

T-cell lymphomas: tests, treatment by setting, regimens and problems during treatment

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A. Diagnosis and staging tests and what they change

The T-cell lymphoma key: markers that name the entity

	Defining markers	Genetics / virus
PTCL, NOS	One or more pan-T antigens (CD2, CD3, CD5, CD7); often loses CD5 or CD7	No specific change; clonal TCR; diagnosis of exclusion
TFH / AITL	CD4 + two of PD-1, ICOS, CXCL13, BCL6, CD10; CD21 dendritic meshwork	TCR clonal in 75–90%; EBV+ B blasts; IgH clonal in 25%
ALCL	CD30 strong, membrane + Golgi; T antigens variable; no B markers	ALK by IHC or FISH (NPM::ALK); ALK-: DUSP22 in up to a third
NK/T, nasal	CD2, CD56, cytoplasmic CD3, granzyme/TIA-1; surface CD3 negative	EBER positive in virtually all; TCR usually germline
ATLL	CD4, CD25 (most), CD7 lost; dim CD3; FoxP3 in some	HTLV-1 antibodies or provirus PCR
T-PLL	CD7, CD52 strong; CD4+CD8+ in a quarter; TCL1 overexpressed	inv(14)/t(14;14)/t(X;14); HTLV-1 negative

Every case: excision biopsy, expert review, CD30 (it chooses first-line treatment), and HTLV-1 serology where relevant. EBER separates NK/T lymphoma.

T-cell lymphoma key (UpToDate PTCL-NOS, AITL, sALCL, ENKTL, ATLL and T-PLL diagnosis reviews; simplified).

Table A. Diagnosis and staging tests and what they change

Test	When	What it changes	Pitfalls
Excision biopsy (deep biopsies for nasal disease)	Every suspected case	Entity	Cores and superficial biopsies miss architecture or show only necrosis
IHC: CD3, CD4, CD8, CD30, ALK, PD-1/ICOS/CXCL13, CD56, granzyme; EBER	Every biopsy	ALCL ALK±, TFH lymphoma, NK/T, PTCL-NOS	CD30 must be quantified (≥1% counts)

Test	When	What it changes	Pitfalls
HTLV-1 serology (blot or PCR)	Abnormal T cells in blood, hypercalcaemia, origin in endemic areas	ATLL	Healthy carriers can have flower cells
Flow cytometry, TCL1, karyotype/FISH	High T-cell counts	T-PLL vs ATLL vs Sézary	TCL1-negative T-PLL exists (minor criteria)
PET-CT; MRI nose and sinuses	Staging; interim (after 3 cycles) and end of treatment	Stage; response-guided plan	Inflammation and infection take up FDG
LDH, calcium, ferritin, DAT, immunoglobulins	Baseline	IPI/PIT; ATLL; HLH; haemolysis in AITL	Ferritin very high with cytopenias: think HLH
HBV, HCV, HIV	Before treatment	Prophylaxis	—

B. Treatment by setting

First-line evidence: CD30 decides, then age and fitness

ECHELON-2 (452 CD30+ PTCL): 5-year PFS in sALCL (%)



AITL subgroup: 5-year OS (%)



CD30-negative

- Fit, about 65 or younger: CHOEP
- Older or less fit: CHOP
- Swedish registry, ≤60 years: CHOEP PFS HR 0.49 vs CHOP
- Interim PET after 3 cycles

ECHELON-2 improved PFS and OS for the whole trial; the 72 patients with non-ALCL subtypes showed no significant difference (not powered for them). CD30 counts as positive at ≥1% of tumour cells (UpToDate). Systemic ALCL, ALK+ or ALK-: BV-CHP rather than CHOP. Stage I, favourable, in remission: add RT.

First line (Horwitz 2019 and 2022, ECHELON-2; Ellin 2014, Swedish registry; UpToDate initial PTCL and sALCL reviews).

Table B. Treatment by setting

Setting	Standard choice	Key evidence	Notes
CD30-positive PTCL (incl. all systemic ALCL)	BV-CHP × 6	ECHELON-2	Benefit clearest in ALCL
CD30-negative PTCL, fit ≤65	CHOEP × 6	Ellin 2014	Interim PET after 3 cycles
CD30-negative PTCL, older or less fit	CHOP × 6	UpToDate initial PTCL review	RT for residual disease
PTCL/ALK- ALCL, advanced, fit, CR	Observation or autologous HCT	NLG-T-01	No randomised proof of survival gain
ALK+ ALCL, CR	Observation	UpToDate sALCL review	No transplant in first CR
Stage I favourable PTCL, CR/PR	Adjuvant RT	UpToDate initial PTCL review	—
Relapsed sALCL, late or BV-naïve	BV	Pro 2012	Then HCT if fit
Relapsed ALK+ ALCL, early or BV-refractory	Crizotinib	Mossé 2013	Young patients best studied
Relapsed PTCL, transplant-eligible	Combination salvage → auto or allo HCT	UpToDate relapsed PTCL review	Newer agent if early or multiple relapse

Setting	Standard choice	Key evidence	Notes
Relapsed PTCL, not eligible	Sequential single agents	BELIEF, PROPEL	Trials; palliative care
NK/T, localised	Asparaginase- or platinum-based chemotherapy + RT (concurrent or sandwich)	JCOG0211, Kim 2009	No anthracyclines; CR → observe
NK/T, advanced	m-SMILE, DDGP or P-GEMOX → HCT	SMILE	Relapse: PD-1 antibody before auto-HCT
ATLL, aggressive types	VCAP-AMP-VECP ± mogamulizumab (or CHOP if unfit), IT prophylaxis → allo-HCT	JCOG9801, Ishida 2015	No mogamulizumab before allo-HCT; chronic/smouldering: watch
T-PLL, active	IV alemtuzumab (+ pentostatin if suboptimal) → HCT in CR	Dearden 2001	Inactive: watch with monthly counts

C. Regimens: evidence and best fit

Relapsed or refractory disease: biopsy, then choose by ALK, BV exposure and transplant plan

sALCL, late, BV-naïve

- Brentuximab vedotin alone
- Responses 73% (CR 46%)
- Then auto-HCT if fit

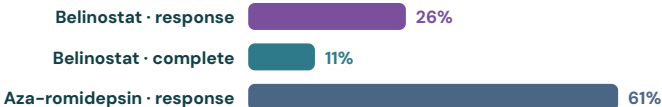
sALCL, early or BV-refractory

- ALK+: crizotinib (88% response in young patients)
- ALK-: belinostat, pralatrexate or romidepsin

PTCL-NOS / AITL

- Transplant-eligible: combination salvage → HCT
- Early relapse or multiple relapses: newer agents
- Not eligible: sequential single agents

Single-agent activity in relapsed PTCL (%)



Oral azacitidine vs investigator's choice in TFH lymphoma (ORACLE): median PFS 5.6 vs 2.8 months, primary endpoint not met. Transplant is the only route to long-term control. No prior auto-HCT and CR to salvage → autologous; prior auto-HCT, PR, or several lines needed → allogeneic (reduced intensity if older).

Relapsed disease (Pro 2012 and 2017, BV; Mossé 2013 and paediatric crizotinib series; O'Connor 2015, BELIEF; Falchi 2021; Dupuis 2024, ORACLE; UpToDate reviews).

Table C. Regimens and drugs: evidence and best fit

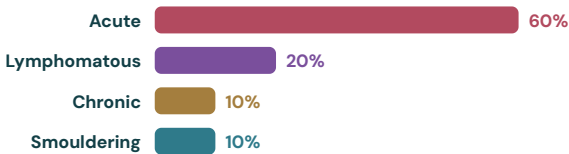
Regimen or drug	Best fit	Evidence	Main toxicity
BV-CHP	CD30-positive PTCL, all systemic ALCL	ECHELON-2: sALCL 5-year PFS 61% vs 48%	Neuropathy, neutropenia
CHOEP	Fit, ≤65, CD30-negative	Swedish registry: PFS HR 0.49 vs CHOP (≤60)	More myelosuppression than CHOP
CHOP	Older or less fit	Historical standard	Neutropenia, neuropathy, cardiotoxicity
Brentuximab vedotin alone	Relapsed CD30+ disease; frail sALCL	Relapsed sALCL: 73% response, 46% complete	Peripheral neuropathy
Crizotinib	Relapsed ALK+ ALCL	88% response in patients ≤21 years	See product information
Belinostat / pralatrexate / romidepsin	Relapsed PTCL, ALK- ALCL	Belinostat: 26% response (11% complete)	Belinostat: nausea (42%), fatigue, fever; cytopenias

Regimen or drug	Best fit	Evidence	Main toxicity
Oral azacitidine (± romidepsin)	Relapsed TFH lymphoma	ORACLE: PFS 5.6 vs 2.8 months (not significant); combination 61% response (phase 2)	Cytopenias, GI effects
Autologous / allogeneic HCT	Responding relapse; selected first CR	Only route to long-term control after relapse	Transplant-related mortality (allo)

D. Managing problems during treatment

Leukaemic T-cell neoplasms: ATLL and T-PLL

ATLL clinical variants (% of cases)



T-PLL criteria (all 3 major, or 2 + 1 minor)

- Over 5000/ μ L T-PLL-phenotype cells in blood or marrow
- Clonal T cells (TCR PCR or flow)
- 14q32 or Xq28 abnormality, or TCL1/MTCPI expression
- Minor: chromosome 11 (ATM), 8, 5, 12, 13, 22; spleen or effusions

ATLL: HTLV-1 test in every suspected case; hypercalcaemia (up to 70% in acute), lytic bone, opportunistic infections incl. Strongyloides; acute and lymphomatous: survival in months. ATLL: acute, lymphomatous, unfavourable chronic $\rightarrow$ VCAP-AMP-VECP ($\pm$ mogamulizumab) or CHOP if older, intrathecal prophylaxis, allogeneic HCT if a donor; chronic, smouldering $\rightarrow$ watch. T-PLL: inactive (15–20%) $\rightarrow$ watch with monthly counts; active $\rightarrow$ IV alemtuzumab (CR in most), add pentostatin if suboptimal, then HCT in CR (allogeneic if young and fit).

ATLL and T-PLL (UpToDate ATLL and T-PLL diagnosis and treatment reviews; Staber 2019; Tsukasaki 2007; Dearden 2001).

Table D. Managing problems during treatment

Problem	Prevent	Recognise	Act
Hypercalcaemia (ATLL)	Check calcium at diagnosis and during treatment	Confusion, thirst, constipation, kidney injury	IV fluids and calcium-lowering treatment; treat the lymphoma
HLH	High suspicion in febrile cytopenic patients	Fever, splenomegaly, ferritin very high, falling fibrinogen	Urgent specialist treatment alongside the lymphoma
Peripheral neuropathy (BV, vincristine)	Ask about tingling every cycle	Numbness, weakness, falls	Dose delay or reduction per protocol
Hepatitis B reactivation	HBsAg and anti-HBc before treatment	Rising ALT, HBV DNA	Antiviral prophylaxis; hepatology
Infections (incl. Strongyloides in ATLL)	Screen and treat Strongyloides before steroids in people from endemic areas; non-live vaccines	Fever, diarrhoea, chest signs	Early antibiotics; specialist advice
Tumour lysis	Hydration $\pm$ allopurinol in bulky disease	Rising potassium, phosphate, uric acid, creatinine	Monitor closely in the first days