Meet Diane,* a 60-year-old with multiple myeloma experiencing relapse following frontline ASCT

Kyprolis® (carfilzomib) for injection

18 months after undergoing ASCT, Diane remains on lenalidomide maintenance. She is usually active; however, she is now presenting with worsening fatigue and back pain.

*Hypothetical patient profile.

Presentation at diagnosis

- R-ISS stage I IgG-ƛ myeloma
- Standard-risk cytogenetics[1,†]
- ECOG PS: 0

Treatment history

Frontline		Maintenance	First relapse
Induction VRd x 4 cycles	ASCT	Lenalidomide 18 months	

†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‡

- ☑ Symptomatic relapse
- ☑ Prior lenalidomide exposure
- ☑ ECOG PS: 0

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

ASCT = autologous stem cell transplant; R-ISS = Revised International Staging System; IgG-ƛ = immunoglobulin G-lambda; ECOG PS = Eastern Cooperative Oncology Group performance status; VRd = bortezomib + lenalidomide + dexamethasone.

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®

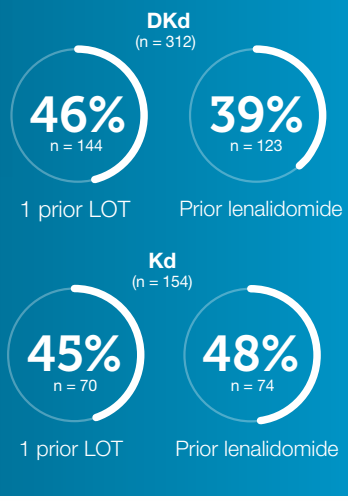
CARDIAC TOXICITIES

- 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 standard-risk patient like Diane, consider a triplet with proven power at first relapse

Select baseline characteristics[2]
CANDOR trial participants

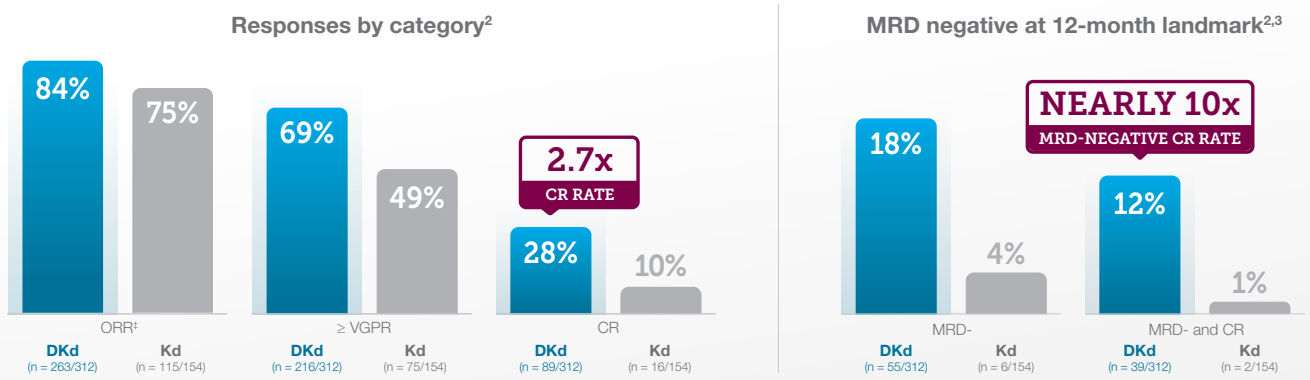


CANDOR evaluated the efficacy and safety of KYPROLIS® + daratumumab + dexamethasone in RRMM

DKd vs Kd study design (CANDOR): Phase 3, randomized, open-label, multicenter trial that compared DKd to Kd in patients with relapsed or refractory multiple myeloma who had received 1 to 3 prior lines of therapy. 466 patients were randomized 2:1 to receive DKd (n = 312) or Kd (n = 154) with KYPROLIS® 56 mg/m² twice weekly for 28-day cycles until disease progression or unacceptable toxicity. The primary endpoint was PFS. Select secondary endpoints included ORR, MRD negativity (MRD-), CR rate at 12 months, and safety.[1,2]

Primary Endpoint: In the ITT population, mPFS was 28.6 months in the DKd group vs 15.2 months in the Kd group[1,*]

DKd delivered deep responses with high MRD negativity rates[†]



*Primary results were reported after a median follow-up of ~17 months. Median PFS was not reached for DKd vs 15.8 months for Kd (HR=0.63; 95% CI: 0.46-0.85; *P*=0.0014, one-sided)

†MRD-negative CR (at the 10^{-5} level) is defined as achievement of CR per the IMWG-URC and MRD-negative status as assessed by the next generation sequencing assay (ClonoSEQ) at the 12-month landmark (from 8 months to 13 months window).

‡ORR was defined as proportion of patients with PR or better.

§Based on sensitivity limits of detecting < 1 in 10^4 to 10^6 cells for MRD-negative CR vs < 5% for CR.

CR = complete response; DKd = carfilzomib + daratumumab + dexamethasone; IMWG-URC = International Myeloma Working Group-Uniform Response Criteria; ITT = intention-to-treat; Kd = carfilzomib + dexamethasone; LOT = line of therapy; mg/m² = milligrams per meter squared; mPFS = median progression free survival; MRD = minimal residual disease; ORR = overall response rate; PFS = progression-free survival; RRMM = relapsed/refractory multiple myeloma; VGPR = very good partial response.

VIEW DKd 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 >

Exploratory analysis for specific patient populations

PFS favorability was consistent across clinically relevant subgroups[2]

Previous lenalidomide exposure

DKd (57/123)* **25.9 months**

Kd (47/74)* **11.1 months**

(HR = 0.49; 95% CI: 0.33-0.74)
*Number of events / patients

Lenalidomide-refractory patients

DKd (46/99)* **28.1 months**

Kd (35/55)* **11.1 months**

(HR = 0.46; 95% CI: 0.28-0.73)
*Number of events / patients

Post hoc analysis: These results represent pre-specified subgroup analyses of the CANDOR study; however, these analyses were not study objectives and the study was therefore not powered or adjusted for multiplicity to assess efficacy in these subgroups.

Most common adverse events in CANDOR (all grades): Occurring in ≥ 15% of patients in either the DKd or Kd study arm, respectively, were infusion-related reactions (41% vs 28%); respiratory tract infection (40% vs 29%); pneumonia (18% vs 12%); bronchitis (17% vs 12%); thrombocytopenia (37% vs 30%); anemia (33% vs 31%); diarrhea (32% vs 14%); nausea (18% vs 13%); hypertension (31% vs 28%); fatigue (32% vs 28%); pyrexia (20% vs 15%); cough (21% vs 21%); dyspnea (20% vs 22%); insomnia (18% vs 11%); and back pain (16% vs 10%).

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%); bronchitis (1.9% vs 0%); and diarrhea (1.6% vs 0%).

CI = confidence interval; HR = hazard ratio.

VIEW DKd PIVOTAL DATA >

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®.

CLICK HERE FOR ADDITIONAL IMPORTANT SAFETY INFORMATION >

References: 1. Usmani S, Quach H, Mateos MV, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): updated outcomes from a randomised, multicentre, open-label, phase 3 study. *Lancet Oncol*. 2022;23:65-76. **2.** KYPROLIS® (carfilzomib) prescribing information, Onyx Pharmaceuticals Inc., an Amgen Inc. subsidiary. **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.

AMGEN Oncology

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- 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.

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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 contributary 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.