/21 (10%)	1/9 (11%)	0/9 (0%)
Secondary neoplasia	1/18 (6%)	0/21 (0%)	1/9 (11%)	0/9 (0%)
Total	18/54 (33%)	21/49 (43%)	9/41 (22%)	9/26 (35%)

[#] seven patients randomized to AlloSCT are included

Supplemental Table 4: Details of treatment-related deaths on study.

Study treatment related deaths	AlloSCT n=8	Cause of death
until day 100 after transplantation	4	– acute GvHD (2) – CMV pneumonia – unknown infection during aplasia
until 1 year after transplantation	2	– hepatic failure due to EBV-positive PTLD – varicella-encephalitis and septicaemia
late therapy-related death	2	– cGvHD – 18 months after transplantation – sepsis, pneumonia – 19 months after transplantation with ongoing cGvHD

Supplemental Table 5: Incidence and severity of acute and chronic GvHD

GvHD	patients with documented GvHD n=19
Max. overall grade of acute GvHD[22]	
0	3 (16%)
1	3 (16%)
2	6 (32 %)
3	4 (21%)
4	3* (16%)
Chronic GvHD[23]	
None	10 (53%)
Limited	7** (37%)
Extensive	1 (5%)
Unknown	1 (5%)

* 2 patients died of acute GvHD

** 1 patient died of chronic GvHD

Supplemental Table 6: Number of patients with non-hematological adverse events grade 3-5 and hematotoxicity grade 3-4 after CHOEP. For details on infections see supplemental table 8.

	AutoSCT n=54	**AlloSCT n=49**
Non-haematological adverse events grade 3-5		
Nausea	0/54 (0%)	2/49 (4%)
Vomiting	1/54 (2%)	0/49 (0%)
Diarrhea	2/54 (4%)	2/49 (4%)
Constipation	0/54 (0%)	1/49 (2%)
Mucositis/ stomatitis	4/54 (7%)	3/49 (6%)
Cardiac arrhythmia	1/54 (2%)	0/49 (0%)
Cardiac general	1/54 (2%)	0/49 (0%)
Haemorrhage/ bleeding	2/54 (4%)	1/49 (2%)
Renal/ genitourinary	2/54 (4%)	1/49 (2%)
Neuropathy sensory	2/54 (4%)	0/49 (0%)
Mood alteration	0/54 (0%)	0/49 (0%)
Allergic reaction/ hypersensitivity	1/54 (2%)	0/49 (0%)
Infections	10/54 (19%)	12/49 (24%)
Haematological adverse events		
Leukocytopenia grade 4*	23/40 (58%)	21/34 (62%)
Thrombocytopenia grade 3, 4*	8/35 (23%)	7/30 (23%)
Anemia grade 3, 4	20/54 (37%)	14/49 (29%)

* some patients without documentation of blood values within the nadir

Supplemental Table 7: Non-haematological adverse events grade 3-5 and haematotoxicity grade 3-4 after DHAP.

	AutoSCT n=38	AlloSCT n=39
Non-haematological adverse events grade 3-5		
Nausea	1/38 (3%)	0/38 (0%)
Vomiting	1/38 (3%)	0/38 (0%)
Diarrhoea	1/38 (3%)	1/38 (3%)
Constipation	0/38 (0%)	0/38 (0%)
Mucositis/ stomatitis	1/38 (3%)	0/38 (0%)
Cardiac arrhythmia	0/38 (0%)	0/38 (0%)
Cardiac general	0/38 (0%)	0/38 (0%)
Haemorrhage/ bleeding	0/38 (0%)	0/38 (0%)
Renal/ genitourinary	0/38 (0%)	1/38 (3%)
Neuropathy sensory	0/38 (0%)	0/38 (0%)
Mood alteration	0/38 (0%)	0/38 (0%)
Allergic reaction/ hypersensitivity	0/38 (0%)	1/38 (3%)
Infections	3*/38 (19%)	0/38 (0%)
Haematological adverse events		
Leukocytopenia grade 4**	2/11 (18%)	6/16 (38%)
Thrombocytopenia grade 3, 4**	13/18 (72%)	17/22 (77%)
Anemia grade 3, 4	10/37 (27%)	5/39 (13%)

* type of infection: 1x bacterial, 2x unknown

** some patients without documentation of blood values within the nadir

Supplemental Table 8: Infectious events grade 3-5 following CHOEP.

Multiple etiologies per event were reported.

	AutoSCT n=54	**AlloSCT n=49**
Infections grade 3-5/ documented courses	18/193 (9%)	16/184 (9%)
Bacterial	10/18 (56%)	9/16 (56%)
Fungal	6*/18 (33%)	2*/16 (12%)
Viral	2/18 (11%)	2**/16 (12%)
Unknown	12/18 (67%)	11/16 (69%)

* 2 (1/1) Aspergillus

** 1 CMV

Supplemental Table 9: Infectious events grade 3-5 following BEAM/ AutoSCT or FBC/ AlloSCT. Multiple etiologies per event were reported.

	BEAM/ AutoSCT[#] n=41	**FBC/ AlloSCT n=26**
Infections grade 3-5 per patient	13/41 (32%)	10/26 (38%)
Bacterial	10*/13 (77%)	7/10 (70%)
Fungal	1/13 (8%)	0/10 (0%)
Viral	1/13 (8%)	4**/10 (40%)
Other	0/13 (0%)	1***/10 (10%)
Unknown	10/13 (77%)	9/10 (90%)

[#] seven patients randomized to AlloSCT are included

* 1 Mycobacterium

** 2 CMV

*** 1 septic shock of unknown cause