

AN IMPORTANT PIECE

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

EFFICACY
+
TOLERABILITY

Beleodaq[®]
(belinostat) for injection

BELEODAQ (belinostat) is an **HDAC inhibitor** for adult patients with R/R PTCL¹ 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

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- **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.

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 Response Rate, Duration of Response, and Time to Response with BELEODAQ® (belinostat)^{1,3}

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 CRITERIA³

- 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 BELEODAQ³

- **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 syndrome³

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.

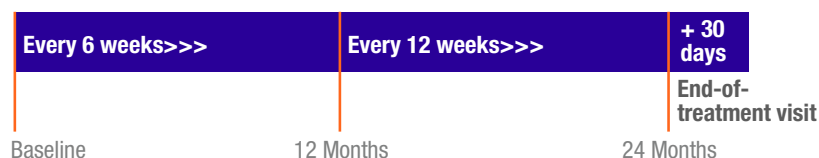
STUDY ENDPOINTS

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 treatment¹



- 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

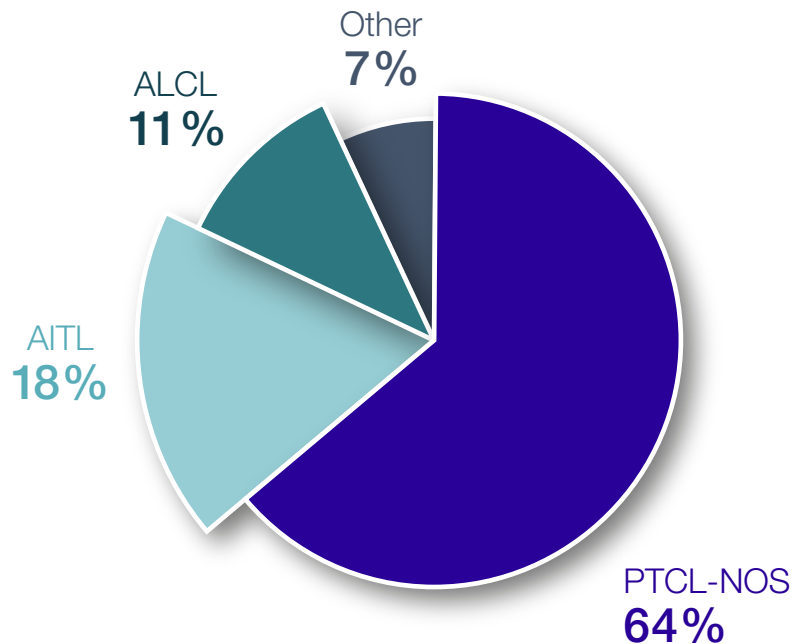
Warnings and Precautions

- **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.

BELIEF Included Patients With R/R PTCL Who Were Representative of a Broad PTCL Patient Population^{1,3}

BELEODAQ® (belinostat) was studied across a range of PTCL subtypes¹

PTCL subtypes studied¹
(N = 120, based on central diagnosis)



PTCL-NOS, AITL, and ALCL are the 3 most common subtypes of PTCL²

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.

The **median age** was **64 years** (range, 29-81)^{1,3}

- 48% of patients (n = 62) **≥65 years¹**
- 10% of patients (n = 13) **≥75 years¹**

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% corticosteroids³

21% of patients (n = 25) underwent a hematopoietic stem cell transplant (HSCT) before entering the BELIEF trial³

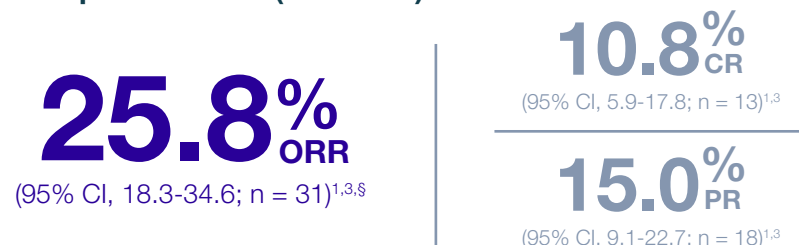
The BELIEF trial included patients with baseline platelet counts between ≥50,000/ μ L and <100,000/ μ L³

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.



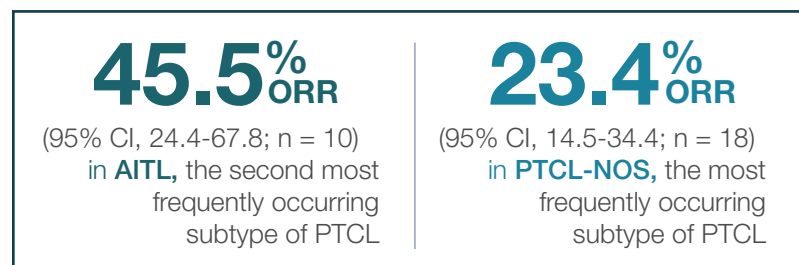
BELEODAQ® (belinostat) Exceeded the Target 20% Response Rate Considered Clinically Meaningful for the Study^{3,*}

Response rate (N = 120)^{1,3,†}



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

Efficacy was observed in the 2 most common PTCL subtypes^{1,3}



*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 transplant²

- **7.5%** of patients proceeded to HSCT after treatment with BELEODAQ¹

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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** weeks¹
- **61%** achieved a response within **4.3 to 6.4** weeks³
- Responses occurred up to **50.4** weeks after the first dose of BELEODAQ¹

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
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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 assessment³
- 13.6 months³ (95% CI, 4.5-29.4; n = 31)

Responses were observed in patients who achieved a CR¹

DoR >29 months³	For those who achieved a CR (n = 13), median DoR was not only reached but exceeded ³
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Warnings and Precautions

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Duration of Exposure and Incidence of Adverse Events (AEs)

- Most patients (113 of 129) remained on the target dose (1000 mg/m²)^{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 AEs¹
 - 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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**AEs occurring in ≥10% of patients
(N = 129) with R/R PTCL (NCI-CTCAE grades 1 to 4)¹**

PERCENTAGE OF PATIENTS

AEs	ALL GRADES	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

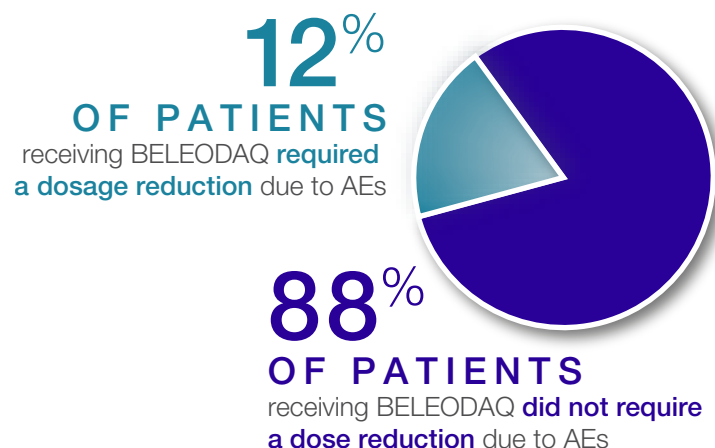
NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; LDH, lactate dehydrogenase.

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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Tolerability Established With the BELIEF Trial^{1,3}

Most patients tolerated the target dose of BELEODAQ^{®1,3}



In studies, BELEODAQ has not been associated with clinically relevant changes in heart rate or PR- or QRS-interval duration³

- Dose reductions due to prolonged QTc or increased transaminases occurred in 2 of 129 patients³
- 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 repolarization³
- Pharmacokinetic and pharmacodynamic analysis showed no correlation between BELEODAQ concentration and QTc changes from baseline³

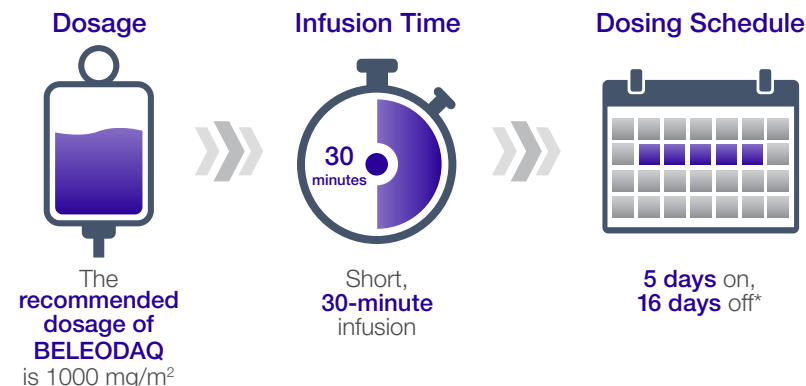
BELEODAQ is the only agent that the FDA has approved for the treatment of R/R PTCL that was studied in patients (N = 120) with platelet counts down to 50,000/ μ L³

- R/R PTCL patients with platelet counts <100,000/ μ L are typically ineligible for clinical trials⁴

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 required¹



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

- Monitor complete blood counts at baseline and weekly¹
- Perform serum chemistry tests, including renal and hepatic functions, prior to the start of the first dose of each cycle¹

Use in patients with renal impairment¹

- 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 \leq 39 mL/min

Dose modifications for patients with reduced UGT1A1 activity are recommended¹

Dosage modification instructions are available for hematologic toxicities, nonhematologic toxicities, and for patients with reduced UGT1A1 activity in the full PI¹

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

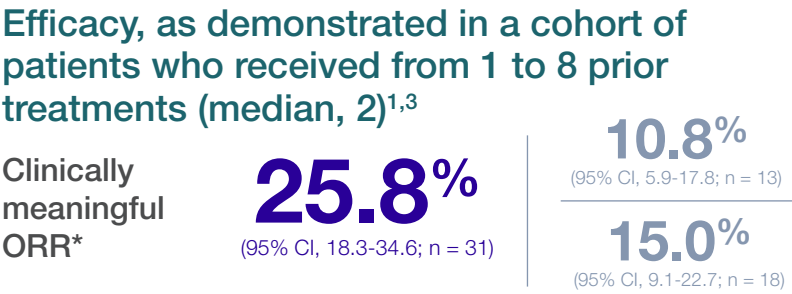
Modifying the dosage may allow for the possibility of continued treatment in some patients

Select Important Administration Information

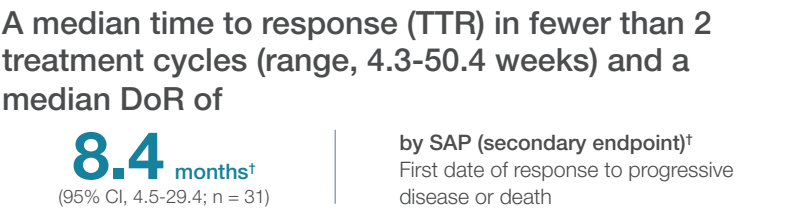
Preparation and Administration Precautions

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

BELEODAQ Provides:

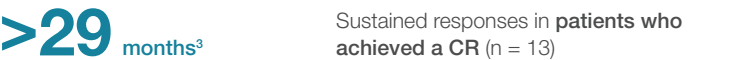


An additional 15.0% had stable disease (n = 18)³



13.6 months³ (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



^{*}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 ³Patients who died were censored at their last tumor assessment.³

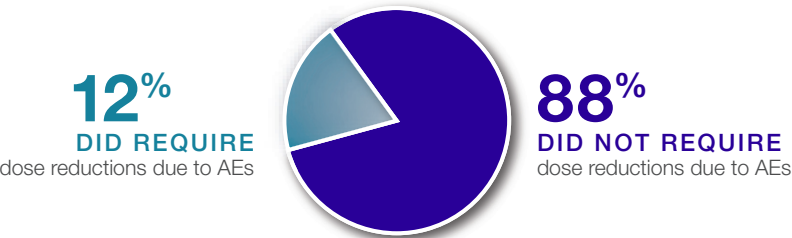
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Adverse Reactions

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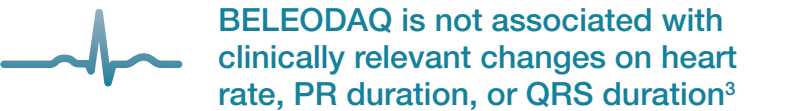
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Tolerability for patients with R/R PTCL at first and subsequent relapse^{1,3}



Grade 3 to 4 AEs (N = 129) ¹	anemia (11%)	pruritus (3%)	phlebitis (1%)
	thrombocytopenia (7%)	diarrhea (2%)	rash (1%)
	dyspnea (6%)	pyrexia (2%)	constipation (1%)
	fatigue (5%)	increased blood LDH (2%)	vomiting (1%)
	hypokalemia (4%)	decreased appetite (2%)	nausea (1%)
	prolonged QT (4%)	chills (1%)	
	hypotension (3%)	abdominal pain (1%)	

- No change in recommended dosage for platelet counts $\geq 25,000/\mu\text{L}$ ¹
- Platelet count should be $\geq 50,000/\mu\text{L}$ prior to the start of each cycle and prior to resuming treatment following toxicity



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.

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

EFFICACY + TOLERABILITY

Delivered in a short, 30-minute IV infusion¹

- 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 required¹



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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BEL-0155

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