Supplementary files

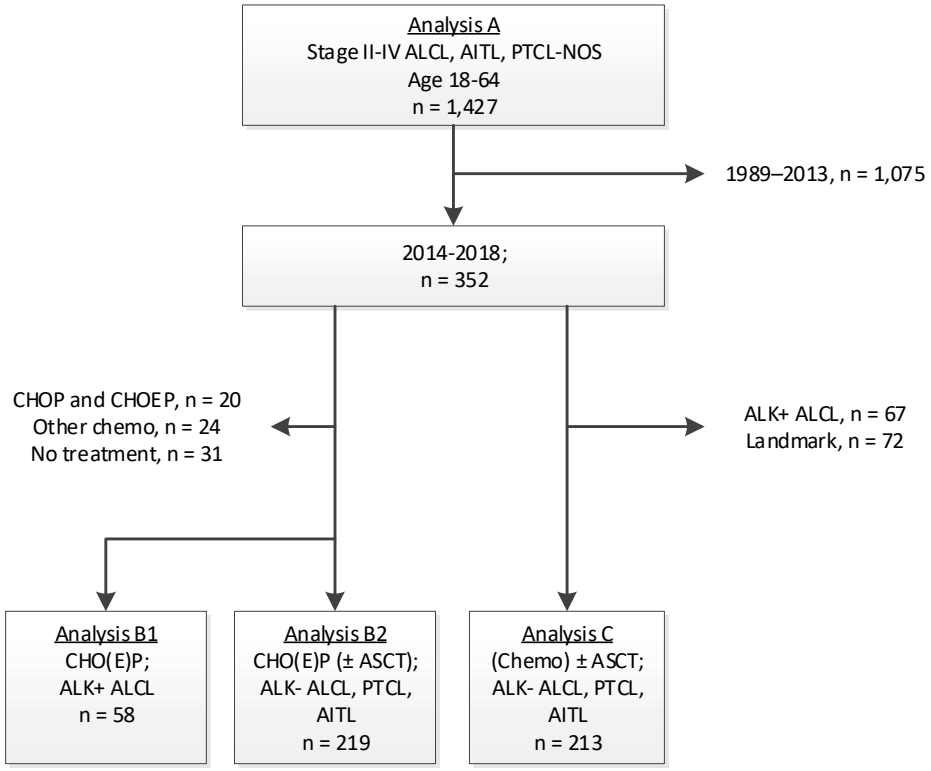
Netherlands Cancer Registry

The nationwide population-based Netherlands Cancer Registry (NCR) is maintained and hosted by the Netherlands Comprehensive Cancer Organization (IKNL) and has nationwide coverage of at least 95% of all malignancies since 1989. The NCR relies on comprehensive case notification through the Nationwide Histopathology and Cytopathology Data Network and the Nationwide Registry of Hospital Discharges (i.e. inpatient and outpatient discharges). Information on dates of birth and diagnosis, sex, topography and morphology, hospital type of diagnosis, and first-line therapy is routinely recorded in the NCR by trained registrars of the NCR through retrospective medical records review. Information on last known vital status for all patients (i.e. alive, dead, or emigration) is obtained through annual linkage with the Nationwide Population Registries Network that holds vital statistics on all residents of the Netherlands. Unique to the NCR, since January 1st, 2014, detailed information on diagnostic and treatment characteristics for all hematological malignancies diagnosed in the Netherlands is also routinely recorded.

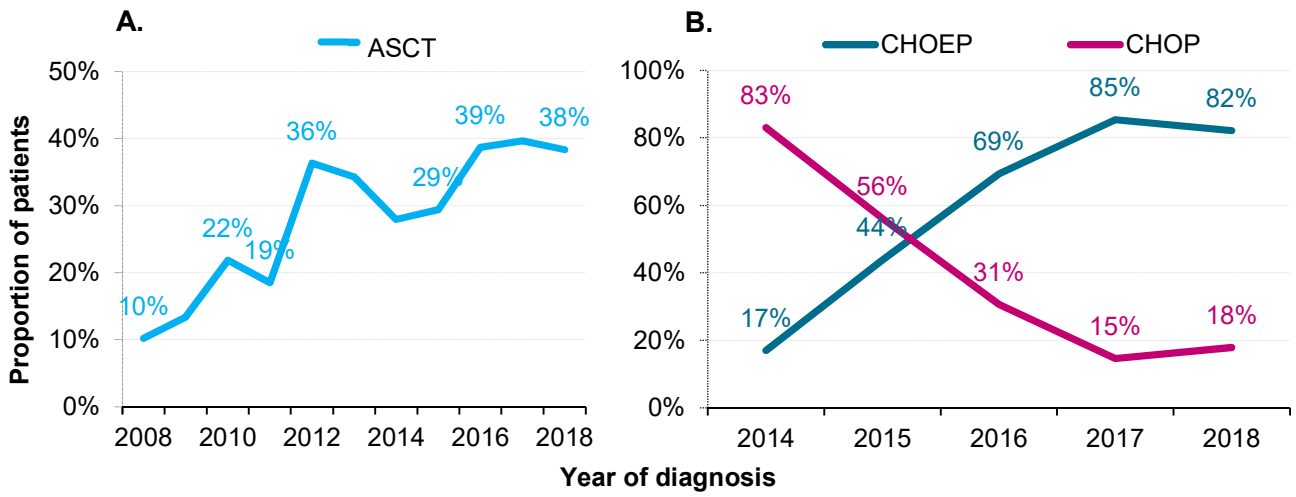
Selection of patients with T-NHL

We selected patients with PTCL using the International Coding system of Disease - Oncology (ICD-O) of the World Health Organization (WHO) morphology codes 9702-9705, and 9714-9715. Patients with T-cell follicular helper lymphoma (TFH) were recoded as AITL. In the WHO classification of 2008 (4th edition), ALK+ ALCL was listed as a distinct entity, whereas ALK-negative (ALK-) ALCL was considered a provisional entity. In the WHO classification of 2017 (revised 4th edition), both ALK+ ALCL and ALK- ALCL are listed as a distinct entity.

Supplementary Figure 1. Flowchart of patients with advanced ALCL, AITL and PTCL NOS <65 years included for analysis A, B and C.

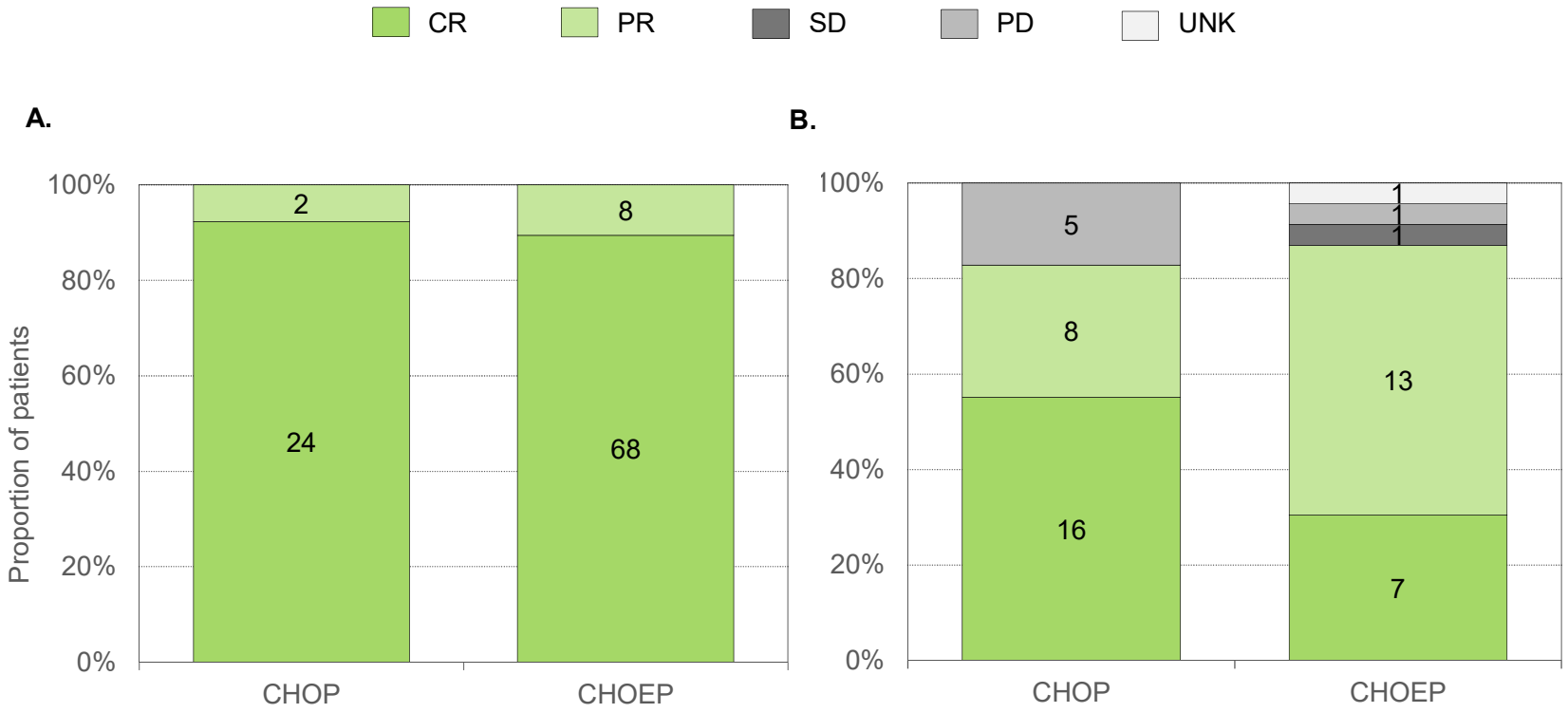


Supplementary Figure 2. The implementation of autologous stem cell transplantation (ASCT) and etoposide in first-line treatment strategies for patients <65 years with stage II-IV anaplastic large T-cell lymphoma, angioimmunoblastic T-cell lymphoma and peripheral T-cell lymphoma not otherwise specified over time in the Netherlands. Panel A shows a line graph depicting the annual proportion of patients who received ASCT between 2008 and 2018. The denominator includes all patients with or without first-line therapy. Panel B shows the implementation of etoposide for patients diagnosed between 2014 and 2018. Here, the denominator includes only patients who received CHOP with or without addition of etoposide.



Supplemental Figure 3.

Best tumor response for patients with ALK- ALCL, AITL or PTCL NOS who received CHOP or CHOEP with (**Panel A**) or without consolidation with ASCT (**Panel B**).



Supplementary Table 1. Cox regression analyses for overall survival in peripheral T-cell lymphoma diagnosed in 1989-2018.

	Univariable			**Multivariable**		
	HR	95% CI	P-value	HR	95% CI	P-value
Calendar period						
1989-2008	1	reference	-	1	reference	-
2009-2018	0.78	0.68-0.90	<0.01	0.80	0.69-0.94	<0.01
Age at diagnosis	1.04	1.03-1.04	<0.01	1.03	1.03-1.04	<0.01
Gender						
Male	1	reference	-	-	-	-
Female	0.91	0.79-1.04	0.15	-	-	-
Subtype						
ALK+ ALCL	1	reference	-	1	reference	-
ALK- ALCL	2.23	1.46-3.39	<0.01	1.62	1.06-2.47	0.03
ALCL	2.15	1.53-3.03	<0.01	1.59	1.10-2.30	0.01
PTCL	3.39	2.46-4.66	<0.01	2.24	1.61-3.14	<0.01
AITL	2.64	1.88-3.69	<0.01	1.58	1.11-2.24	0.01

Abbreviations: HR; hazard ratio, CI; confidence interval, ALCL; Anaplastic large T-cell lymphoma, PTCL; Peripheral T-cell lymphoma, not otherwise specified, AITL; Angioimmunoblastic T-cell lymphoma

Supplemental Table 2. Univariable Cox regression analyses for overall survival in peripheral T-cell lymphoma diagnosed in 2014-2018.

	Univariable		
	HR	95% CI	P-value
Chemotherapy			
CHOEP	1	reference	-
CHOP	1.64	1.14-2.35	<0.01
Age at diagnosis	1.03	1.01-1.05	<0.01
Gender			
Male	1	reference	-
Female	0.96	0.66-1.39	0.82
Subtype			
ALK+ ALCL	1	reference	-
ALK- ALCL	1.43	0.68-3.01	0.34
PTCL NOS	3.46	1.91-6.29	<0.01
AITL	2.13	1.16-3.90	0.01
IPI-score			
0-2	1	reference	-
3-5	2.47	1.71-3.56	<0.01
Autologous stem cell transplantation*			
yes	1	reference	
no	4.04	2.54-6.43	<0.01

Abbreviations: IPI; international prognostic index, HR; hazard ratio, CI; confidence interval, ALCL; Anaplastic large T-cell lymphoma, PTCL; Peripheral T-cell lymphoma, not otherwise specified, AITL; Angioimmunoblastic T-cell lymphoma, CHOP; cyclophosphamide, doxorubicin, vincristine and prednisone, CHOEP; cyclophosphamide, doxorubicin, vincristine prednisone and etoposide.
*Autologous stem cell transplantation included as time-dependent covariable.

Supplemental Table 3. Univariable Cox regression analyses for overall survival in ALK+ ALCL (**Panel A**) and ALK- ALCL, AITL and PTCL NOS (**Panel B**) in 2014-2018.

	Panel A: ALK+ ALCL			**Panel B: ALK- ALCL, AITL, PTCL NOS**		
	HR	95% CI	P-value	HR	95% CI	P-value
Chemotherapy						
CHOEP	1	reference		1	reference	
CHOP	4.73	1.32-17.00	0.02	1.55	1.06-2.28	0.03
Age at diagnosis	1.00	0.96-1.04	0.87	1.03	1.01-1.05	0.01
Gender						
Male	1	reference		1	reference	
Female	0.72	0.24-2.15	0.56	1.07	0.72-1.60	0.73
Subtype						
ALK- ALCL	*n.a.*	*n.a.*		1	reference	
PTCL NOS	*n.a.*	*n.a.*		2.43	1.34-4.41	<0.01
AITL	*n.a.*	*n.a.*		1.49	0.81-2.72	0.20
IPI-score						
0-2	1	reference		1	reference	
3-5	4.94	1.36-17.86	0.02	2.11	1.43-3.12	<0.01
Autologous stem cell transplantation*						
yes	*n.a*	*n.a.*		1	reference	
no	*n.a.*	*n.a.*		6.17	3.84-9.91	<0.01

Abbreviations: IPI; international prognostic index, HR; hazard ratio, CI; confidence interval, ALCL; Anaplastic large T-cell lymphoma, PTCL; Peripheral T-cell lymphoma, not otherwise specified, AITL; Angioimmunoblastic T-cell lymphoma, CHOP; cyclophosphamide, doxorubicin, vincristine and prednisone, CHOEP; cyclophosphamide, doxorubicin, vincristine prednisone and etoposide, n.a.; not applicable.
*Autologous stem cell transplantation included as time-dependent covariable.

Supplemental Table 4. 5-year overall survival estimates of patients <65 years with stage II-IV disease according to ALK-ALCL, AITL or PTCL NOS separately, measured following the 9-months landmark. **Panel A** presents the 5-year OS for patients who received ASCT and patients who only received chemotherapy (no ASCT). In **Panel B**, 5-year OS is presented for patients who achieved CR in first-line following induction chemotherapy, with or without consolidation with ASCT.

	Panel A		**Panel B**	
	ASCT	no ASCT	ASCT	no ASCT
ALK- ALCL				
Number of patients	*28*	*16*	*22*	*6*
5-year OS (95% CI)	96% (77%-99%)	47% (20%-70%)	100%	44% (7%-78%)
AITL				
Number of patients	*48*	*46*	*31*	*18*
5-year OS (95% CI)	76% (55%-88%)	39% (19%-58%)	87% (69%-95%)	27% (2%-66%)
PTCL NOS				
Number of patients	*41*	*34*	*33*	*8*
5-year OS (95% CI)	68% (50%-81%)	49% (30%-66%)	67% (46%-81%)	60% (20%-85%)

Abbreviations: OS; overall survival, CI; confidence interval, ASCT; autologous stem cell transplantation, ALCL; Anaplastic large T-cell lymphoma, PTCL NOS; Peripheral T-cell lymphoma, not otherwise specified, AITL; Angioimmunoblastic T-cell lymphoma.