Pomalyst®
(pomalidomide) capsules
1 · 2 · 3 · 4 mg

POMALYST® (pomalidomide) Patient Case Study: Mary

A hypothetical patient receiving a triplet regimen with POMALYST and presenting with Grade 4 thrombocytopenia*

POMALYST Indication
POMALYST® (pomalidomide) is a thalidomide analogue indicated, in combination with dexamethasone, for adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy.

POMALYST + dexamethasone + daratumumab Indication
POMALYST + dexamethasone + daratumumab is indicated for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

SELECTED IMPORTANT SAFETY INFORMATION
POMALYST has Boxed WARNINGS for EMBRYO-FETAL TOXICITY, and VENOUS and ARTERIAL THROMBOEMBOLISM. POMALYST is only available through the POMALYST REMS® program.
More information on the REMS program is available at www.CelgeneRiskManagement.com or by calling 1-888-423-5436.

*This is a hypothetical case study. Each patient is different, and healthcare providers should determine what treatment regimen is right for each patient.

Information about POMALYST + dexamethasone + daratumumab does not appear in the POMALYST Prescribing Information (PI). Please see the daratumumab full PI for a complete discussion of Important Safety Information at www.darzalexhcp.com/iv.

This AE is not the only one you can expect for your patients.
Please see the full Prescribing Information for more details.

Please see Important Safety Information throughout and on pages 6-9, and see full Prescribing Information for POMALYST and REVLIMID, including Boxed WARNINGS.

POMALYST SELECTED IMPORTANT SAFETY INFORMATION

WARNING: EMBRYO-FETAL TOXICITY and VENOUS AND ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

- **POMALYST is contraindicated in pregnancy. POMALYST is a thalidomide analogue. Thalidomide is a known human teratogen that causes severe birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting POMALYST treatment.**
- **Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after stopping POMALYST treatment.**

POMALYST is only available through a restricted distribution program called POMALYST REMS®.

Venous and Arterial Thromboembolism

- **Deep venous thrombosis (DVT), pulmonary embolism (PE), myocardial infarction, and stroke occur in patients with multiple myeloma treated with POMALYST. Prophylactic antithrombotic measures were employed in clinical trials. Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.**

CONTRAINDICATIONS FOR DARATUMUMAB

Daratumumab is contraindicated in patients with a history of severe hypersensitivity (e.g., anaphylactic reactions) to daratumumab or any of the components of the formulation.

Daratumumab is associated with the following Warnings and Precautions: Infusion-Related Reactions, Interference With Cross-Matching and Red Blood Cell Antibody Screening, Neutropenia, Thrombocytopenia, Interference With Determination of Complete Response, and Embryo-Fetal Toxicity.

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Mary, 59

A hypothetical patient receiving a triplet regimen with POMALYST® (pomalidomide) and presenting with Grade 4 thrombocytopenia

PATIENT HISTORY

- Diagnosed with IgG k MM ISS Stage II
- **Presentation at diagnosis:** increased back pain with M spike of 4 g/dL
- **SLiM-CRAB criteria features:**
  - 70% BMPCs
  - High k/l-light chain ratio (122)
  - Lumbar spine MRI showing several lytic lesions
  - Mild anemia (Hb, 10.9 g/dL)
- **Platelets:** 80,000 per mcL (normal)
- **Comorbidities:** none
- **Cytogenetics:** del(17)p
- **Prior therapies:** REVLIMID® (lenalidomide), proteasome inhibitor (PI), auto-HSCT, and maintenance

auto-HSCT, autologous hematopoietic stem cell transplantation; BMPC, bone marrow plasma cell; Hb, hemoglobin; IgG, immunoglobulin G; ISS, International Staging System; M spike, monoclonal protein spike; MRI, magnetic resonance imaging; PI, proteasome inhibitor.

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Mary, 59

A hypothetical patient receiving a triplet regimen with POMALYST® (pomalidomide) and presenting with Grade 4 thrombocytopenia

PROGRESSED AFTER REVLIMID® (lenalidomide) and a PI

- **M protein**: spike from 0.7 g/dL to 1.3 g/dL in 1 year
- **FLC**: increased by >20 mg/dL
- **Bone lesions**: leg pain; repeat bone imaging showed new lesions
- **Anemia**: Hb level decreased to 8.9 mg/dL

TREATED WITH POMALYST + DEX + DARA

Treatment Plan

POMALYST: 4 mg* + **dara:** 16 mg/kg† + **dex:** 40 mg‡

MONITOR CBC WEEKLY FOR THE FIRST 8 WEEKS AND MONTHLY THEREAFTER.

At 2 months, Grade 4 thrombocytopenia occurred. Platelets decreased to 23,500 per mcL.

What action can be taken to help Mary stay on treatment after her platelets decreased below 25,000 per mcL?

*POMALYST 4 mg orally once daily on Days 1-21 of each 28-day cycle.
†Dara 16 mg/kg IV weekly (Weeks 1-8). Monitor CBCs periodically during treatment according to manufacturer's Prescribing Information (PI) for background therapies. Consider withholding dara until recovery of platelets. **Please see additional dosing and dose modification information in the full daratumumab PI.**
‡Dex 40 mg IV or oral weekly. On dara infusion days, 20 mg of the dex dose was given as a pre-infusion medication between 1 and 3 hours before dara and the remainder given the day after the infusion.

CBC, complete blood count; dara, daratumumab; dex, dexamethasone; FLC, free light chain; Hb, hemoglobin; M protein, monoclonal protein; PI, proteasome inhibitor.

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Mary, 59

A hypothetical patient receiving a triplet regimen with POMALYST® (pomalidomide) and presenting with Grade 4 thrombocytopenia

PATIENT TAKING POMALYST + DEX + DARA

Previously treated with REVLIMID® (lenalidomide) and a PI

Patient received POMALYST + dex + dara for 2 months when Grade 4 thrombocytopenia occurred.

POMALYST was withheld and CBC monitored weekly for 2 weeks.

Treatment restarted when platelets returned to 52,000 per mcL.

POMALYST: 3 mg* + **dara:** 16 mg/kg† + **dex:** 40 mg‡

POMALYST REDUCED FROM 4 MG TO 3 MG UPON RESUMING TREATMENT.

Treatment continued

For more information on dose modifications, visit pomalysthcp.com/nurses/dosing.

*POMALYST 3 mg orally once daily on Days 1-21 of each 28-day cycle.
†Dara 16 mg/kg IV weekly (Weeks 1-8). Monitor CBCs periodically during treatment according to manufacturer's Prescribing Information (PI) for background therapies. Consider withholding dara until recovery of platelets. **Please see additional dosing and dose modification information in the full daratumumab PI.**
‡Dex 40 mg IV or oral weekly. On dara infusion days, 20 mg of the dex dose was given as a pre-infusion medication between 1 and 3 hours before dara and the remainder given the day after the infusion.

CBC, complete blood count; dara, daratumumab; dex, dexamethasone; PI, proteasome inhibitor.

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Indications and Important Safety Information

POMALYST Indication

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POMALYST + dexamethasone + daratumumab Indication

POMALYST + dexamethasone + daratumumab is indicated for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

Information about POMALYST + dexamethasone + daratumumab does not appear in the POMALYST Prescribing Information (PI). Please see the daratumumab full PI for a complete discussion of Important Safety Information at www.darzalexhcp.com/iv.

Important Safety Information

POMALYST Boxed WARNINGS

WARNING: EMBRYO-FETAL TOXICITY and VENOUS AND ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

- **POMALYST is contraindicated in pregnancy. POMALYST is a thalidomide analogue. Thalidomide is a known human teratogen that causes severe birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting POMALYST treatment.**
- **Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after stopping POMALYST treatment.**

POMALYST is only available through a restricted distribution program called POMALYST REMS®.

Venous and Arterial Thromboembolism

- **Deep venous thrombosis (DVT), pulmonary embolism (PE), myocardial infarction, and stroke occur in patients with multiple myeloma treated with POMALYST. Prophylactic antithrombotic measures were employed in clinical trials. Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.**

CONTRAINDICATIONS FOR POMALYST

- **Pregnancy:** POMALYST can cause fetal harm and is contraindicated in females who are pregnant. If the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to a fetus.
- **Hypersensitivity:** POMALYST is contraindicated in patients who have demonstrated severe hypersensitivity (e.g., angioedema, anaphylaxis) to pomalidomide or any of the excipients.

CONTRAINDICATIONS FOR DARATUMUMAB

- Daratumumab is contraindicated in patients with a history of severe hypersensitivity (e.g., anaphylactic reactions) to daratumumab or any of the components of the formulation.

Please see full Prescribing Information, including Boxed WARNINGS, for POMALYST. Please see the dara full Prescribing Information for a discussion of Important Safety Information at www.darzalexhcp.com/iv.

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WARNINGS AND PRECAUTIONS FOR POMALYST

- **Embryo-Fetal Toxicity & Females of Reproductive Potential: See Boxed WARNINGS**
  - Males: Pomalidomide is present in the semen of patients receiving the drug. Males must always use a latex or synthetic condom during any sexual contact with females of reproductive potential while taking POMALYST and for up to 4 weeks after discontinuing POMALYST, even if they have undergone a successful vasectomy. Males must not donate sperm.
  - Blood Donation: Patients must not donate blood during treatment with POMALYST and for 4 weeks following discontinuation of POMALYST therapy because the blood might be given to a pregnant female patient whose fetus must not be exposed to POMALYST.
- **POMALYST REMS Program: See Boxed WARNINGS**
  - Prescribers and pharmacies must be certified with the **POMALYST REMS** program by enrolling and complying with the REMS requirements; pharmacies must only dispense to patients who are authorized to receive POMALYST. Patients must sign a Patient-Physician Agreement Form and comply with REMS requirements; female patients of reproductive potential who are not pregnant must comply with the pregnancy testing and contraception requirements and males must comply with contraception requirements.
  - Further information about the **POMALYST REMS** program is available at **www.CelgeneRiskManagement.com** or by telephone at 1-888-423-5436.
- **Venous and Arterial Thromboembolism: See Boxed WARNINGS.** Patients with known risk factors, including prior thrombosis, may be at greater risk, and actions should be taken to try to minimize all modifiable factors (e.g., hyperlipidemia, hypertension, smoking). Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.
- **Increased Mortality With Pembrolizumab:** In clinical trials in patients with multiple myeloma, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.
- **Hematologic Toxicity:** Neutropenia (46%) was the most frequently reported Grade 3 or 4 adverse reaction in patients taking POMALYST in clinical trials, followed by anemia and thrombocytopenia. Monitor complete blood counts weekly for the first 8 weeks and monthly thereafter. Patients may require dose interruption and/or modification.
- **Hepatotoxicity:**
  - Hepatic failure, including fatal cases, has occurred in patients treated with POMALYST. Elevated levels of alanine aminotransferase and bilirubin have also been observed in patients treated with POMALYST. Monitor liver function tests monthly. Stop POMALYST upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered.
- **Severe Cutaneous Reactions:** Severe cutaneous reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported. DRESS may present with a cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, fever, and/or lymphadenopathy with systemic complications such as hepatitis, nephritis, pneumonitis, myocarditis, and/or pericarditis. These reactions can be fatal. Consider POMALYST interruption or discontinuation for Grade 2 or 3 skin rash. Permanently discontinue POMALYST for Grade 4 rash, exfoliative or bullous rash, or any other severe cutaneous reactions such as SJS, TEN or DRESS.
- **Dizziness and Confusional State:** In patients taking POMALYST in clinical trials, 14% experienced dizziness (1% Grade 3 or 4) and 7% a confusional state (3% Grade 3 or 4). Instruct patients to avoid situations where dizziness or confusional state may be a problem and not to take other medications that may cause dizziness or confusional state without adequate medical advice.
- **Neuropathy:** In patients taking POMALYST in clinical trials, 18% experienced neuropathy (2% Grade 3 in one trial) and 12% peripheral neuropathy.
- **Second Primary Malignancies:** Cases of acute myelogenous leukemia have been reported in patients receiving POMALYST as an investigational therapy outside of multiple myeloma.
- **Tumor Lysis Syndrome (TLS):** TLS may occur in patients treated with POMALYST. Patients at risk are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.
- **Hypersensitivity:** Hypersensitivity, including angioedema, anaphylaxis, and anaphylactic reactions to POMALYST have been reported. Permanently discontinue POMALYST for angioedema or anaphylaxis.

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WARNINGS AND PRECAUTIONS FOR DARATUMUMAB

- **Infusion-Related Reactions:** Daratumumab can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening and fatal outcomes have been reported. Interrupt daratumumab infusion for infusion-related reactions of any severity. Permanently discontinue the infusion in case of anaphylactic reactions or life-threatening infusion reactions and institute appropriate emergency care.
- **Interference With Cross-Matching and Red Blood Cell Antibody Screening:** Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test), which may persist for up to 6 months after the last daratumumab infusion. Type and screen patients prior to starting treatment. Inform blood banks that a patient has received daratumumab.
- **Neutropenia:** Monitor complete blood cell counts periodically during treatment. Monitor patients with neutropenia for signs of infection. Consider withholding daratumumab until recovery of neutrophils.
- **Thrombocytopenia:** Monitor complete blood cell counts periodically during treatment. Consider withholding daratumumab until recovery of platelets.
- **Interference With Determination of Complete Response:** Daratumumab can interfere with the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.
- **Embryo-Fetal Toxicity:** Can cause fetal harm. Advise pregnant women of the potential risk to a fetus and advise females of reproductive potential to use effective contraception.

ADVERSE REACTIONS FOR POMALYST + dexamethasone

The most common adverse reactions for POMALYST (≥30%) included fatigue and asthenia, neutropenia, anemia, constipation, nausea, diarrhea, dyspnea, upper-respiratory tract infections, back pain, and pyrexia.

In the phase III trial, nearly all patients treated with POMALYST + low-dose dex experienced at least one adverse reaction (99%). Adverse reactions (≥15% in the POMALYST + low-dose dex arm and ≥2% higher than control) included neutropenia (51%), fatigue and asthenia (47%), upper respiratory tract infection (31%), thrombocytopenia (30%), pyrexia (27%), dyspnea (25%), diarrhea (22%), constipation (22%), back pain (20%), cough (20%), pneumonia (19%), bone pain (18%), edema peripheral (17%), peripheral neuropathy (17%), muscle spasms (15%), and nausea (15%). Grade 3 or 4 adverse reactions (≥15% in the POMALYST + low-dose dex arm and ≥1% higher than control) included neutropenia (48%), thrombocytopenia (22%), and pneumonia (16%).

ADVERSE REACTIONS FOR POMALYST + dexamethasone + daratumumab

The most common adverse reactions (≥20%) included neutropenia (95%), lymphopenia (94%), thrombocytopenia (75%), anemia (57%), infusion reactions (50%), fatigue (50%), upper respiratory tract infection (50%), cough (43%), diarrhea (38%), constipation (33%), dyspnea (33%), nausea (30%), muscle spasms (26%), pyrexia (25%), back pain (25%), insomnia (23%), arthralgia (22%), vomiting (21%), dizziness (21%), and chills (20%). Grade 3 or 4 hematology laboratory abnormalities included: neutropenia (82%), lymphopenia (71%), anemia (30%), and thrombocytopenia (20%).

DRUG INTERACTIONS FOR POMALYST

Avoid concomitant use of POMALYST with strong inhibitors of CYP1A2. If concomitant use of a strong CYP1A2 inhibitor is unavoidable, reduce POMALYST dose to 2 mg.

USE IN SPECIFIC POPULATIONS FOR POMALYST

- **Pregnancy: See Boxed WARNINGS.** If pregnancy does occur during treatment, immediately discontinue the drug and refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. There is a POMALYST pregnancy exposure registry that monitors pregnancy outcomes in females exposed to POMALYST during pregnancy as well as female partners of male patients who are exposed to POMALYST. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to POMALYST to the FDA via the MedWatch program at 1-800-FDA-1088 and also to Celgene Corporation at 1-888-423-5436.
- **Lactation:** There is no information regarding the presence of pomalidomide in human milk, the effects of POMALYST on the breastfed child, or the effects of POMALYST on milk production. Pomalidomide was excreted in the milk of lactating rats. Because many drugs are excreted in human milk and because of the potential for adverse reactions in a breastfed child from POMALYST, advise women not to breastfeed during treatment with POMALYST.
- **Pediatric Use:** Safety and effectiveness have not been established in pediatric patients.

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- **Geriatric Use:** No dosage adjustment is required for POMALYST based on age. Patients >65 years of age were more likely than patients ≤65 years of age to experience pneumonia.
- **Renal Impairment:** For patients with severe renal impairment requiring dialysis, reduce the recommended dosage to 3 mg orally daily. Take dose of POMALYST following hemodialysis on hemodialysis days.
- **Hepatic Impairment:** In patients with mild to moderate hepatic impairment, reduce POMALYST dosage to 3 mg orally daily and to 2 mg orally daily in patients with severe hepatic impairment.
- **Smoking Tobacco:** Advise patients that smoking may reduce the efficacy of POMALYST. Cigarette smoking reduces pomalidomide AUC due to CYP1A2 induction.

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Bristol Myers Squibb™

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