

DKd offers a powerful and durable treatment option for your patients with multiple myeloma at first relapse¹

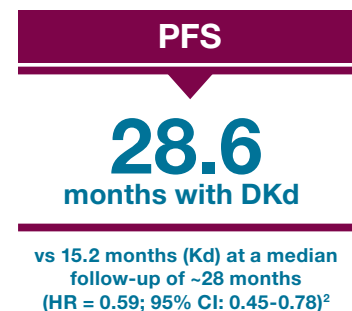
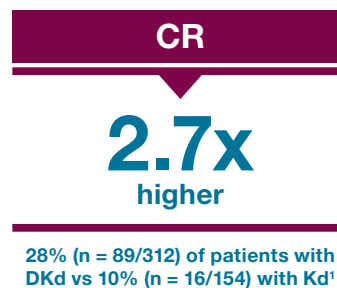
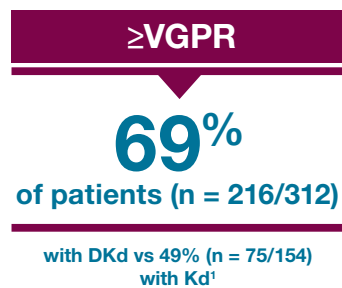
Patients that may benefit from DKd:

- ✓ Refractory to, or progressed on, lenalidomide
- ✓ High- or standard-risk*
- ✓ Need a powerful triplet
- ✓ Want a once-weekly dosing option



Deep and Durable

DKd delivered higher \geq VGPR, CR, ORR, and reduced risk of disease progression or death vs Kd alone^{1,2}



- **PFS:** DKd reduced the risk of disease progression or death by 41% vs Kd²
- **ORR:** Patients in the DKd arm achieved an ORR of 84% vs 75% for the Kd arm ($P = 0.0040$, one-sided)^{1,3,†}



Phase 3 DKd vs Kd Study (CANDOR)^{1,3,4}

Study design (N = 466)

- Randomized 2:1, open-label, multicenter study in patients with RRMM
- KYPROLIS® dosing: DKd 56 mg/m² twice weekly vs Kd 56 mg/m² twice weekly for 28-day cycles until disease progression or unacceptable toxicity
- Eligible patients had 1 to 3 prior lines of therapy[‡]
 - Median prior lines of therapy: 2
 - Median age (min, max): 64 (29-84)
 - ECOG PS scores of 0-2: 99%

Prior therapies (N = 466)[§]

- Bortezomib: 90%
- Lenalidomide: 42%
- Refractory to lenalidomide: 33%

Study endpoints

- Primary: Progression-free survival
- Select secondary: ORR, CR, and safety

*High-risk defined as a patient with cytogenetic abnormalities that are considered high-risk, including t(4; 14), t(14; 16), or del17p. Standard-risk defined as a patient without cytogenetic abnormalities that are considered high risk.³

[†]Overall response rate was defined as proportion of patients with PR or better.³

[‡]Subjects with number of prior regimens > 3 was 0 in the DKd arm and 1 in the Kd arm.¹

[§]Prior treatment subgroups were balanced across treatment arms.³

DKd = KYPROLIS®+Darzalex® (daratumumab) and dexamethasone; \geq VGPR = very good partial response or better; CR = complete response; ORR = overall response rate; Kd = KYPROLIS®+dexamethasone; PFS = progression-free survival; HR = hazard ratio; CI = confidence interval; RRMM = relapsed or refractory multiple myeloma; ECOG PS = Eastern Cooperative Oncology Group Performance Status; PR = partial response.

INDICATION

- KYPROLIS® (carfilzomib) is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone or with daratumumab and dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.

IMPORTANT SAFETY INFORMATION FOR KYPROLIS

Cardiac Toxicities

- New onset or worsening of pre-existing cardiac failure (e.g., congestive heart failure, pulmonary edema, decreased ejection fraction), cardiomyopathy, myocardial ischemia, and myocardial infarction including fatalities have occurred following administration of KYPROLIS. Some events occurred in patients with normal baseline ventricular function. Death due to cardiac arrest has occurred within one day of administration.
- Monitor patients for signs or symptoms of cardiac failure or ischemia. Evaluate promptly if cardiac toxicity is suspected. Withhold KYPROLIS for Grade 3 or 4 cardiac adverse reactions until recovery, and consider whether to restart at 1 dose level reduction based on a benefit/risk assessment.





A once-weekly dosing option for your patients^{1,3,*}

	2nd-generation PI + mAb + dex DKd once weekly
	Infusion time 30 minutes
	KYPROLIS® priming dose 20 mg/m ² on Day 1 of Cycle 1 to evaluate tolerability
	Target KYPROLIS® therapeutic dose 70 mg/m ² starting Day 8 of Cycle 1
Treatment schedule <ul style="list-style-type: none"> • Administer KYPROLIS® 70 mg/m² 1 day each week for 3 weeks • Follow with a 13-day rest period, as part of a 28-day treatment cycle • Continue until disease progression or unacceptable toxicity occurs 	

- DKd also offers a twice-weekly, 56-mg/m² dosing option with a 20-mg/m² priming dose^{1,†}
Refer to Darzalex® (daratumumab) and dexamethasone Prescribing Information for additional dosage information on that product.

Manage hydration throughout treatment¹

Adequate hydration is required prior to dosing in Cycle 1, especially in patients at high risk of tumor lysis syndrome or renal toxicity. Hydration should be monitored throughout treatment and adjusted according to individual patient needs, especially in patients with or at risk for cardiac failure.

Please see the [full Prescribing Information](#) for KYPROLIS® for dosing and administration.



Adverse reactions were consistent with the known safety profiles of each medication

- **Most common adverse reactions (all grades):** Occurring in ≥ 15% of patients in either the DKd or Kd study arm, respectively, were infusion-related reactions^a (41% vs 28%); respiratory tract infection^b (40%^c vs 29%); pneumonia (18%^c vs 12%); bronchitis (17% vs 12%); thrombocytopenia^d (37% vs 30%); anemia^e (33% vs 31%); diarrhea (32% vs 14%), nausea (18% vs 13%); hypertension (31% vs 28%); fatigue^f (32% vs 28%); pyrexia (20% vs 15%); cough^g (21% vs 21%); dyspnea (20% vs 22%); insomnia (18% vs 11%); back pain (16% vs 10%)¹
- **Most frequent serious adverse reactions:** Reported in the DKd and Kd arms, respectively, were pneumonia (14% vs 9%), pyrexia (4.2% vs 2.0%), influenza (3.9% vs 1.3%), sepsis (3.9% vs 1.3%), anemia (2.3% vs 0.7%), diarrhea (1.6% vs 0%), and bronchitis (1.9% vs 0%)¹

*Once-weekly dosing was demonstrated in the EQUULEUS study, a phase 1b, open-label, multicohort study (N = 85) which evaluated the combination of once-weekly KYPROLIS® with IV daratumumab and dexamethasone in patients with relapsed or refractory multiple myeloma who received 1 to 3 prior lines of therapy. KYPROLIS® was administered weekly on Days 1, 8, and 15 of each 28-day cycle at a dose of 70 mg/m² with a priming dose of 20 mg/m² on Day 1 of Cycle 1. Safety and tolerability of DKd were evaluated as primary endpoints. Overall response rate and overall survival were evaluated as secondary endpoints. Results from the EQUULEUS study set a precedent of DKd regimen safety and efficacy for the phase 3 CANDOR study and provided the rationale for the once-weekly dosing of DKd.^{1,5}

[†]Twice-weekly dosing was demonstrated in the phase 3 CANDOR study.^{1,3}

^aThe incidence of infusion related reactions is based on a group of symptoms (including hypertension, pyrexia, rash, myalgia, hypotension, blood pressure increased, urticaria, acute kidney injury, bronchospasm, face edema, hypersensitivity, rash, syncope, wheezing, eye pruritus, eyelid edema, renal failure, swelling face) related to infusion reactions which occurred within 1 day after DKd or Kd administration.

^bRespiratory tract infection includes respiratory tract infection, lower respiratory tract infection, upper respiratory tract infection, and viral upper respiratory tract infection.

^cIncludes fatal adverse reactions.

^dThrombocytopenia includes platelet count decreased and thrombocytopenia.

^eAnemia includes anemia, hematocrit decreased, and hemoglobin decreased.

^fFatigue includes fatigue and asthenia.

^gCough includes productive cough and cough.

DKd = KYPROLIS®+Darzalex® (daratumumab) and dexamethasone; PI = proteasome inhibitor; mAb = monoclonal antibody; dex = dexamethasone;
Kd = KYPROLIS®+dexamethasone; IV = intravenous.

IMPORTANT SAFETY INFORMATION FOR KYPROLIS

Cardiac Toxicities (cont'd)

- While adequate hydration is required prior to each dose in Cycle 1, monitor all patients for evidence of volume overload, especially patients at risk for cardiac failure. Adjust total fluid intake as clinically appropriate.
- For patients ≥ 75 years, the risk of cardiac failure is increased. Patients with New York Heart Association Class III and IV heart failure, recent myocardial infarction, conduction abnormalities, angina, or arrhythmias may be at greater risk for cardiac complications and should have a comprehensive medical assessment prior to starting treatment with KYPROLIS and remain under close follow-up with fluid management.



IMPORTANT SAFETY INFORMATION FOR KYPROLIS (cont'd)

Acute Renal Failure

- Cases of acute renal failure, including some fatal renal failure events, and renal insufficiency (including renal failure) have occurred. Acute renal failure was reported more frequently in patients with advanced relapsed and refractory multiple myeloma who received KYPROLIS monotherapy. Monitor renal function with regular measurement of the serum creatinine and/or estimated creatinine clearance. Reduce or withhold dose as appropriate.

Tumor Lysis Syndrome

- Cases of Tumor Lysis Syndrome (TLS), including fatal outcomes, have occurred. Patients with a high tumor burden should be considered at greater risk for TLS. Adequate hydration is required prior to each dose in Cycle 1, and in subsequent cycles as needed. Consider uric acid lowering drugs in patients at risk for TLS. Monitor for evidence of TLS during treatment and manage promptly, and withhold until resolved.

Pulmonary Toxicity

- Acute Respiratory Distress Syndrome (ARDS), acute respiratory failure, and acute diffuse infiltrative pulmonary disease such as pneumonitis and interstitial lung disease have occurred. Some events have been fatal. In the event of drug-induced pulmonary toxicity, discontinue KYPROLIS.

Pulmonary Hypertension

- Pulmonary arterial hypertension (PAH) was reported. Evaluate with cardiac imaging and/or other tests as indicated. Withhold KYPROLIS for PAH until resolved or returned to baseline and consider whether to restart based on a benefit/risk assessment.

Dyspnea

- Dyspnea was reported in patients treated with KYPROLIS. Evaluate dyspnea to exclude cardiopulmonary conditions including cardiac failure and pulmonary syndromes. Stop KYPROLIS for Grade 3 or 4 dyspnea until resolved or returned to baseline. Consider whether to restart based on a benefit/risk assessment.

Hypertension

- Hypertension, including hypertensive crisis and hypertensive emergency, has been observed, some fatal. Control hypertension prior to starting KYPROLIS. Monitor blood pressure regularly in all patients. If hypertension cannot be adequately controlled, withhold KYPROLIS and evaluate. Consider whether to restart based on a benefit/risk assessment.

Venous Thrombosis

- Venous thromboembolic events (including deep venous thrombosis and pulmonary embolism) have been observed. Provide thromboprophylaxis for patients being treated with the combination of KYPROLIS with dexamethasone or with lenalidomide plus dexamethasone or with daratumumab and dexamethasone. The thromboprophylaxis regimen should be based on an assessment of the patient's underlying risks.
- For patients using hormonal contraception associated with a risk of thrombosis, consider an alternative method of effective contraception during treatment.

Infusion-Related Reactions

- Infusion-related reactions, including life-threatening reactions, have occurred. Signs and symptoms include fever, chills, arthralgia, myalgia, facial flushing, facial edema, laryngeal edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina. These reactions can occur immediately following or up to 24 hours after administration. Premedicate with dexamethasone to reduce the incidence and severity of infusion-related reactions.

Hemorrhage

- Fatal or serious cases of hemorrhage have been reported. Hemorrhagic events have included gastrointestinal, pulmonary, and intracranial hemorrhage and epistaxis. Promptly evaluate signs and symptoms of blood loss. Reduce or withhold dose as appropriate.

Thrombocytopenia

- KYPROLIS causes thrombocytopenia with recovery to baseline platelet count usually by the start of the next cycle. Monitor platelet counts frequently during treatment. Reduce or withhold dose as appropriate.

Hepatic Toxicity and Hepatic Failure

- Cases of hepatic failure, including fatal cases, have occurred. KYPROLIS can cause increased serum transaminases. Monitor liver enzymes regularly regardless of baseline values. Reduce or withhold dose as appropriate.

Thrombotic Microangiopathy

- Cases of thrombotic microangiopathy, including thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), including fatal outcome have occurred. Monitor for signs and symptoms of TTP/HUS. Discontinue if diagnosis is suspected. If the diagnosis of TTP/HUS is excluded, KYPROLIS may be restarted. The safety of reinitiating KYPROLIS is not known.

Posterior Reversible Encephalopathy Syndrome (PRES)

- Cases of PRES have occurred in patients receiving KYPROLIS. If PRES is suspected, discontinue and evaluate with appropriate imaging. The safety of reinitiating KYPROLIS is not known.

Progressive Multifocal Leukoencephalopathy (PML)

- Cases of PML, including fatal cases, have occurred. In addition to KYPROLIS, other contributory factors may include prior or concurrent use of immunosuppressive therapy. Consider PML in any patient with new onset of or changes in pre-existing neurological signs or symptoms. If PML is suspected, discontinue and initiate evaluation for PML including neurology consultation.

Increased Fatal and Serious Toxicities in Combination with Melphalan and Prednisone in Newly Diagnosed Transplant-ineligible Patients

- In a clinical trial of transplant-ineligible patients with newly diagnosed multiple myeloma comparing KYPROLIS, melphalan, and prednisone (KMP) vs bortezomib, melphalan, and prednisone (VMP), a higher incidence of serious and fatal adverse reactions was observed in patients in the KMP arm. KMP is not indicated for transplant-ineligible patients with newly diagnosed multiple myeloma.

Embryo-fetal Toxicity

- KYPROLIS can cause fetal harm when administered to a pregnant woman.
- Advise pregnant women of the potential risk to a fetus. Females of reproductive potential should use effective contraception during treatment with KYPROLIS and for 6 months following the final dose. Males of reproductive potential should use effective contraception during treatment with KYPROLIS and for 3 months following the final dose.

Adverse Reactions

- The most common adverse reactions in the combination therapy trials: anemia, diarrhea, fatigue, hypertension, pyrexia, upper respiratory tract infection, thrombocytopenia, cough, dyspnea, and insomnia.

Please see additional Important Safety Information on pages 1 and 2 or in the accompanying [full Prescribing Information](#).

Get more information about DKd at
www.kyprolis-hcp.com

References: 1. KYPROLIS® (carfilzomib) prescribing information, Onyx Pharmaceuticals Inc., an Amgen, Inc. subsidiary. 2. Dimopoulos M, Quach H, Mateos MV, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone in relapsed or refractory multiple myeloma: updated efficacy and safety results of the Phase 3 CANDOR study. Poster presented at: 62nd ASH Annual Meeting & Exposition; December 5-8, 2020 [virtual conference]. 3. Dimopoulos M, Quach H, Mateos MV, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): results from a randomised, multicentre, open-label, phase 3 study. *Lancet*. 2020;396:186-197. 4. Dimopoulos M, Quach H, Mateos MV, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): results from a randomised, multicentre, open-label, phase 3 study [supplementary appendix]. *Lancet*. 2020;396:186-197. 5. Chari A, Martinez-Lopez J, Mateos M, et al. Daratumumab plus carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma. *Blood*. 2019;134:421-431.

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