

How Should We Manage Relapsed T-Cell Lymphoma?

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City of Hope

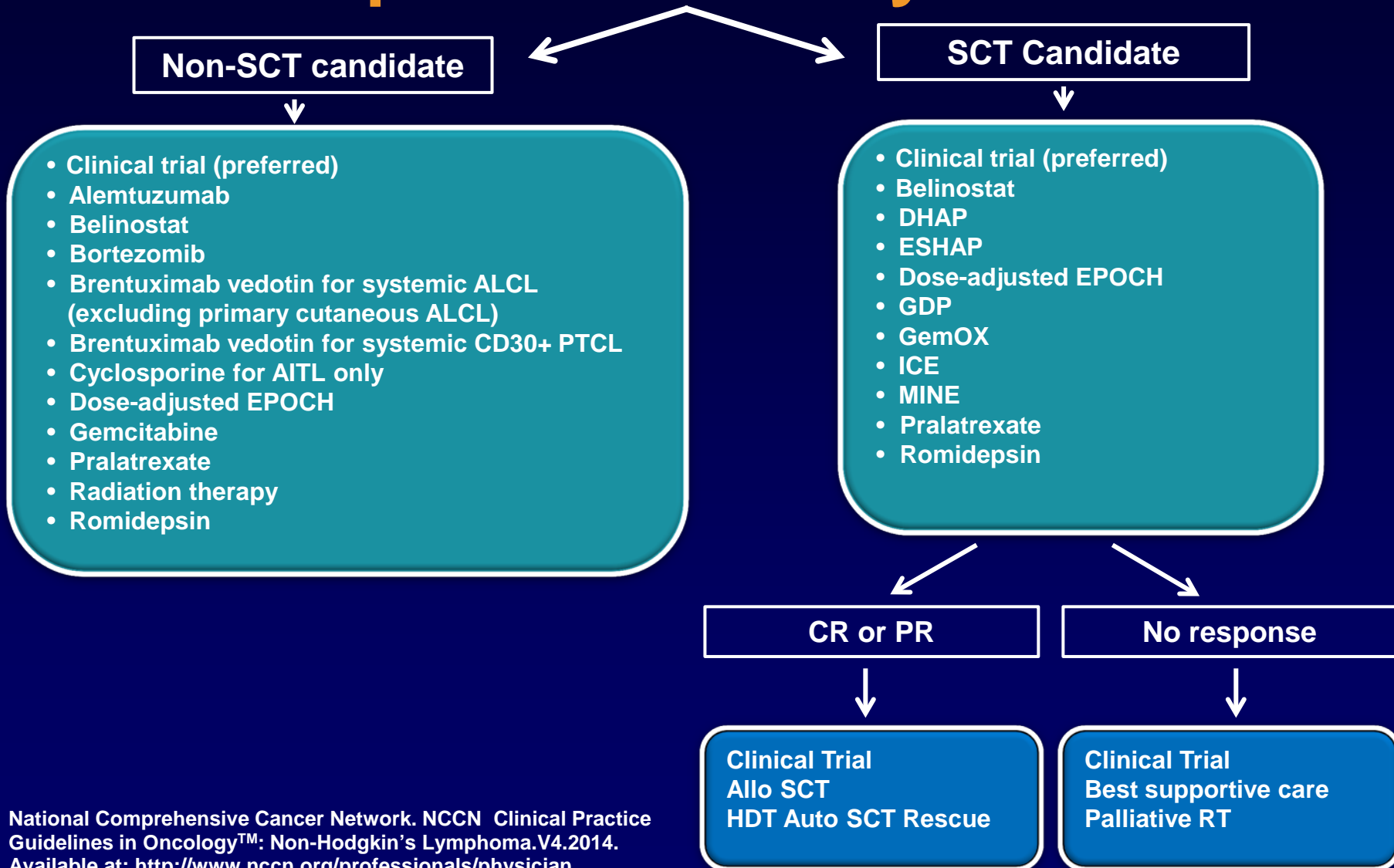
Duarte, California, United States

Relapsed PTCL-NOS

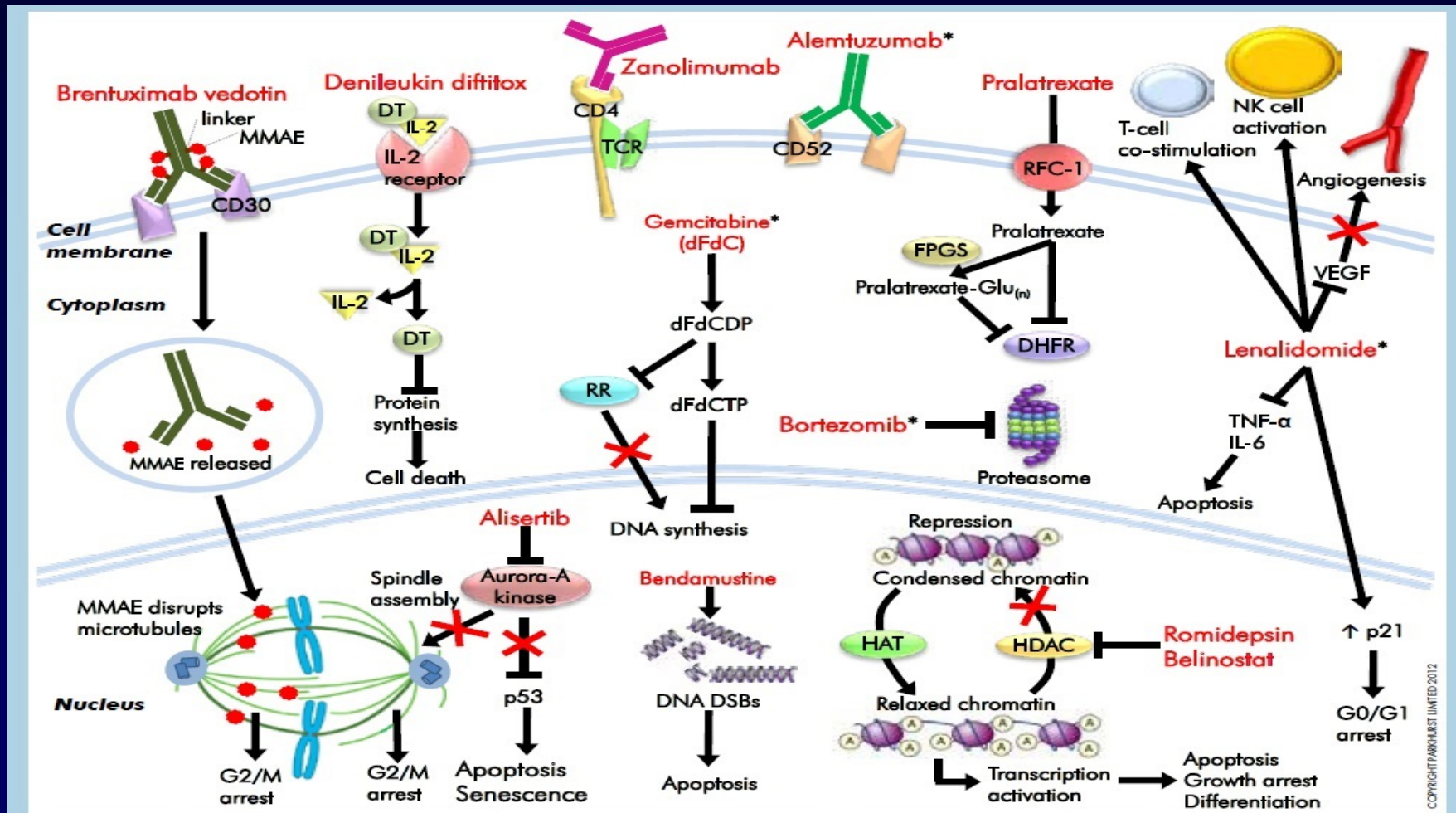
- Relapse is common
- Reinduction chemotherapy followed by autologous or allogeneic transplantation may cure a limited subset
- Sequential single agents may extend life expectancy and/or palliate symptoms
- Clinical trials with novel agents or new combinations continue to evolve

PTCL-NOS, peripheral T-cell lymphoma not otherwise specified

NCCN Guidelines: Relapsed/Refractory PTCL



Therapeutic Options for T-Cell Lymphomas



* approved by Health Canada; MMAE=monomethyl auristatin E; DT=diphtheria toxin; IL-2=interleukin 2; TCR=T-cell receptor; dFdCDP=gemcitabine diphosphate; dFdCTP=gemcitabine triphosphate; RR=ribonucleotide reductase; RFC-1=reduced folate carrier; FPGS=folypolyglutamate synthase; Glu=glutamate; DHFR=dihydrofolate reductase; NK=natural killer; VEGF=vascular endothelial growth factor; TNF-α=tumour necrosis factor-alpha; IL-6=interleukin 6; DSB=double-strand breaks; HAT=histone acetyltransferase; HDAC=histone deacetylase; A=acetyl group.

Single Agents For Relapsed or Refractory PTCL

Author	Agent (off label use)	RR
Dearden et al 1991 ¹	Pentostatin	0/6
Zinzani et al 1998 ²	Gemcitabine	5/8
Enblad et al 2004 ³	Alemtuzumab	5/14
Dang et al 2006 ⁴	Denileukin diftitox	8/19
Zinzani et al 2007 ⁵	Bortezomib	1/2
Czuczman et al 2007 ⁶	Nelarabine	1/8

1. Dearden C, et al. *Br J Cancer*. 1991;64(5):903-906; 2. Zinzani PL, et al. *Ann Oncol*. 1998;9(12):1351-1353; 3. Enblad G, et al. *Blood*. 2004;103(8):2920-2924; 4. Dang NH, et al. *Br J Haematol*. 2007;136(3):439-447; 5. Zinzani PL, et al. *J Clin Oncol*. 2007;25(27):4293-4297; 6. Czuczman MS, et al. *Leuk Lymphoma*. 2007;48(1):97-103.

PROPEL Pivotal Trial: Pralatrexate in Relapsed/Refractory PTCL



*No premedications were required. Patients received vitamin B12 q 8-10 weeks, and 1 mg of oral folic acid daily.

Outcome	Evaluable Patients N = 109
ORR	29%
CR	11%
PR	18%
Median DOR	10.1 months
Median PFS	3.5 months
Median OS	14.5 months

ORR by Histology:

PTCL-NOS: 32%; AILT: 8%; ALCL: 35%; transformed MF: 25%; other: 38%

PROPEL Pivotal Trial

Adverse Events \geq Gr 3 Occurring in $\geq 3\%$ of Patients (N = 111)

	Any Grade	Grade 3	Grade 4
Mucosal inflammation	71%	18%	4%
Thrombocytopenia	41%	14%	19%
Nausea	41%	4%	0%
Fatigue	36%	5%	2%
Anemia	34%	16%	2%
Neutropenia	25%	14%	8%
Dyspnea	19%	7%	0%
Hypokalemia	16%	4%	1%
Abnormal LFTs	13%	5%	0%
Abdominal pain	12%	4%	0%
Leukopenia	11%	4%	4%
Febrile neutropenia	5%	5%	0%
Sepsis	5%	3%	2%
Hypotension	5%	3%	1%

Romidepsin in Relapsed/Refractory PTCL

PTCL failing ≥ 1
systemic therapy
N = 130
PTCL-NOS (69),
AITL (27), ALCL
(ALK-1-neg) (21),
Other (13)

Romidepsin

14 mg/m² IV on Days 1, 8, 15
every 28 days

- Median age: 61 years (range, 20-83)
- Median of 2 prior regimens (range, 1-8)
- 62% refractory to frontline therapy

- Primary endpoint
CR/CRu (by IRC)
- Secondary endpoints
ORR, DOR

Outcomes	Romidepsin N = 131
CR/CRu	15%
ORR	25%
Median DOR	28 months (range <1–48+)
Median PFS	4 months
Median OS	11.3 months

Romidepsin in Relapsed/Refractory PTCL Toxicity

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Belinostat: The BELIEF Trial

International, phase II
study in patients with
relapsed/refractory
PTCL
N = 129

Belinostat 1000 mg/m²
d 1-5 of 21-day cycle

Primary endpoint: ORR

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Outcomes

Belinostat
N = 120

Belinostat: The BELIEF Trial

Grade ≥ 3 Treatment-Emergent AEs

Adverse Event	Incidence N = 129
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Lenalidomide in Relapsed/Refractory PTCL

- T-cell lymphoma*
- WHO PS ≤ 3
- Previously treated or untreated
- Not suitable for standard Tx, N = 24

Lenalidomide 25 mg PO
QD, days 1-21 of 28-day
cycle until disease
progression, death, or
unacceptable toxicity

- Primary endpoint:
- ORR
- Secondary endpoints:
- PFS, OS, safety

Histology	N	CR	PR	ORR (%)
All	23	0	7	30

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Bendamustine in Relapsed/Refractory T-Cell Lymphomas: BENTLY Trial

N = 60

- Multicenter, single-arm phase II study
- ≤ 3 prior lines chemotherapy
- Prior treatment: Median 1

T-cell lymphoma subtypes (n):

- AILT (32)
- PTCL-NOS (23)
- ALCL (2)
- EATL (1)
- MF (2)

**Bendamustine 120
mg/m² IV on days 1,2
every
3 weeks for 3 cycles**

**If no PD, additional 3
cycles of bendamustine**

**Primary endpoint:
OR**

**Secondary endpoints:
Safety, tolerability,
DOR, PFS, OS**

Outcomes

Alisertib: Phase II Trials (S1108) in PTCL

Category	Response, n (%)
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Adverse Event	n = 37 n (%)
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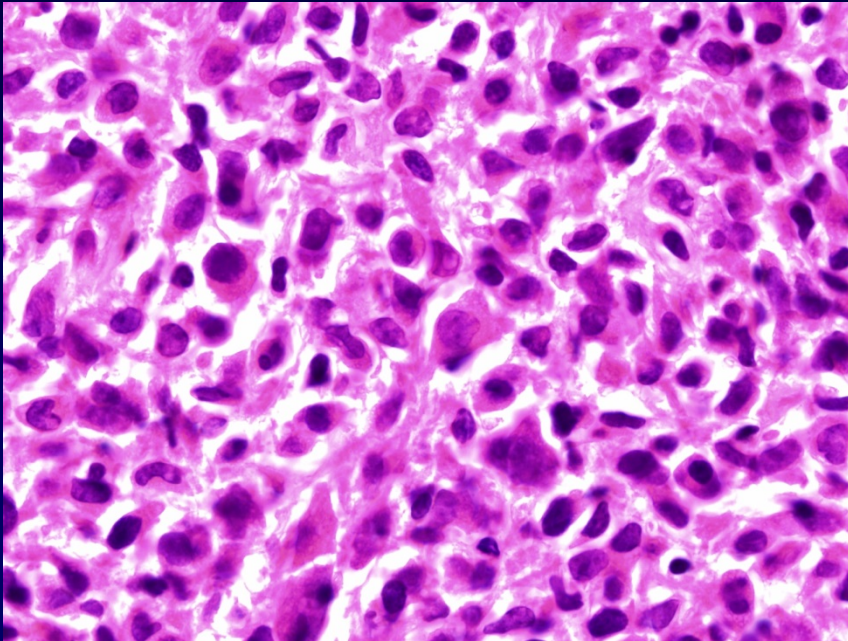
IPI-145: Oral PI3K- δ , γ Inhibitor

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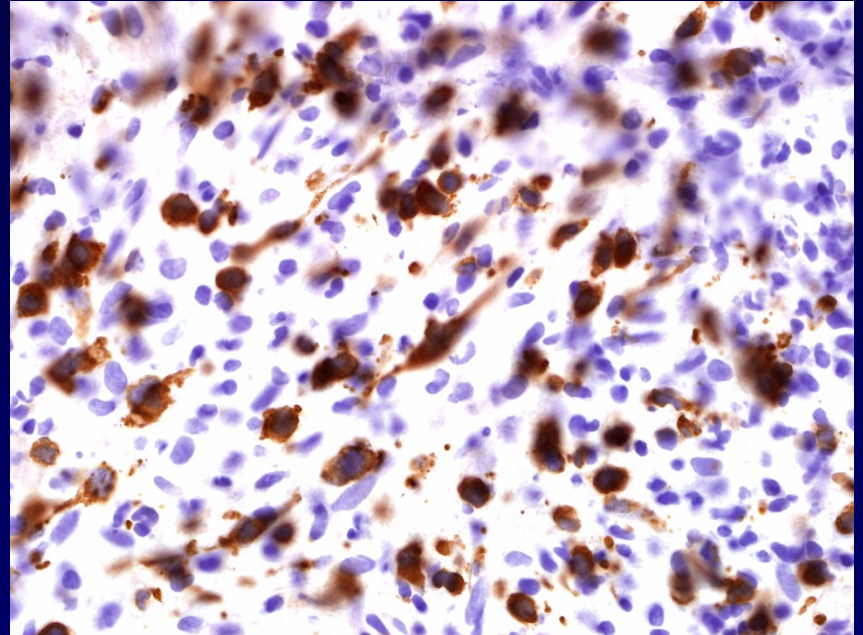
PI3K Isoform		PI3K-δ		PI3K-γ		
Population	Evaluable Patients, n	ORR	Best Response, n (%)			
			CR	PR	SD	CD

Lymph Node Biopsy

ALCL



CD30+



Brentuximab Vedotin: 3-Year Survival Results in Relapsed/Refractory ALCL

Phase II ongoing study

N = 58

62% primary refractory disease

26% had failed prior autoSCT

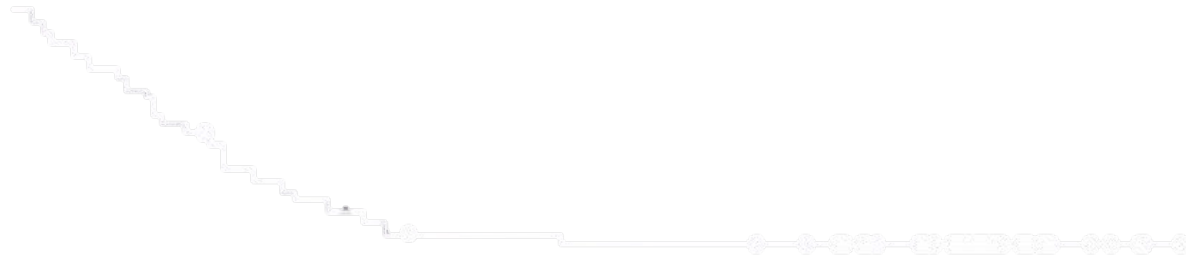
72% ALK⁻ disease

Brentuximab vedotin
1.8 mg/kg IV every 3 weeks
up to 16 cycles

Primary endpoint:
ORR

Response / Outcome

Brentuximab Vedotin: 3-Year Survival Results in Relapsed/Refractory ALCL



Brentuximab Vedotin: 3-Year Survival Results AEs in $\geq 20\%$ of Patients

Adverse Event	Any Grade, N = 58
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Brentuximab Vedotin in Relapsed T-Cell Lymphomas

Phase II, open-label
N = 35

AITL (13)
PTCL NOS (22)

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Brentuximab vedotin
1.8 mg/kg every 3 weeks
until progression or
unacceptable toxicity

Primary endpoint: ORR

Secondary endpoints:
Safety, correlation of
CD30 expression with
response, response
duration, PFS

AITL
n = 13

PTCL-NOS
n = 21

Total
N = 34

Crizotinib in ALK Rearranged Lymphoma

Chemoresistant

N = 11

ALCL histology: n = 9

DLBCL: n = 2

**Crizotinib 250 mg
twice daily**

**Primary endpoint:
ORR**

Response / Outcome

N = 11

Open-label phase Ib

N = 15

14 patients with ALK+ ALCL

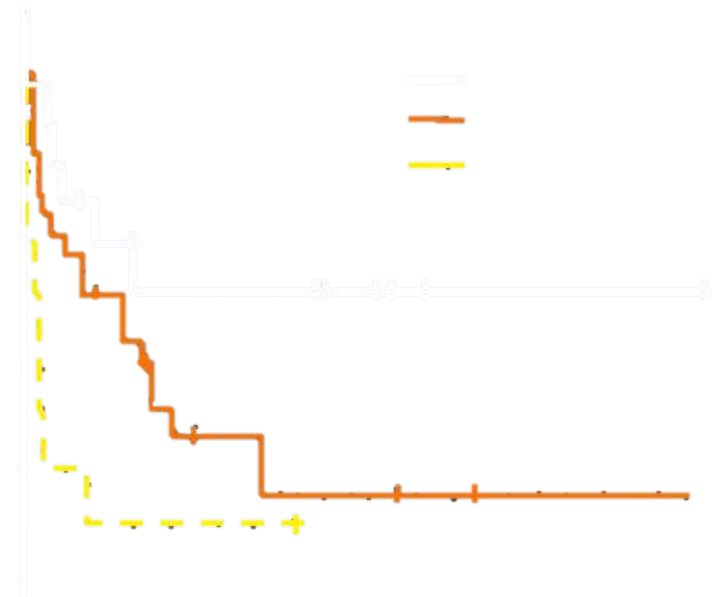
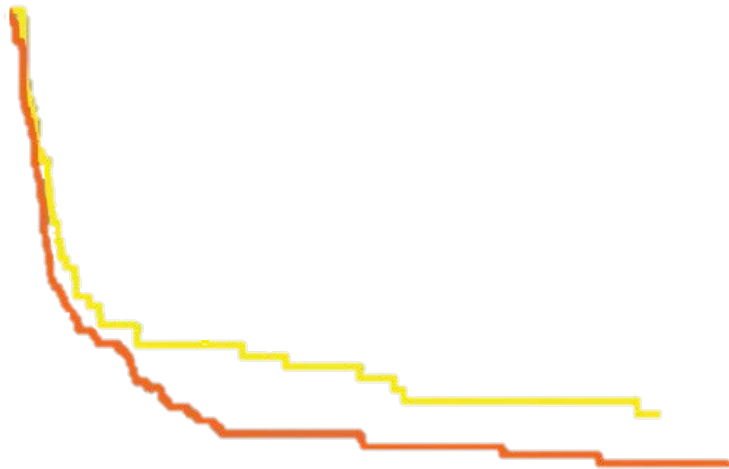
1 patient with ALK+ DLBCL

**Crizotinib 250 mg
twice daily**

**Primary endpoint:
ORR**

Response / Outcome

Autologous Transplantation in Relapsed PTCL



Mogamulizumab

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Summary

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