

Meet Alice,* a 77-year-old with multiple myeloma showing signs of symptomatic progression on frontline DRd

Kyprolis®
(carfilzomib) for injection

Alice presents with worsening back pain, fatigue, and weakness. She has a history of type 2 diabetes and COPD limiting her physical activity.



*Hypothetical patient profile.

Presentation at diagnosis

- Transplant-ineligible
- Standard-risk cytogenetics^{1,†}
- ECOG PS: 2
- Assessed as frail

Treatment history



[†]Standard-risk is defined as having any cytogenetics other than the abnormalities t(4;14), t(14;16), t(14;20), or del(17p).

Select treatment considerations at first relapse[‡]



Refractory to IMiD



Refractory to anti-CD38 mAb



Peripheral neuropathy



Standard-risk cytogenetics



ECOG PS: 2

[‡]There are many patient and disease related factors that can affect treatment choice, not limited to the above select considerations^{2,3}

COPD = chronic obstructive pulmonary disease; DRd = daratumumab + lenalidomide + dexamethasone; ECOG PS = Eastern Cooperative Oncology Group performance status; IMiD = immunomodulatory imide drugs; mAb = monoclonal antibody.

References: **1.** Sonneveld P, Avet-Loiseau H, Lonial S, et al. Treatment of multiple myeloma with high-risk cytogenetics: a consensus of the International Myeloma Working Group. *Blood*. 2016;127(24):2955-2962. **2.** Moreau P, Kumar SK, San Miguel J, et al. Treatment of relapsed and refractory multiple myeloma: recommendations from the International Myeloma Working Group. *Lancet Oncol*. 2021;22: e105-e118. **3.** Kumar S, Baizer L, Callander N, et al. Gaps and opportunities in the treatment of relapsed-refractory multiple myeloma: Consensus recommendations of the NCI Multiple Myeloma Steering Committee. *Blood Cancer J*. 2022;12(6):98.

INDICATIONS

- KYPROLIS® (carfilzomib) is indicated in combination with dexamethasone, or with lenalidomide plus dexamethasone, or with daratumumab plus dexamethasone, or with daratumumab plus hyaluronidase-fihj plus dexamethasone, or with isatuximab plus dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
- KYPROLIS® is indicated as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more 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.

[CLICK HERE FOR ADDITIONAL IMPORTANT SAFETY INFORMATION >](#)

For a frail patient like Alice, discover the progression-free potential of a doublet at first relapse



ENDEAVOR demonstrated the efficacy and safety of KYPROLIS® + dexamethasone (Kd) in RRRM^{1,2}

Phase 3, randomized, open-label, multicenter superiority study that compared Kd to Vd in adult patients with relapsed or refractory multiple myeloma who had received 1 to 3 prior lines of therapy. A total of 929 patients were randomized 1:1 to receive Kd (n = 464) or Vd (n = 465). Patients received KYPROLIS® at a starting dose of 20 mg/m² that was increased to 56 mg/m² on cycle 1, day 8 onward for 28-day cycles until disease progression or unacceptable toxicity. The primary endpoint was PFS. Select secondary endpoints included OS, ORR, DOR, and safety.

Primary Endpoint: Median PFS in the ITT Population
18.7 months in the Kd group vs 9.4 months in the Vd group
(HR = 0.53; 95% CI: 0.44-0.65; P < 0.0001, one-sided)

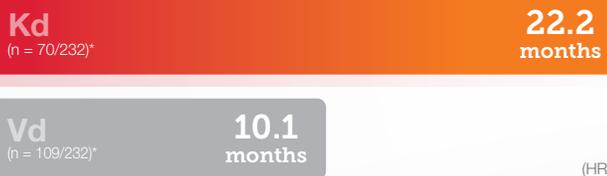
Exploratory subgroup analysis for specific patient populations

Patients experienced

5x LESS PN

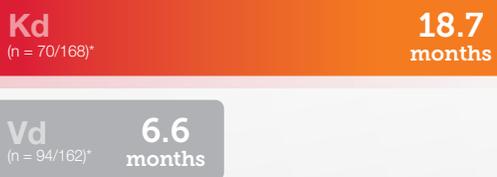
(Grade ≥ 2) with Kd with KYPROLIS® 56 mg/m² vs Vd; 7% with Kd (n = 463; 95% CI: 5-9) vs 35% with Vd (n = 456; 95% CI: 31-39)²

Median PFS at first relapse³



(HR = 0.45; 95% CI: 0.33-0.61)
*Number of events / patients

Median PFS in frail patients^{4,†}



(HR = 0.50; 95% CI: 0.36-0.68)
*Number of events / patients

Study was not powered for PFS efficacy in either subgroup, and estimation of PFS was not a study objective.

[†]Patients who scored ≥2 by proxy algorithm were categorized as frail-subgroup patients. Frail-subgroup patients represented 36% (168/464) and 35% (162/465) of patients in the Kd and Vd arms, respectively.

Adverse events were consistent with known safety profiles of each medication. Common adverse events seen (≥ 20% incidence);

Occurring in the Kd vs Vd arms, respectively were, anemia (39% vs 27%); diarrhea (30% vs 38%); fatigue (29% vs 28%); dyspnea (28% vs 13%); pyrexia (28% vs 14%); insomnia (26% vs 26%); cough (25% vs 14%); hypertension (25% vs 9%); peripheral edema (22% vs 17%); asthenia (20% vs 16%); and upper respiratory tract infection (20% vs 15%).

Adverse reactions of interest in the Kd vs Vd arms, respectively: Peripheral neuropathy (19% vs 52%); acute renal failure (8% vs 5%); cardiac failure (8% vs 3%); pneumonia (9% vs 11%); ischemic heart disease (3% vs 2%); and pulmonary hypertension (1% vs 1%).

ECOG PS = Eastern Cooperative Oncology Group performance status; CI = confidence interval; HR = hazard ratio; DOR = duration of response; Kd = carfilzomib + dexamethasone; mg/m² = milligrams per meter squared; ORR = overall response rate; OS = overall survival; PFS = progression-free survival; PN = peripheral neuropathy; RRRM = relapsed refractory multiple myeloma; Vd = bortezomib + dexamethasone.

[VIEW Kd PIVOTAL DATA >](#)

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.

[CLICK HERE FOR ADDITIONAL IMPORTANT SAFETY INFORMATION >](#)

References: 1. Dimopoulos MA, Moreau P, Palumbo A, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. *Lancet Oncol.* 2016;17:27-38. 2. KYPROLIS® (carfilzomib) prescribing information, Onyx Pharmaceuticals Inc., an Amgen Inc. subsidiary. 3. Moreau P, Joshua D, Chng WJ, et al. Impact of prior treatment on patients with relapsed multiple myeloma treated with carfilzomib and dexamethasone vs bortezomib and dexamethasone in the phase 3 ENDEAVOR study. *Leukemia.* 2017;31:115-122. 4. Facon T, Niesvizky R, Mateos MV, et al. Efficacy and safety of carfilzomib-based regimens in frail patients with relapsed and/or refractory multiple myeloma. *Blood Adv.* 2020;4:5449-5459.

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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.
- 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.

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 occurring in at least 20% of patients taking KYPROLIS® in the combination therapy trials: anemia, diarrhea, hypertension, fatigue, upper respiratory tract infection, thrombocytopenia, pyrexia, cough, dyspnea, and insomnia.
- The most common adverse reactions occurring in at least 20% of patients taking KYPROLIS® in monotherapy trials: anemia, fatigue, thrombocytopenia, nausea, pyrexia, dyspnea, diarrhea, headache, cough, edema peripheral.

Please see full Prescribing Information [here](#).