Meet Allen,* a 64-year-old with multiple myeloma experiencing his first relapse four years after ASCT

Kyprolis® (carfilzomib) for injection

After frontline triplet therapy followed by ASCT and 24 months of lenalidomide, Allen remained in CR during maintenance. He presents with mild back pain and evidence of increased plasma cells in his bone marrow while maintaining a good performance status.

*Hypothetical patient profile.

Presentation at diagnosis

- Standard-risk cytogenetics[1,†]
- ECOG PS: 1

Treatment history

Frontline		Maintenance	No treatment	
Induction VRd x 4 cycles	ASCT	Lenalidomide 2 years	1 year	**First relapse**

†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‡

- ☑ Lenalidomide sensitive
- ☑ ECOG PS: 1

‡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; CR = complete response; 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 ›

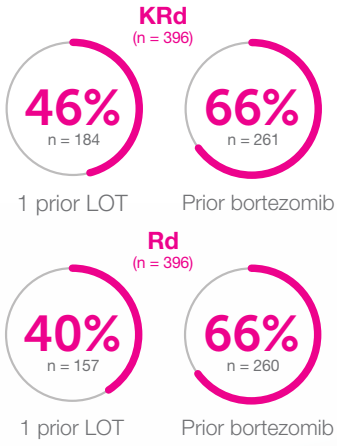
For first relapse in a fit, lenalidomide-sensitive patient like Allen, consider the proven power of KYPROLIS® in combination with Rd

ASPIRE demonstrated the efficacy and safety of KYPROLIS® + Rd in RRMM[1]

KRd vs Rd study design (ASPIRE): Randomized, open-label, multicenter, phase 3 study in relapsed or refractory multiple myeloma patients who had received 1 to 3 prior lines of therapy. Seven hundred ninety-two patients were randomized 1:1 to receive KRd (n = 396) or Rd (n = 396). Per protocol, patients received up to 18 cycles of KYPROLIS® 27 mg/m^2 twice-weekly with Rd, unless discontinued for toxicity or disease progression, and then continued treatment with Rd alone to progression or unacceptable toxicity. The primary endpoint was PFS. Select secondary endpoints included OS and ORR.[1]

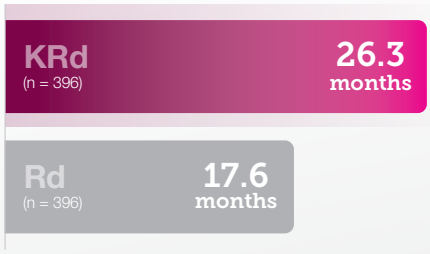
Select baseline characteristics

ASPIRE trial participants



Adding KYPROLIS® to Rd significantly prolonged PFS and OS[3]

PFS in the ITT population



(HR = 0.69; 95% CI: 0.57-0.83, *P* = 0.0001, two-sided)

+7.9 MONTH IMPROVEMENT in median overall survival[3]

48.3 months with KRd (n = 396) vs 40.4 months with Rd (n = 396)

(HR = 0.79; 95% CI: 0.67-0.95; *P* = 0.0091, two-sided)[3]

POST HOC ANALYSIS: KRd improved mPFS at first relapse by **12 MONTHS** vs Rd alone. 29.6 months KRd (n = 184) vs 17.6 months Rd (n = 157)[2]
(HR = 0.71; 95% CI: 0.53-0.96)

POST HOC ANALYSIS: Demonstration of PFS efficacy by prior lines of therapy was not a study objective. The study was not powered to evaluate PFS efficacy within this subgroup. KYPROLIS® was discontinued after Cycle 18 per protocol.

Most common adverse reactions (≥ 20%) in KRd vs Rd arms, respectively: anemia (43% vs 41%); neutropenia (40% vs 35%); thrombocytopenia (29% vs 24%); diarrhea (44% vs 37%); fatigue (33% vs 32%); cough (30% vs 18%); pyrexia (30% vs 22%); upper respiratory tract infection (30% vs 21%); hypokalemia (30% vs 15%); muscle spasms (27% vs 21%); pneumonia (23% vs 17%); viral upper respiratory tract infection (20% vs 18%); nausea (21% vs 14%); bronchitis (20% vs 15%); constipation (21% vs 18%); insomnia (21% vs 17%); back pain (19% vs 21%).

Grade ≥ 3 AEs of interest (grouped terms; KRd vs Rd): acute renal failure (3.8% vs 3.3%), cardiac failure (4.3% vs 2.1%), ischemic heart disease (3.8% vs 2.3%), hypertension (6.4% vs 2.3%), hematopoietic thrombocytopenia (20.2% vs 14.9%) and peripheral neuropathy (2.8 vs 3.1).[4]

CI = confidence interval; HR = hazard ratio; ITT = intention-to-treat; KRd = carfilzomib + lenalidomide + dexamethasone; LOT = line of therapy; ORR = overall response rate; OS = overall survival; PFS = progression-free survival; Rd = lenalidomide + dexamethasone; RRMM = relapsed refractory multiple myeloma.

VIEW KRd 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.

CLICK HERE FOR ADDITIONAL IMPORTANT SAFETY INFORMATION >

References: 1. Stewart AK, Rajkumar SV, Dimopoulos MA, et al. Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. *N Engl J Med*. 2015;372:142-152. **2.** Dimopoulos MA, Stewart AK, Masszi T, et al. Carfilzomib-lenalidomide-dexamethasone vs lenalidomide-dexamethasone in relapsed multiple myeloma by previous treatment. *Blood Cancer J*. 2017;7:e554. **3.** KYPROLIS® (carfilzomib) prescribing information, Onyx Pharmaceuticals Inc., an Amgen Inc. subsidiary. **4.** Siegel DS, Dimopoulos MA, Ludwig H, et al. Improvement in overall survival with carfilzomib, lenalidomide, and dexamethasone in patients with relapsed or refractory multiple myeloma. *J Clin Oncol*. 2018;36(8):728-734.

AMGEN Oncology

INDICATIONS

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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 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.