AN IMPORTANT PIECE

WHEN CONSIDERING A TREATMENT FOR ADULT PATIENTS WITH
PTCL AT FIRST RELAPSE

BELEODAQ (belinostat) is an **HDAC inhibitor for adult patients with R/R PTCL**[1] and is a single-agent treatment included in the National Comprehensive Cancer Network® (NCCN®) Guidelines as a Category 2A preferred second-line and subsequent therapy for PTCL-NOS; AITL; EATL; MEITL; nodal PTCL, TFH; and FTCL, **regardless of intention to proceed to transplant.**[2]

See NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for T-Cell Lymphomas, Version 1.2021 for complete recommendations. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Indications and Usage

BELEODAQ® (belinostat) is a histone deacetylase inhibitor indicated for the treatment of adult patients with relapsed or refractory (R/R) peripheral T-cell lymphoma (PTCL). This indication is approved under accelerated approval based on tumor response rate and duration of response. An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.

Select Important Safety Information

Warnings and Precautions

- **Hematologic Toxicity:** BELEODAQ can cause thrombocytopenia, leukopenia (neutropenia and lymphopenia), and/or anemia; monitor blood counts weekly during treatment and modify dosage as necessary.
- **Infections:** Serious and sometimes fatal infections, including pneumonia and sepsis, have occurred with BELEODAQ. Do not administer BELEODAQ to patients with an active infection. Patients with a history of extensive or intensive chemotherapy may be at a higher risk of life-threatening infections.

Please see additional Important Safety Information on pages 1 and 2. Please see accompanying full Prescribing Information or visit www.BELEODAQ.com.

Beleodaq®
(belinostat) for injection
500 mg per vial for intravenous infusion

BELEODAQ Is for Adult Patients With

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- **Infections:** Serious and sometimes fatal infections, including pneumonia and sepsis, have occurred with BELEODAQ. Do not administer BELEODAQ to patients with an active infection. Patients with a history of extensive or intensive chemotherapy may be at a higher risk of life-threatening infections.
- **Hepatotoxicity:** BELEODAQ can cause fatal hepatotoxicity and liver function test abnormalities. Monitor liver function tests before treatment and before the start of each cycle. Interrupt or adjust dosage until recovery, or permanently discontinue BELEODAQ based on the severity of the hepatic toxicity.
- **Tumor Lysis Syndrome:** Tumor lysis syndrome has occurred in BELEODAQ-treated patients in the clinical trial of patients with relapsed or refractory PTCL. Monitor patients with advanced stage disease and/or high tumor burden, and take appropriate precautions.
- **Gastrointestinal Toxicity:** Nausea, vomiting, and diarrhea occur with BELEODAQ and may require the use of antiemetic and antidiarrheal medications.

Please see accompanying full Prescribing Information (PI) or visit www.BELEODAQ.com for full PI.

PTCL at First or Subsequent Relapse[1]

Important Safety Information

Warnings and Precautions

- **Embryo-Fetal Toxicity:** BELEODAQ can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the risk to a fetus. Advise females of reproductive potential to use an effective method of contraception during treatment with BELEODAQ and for 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with BELEODAQ and for 3 months after the last dose.

Adverse Reactions

- The most common adverse reactions observed in more than 25% of patients with relapsed or refractory PTCL in the trial, who were treated with BELEODAQ, were nausea (42%), fatigue (37%), pyrexia (35%), anemia (32%), and vomiting (29%).
- Sixty-one patients (47.3%) experienced serious adverse reactions while taking BELEODAQ or within 30 days after their last dose of BELEODAQ. The most common serious adverse reactions (>2%) were pneumonia, pyrexia, infection, anemia, increased creatinine, thrombocytopenia, and multi-organ failure.

Drug Interactions

- BELEODAQ is primarily metabolized by *UGT1A1*. Avoid concomitant administration of BELEODAQ with strong inhibitors of *UGT1A1*.

Use in Specific Populations

- **Lactation:** Due to the potential for serious adverse reactions in the breastfed child, advise patients that breastfeeding is not recommended during treatment with BELEODAQ and for 2 weeks after the last dose.
- **Pregnancy Testing:** BELEODAQ can cause fetal harm when administered to a pregnant woman. Pregnancy testing is recommended for females of reproductive potential prior to initiating BELEODAQ.
- **Pediatric Use:** The safety and effectiveness of BELEODAQ in pediatric patients have not been established.

The BELIEF Trial Evaluated Overall R and Time to Response With

BELIEF was a single-arm, open-label, nonrandomized, international phase 2 study of 129 adult patients with R/R PTCL[1,3]

- 120 of the 129 had histologically confirmed PTCL and were evaluable for efficacy[1,3]
- The median time from PTCL diagnosis was 12.0 months (range, 2.6-266.4)[3]

SELECT INCLUSION CRITERIA[3]

- Aged ≥18 years
- PTCL by histologic confirmation
- At least 1 prior systemic therapy
- Eastern Cooperative Oncology Group (ECOG) Performance Status score 0-2
- ANC ≥1000/µL
- Platelets ≥50,000/µL

DOSING OF BELEODAQ[3]

- **1000 mg/m² by intravenous (IV) infusion over 30 minutes**, once daily on days 1-5 of a 21-day cycle*
- Two dose reductions for toxicity were permitted in 25% increments, after which BELEODAQ was discontinued

*Cycles were repeated every 3 weeks until disease progression, death, unacceptable toxicity, hematopoietic stem cell transplantation (HSCT), loss to follow-up, or patient or investigator decision

The BELIEF trial excluded patients with precursor and adult T-cell lymphoma (TCL) or leukemia, prolymphocytic leukemia, T-cell large granular lymphocytic leukemia, primary cutaneous anaplastic large cell lymphoma (ALCL), mycosis fungoides, and Sézary syndrome[3]

Please see additional Important Safety Information on pages 1 and 2.
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esponse Rate, Duration of Response, BELEODAQ® (belinostat)[1,3]

STUDY ENDPOINTS

PRIMARY[1,3]	SECONDARY[1,3]
ORR† (overall response rate) (complete response [CR] and partial response [PR])	Duration of response (DoR) and time to response (TTR)

†ORR per the independent review committee (IRC) using the International Working Group (IWG) Criteria.[1,3]

STUDY ASSESSMENTS

- Response was evaluated every 6 weeks for the first 12 months and then every 12 weeks until 2 years from the start of study treatment[1]

- DoR was calculated using 2 methods per IRC based on both the statistical analyses plan (SAP) and IWG beginning when response criteria were first met (CR and PR)[3]
  - The end date chosen for the SAP was the date of either progressive disease (PD) or death
  - The end date per IWG criteria was the first subsequent date that relapse or progression was documented with patients who died, censored at their last tumor assessment

Select Important Safety Information

Warnings and Precautions

- **Hepatotoxicity:** BELEODAQ can cause fatal hepatotoxicity and liver function test abnormalities. Monitor liver function tests before treatment and before the start of each cycle. Interrupt or adjust dosage until recovery, or permanently discontinue BELEODAQ based on the severity of the hepatic toxicity.

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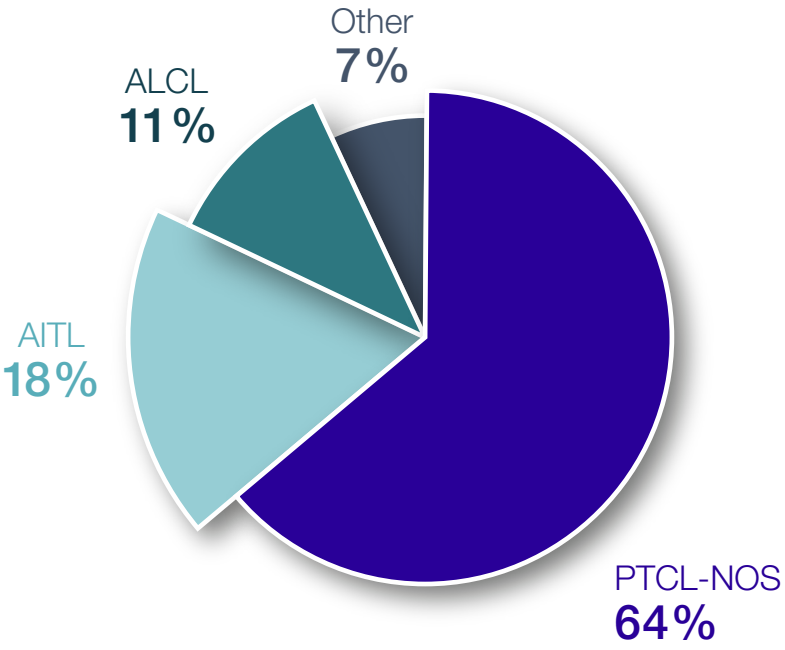
BELEODAQ® (belinostat) was studied across a range of PTCL subtypes[1]

PTCL subtypes studied[1]
(N = 120, based on central diagnosis)



PTCL-NOS, AITL, and ALCL are the 3 most common subtypes of PTCL[2]

Select Important Safety Information

Warnings and Precautions

- **Tumor Lysis Syndrome:** Tumor lysis syndrome has occurred in BELEODAQ-treated patients in the clinical trial of patients with relapsed or refractory PTCL. Monitor patients with advanced stage disease and/or high tumor burden, and take appropriate precautions.
- **Gastrointestinal Toxicity:** Nausea, vomiting, and diarrhea occur with BELEODAQ and may require the use of antiemetic and antidiarrheal medications.

With R/R PTCL Who Were PTCL Patient Population[1,3]

The **median age** was **64 years** (range, 29-81)[1,3]

- 48% of patients (n = 62) **≥65 years**[1]
- 10% of patients (n = 13) **≥75 years**[1]

Patients were treated with BELEODAQ after failing at least 1 prior systemic therapy[1,3]

- Patients received a median of 2 prior treatments (range, 1-8)[1,3]
- Some patients were heavily pretreated with up to 8 prior treatments
- Prior systemic regimens (N = 120) included 97% CHOP or CHOP-like regimens, 68% other multiagent regimens, 25% single-agent regimens, and 3% corticosteroids[3]

21% of patients (n = 25) underwent a hematopoietic stem cell transplant (HSCT) before entering the BELIEF trial[3]

The BELIEF trial included patients with baseline platelet counts between ≥50,000/µL and <100,000/µL[3]

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BELEODAQ® (belinostat) Exce Rate Considered Clinically

Response rate (N = 120)[1,3,†]

25.8% ORR
(95% CI, 18.3-34.6; n = 31)[1,3,§]

10.8% CR
(95% CI, 5.9-17.8; n = 13)[1,3]

15.0% PR
(95% CI, 9.1-22.7; n = 18)[1,3]

An additional 15.0% had stable disease (n = 18)[3]

Efficacy was observed in the 2 most common PTCL subtypes[1,3]

45.5% ORR
(95% CI, 24.4-67.8; n = 10) in **AITL,** the second most frequently occurring subtype of PTCL

23.4% ORR
(95% CI, 14.5-34.4; n = 18) in **PTCL-NOS,** the most frequently occurring subtype of PTCL

*The primary study endpoint of ORR was based on an independent review, where a 20% ORR was considered clinically meaningful.[3]

†Sample size was based on a 2-stage optimal design, with a hypothesized ORR of the alternate hypothesis (p1 = 20%) for BELEODAQ and a minimal or uninteresting ORR of null hypothesis (p0 = 9%).[3]

§No meaningful difference in response rate was observed between patients ≥75 years and those <75 years.[1]

BELEODAQ® (belinostat) is included in the NCCN® Guidelines as a category 2A preferred second-line and subsequent therapy for **PTCL-NOS; AITL; EATL; MEITL; nodal PTCL, TFH; and FTCL,** regardless of intention to proceed to transplant[2]

- **7.5%** of patients proceeded to HSCT after treatment with BELEODAQ[1]

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Durable responses occurred with BELEODAQ

Patients achieved median time to response (TTR) in fewer than 2 treatment cycles (n = 31)[1,3]

- Median TTR was **5.6** weeks[1]
- **61%** achieved a response within **4.3 to 6.4** weeks[3]
- Responses occurred up to **50.4** weeks after the first dose of BELEODAQ[1]

DoR was calculated using 2 methods[1,3]

- Calculations for both methods began when a patient first met response criteria (CR or PR)

DoR as determined by SAP criteria was used by the FDA to evaluate durability and is included in the required labeling

8.4 months[1,3]
(95% CI, 4.5-29.4; n = 31)

SAP criteria
DoR measured from the first date of response to PD or death.[1] DoR definition of SAP differs from the more commonly used IWG definition[3]

DoR as determined by IWG criteria is a post-hoc analysis and is not included in the Prescribing Information

- **IWG criteria:** DoR measured from the first date of response to subsequent date that relapse or progression was documented with patients who died censored at their last tumor assessment[3]
- 13.6 months[3] (95% CI, 4.5-29.4; n = 31)

Responses were observed in patients who achieved a CR[1]

DoR >29 months[3]

For those who achieved a CR (n = 13), median DoR was not only reached but exceeded[3]

Trial Results

Select Important Safety Information

Warnings and Precautions

- **Embryo-Fetal Toxicity:** BELEODAQ can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the risk to a fetus. Advise females of reproductive potential to use an effective method of contraception during treatment with BELEODAQ and for 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with BELEODAQ and for 3 months after the last dose.

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- Most patients (113 of 129) remained on the target dose (1000 mg/m^2)[1,3]
  - Dosage adjustments due to AEs occurred in 16 of 129 patients treated with BELEODAQ
- The relative dose intensity (doses administered vs planned) was 98%[3]
- Treatment duration ranged from 1 to 33 cycles (median, 2 cycles)[1]
- Twenty-five patients (19.4%) discontinued treatment with BELEODAQ due to AEs[1]
  - The AEs reported most frequently as the reason for discontinuation of treatment included anemia, febrile neutropenia, fatigue, and multi-organ failure
- Treatment-emergent AEs (TEAEs) occurred in 97% of patients and were generally mild to moderate in severity[1,3]
  - The most common AEs were nausea, fatigue, pyrexia, anemia, and vomiting
- Grade 3/4 AEs occurring in ≥5% of patients (N = 129) were anemia (11%), thrombocytopenia (7%), dyspnea (6%), and fatigue (5%)[1]
- 47% (n = 61) experienced serious AEs (SAEs)[1,3]
  - No clinically meaningful difference in SAEs was observed in patients based on age (<65 years vs ≥65 years or <75 years vs ≥75 years)

Select Important Administration Information

Drug Interactions

- BELEODAQ is primarily metabolized by *UGT1A1*. Avoid concomitant administration of BELEODAQ with strong inhibitors of *UGT1A1*.

Use in Specific Populations

Lactation: Due to the potential for serious adverse reactions in the breastfed child, advise patients that breastfeeding is not recommended during treatment with BELEODAQ and for 2 weeks after the last dose.

Pregnancy Testing: BELEODAQ can cause fetal harm when administered to a pregnant woman. Pregnancy testing is recommended for females of reproductive potential prior to initiating BELEODAQ.

Pediatric Use: The safety and effectiveness of BELEODAQ in pediatric patients have not been established.

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dence of Adverse Events (AEs)

AEs occurring in ≥10% of patients (N = 129) with R/R PTCL (NCI-CTCAE grades 1 to 4)[1]

AEs	PERCENTAGE OF PATIENTS: ALL GRADES	PERCENTAGE OF PATIENTS: GRADES 3 TO 4
All AEs	97	61
Nausea	42	1
Fatigue	37	5
Pyrexia	35	2
Anemia	32	11
Vomiting	29	1
Constipation	23	1
Diarrhea	23	2
Dyspnea	22	6
Rash	20	1
Peripheral edema	20	0
Cough	19	0
Thrombocytopenia	16	7
Pruritus	16	3
Chills	16	1
Increased blood LDH	16	2
Decreased appetite	15	2
Headache	15	0
Infusion site pain	14	0
Hypokalemia	12	4
Prolonged QT interval	11	4
Abdominal pain	11	1
Hypotension	10	3
Phlebitis	10	1
Dizziness	10	0

NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; LDH, lactate dehydrogenase.

Note: AEs are listed by order of incidence in the all-grades category first, then in the grades 3 to 4 category, as measured by NCI-CTCAE version 3.0.

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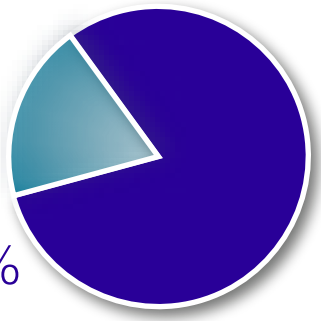
Most patients tolerated the target dose of BELEODAQ®[1,3]

12%

OF PATIENTS

receiving BELEODAQ **required a dosage reduction** due to AEs



88%

OF PATIENTS

receiving BELEODAQ **did not require a dose reduction** due to AEs

In studies, BELEODAQ has not been associated with clinically relevant changes in heart rate or PR- or QRS-interval duration[3]

- Dose reductions due to prolonged QTc or increased transaminases occurred in 2 of 129 patients[3]
- Independent central review of electrocardiogram (ECG) data identified these 2 patients with grade 3 QT prolongation and concluded that BELEODAQ had no effect on cardiac repolarization[3]
- Pharmacokinetic and pharmacodynamic analysis showed no correlation between BELEODAQ concentration and QTc changes from baseline[3]

BELEODAQ is the only agent that the FDA has approved for the treatment of R/R PTCL that was studied in patients (N = 120) with platelet counts down to 50,000/µL[3]

- R/R PTCL patients with **platelet counts <100,000/µL** are typically **ineligible for clinical trials**[4]

Please see additional Important Safety Information on pages 1 and 2. Please see accompanying full Prescribing Information (PI) or visit www.BELEODAQ.com for full PI.

Just a short, 30-minute IV infusion

No recommended pretreatment required[1]

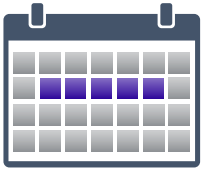
Dosage

The **recommended dosage of BELEODAQ** is 1000 mg/m^2

Infusion Time

Short, **30-minute** infusion

Dosing Schedule



5 days on, **16 days** off*

*Repeat every 21 days until disease progression or unacceptable toxicity.[1]

- Monitor complete blood counts at baseline and weekly[1]
- Perform serum chemistry tests, including renal and hepatic functions, prior to the start of the first dose of each cycle[1]

Use in patients with renal impairment[1]

- BELEODAQ exposure **is not altered in patients** with creatinine clearance (CrCl) >39 mL/min
- There is insufficient data to recommend a dose of BELEODAQ in patients with CrCl ≤39 mL/min

Dose modifications for patients with reduced *UGT1A1* activity are recommended[1]

Dosage modification instructions are available for hematologic toxicities, nonhematologic toxicities, and for patients with reduced *UGT1A1* activity in the full PI[1]

- See accompanying full Prescribing Information or visit **www.BELEODAQ.com** for full PI

Modifying the dosage may allow for the possibility of continued treatment in some patients

Select Important Administration Information

Preparation and Administration Precautions

- As with other potentially cytotoxic anticancer agents, exercise care in the handling and preparation of solutions prepared with BELEODAQ.

Efficacy, as demonstrated in a cohort of patients who received from 1 to 8 prior treatments (median, 2)[1,3]

Clinically meaningful ORR*

25.8%
(95% CI, 18.3-34.6; n = 31)

10.8%
(95% CI, 5.9-17.8; n = 13)

15.0%
(95% CI, 9.1-22.7; n = 18)

An additional 15.0% had stable disease (n = 18)[3]

Response in the **2 most common** PTCL subtypes[1,3]

45.5%
ORR in AITL
(95% CI, 24.4-67.8; n = 10)

23.4%
ORR in PTCL-NOS
(95% CI, 14.5-34.4; n = 18)

A median time to response (TTR) in fewer than 2 treatment cycles (range, 4.3-50.4 weeks) and a median DoR of

8.4 months†
(95% CI, 4.5-29.4; n = 31)

by SAP (secondary endpoint)†
First date of response to progressive disease or death

13.6 months[3] (95% CI, 4.5-29.4; n = 31) by IWG (post-hoc analysis)‡

First date of response to first subsequent date that relapse or PD was documented

>29 months[3]

Sustained responses in **patients who achieved a CR** (n = 13)

*The primary study endpoint of ORR was based on independent review, where a 20% ORR was considered clinically meaningful.[3] †The SAP definition of DoR used by the FDA to evaluate durability, which is included in the required labeling, differs from the more commonly used IWG definition.[3] ‡Patients who died were censored at their last tumor assessment.[3]

Select Important Safety Information

Adverse Reactions

- The most common adverse reactions observed in more than 25% of patients with relapsed or refractory PTCL in the trial, who were treated with BELEODAQ, were nausea (42%), fatigue (37%), pyrexia (35%), anemia (32%), and vomiting (29%).

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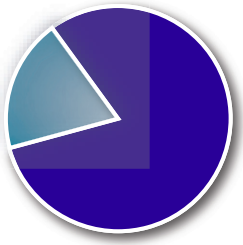
Tolerability for patients with R/R PTCL at first and subsequent relapse[1,3]

12%
DID REQUIRE
dose reductions due to AEs



88%
DID NOT REQUIRE
dose reductions due to AEs

Grade 3 to 4 AEs (N = 129)[1]

- anemia (11%)
- thrombocytopenia (7%)
- dyspnea (6%)
- fatigue (5%)
- hypokalemia (4%)
- prolonged QT (4%)
- hypotension (3%)
- pruritus (3%)
- diarrhea (2%)
- pyrexia (2%)
- increased blood LDH (2%)
- decreased appetite (2%)
- chills (1%)
- abdominal pain (1%)
- phlebitis (1%)
- rash (1%)
- constipation (1%)
- vomiting (1%)
- nausea (1%)

No change in recommended dosage for platelet counts ≥25,000/µL[1]

- Platelet count should be ≥50,000/µL prior to the start of each cycle and prior to resuming treatment following toxicity

BELEODAQ is not associated with clinically relevant changes on heart rate, PR duration, or QRS duration[3]

Select Important Safety Information

Adverse Reactions

- Sixty-one patients (47.3%) experienced serious adverse reactions while taking BELEODAQ or within 30 days after their last dose of BELEODAQ. The most common serious adverse reactions (>2%) were pneumonia, pyrexia, infection, anemia, increased creatinine, thrombocytopenia, and multi-organ failure.

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BELEODAQ® (belinostat) is for adult patients with PTCL at first or subsequent relapse

EFFICACY + TOLERABILITY

Delivered in a short, 30-minute IV infusion[1]

- 5 days on and 16 days off. One cycle of BELEODAQ comprises 5 consecutive, once-daily, 30-minute infusions followed by 16 treatment-free days
- Cycles can be repeated every 21 days until PD or unacceptable toxicity

No recommended pretreatment required[1]

STAR®
Specialty Therapy Access Resources

Specialty Therapy Access Resources® (STAR®) is a reimbursement support, copay assistance, and patient assistance program designed to help patients and healthcare professionals gain appropriate access to BELEODAQ

1-888-53-STAR-7 or 1-888-537-8288
Fax: 1-866-930-1562
AcrotechPatientAccess.com

References

1. BELEODAQ® [Prescribing Information], Acrotech Biopharma, LLC; January 2020. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for T-Cell Lymphomas V.1.2021. © 2021 National Comprehensive Cancer Network, Inc. All rights reserved. Accessed February 25, 2021. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. **3.** O'Connor O, et al. *J Clin Oncol*. 2015;33:2492-2499. **4.** Savage KJ, et al. *Blood*. 2014;124:3075. doi.org/10.1182/blood.V124.21.3075.3075.

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