Webinars

Cutaneous Lymphoma

EuroBloodNet Topic on Focus

AGGRESSIVE CTCL part 2
Clinical management and treatment data

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European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

Conflicts of interest

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- **INNATE PHARMA**
- **4SC**
- **ANTHELIOS**

Learning objectives

AGGRESSIVE CTCLs

- CLINICAL & PROGNOSTIC FEATURES WITH TREATMENT IMPLICATIONS

TWO MAIN CHARACTERISTICS…

	FREQUENCY % PCL	DSS 5-YEAR SURVIVAL %
Extranodal NK/T-cell lymphoma, nasal type	<1%	16%
Primary cutaneous gamma/delta TCL	<1%	11%
Primary cutaneous aggressive epidermotropic CD8+ T-cell Lymphoma (AECTCL)	<1%	31%
Primary cutaneous peripheral T-cell lymphoma, NOS	2%	15%
Blastic plasmacytoid dendritic cell neoplasm (BPDCN) Blastic NK-cell lymphoma (WHO classification) CD4+/CD56+ haematodermic neoplasia (WHO-EORTC classification)	Very rare	12 mo median

blood Special Report

CME Article

The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas

Rein Willemze,[1] Lorenzo Cerroni,[2] Werner Kempf,[3] Emilio Berti,[4] Fabio Facchetti,[5] Steven H. Swerdlow,[6] and Elaine S. Jaffe[7]

[1]Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; [2]Department of Dermatology, Medical University of Graz, Graz, Austria; [3]Kempf und Pfaltz Histologische Diagnostik and Department of Dermatology, University Hospital Zurich, Zurich, Switzerland; [4]Department of Dermatology, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy; [5]Department of Pathology, University of Brescia, Brescia, Italy; [6]Division of Hematopathology, University of Pittsburgh School of Medicine, Pittsburgh, PA; and [7]Hematopathology Section, Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, MD

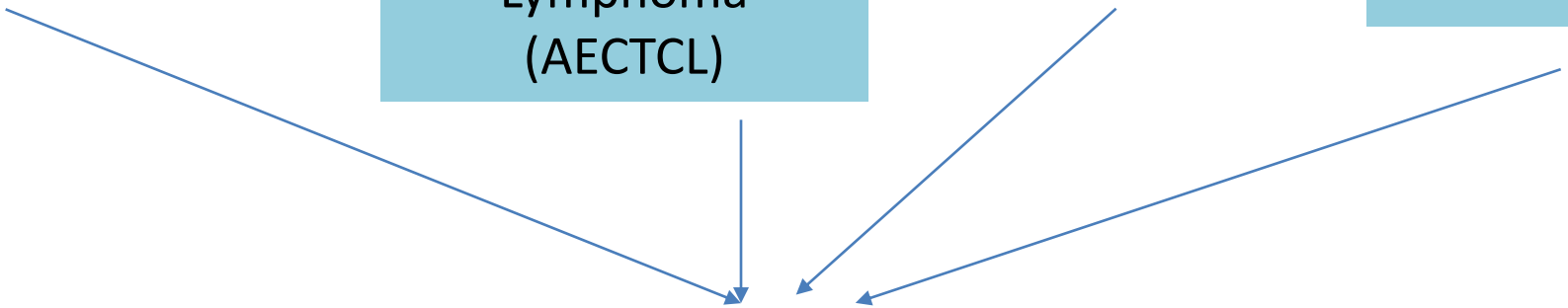
POOR PROGNOSIS

Primary cutaneous gamma/delta TCL

Primary cutaneous aggressive epidermotropic CD8+ T-cell Lymphoma (AECTCL)

Extranodal NK/T-cell lymphoma, nasal type

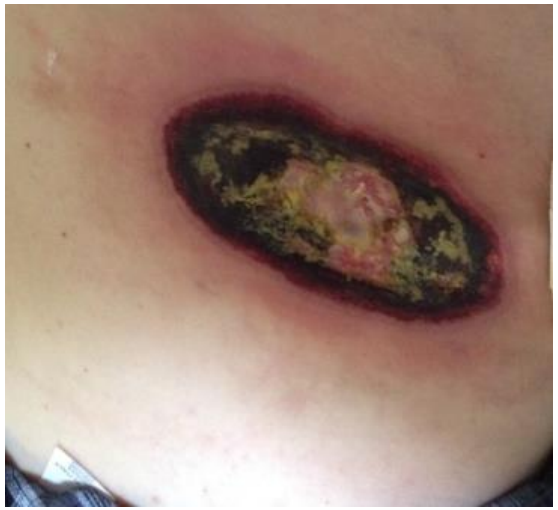
Primary cutaneous peripheral T-cell lymphoma, NOS

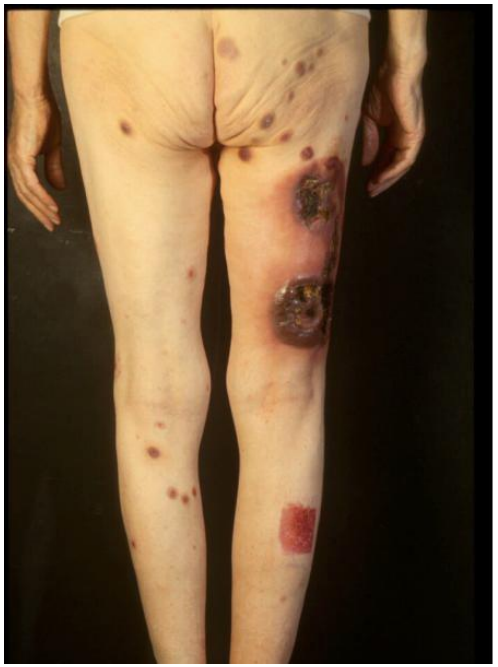


Wide-spread ulcerated plaque tumours

Frequent extracutaneous involvement

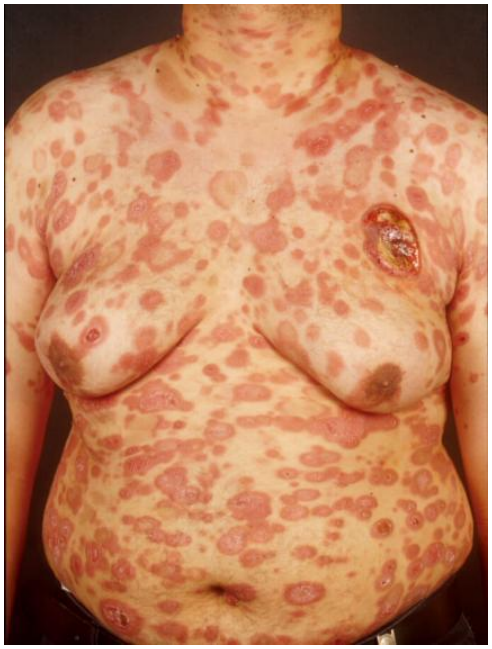
SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA



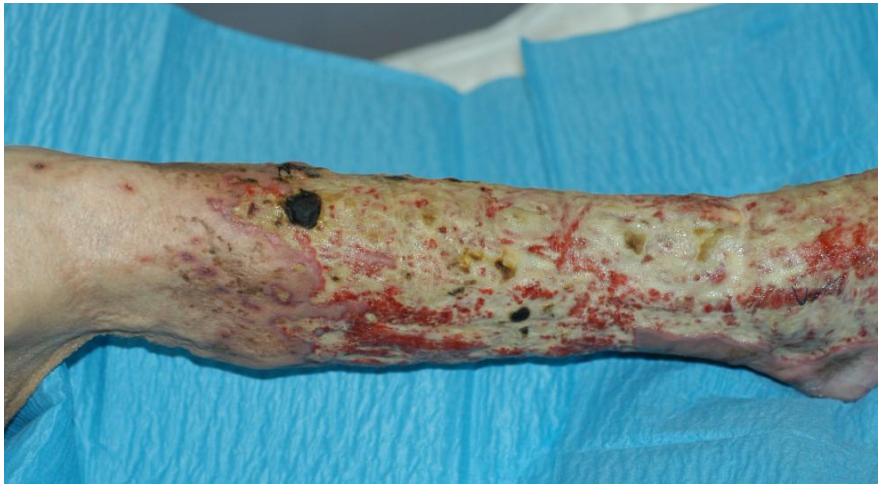


Primary cutaneous aggressive epidermotropic CD8+ T-cell Lymphoma (AECTCL)

PTCL, NOS



Cutaneous gamma delta T-cell lymphoma



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Cutaneous Lymphoma
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Learning objectives

AGGRESSIVE CTCLs

- CLINICAL & PROGNOSTIC FEATURES WITH TREATMENT IMPLICATIONS
- CLINICAL STAGING

AFTER DIAGNOSIS and BEFORE TREATMENT
CLINICAL STAGING CTCL, non MF/SS

T1: Solitary skin involvement
T1a: a solitary lesion <5 cm diameter
T1b: a solitary >5 cm diameter
T2: Regional skin involvement: multiple lesions limited to 1 body region or 2 contiguous body regions*
T2a: all-disease-encompassing in a <15-cm-diameter circular area
T2b: all-disease-encompassing in a >15- and <30-cm-diameter circular area
T2c: all-disease-encompassing in a >30-cm-diameter circular area
T3: Generalized skin involvement
T3a: multiple lesions involving 2 noncontiguous body regions
T3b: multiple lesions involving ≥3 body regions

Kim Y, et al. Blood 2007

ITALIAN GROUP FOR CUTANEOUS LYMPHOMA guidelines of treatment

- To confirm the primary cutaneous origin
- To detect extracutaneous involvement

diagnosis	staging
CGT-TCL, AECTCL, PTL-NOS	CT, PET, bone marrow biopsy
SPTL with HPS	CT, PET, bone marrow biopsy

Pimpinelli N, Berti E, Pileri A, Albrti-Violetti S, Quagllino p, Fava P, et al

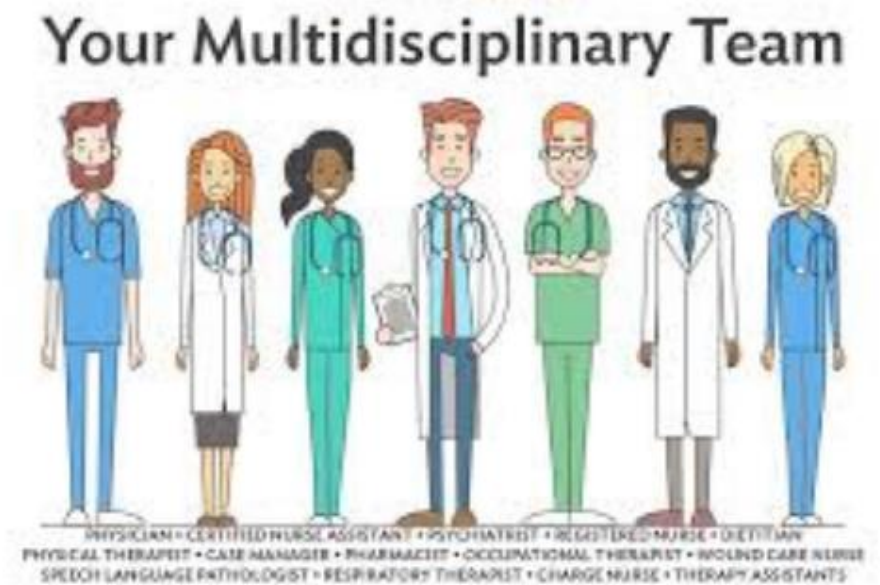
Learning objectives

AGGRESSIVE CTCLs

- CLINICAL & PROGNOSTIC FEATURES WITH TREATMENT IMPLICATIONS
- CLINICAL STAGING
- MULTI-DISCIPLINARY APPROACH

MULTI-DISCIPLINARY TEAM

- HAEMATOLOGIST
- DERMATOLOGIST
- RADIATION ONCOLOGIST
- PATHOLOGIST
- NURSE TEAM for SKIN CARE
- OTHERS..



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Learning objectives

AGGRESSIVE CTCLs

- CLINICAL & PROGNOSTIC FEATURES WITH TREATMENT IMPLICATIONS
- CLINICAL STAGING
- MULTI-DISCIPLINARY APPROACH
- TREATMENT: CHEMOTHERAPY

- VERY FEW LITERATURE DATA SPECIFICALLY FOCUSED ON THESE RARE PRIMARY CUTANEOUS ENTITIES
- TREATMENTS ARE MUTUATED FROM THE HAEMATOLOGIST GUIDELINES

MONOCHEMOTHERAPY

Patients	Responses (%)	CR (%)	Response dura (months)
526	329 (62)	91 (33)	3-22

POLICHEMOTHERAPY

331	269 (81)	125 (37.7)	3.5 (5-41)

n PA, Ann Intern Med, 1994

Table 11. Key clinical studies of systemic chemotherapy in cutaneous T-cell lymphoma

Therapy examples*	Efficacy	Comments
CHOP-based[67]	ORR stage IIB: 66%	Myelosuppression with risk of infection; very short remission duration
EPOCH[61]	ORR stage IIB-IV: 80%	Myelosuppression with risk of infection; short remission duration
CMED/ABV[42,62]	ORR stage III-IV: 81%	Myelosuppression with risk of infection; median DFS of 7 months and 27% 5-year DFS
Pegylated liposomal doxorubicin[65]	ORR stage IA-IV: 88%	Single agent; well tolerated; infusion-related events; no comparisons with standard anthracyclines
Pentostatin[64]	ORR stage IIB: 75% Stage III: 58% Stage IV: 50%	Numerous trials and regimens used; activity in PTCL; perhaps best activity in SS; prolonged therapy needed in some cases; lymphopenia
Fludarabine plus IFN-α[55]	ORR stage IIA-IVA: 58% stage IVB: 40%	Neutropenia common
Fludarabine plus cyclophosphamide[66]	ORR stage IIB-III: 55%	Appears higher RR to fludarabine-alone; lymphopenia and prolonged myelosuppression in some patients; stem cell collection yields are lower
Gemcitabine[63]	ORR stage IIB-III: 70%	Neutropenia; recent evidence that toxicities (rash, infection) may be higher in patients with CTCL (see "Systemic chemotherapy")
2-Chlorodeoxyadensine[68]	ORR stage IIA-IV: 28%	Median duration or response of 4.5 months; bone marrow suppression and infections in 62%

CR indicates complete response; CRR, complete response rate; EPOCH, etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone; ORR, overall response rate; PR, partial response; PUVA, ultraviolet A light with oral methoxypsoralen; and DFS, disease-free survival.

*See "Systemic chemotherapy" for more details and other trial results.

BLOOD, 2011

Literature studies on systemic treatment options in advanced-phase CTCL

Author, year	Drug/ regimen	No of patients	Disease /stage	ORR %	CR %	Remission duration median (mo)	TTP/ PFS median (mo)
Fierro, 1998	COP/CHOP	35	MF IIB-IV, SS, PTCLU	40%	23%	5.7	4.5
Marchi, 2005	Gemcitabine	32	MF IIB-IV, SS, PTCLU	75%	22%	10 (CRs)	10
Olsen, 2007	Vorinostat	74	IB-IVA MF/SS	29.7%	1%	>6.1	4.9
Jidar, 2009	Gemcitabine	23	MF IIB-IV, SS, PTCLU	62.5%	6.25%	-	-
Whittaker, 2010	Romidepsine	96	MF IB-IV, SS	34%	6.2%	15	-
Dummer, 2012	Peg-doxo	49	MF IIB, IV	40.8%	6.1%	6	7.4
Illidge, 2013	Gemcitabine + bexarotene	30	MF IB-IVA	31%	0	-	5.3
De Masson, 2014	Alemtuzumab	39	MF II-IVB /SS	51%	18%	4	3.4
Dummer, 2014	Forodesine	144	IB- IVA MF/SS	11%	0%	6.3	-

MF= Mycosis fungoides; SS= Sézary syndrome; PTCLU= Peripheral T-cell lymphoma, unspecified
RR=Response Rate; CR=Complete Remission; TTP=Time-To-Progression; PFS: Progression-Free-Survival

Gemcitabine as Frontline Treatment for Cutaneous T-Cell Lymphoma

Phase II Study of 32 Patients

Enrica Marchi, M.D.[1]
Lapo Alinari, M.D.[1]
Monica Tani, M.D.[1]
Vittorio Stefoni, M.D.[1]
Nicola Pimpinelli, M.D.[2]
Emilio Berti, M.D.[3]
Livio Pagano, M.D.[4]
Maria Grazia Bernengo, M.D.[5]
Francesco Zaja, M.D.[6]
Serena Rupoli, M.D.[7]
Stefano Pileri, M.D.[1]
Michele Baccarani, M.D.[1]
Pier Luigi Zinzani, M.D.[1]

BACKGROUND. Based on the activity of gemcitabine in heavily pretreated patients with cutaneous T-cell lymphoma (CTCL), the objective of the current study was to determine the role of gemcitabine in the treatment of patients with advanced, untreated CTCL.

METHODS. Between June 2002 and February 2004, 32 untreated patients with mycosis fungoides (MF) (n = 26 patients); peripheral T-cell lymphoma, unspecified (PTCLU) with exclusive skin involvement (n = 5 patients); and Sezary syndrome (SS) (n = 1 patient) were enrolled in a 7-institution, Phase II trial and treated with gemcitabine. This drug was given on Days 1, 8, and 15 of a 28-day schedule at a dose of 1200 mg/m^2 intravenously over 30 minutes for a total of 6 cycles.

RESULTS. Of the 32 patients studied, 7 (22%) achieved a complete response (CR) and 17 (53%) achieved a partial response (PR), whereas the remaining 8 patients showed no benefit from the treatment. Five of the CRs were confirmed histologically. The CR and PR rates were found to be the same for patients with MF and

TABLE 2
Treatment Outcome

	Total (n = 32 patients)	MF (n = 26 patients)	PTCLU (n = 5 patients)	SS (n = 1 patient)
CR	7 (22%)	6 (23%)	1 (20%)	—
PR	17 (53%)	13 (50%)	4 (80%)	—
No response	8 (25%)	7 (27%)	—	1 (100%)
CR + PR	24 (75%)	19 (73%)	5 (100%)	—

MF: mycosis fungoides; PTCLU: peripheral T-cell lymphoma, unspecified; SS: Sezary syndrome; CR: complete response; PR: partial response.

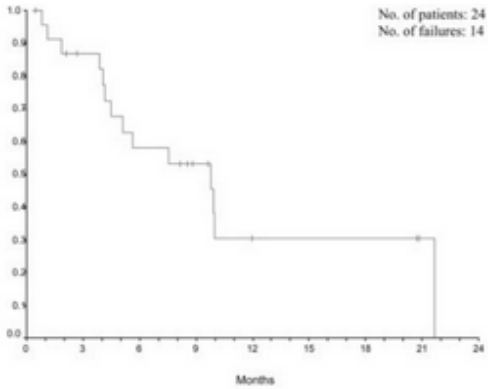
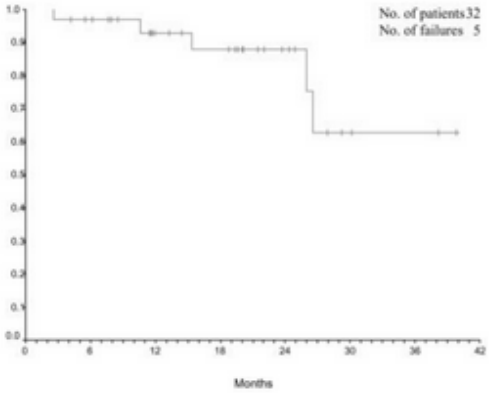


FIGURE 1. Progression-free survival curve of all responding patients.

TABLE 1
Characteristics of the Study Group

Characteristic	
M:F ratio	22:10
Age in yrs	
Median	58
Range	25–77
Histology	
MF	26 (81%)
PTCLU	5 (16%)
SS	1 (3%)
Previous treatments (n = 22 patients)	
Radiotherapy	4
PUVA	10
PUVA plus local radiotherapy	8
TNM classification/Ann Arbor stage	
MF (T3 or T4, N0,M0)	26
PTCLU (Stage IV, skin)	5

M:F: male-to-female; MF: mycosis fungoides; PTCLU: peripheral T-cell lymphoma, unspecified; SS: Sezary syndrome; PUVA: psoralen and ultraviolet A radiation therapy.



Cancer [0008-543X] Marchi, Enrica anno:2005 vol:104 fasc:11 pag:2437 -2441

Annals of Hematology (2019) 98:1961–1972
https://doi.org/10.1007/s00277-019-03694-y

ORIGINAL ARTICLE

First-line therapy for T cell lymphomas: a retrospective population-based analysis of 906 T cell lymphoma patients

Andrea Janikova[1] · Renata Chloupkova[2] · Vit Campr[3] · Pavel Klener[4] · Jitka Hamouzova[4] · David Belada[5] · Vit Prochazka[6] · Robert Pytlik[4] · Jan Pirnos[7] · Juraj Duras[8] · Heidi Mocikova[9,10] · Zbynek Bortlicek[2] · Natasa Kopalova[1] · Jiri Mayer[1] · Marek Trneny[4]

Received: 16 July 2018 / Accepted: 15 April 2019 / Published online: 8 May 2019

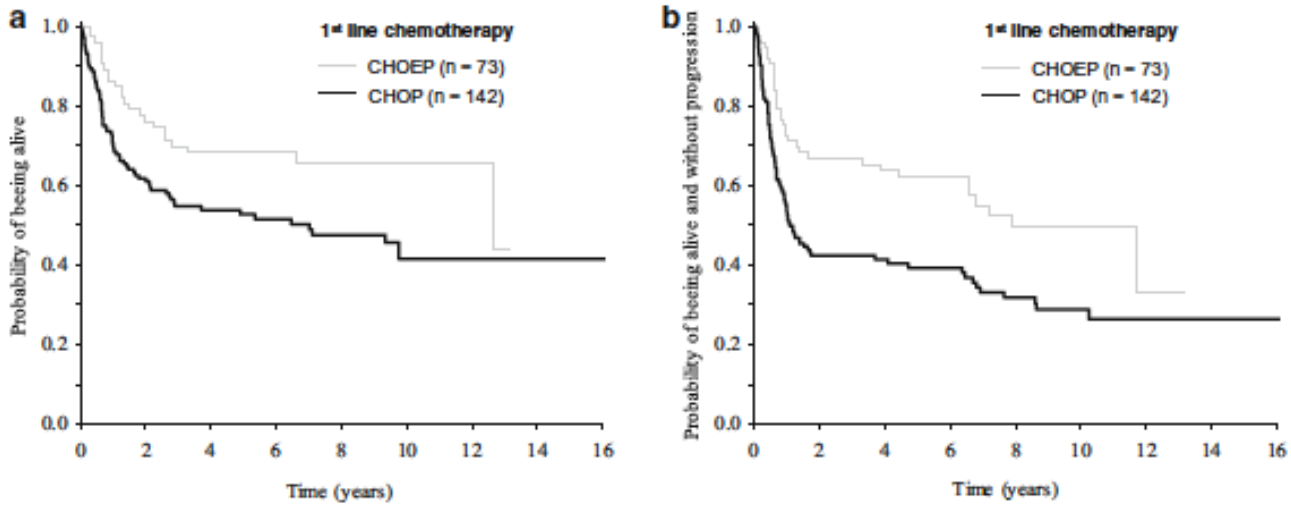


Fig. 2 Overall survival from diagnosis according to IPI (**a**) and PIT (**b**) score

European Reference Network for rare or low complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

EuroBloodNet Topic on Focus

> Dermatology. 1997;194(3):268-72. doi: 10.1159/000246116.

Combination of etoposide, idarubicin, cyclophosphamide, vincristine, prednisone and bleomycin (VICOP-B) in the treatment of advanced cutaneous T-cell lymphoma

M T Fierro [1], G C Doveil, P Quaglino, P Savoia, A Verrone, M G Bernengo

Affiliations + expand

PMID: 9187846 DOI: 10.1159/000246116

Abstract

Background: Response of cutaneous T-cell lymphoma (CTCL) to systemic chemotherapy is unsatisfactory: despite an initially high response rate (RR), duration is always short-lived.

Objective: To investigate the capability of a third-generation regimen including idarubicin in improving RR and response duration in CTCL patients.

Methods: Twenty-five patients with advanced CTCL (stages IIB and IV) were treated with a 12-week polychemotherapeutic regimen (VICOP-B), which foresees the use of idarubicin in association with etoposide, cyclophosphamide, vincristine, prednisone and bleomycin.

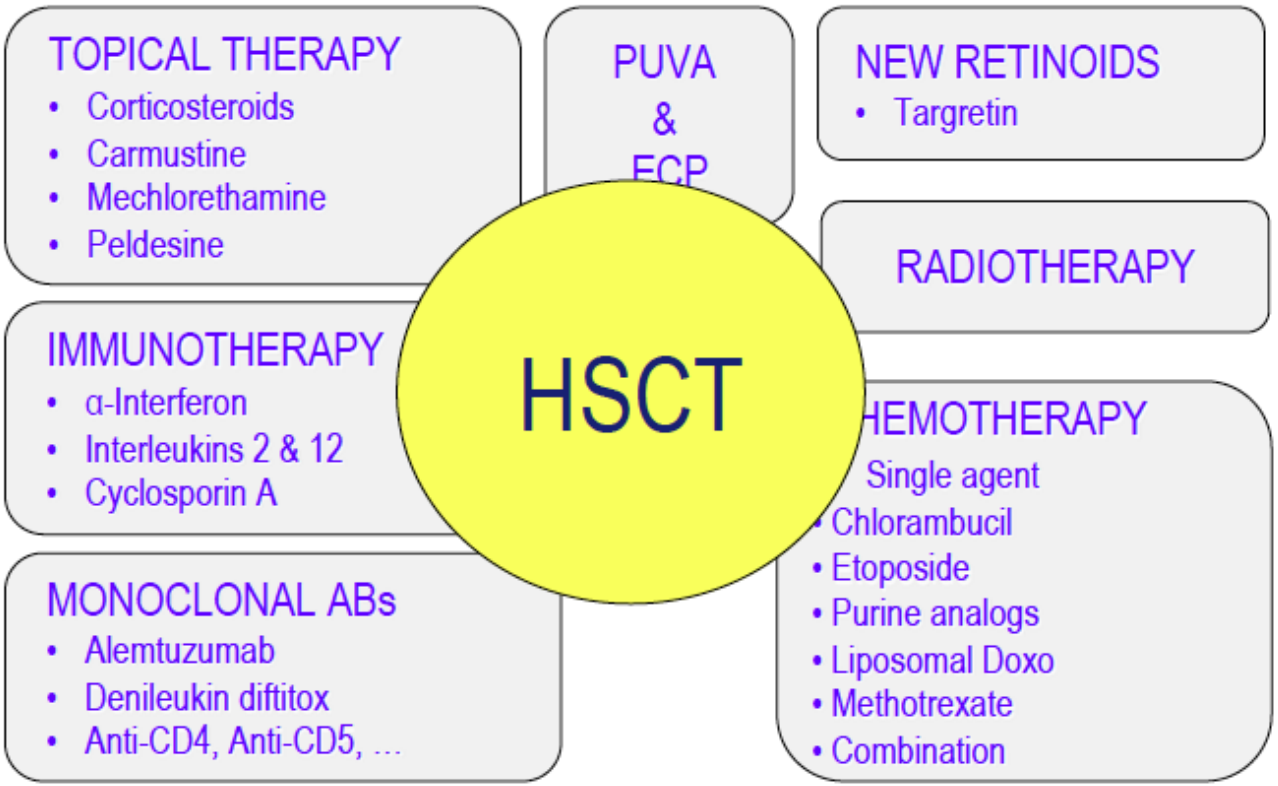
Results: The overall objective RR was 80% (36% complete response). The mycosis fungoides (MF) RR was 84%, with a median duration of 8.7 months. The pleomorphic-lymphoma RR was higher (100%), but the corresponding response duration was shorter (median: 3 months). No responses were documented in Sézary syndrome.

Learning objectives

AGGRESSIVE CTCLs

- CLINICAL & PROGNOSTIC FEATURES WITH TREATMENT IMPLICATIONS
- CLINICAL STAGING
- MULTI-DISCIPLINARY APPROACH
- TREATMENT: CHEMOTHERAPY
- TREATMENT: ALLOGENEIC TRANSPLANT

Management of advanced stage primary CTCL



VOLUME 32 · NUMBER 29 · OCTOBER 10 2014

JOURNAL OF CLINICAL ONCOLOGY

Long-Term Outcome of Allogeneic Hematopoietic Cell Transplantation for Patients With Mycosis Fungoides and Sézary Syndrome: A European Society for Blood and Marrow Transplantation Lymphoma Working Party Extended Analysis

To the Editor: In 2010, the European Society for Blood and Marrow Transplantation (EBMT) reported an overall survival (OS) of 66% at 1 year and 54% at 3 years after allogeneic hematopoietic cell transplantation (HCT) in patients with advanced-stage mycosis fungoides and Sézary syndrome (MF/SS).[1] The main shortcoming of this initial report was a limited follow-up of only 36 months; in particular, for a series in which 73% of the cases received reduced-intensity conditioning before HCT. Here, we present an extended analysis of this experience, with a median follow-up in survivors of 7 years (longest follow-up: 12 years; interquartile range: 6 to 9 years). The analysis focuses on nonrelapse mortality (NRM), cumulative incidence of relapse/progression, progression-free survival (PFS), OS, and the impact of disease and transplant factors on long-term patient outcome.

All 60 patients with European Organisation for Research and Treatment of Cancer/International Society for Cutaneous Lymphomas advanced-stage (TNM stages IIB and higher)[2] MF (n = 36) and SS (n = 24) reported to the EBMT for a first allogeneic HCT between 1997 and 2007 and who were included in our original series were reanalyzed. The sample included 37 men and 23 women; median age at transplant was 46.5 years (range, 22 to 66 years). There were 45 matched related and 15 matched unrelated donors; 44 (73%) had TNM stage IV disease,[2] and 40 (67%) were at advanced disease phase at transplantation, defined as either those on third or later complete

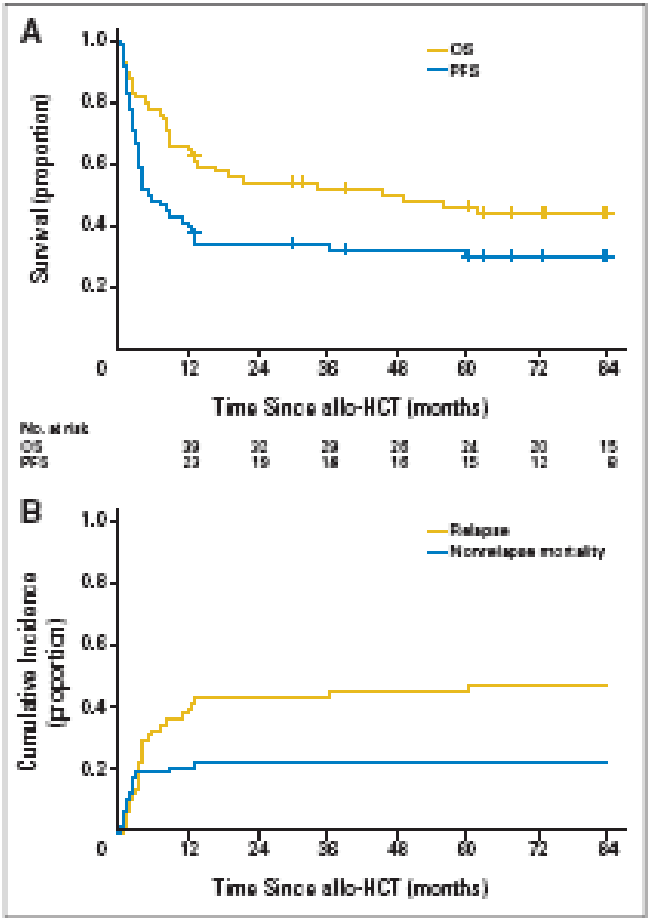


Fig 1. (A) Long-term probability of overall survival (OS) and progression-free survival (PFS), and (B) cumulative incidence of nonrelapse mortality and disease relapse or progression after allogeneic hematopoietic cell transplantation in patients with mycosis fungoides and Sézary syndrome.

THERAPY OF AGGRESSIVE non MF/SS CTCLs…

	DSS 5-YEAR SURVIVAL %	THERAPY
Primary cutaneous gamma/delta TCL	11%	CHOP/CHOP-like, HSCT
Primary cutaneous aggressive epidermotropic CD8+ T-cell Lymphoma (AECTCL)	31%	
Primary cutaneous peripheral T-cell lymphoma, NOS	15%	

Toro JR, Blood. 2003.
Guitart J, et al. Am J Surg Pathol. 2012.
Geller S, et al. Semin Cut Med Surg, 2018.
Plakhouri KM, et al. JAAD case reports, 2017.

Biol Blood Marrow Transplant 26 (2020) 76–82

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Efficacy of Allogeneic Hematopoietic Cell Transplantation in Cutaneous T Cell Lymphoma: Results of a Systematic Review and Meta-Analysis

Madiha Iqbal[1], Tea Reljic[2], Ernesto Ayala[1], Taimur Sher[1], Hemant Murthy[3], Vivek Roy[1], James Foran[1], Han Tun[1], Ambuj Kumar[2], Mohamed A. Kharfan-Dabaja[1,*]

[1] Division of Hematology-Oncology and Blood and Marrow Transplantation Program, Mayo Clinic, Jacksonville, Florida
[2] Program for Comparative Effectiveness Research, Morsani College of Medicine, University of South Florida, Tampa, Florida
[3] Blood and Marrow Transplantation and Malignant Hematology Program, University of Florida Health Cancer Center, Gainesville, Florida

Table 1
Characteristics of Eligible Studies

Author, Year of Publication, Reference	Institution or Group/Years of Recruitment/Study Type	No. of Patients Enrolled	No. of Patients Included in Analysis and Gender	Median Age for Patients Enrolled(yr) (range)	Donor Status	Cell Source	Conditioning Regimen	Median Number of Prior Regimens (range)	Disease Status at Time of HCT	Outcomes
Delioukina et al., 2012 [15]	City of Hope (2001-2008) Retrospective	27*	11†	50 (19-68)	MUD = 5 Sibling = 6	BM = 3* PBSC = 24*	RIC = 11	6 (4-9)	CR = 1 PR = 1 PD = 9	OS = 45% PFS = 45% (2 year)
Duarte et al., 2010 [21]	EBMT (1997-2007) Retrospective	60 MF = 36 SS = 24	60 M = 37 F = 23	46.5 (22-66)	MRD = 45 MUD = 15	BM = 10 PBSC = 50	RIC = 44 MAC = 16	4 (1-12)	Early phase** = 20 Advanced phase = 40	OS = 66% PFS = 42% (1 year) OS = 54% PFS = 34% (3 year)
Duvic et al., 2010 [22]	MD Anderson (2001-2008) Single center	19	19 M = 9 F = 10	50 (21-63)	MRD = 12 MUD = 7	BM = 5 PBSC = 14	NMA = 19	4 (1-7)	CR = 4 PR = 4 PD = 6 SD = 5	OS = 79% PFS = 53% (2 year)
Hosing et al., 2015 [14]	MD Anderson (2001-2013) Prospective	47	47 M = 20 F = 27	51.5 (19-72)	MRD = 21 MUD = 24 MMRD = 2	BM = 12 PBSC = 35	RIC = 42 NMA = 2 MAC = 3	6 (2-11)	CR = 7 PR = 28 SD/PD = 12	OS = 51% PFS = 26% (4 year)
Lechowicz et al., 2014 [33]	CIMBTR (2000-2009) Retrospective	129	129 M = 70 F = 59	51 (27-72) NMA/RIC 44 (22-63) MAC	MRD = 64 MUD = 56 MMRD = 9	BM = 18 PBSC = 107 Cord blood = 4	RIC/NMA = 83 MAC = 46	ND	First CR = 3 Second CR = 5 REL1 = 10 ≥REL2 = 18 Missing = 49 PD = 44	OS = 54% PFS = 31% (1 year) OS = 32% PFS = 17% (5 year)

BM indicates bone marrow; PBSC, peripheral blood stem cells; MUD, matched unrelated donor; MRD, matched related donor; MMRD, mismatched related donor; MAC, myeloablative conditioning; RIC, reduced intensity conditioning; NMA, nonmyeloablative; CR, complete remission; PR, partial remission; PD, progressive disease; REL1, first relapse; REL2, second relapse; SD, stable disease; ND, not described; OS, overall survival; PFS, progression-free survival; EBMT, European Society for Blood and Marrow Transplantation; CIMBTR, Center for International Blood and Marrow Transplant Research.

* Includes all histologies (CTCL = 11).

** Defined as 1st or 2nd CR, PR, relapse with 3 or fewer lines of therapy.

† Gender not specified for MF and SS.

Biol Blood Marrow Transplant 26 (2020) 76–82

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Efficacy of Allogeneic Hematopoietic Cell Transplantation in Cutaneous T Cell Lymphoma: Results of a Systematic Review and Meta-Analysis

Madiha Iqbal[1], Tea Reljic[2], Ernesto Ayala[1], Taimur Sher[1], Hemant Murthy[3], Vivek Roy[1], James Foran[1], Han Tun[1], Ambuj Kumar[2], Mohamed A. Kharfan-Dabaja[1,*]

[1] Division of Hematology-Oncology and Blood and Marrow Transplantation Program, Mayo Clinic, Jacksonville, Florida
[2] Program for Comparative Effectiveness Research, Morsani College of Medicine, University of South Florida, Tampa, Florida
[3] Blood and Marrow Transplantation and Malignant Hematology Program, University of Florida Health Cancer Center, Gainesville, Florida

This systematic review and meta-analysis demonstrates that allo-HCT is an effective treatment for patients with CTCLs.
Encouraging pooled OS rates of 59% (95% CI, 50% to 69%) were observed despite the fact that most patients had advanced/resistant disease and were not in complete remission at the time of allografting).
However, a lower pooled PFS rate of 36% (95% CI, 27% to 45%) was observed, highlighting the risk of disease relapse even after allo-HCT

Learning objectives

AGGRESSIVE CTCLs

- CLINICAL & PROGNOSTIC FEATURES WITH TREATMENT IMPLICATIONS
- CLINICAL STAGING
- MULTI-DISCIPLINARY APPROACH
- TREATMENT: CHEMOTHERAPY
- TREATMENT: ALLOGENEIC TRANSPLANT
- TREATMENT: A COMPREHENSIVE SCENARIO

AGGRESSIVE CUTANEOUS T-CELL LYMPHOMA

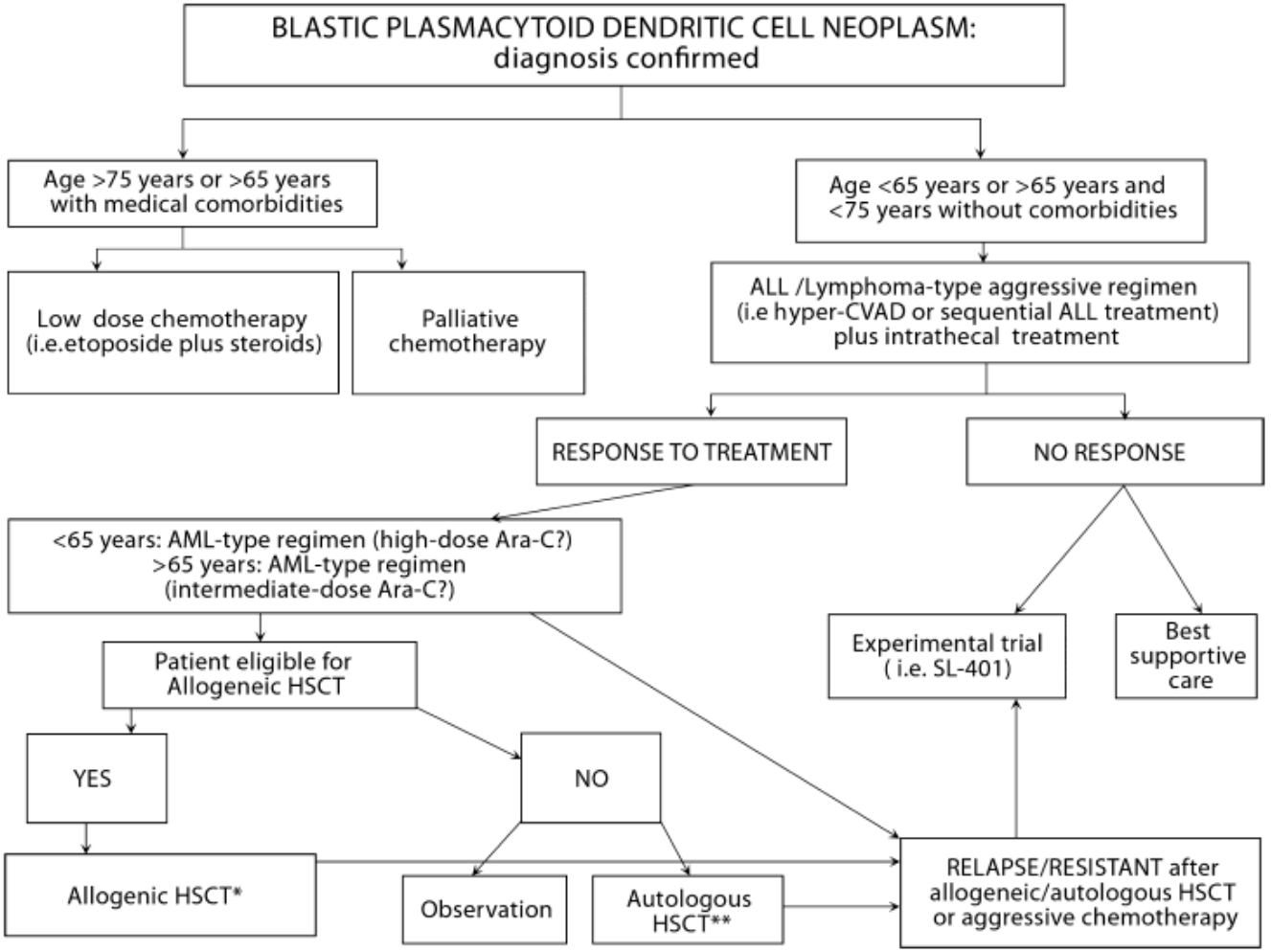
MULTI-DISCIPLINARY TEAM

RADIO-THERAPY
Solitary lesions
Improve response

CHEMOTHERAPY
(MONO/POLY)
CHOP/CHOEP

ALLO-TRANSPLANT
Age/comorbidities

CLINICAL TRIAL


BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM: diagnosis confirmed
Age >75 years or >65 years with medical comorbidities
Age <65 years or >65 years and <75 years without comorbidities
Low dose chemotherapy (i.e.etoposide plus steroids)
Palliative chemotherapy
ALL /Lymphoma-type aggressive regimen (i.e hyper-CVAD or sequential ALL treatment) plus intrathecal treatment
RESPONSE TO TREATMENT
NO RESPONSE
<65 years: AML-type regimen (high-dose Ara-C?) >65 years: AML-type regimen (intermediate-dose Ara-C?)
Experimental trial (i.e. SL-401)
Best supportive care
Patient eligible for Allogeneic HSCT
YES
NO
Allogenic HSCT*
Observation
Autologous HSCT**
RELAPSE/RESISTANT after allogeneic/autologous HSCT or aggressive chemotherapy

Learning objectives

AGGRESSIVE CTCLs

- CLINICAL & PROGNOSTIC FEATURES WITH TREATMENT IMPLICATIONS
- CLINICAL STAGING
- MULTI-DISCIPLINARY APPROACH
- TREATMENT: CHEMOTHERAPY
- TREATMENT: ALLOGENEIC TRANSPLANT
- TREATMENT: A COMPREHENSIVE SCENARIO
- FUTURE PERSPECTIVES

Table 2. Summary of the results from the main studies with new drugs in CTCL

Target	Drug	Phase	No of pts	Inclusion	ORR	Disease outcome	Drug approva
CD30	Brentuximab vedotin	III randomized vs best clinical choice (Bexarotene or Methotrexate) [29]	128	CD30-positive mycosis fungoides or primary cutaneous anaplastic large-cell lymphoma	56.3% vs 12.5% (ORR4); MF IIB: 63%;CD30+ anaplastic:75%	Median PFS: 16.7 vs 3.5 months	FDA/EMA
CD47	TTI-621	I	9	relapsed or refractory MF/SS			
CD52	Alemtuzumab						
CCR4	Mogamulizumab	III randomized vs Vorinostat [36]	372	MF/SS stage Ib to IV with at least one systemic therapy.	28% vs 5%; RR in SS 37%; 68% in the blood	PFS median 7.7 vs 3.1; p<0.0001	FDA/EMA
CD158k	IPH4102	I open-label dose-escalation and cohort expansion [43]	44	dose-escalation: relapsed/ refractory CTCL stage>=IB, at least 5% skin-infiltrating or phenotypically abnormal circulating T-cells expressing KIR3DL2; cohort expansion: SS/MF patients with large cell transformation, independently from KIR3DL2	36.4%; in SS 42.9% global and 55.9% in the blood	Median DOR: 13.8 months	-
PI3K-δ,γ	Duvelisib	I [46]	19	CTCL	31.6%	-	-
NfKb	Bortezomib	II [57]	12	CTCL	67%	DOR from 7 to > 14 months	-
HDAC	Vorinostat	Open-label phase IIb trial [59]	74	IB-IVA MF/SS, at least two prior systemic therapies, at least one of which Bexarotene	29.7% (32% pruritus relief)	Median DOR NR (>185 days). Median TTP 4.9 mo, 9.8 months stage IIB or higher responders.	FDA
HDAC	Vorinostat	II [60]	33	Refractory CTCL	RR 24%; 14/31 patients had pruritus relief (45%)	Median DOR: 15.1 weeks; median TTP: 30.2 weeks	FDA
HDAC	Romidepsin	II [61]	84	relapsed or refractory CTCL stage-IA to IVB and ECOG 0–2	RR 35% and 31% for patients with and without prior chemotherapy	Median DOR 23 months	FDA
HDAC	Romidepsin	pivotal, single-arm, open-label, phase II [62]	96	stage IB-IVA CTCL at least 1 prior systemic therapy	RR 34%, 38% IIB-IV;pruritus relief 43%	Median DOR 15 months	FDA
HDAC	Resminostat	III maintenance randomized vs placebo	190	MF/SS stage IIB to IV in response or SD after a previous therapy.	-	-	Trial Ongoing
HDAC	Quisinostat	II [130]	26	MF stage Ib to IVA with at least one systemic therapy	RR 24%, pruritus relief in responders	DOR in skin ranged from 2.8 to 6.9 months. Median PFS was 5.1 months.	
miR-155	MRG-106, cobomarsen	II randomized versus Vorinostat	126	CTCL and ATLL	-	-	Trial ongoing
PD-1	Nivolumab	I open-label dose-escalation, cohort-expansion basket [104]	13	MF heavily pretreated	15%	DOR up to 81 weeks	-
PD-1	Pembrolizumab	II [105]	24	MF/SS patients (23 of 24 with stage IIB to IV) and heavily pretreated	38	8 durable responses (median DOR not reached > 58 weeks)	-
PD-1	Atezolizumab	II	25	stage IIb-IV MF/SS patients relapsed/refractory	-	-	Trial ongoing

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QUAGLINO P , et al. Journal Investigative Dermatology 2020 in press

Webinars
Cutaneous Lymphoma
EuroBloodNet Topic on Focus

2017

International Journal of Dermatology

Case report

Primary cutaneous aggressive epidermotropic cytotoxic CD8+ T-cell lymphoma: long-term remission after brentuximab vedotin

Benoit M. Cyrenne[1], BS, Antonio Subtil[2], MD, Michael Girardi[1], MD, and Francine Foss[3], MD

JAMA Dermatol. 2016 Dec 1;152(12):1388-1390. doi: 10.1001/jamadermatol.2016.3117.

Cutaneous Gamma-Delta T-Cell Lymphoma Successfully Treated With Brentuximab Vedotin.

Rubio-Gonzalez B[1], Zain J[2], Garcia L[3], Rosen ST[2], Querfeld C[4].

⊕ **Author information**

PMID: 27653662 DOI: 10.1001/jamadermatol.2016.3117

[Indexed for MEDLINE]

What is AFM13?

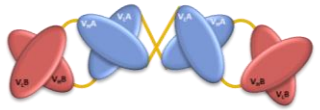
AFM13 is a tetravalent bispecific chimeric (anti-human CD30 x anti-human CD16A) recombinant antibody construct being developed for the indication of Hodgkin lymphoma (HL) and other CD30-positive T-Cell malignancies

NK cells have high number of activating receptors (e.g., CD16A)

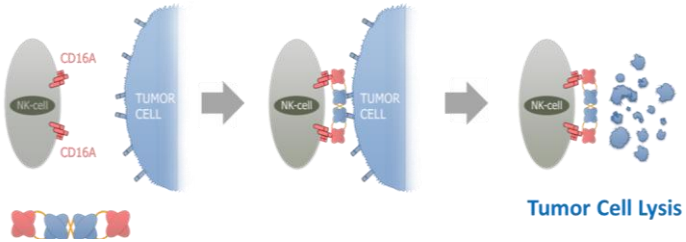
AFM13

- >1000x higher affinity for CD16A than monoclonal antibodies
- Binding largely unaffected by competing IgG
- Overcome CD16A polymorphism (V/F)

AFM13 binds the CD30 target and engages CD16A-positive cells leading to lysis of CD30-positive tumor cells



AFM13 specifically recruits NK-cells, no binding to neutrophils



Background

Title:

A Phase II Open-label Multicenter Study to Assess the Efficacy and Safety of AFM13 in Patients with Relapsed or Refractory CD30-positive Peripheral T-Cell Lymphoma or Transformed Mycosis Fungoides (REDIRECT)

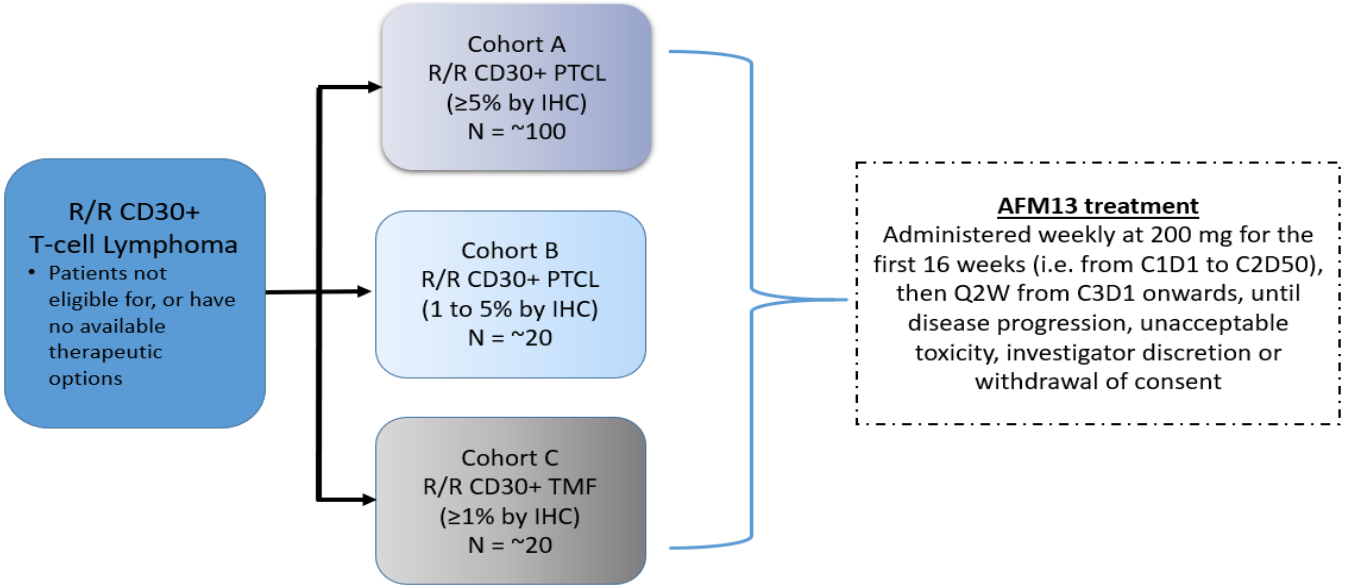
Phase II study. **This feasibility is for the Phase II study**

IMP: **AFM13 bi-specific antibody**

Disease:

Relapsed or Refractory (R/R) CD30-positive PTCL or TMF

AFM13-202 is a Phase 2 study with 3 different cohorts



Please note that at this stage of the study **Cohort C will only be conducted in the US.**
The study consists of a Screening period, Treatment Period, a Final Study Visit, plus Follow-up Assessments.

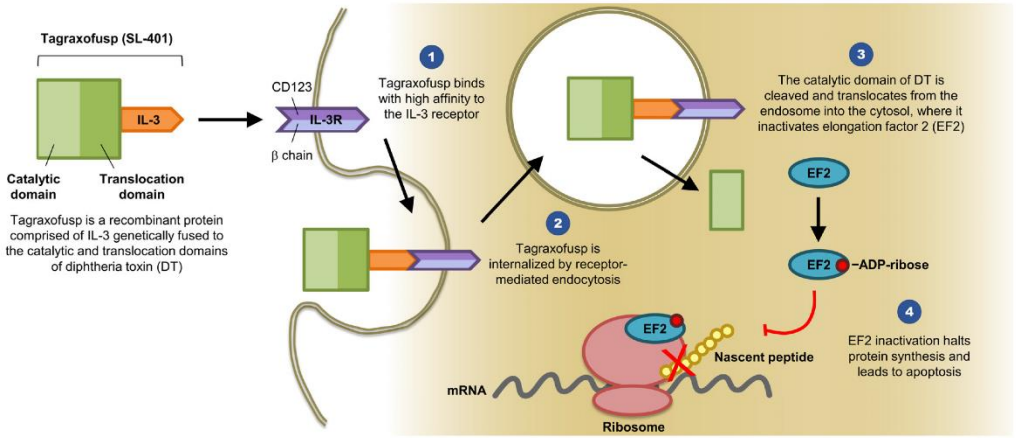
The NEW ENGLAND JOURNAL of MEDICINE

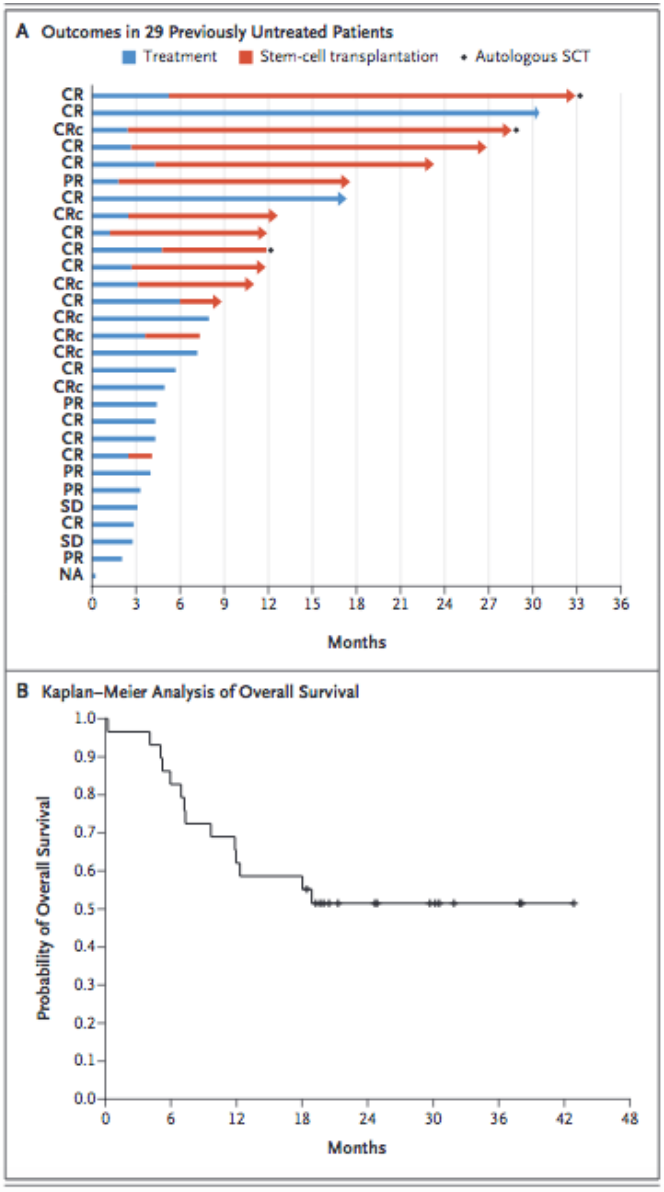
ORIGINAL ARTICLE

Tagraxofusp in Blastic Plasmacytoid Dendritic-Cell Neoplasm

Naveen Pemmaraju, M.D., Andrew A. Lane, M.D., Ph.D., Kendra L. Sweet, M.D., Anthony S. Stein, M.D., Sumithira Vasu, M.D., William Blum, M.D., David A. Rizzieri, M.D., Eunice S. Wang, M.D., Madeleine Duvic, M.D., J. Mark Sloan, M.D., Sharon Spence, M.S., Shay Shemesh, M.S., Christopher L. Brooks, Ph.D., John Balser, Ph.D., Ivan Bergstein, M.D., Jeffrey E. Lancet, M.D., Hagop M. Kantarjian, M.D., and Marina Konopleva, M.D., Ph.D.

ABSTRACT





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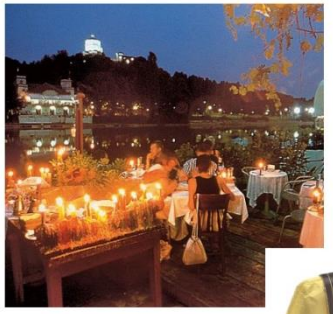
EuroBloodNet Topic on Focus



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