Transcript Details

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Review Regimens for the Treatment of Relapsed/Refractory Multiple Myeloma

Announcer:
Welcome to ReachMD.

This medical industry feature, titled "POMALYST: A Therapy for Relapsed/Refractory Multiple Myeloma," is sponsored by Bristol Myers Squibb. This program is intended for healthcare providers based in the United States. This program is not available for CME credits.

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The treatment landscape for multiple myeloma has been evolving rapidly over the recent years. For appropriate adult patients with Relapsed/Refractory Multiple Myeloma, consider POMALYST (pomalidomide), which can either be used as part of a doublet regimen in combination with dexamethasone or as a triplet regimen with dexamethasone and other medications such as daratumumab or elotuzumab for patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.[1,4,5]

Let's first review select Indications with POMALYST and some Important Safety Information for POMALYST, including Boxed WARNINGS.

Voice Over:
POMALYST and EMPLICITI Indications

POMALYST® (pomalidomide) capsules 1, 2, 3, 4 mg 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.[1]

EMPLICITI® (elotuzumab) is indicated in combination with POMALYST and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.[5]

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.[4]

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.[4]

Important Safety Information for POMALYST, EMPLICITI, and daratumumab

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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.[1] In females of reproductive potential, obtain 2 negative pregnancy tests before starting POMALYST treatment.[1]**
- **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.[1]**

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.[1] Prophylactic antithrombotic measures were employed in clinical trials.[1] Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.[1]**

CONTRAINDICATIONS FOR POMALYST

- Pregnancy: POMALYST can cause fetal harm and is contraindicated in females who are pregnant.[1] If the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to a fetus.[1]
- Hypersensitivity: POMALYST is contraindicated in patients who have demonstrated severe hypersensitivity (e.g., angioedema, anaphylaxis) to pomalidomide or any of the excipients.[1]

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.[4]

Important safety information for POMALYST, including BOXED WARNINGS, and important safety information for EMPLICITI will be provided throughout this podcast. This information can also be accessed at www.POMALYSTHCP.com and www.EMPLICITIHCP.com, respectively.

Important safety information for daratumumab will be provided throughout this podcast. More information about daratumumab can be accessed at www.darzelexhcp.com/iv.

Announcer:
POMALYST + dex: A doublet therapy

POMALYST + dex, a doublet therapy, was studied in a Phase 3 , multicenter, randomized, open-label trial of POMALYST + low-dose dex vs high-dose dex in 455 patients (ITT population) with relapsed/refractory multiple myeloma who had received at least 2 prior treatment regimens, including REVLIMID® (lenalidomide) and bortezomib, and demonstrated disease progression on or within 60 days of last therapy.[1,2] Some key exclusion criteria included serum bilirubin >2.0 mg/dL, aspartate and alanine aminotransferase or AST/ALT ratio >3x ULN, and creatinine clearance or CrCl <45 mL/min.[1,2]

Patients were randomized in a 2:1 fashion. 302 patients in the POMALYST + low-dose dex arm received 4 mg of POMALYST orally on Days 1-21 of 28-day cycles with 40 mg of low-dose dex once daily on Days 1, 8, 15, and 22 of 28-day cycles.[1,2] 153 patients in the high-dose dex arm received 40 mg of dex once daily on Days 1-4, 9-12, and 17-20 of 28-day cycles.[1,2] Patients >75 years received 20 mg of dex in the same respective dosing schedules.[1,2] Patients receiving POMALYST + low-dose dex were required to receive prophylaxis or anti-thrombotic treatment, as well as any other patient with a history of DVT or PE.[1,2] The primary endpoint was

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progression-free survival, or PFS, and a key secondary efficacy endpoint was overall survival or OS.[1,2] Treatment continued until disease progression.[1,2]

THE MAJORITY OF PATIENTS STUDIED WERE REFRACTORY TO REVLIMID

In the study, 94% were refractory to REVLIMID. 79% of patients were refractory to bortezomib and 74% were refractory to both REVLIMID and bortezomib.[1]

To access the full prescribing information for REVLIMID, including BOXED WARNINGS, please visit www.REVLIMIDHCP.com.

Patients had received a median of 5 prior therapies. The median age was 64 years, ranging from 35 to 87 years of age. 59% of the patients were male, 78% were white, 1.5% Black or African American, <1% Asian, and <1% were another race. The Eastern Cooperative Oncology Group or ECOG performance status was 0 in 32%, 1 in 49%, 2 in 17%, and 3 in <1% of patients, and the International Staging System or ISS Stage was I or II in 64%, and III in 32% of patients. 41% of patients had del13q14, del17p13, t(4;14), or t(14;16).

Please see full baseline characteristics in the POMALYST prescribing information at www.POMALYSTHCP.com.

The secondary endpoint demonstrated a 30% reduced risk of death with POMALYST + low-dose dexamethasone vs high-dose dexamethasone.[1] The key secondary efficacy endpoint of median OS for POMALYST + low-dose dexamethasone was 12.4 months with a 95% confidence interval of 10.4 to 15.3 months.[1] For high-dose dexamethasone, the median OS was 8 months with a 95% confidence interval of 6.9 to 9 months.[1] The hazard ratio was 0.70 with a 95% confidence interval of 0.54 to 0.92; the P value was 0.009.[1] The OS data cutoff was March 1, 2013.[1]

For the primary endpoint, POMALYST + low-dose dexamethasone doubled the median PFS of high-dose dexamethasone, 3.6 months with a 95% confidence interval of 3.0 to 4.6 months vs 1.8 months with a 95% confidence interval of 1.6 to 2.1 months.[1,2] The hazard ratio was 0.45, with a 95% confidence interval of 0.35 to 0.59.[1,2] The P value was less than 0.001.[1,2] The PFS data cutoff was September 7, 2012.[1,2]

In the Phase 3 trial, PFS and OS were based on the assessment by the Independent Review Adjudication Committee (IRAC) review at the final PFS and OS analysis.

The safety profile for POMALYST plus dexamethasone included the most common adverse reactions of any grade that occurred in at least 20% of patients in the Pd arm and greater than or equal to 2% higher than the high dose dex arm were neutropenia, fatigue/asthenia, upper respiratory tract infection, thrombocytopenia, pyrexia, dyspnea, diarrhea, constipation, cough and back pain.

Grade 3 or 4 adverse reactions (≥15% in the POMALYST + low-dose dex arm and ≥1% higher than the high-dose dex arm) included neutropenia (48%), thrombocytopenia (22%), and pneumonia (16%).

67% of trial patients experienced at least one dose interruption of POMALYST, while 27% of patients experienced at least one dose reduction of POMALYST and 8% discontinued treatment with POMALYST. The median time to first dose interruption and first dose reduction of POMALYST was 4.1 weeks and 4.5 weeks, respectively, and the majority of patients remained on POMALYST + dex until disease progression or unacceptable toxicities with dose modifications.

Now, let's review the warnings and precautions for POMALYST.

Voice Over:

- Embryo-Fetal Toxicity & Females of Reproductive Potential: See Boxed WARNINGS for POMALYST
  - Males: Pomalidomide is present in the semen of patients receiving the drug.[1] 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.[1] 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.[1]
- 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. [1] Patients must sign a

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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.[1]
    - Further information about the **POMALYST REMS** program is available at **www.CelgeneRiskManagement.com** or by telephone at 1-888-423-5436.[1]
- **Venous and Arterial Thromboembolism: See Boxed WARNINGS for POMALYST.**[1] 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).[1] Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.[1]
- **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.[1] 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.[1]
- **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.[1] Monitor complete blood counts weekly for the first 8 weeks and monthly thereafter.[1] Patients may require dose interruption and/or modification.[1]

Announcer: POMALYST + dex + daratumumab: A triplet therapy

POMALYST + dex + dara, a triplet therapy, was studied in an open-label trial, without a comparator arm, in 103 patients who received a prior proteasome inhibitor and REVLIMID.[3,4] Patients were required to have calculated CrCl ≥45 mL/min/1.73 m^2, AST/ALT ≤2.5x ULN, and total bilirubin ≤2 mg/dL.[3,4]

During weeks 1-8, patients received 16 mg/kg of dara as an intravenous infusion weekly.[3,4] During weeks 9-24, they received the infusion every 2 weeks, followed by every 4 weeks from Week 25 until disease progression.[3,4] In addition, patients received 4 mg of POMALYST once daily orally on Days 1-21 of repeated 28-day cycles and 40 mg/week low-dose oral or intravenous dex, with reduced dose of 20 mg/week for patients >75 years or with a Body Mass Index or BMI <18.5.[3,4] 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 following day.[3,4] For patients on a reduced dex dose, the entire 20-mg dose was given as a pre-infusion medication prior to dara.[3,4] Patients in the trial were treated until disease progression.

THE MAJORITY OF PATIENTS STUDIED WERE REFRACTORY TO REVLIMID

89% of the patients enrolled in the trial were refractory to REVLIMID, while 71% were refractory to bortezomib and 64% of patients were refractory to both REVLIMID and bortezomib.[4]

To access the full prescribing information for REVLIMID, including BOXED WARNINGS, please visit www.REVLIMIDHCP.com.

Patients had received a median of 4 prior lines of therapy, including 74% of patients having undergone ASCT, 98% having received bortezomib, 33% carfilzomib, and with 98% previously treated with the combination of bortezomib and lenalidomide. The median age was 64 years, ranging from 35 to 86. The ECOG performance status was 0 in 27%, 1 in 61%, and 2 in 12% of patients. 87 out of 103 patients had available cytogenetic data, 18% were del17p, 7% were t(4;14) and 1% were t(14;16).

Please see full baseline characteristics for daratumumab in the prescribing information at www.darzalexhcp.com/iv.

The overall response rate was 59.2%, with a 95% confidence interval of 49.1 to 68.8.[4] The overall response rate was comprised of a 7.8% stringent complete response, 5.8% complete response, 28.2% very good partial response, and a 17.5% partial response.[4] The median duration of response was 13.6 months, ranging from 0.9 plus to 14.6 plus months.[4] The median time to response was 1 month, ranging from 0.9 to 2.8 months.[4] Efficacy results were based on overall response rate as determined by Independent Review Committee using IMWG criteria.

The most common adverse reactions occurring in at least 50% of patients are neutropenia, lymphopenia, thrombocytopenia, anemia, infusion reactions, fatigue, and upper respiratory tract infection.

Grade 3/4 hematologic adverse reactions that occurred in at least 20% of patients are lymphopenia, neutropenia, anemia and thrombocytopenia. Neutropenia was the most common adverse reaction in 95% of patients, with 44% of patients presenting with Grade

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1 or 2 at baseline.

The overall incidence of adverse reactions was 49%. Serious adverse reactions reported in greater than 5% of patients included pneumonia, which occurred in 7% of patients.

Let's review the warnings and precautions and adverse reactions for daratumumab.

Voice Over:
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.[4] Permanently discontinue the infusion in case of anaphylactic reactions or life-threatening infusion reactions and institute appropriate emergency care.[4]
- **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.[4]Type and screen patients prior to starting treatment.[4] Inform blood banks that a patient has received daratumumab.[4]
- **Neutropenia:** Monitor complete blood cell counts periodically during treatment.[1] Monitor patients with neutropenia for signs of infection.[4] Consider withholding daratumumab until recovery of neutrophils.[4]
- **Thrombocytopenia:** Monitor complete blood cell counts periodically during treatment.[4] Consider withholding daratumumab until recovery of platelets.[4]
- **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.[4]
- **Embryo-Fetal Toxicity:** Can cause fetal harm.[4] Advise pregnant women of the potential risk to a fetus and advise females of reproductive potential to use effective contraception.[4]

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%).

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.

Announcer:
POMALYST + dex + EMPLICITI: A triplet therapy

POMALYST + dex + EMPLICITI, a triplet therapy, was studied in a Phase 2, randomized, open-label study in 117 patients with RRMM who have received at least 2 prior lines of therapy, including REVLIMID and a PI, and were refractory to the most recent therapy.[5,6,7] Some key exclusion criteria included CrCl <45 mL/min and bilirubin ≥2x ULN or AST/ALT ≥3x ULN. 60 patients were randomized to receive POMALYST + dex + EMPLICITI and 57 patients were randomized to receive POMALYST + dex.[5,6,7] In the triplet arm, patients received 4 mg of POMALYST orally once daily on Days 1-21 of a repeated 28-day cycle.[5,6,7] In Cycles 1 and 2, patients received 10 mg/kg of EMPLICITI IV weekly and dex weekly.[5,6,7] From Cycle 3 onward, patients received EMPLICITI 20 mg/kg IV every 4 weeks and dex weekly.[5,6,7] In the doublet arm, patients received POMALYST + 40 mg of dex weekly, taken orally (20 mg in patients ≥75 years of age).[5,6,7] The primary endpoint was PFS, and a secondary endpoint was ORR.[5,6,7]

On days that EMPLICITI was administered, dex 28 mg was given orally between 3 and 24 hours before EMPLICITI plus 8 mg IV between 45 and 90 minutes before EMPLICITI. For patients >75 years, an oral dose of 8 mg and an IV dose of 8 mg were administered. Premedication with dex, H1 blocker diphenhydramine (25-50 mg orally or IV) or equivalent, H2 blocker, and 650-1000 mg oral acetaminophen prior to EMPLICITI infusion was required. On weeks without an EMPLICITI infusion, dex was given as an oral, 40-mg

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dose (20 mg in patients >75 years).

THE MAJORITY OF PATIENTS STUDIED WERE REFRACTORY TO REVLIMID

87% of the patients enrolled in the trial were refractory to REVLIMID, while 80% were refractory to a proteasome inhibitor, and 70% of patients were refractory to both REVLIMID and a proteasome inhibitor.[5]

To access the full prescribing information for REVLIMID, including BOXED WARNINGS, please visit www.REVLIMIDHCP.com.

Patients had received a median of 3 prior therapies. The median patient age was 67 years, ranging from 36 to 81. 57% of patients were male, 77% of patients were white, 21% were Asians, and 1% were black. The ECOG performance status was 0 in 44%, 1 in 46%, and 2 in 10% of patients, and the ISS Stage was I in 50%, II in 38%, and III in 12% of patients. As determined by FISH, 5% of patients had del(17)p and 11% had t(4;14) chromosomal lab abnormalities.

Please see full baseline characteristics in EMPLICITI Prescribing information at www.EMPLICITIHCP.com.

Study results demonstrated a 46% reduction in the risk of disease progression or death for POMALYST + dexamethasone + EMPLICITI vs POMALYST + dexamethasone.[5] The primary endpoint of median PFS for POMALYST + dexamethasone + EMPLICITI was 10.3 months with a 95% confidence interval of 5.6 to not estimable.[5] The minimum follow-up of PFS was 9.1 months.[5] For POMALYST + dexamethasone, the median PFS was 4.7 months with a 95% confidence interval of 2.8 to 7.2 months.[5] The hazard ratio was 0.54 with a 95% confidence interval of 0.34 to 0.86; the P value was 0.0078.[5] The secondary endpoint of overall response rate for POMALYST + dexamethasone + EMPLICITI was 53.3% with a 95% confidence interval of 40.0 to 66.3, where CR + sCR is 8.3%, VGPR is 11.7%, and PR is 33.3%, compared to 26.3% for POMALYST + dexamethasone, with a 95% confidence interval of 15.5 to 39.7, where CR + sCR is 1.8%, VGPR is 7.0%, and PR is 17.5%.[5] The P value was 0.0029.[5]

Efficacy was evaluated by PFS and ORR as determined by the investigator. ORR was assessed using IMWG response criteria and ORR includes complete response (complete response + stringent complete response), very good partial response, and partial response. The interference of EMPLICITI with the assessment of myeloma protein with immunofixation and serum protein electrophoresis assays may interfere with correct response classification.

The most common adverse reactions of any grade that occurred in at least 20% of patients in the triplet arm and with at least a 5% higher incidence than the doublet arm were constipation and hyperglycemia.

The overall incidence of serious adverse reactions was 22% in patients treated with POMALYST plus dexamethasone and elotuzumab, compared with 15% treated with POMALYST plus dexamethasone.

The most frequent serious adverse reactions were pneumonia and respiratory tract infection.

Sixty-five percent of patients treated in either arm experienced infections of any grade. Grade 3/4 infections were reported in 13% of patients treated with the triplet vs 22% with the doublet. Infusion reactions were reported in 3.3% of patients treated with the triplet.

Five percent of patients discontinued treatment due to adverse reactions with POMALYST plus dexamethasone and elotuzumab, compared with 1.8% with POMALYST plus dexamethasone.

Now, let's review the warnings and precautions for elotuzumab and pomalidomide, followed by the adverse reactions for POMALYST + dexamethasone + elotuzumab and remaining important safety information.

Voice Over continues:
WARNINGS AND PRECAUTIONS FOR POMALYST AND EMPLICITI

- Venous and Arterial Thromboembolism: See Boxed WARNINGS for POMALYST. 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.
- Hepatotoxicity:
  - Hepatic failure, including fatal cases, has occurred in patients treated with POMALYST.[1] Elevated levels of alanine aminotransferase and bilirubin have also been observed in patients treated with POMALYST.[1] Monitor liver function tests monthly.[1] Stop POMALYST upon elevation of liver enzymes.[1] After return to baseline values, treatment at a lower dose may be considered.[1]

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- In the ELOQUENT-2 trial (EMPLICITI + lenalidomide + dexamethasone vs lenalidomide + dexamethasone) (N=635), AST/ALT >3X the upper limit, total bilirubin >2X the upper limit, and alkaline phosphatase <2X the upper limit were 2.5% (EMPLICITI arm) vs 0.6% (control arm).[5] Of 8 patients experiencing hepatotoxicity, 2 patients discontinued treatment while 6 patients had resolution and continued. Stop EMPLICITI upon ≥Grade 3 elevation of liver enzymes.[5] Continuation of treatment may be considered after return to baseline values.[5]

- **Infusion Reactions:**
  - Infusion reactions were reported in 3.3% of patients treated with EMPLICITI in the ELOQUENT-3 trial [EMPLICITI + pomalidomide + dexamethasone (EPd) vs pomalidomide + dexamethasone (Pd)].[5]
  - The only infusion reaction symptom was chest discomfort (2%), which was Grade 1. All the patients who experienced an infusion reaction had them during the first treatment cycle.[5]
  - If a Grade 2 or higher infusion reaction occurs, interrupt the EMPLICITI infusion and institute appropriate medical and supportive measures.[5] If the infusion reaction recurs, stop the EMPLICITI infusion and do not restart it on that day.[5] Severe infusion reactions may require permanent discontinuation of EMPLICITI therapy and emergency treatment.[5]
  - Premedicate with dexamethasone, H1 blocker, H2 blocker, and acetaminophen prior to EMPLICITI infusion.[5]
- **Infections:**
  - In the ELOQUENT-3 trial (N=115), infections were reported in 65% of patients in both the EPd arm and the Pd arm. Grade 3-4 infections were reported in 13% (EPd) and 22% (Pd).[5] Discontinuations due to infections were 7% (EPd) and 5% (Pd).[5] Fatal infections were 5% (EPd) and 3.6% (Pd).[5] Opportunistic infections were reported in 10% (EPd) and 9% (Pd).[5] Herpes zoster was reported in 5% (EPd) and 1.8% (Pd).[5]
  - Monitor patients for development of infections and treat promptly.[5]
- **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 with POMALYST.[1] 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.[1] These reactions can be fatal.[1] Consider POMALYST interruption or discontinuation for Grade 2 or 3 skin rash.[1] Permanently discontinue POMALYST for Grade 4 rash, exfoliative or bullous rash, or any other severe cutaneous reactions such as SJS, TEN or DRESS.[1]
- **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).[1] 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.[1]
- **Neuropathy:** In patients taking POMALYST in clinical trials, 18% experienced neuropathy (2% Grade 3 in one trial) and 12% peripheral neuropathy.[1]
- **Second Primary Malignancies (SPMs):**
  - Cases of acute myelogenous leukemia have been reported in patients receiving POMALYST as an investigational therapy outside of multiple myeloma.[1]
  - In the EMPLICITI ELOQUENT-3 trial (N=115), invasive SPMs were 0% (EPd) and 1.8% (Pd).[1]
  - Monitor patients for the development of SPMs.[1]
- **Tumor Lysis Syndrome (TLS):** TLS may occur in patients treated with POMALYST.[1] Patients at risk are those with high tumor burden prior to treatment.[1] These patients should be monitored closely and appropriate precautions taken.[1]
- **Interference With Determination of Complete Response:** EMPLICITI is a humanized IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis and immunofixation assays used for the clinical monitoring of endogenous M-protein.[5] This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein.[5]
- **Hypersensitivity:** Hypersensitivity, including angioedema, anaphylaxis, and anaphylactic reactions to POMALYST have been reported.[1] Permanently discontinue POMALYST for angioedema or anaphylaxis.[1]

ADVERSE REACTIONS FOR POMALYST AND EMPLICITI

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.[1]

In the phase III trial, nearly all patients treated with POMALYST + low-dose dex experienced at least one adverse reaction (99%).[1]

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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%).[1] 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%).[1]

Serious adverse reactions in the EMPLICITI ELOQUENT-3 trial were 22% (EPd) and 15% (Pd).[5] The most frequent serious adverse reactions in the EPd arm compared to the Pd arm were: pneumonia (13%, 11%) and respiratory tract infection (7%, 3.6%).[5]

The most common adverse reactions in EPd arm (≥20% EPd) and Pd, respectively, were constipation (22%, 11%) and hyperglycemia (20%, 15%).[5]

There are some drug interactions for POMALYST.

Avoid concomitant use of POMALYST with strong inhibitors of CYP1A2.[1] If concomitant use of a strong CYP1A2 inhibitor is unavoidable, reduce POMALYST dose to 2 mg.[1]

USE IN SPECIFIC POPULATIONS FOR POMALYST AND EMPLICITI

- **Pregnancy: See Boxed WARNINGS for POMALYST.** 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.[1] 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.[1] This registry is also used to understand the root cause for the pregnancy.[1] 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.[1]
- **Pregnancy and EMPLICITI Use:** There are no available data on EMPLICITI use in pregnant women to inform a drug-associated risk of major defects and miscarriage.[5]
- **Lactation:** There is no information regarding the presence of pomalidomide or elotuzumab in human milk, the effects of POMALYST or EMPLICITI on the breastfed child, or the effects of POMALYST or EMPLICITI on milk production.[1,5] Pomalidomide was excreted in the milk of lactating rats.[1] 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 or POMALYST in combination with EMPLICITI.[1,5]
- **Pediatric Use:** Safety and effectiveness have not been established in pediatric patients.[1,5]
- **Geriatric Use:** No dosage adjustment is required for POMALYST based on age.[1] Patients >65 years of age were more likely than patients ≤65 years of age to experience pneumonia.[1]
- **Renal Impairment:** For patients with severe renal impairment requiring dialysis, reduce the recommended dosage to 3 mg orally daily.[1] Take dose of POMALYST following hemodialysis on hemodialysis days.[1]
- **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.[1]
- **Smoking Tobacco:**Advise patients that smoking may reduce the efficacy of POMALYST. Cigarette smoking reduces pomalidomide AUC due to CYP1A2 induction.[1]

Please see full Prescribing Information for POMALYST, including Boxed WARNINGS, at www.POMALYSTHCP.com and full Prescribing Information for EMPLICITI at www.EMPLICITIHCP.com.

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

Announcer:
Consider a POMALYST plus dex-containing regimen for your appropriate adult patients with relapsed/refractory multiple myeloma who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor.

This program was sponsored by Bristol Myers Squibb. If you missed any part of this discussion or to find others in this series, visit reachmd.com/industryfeature. This is ReachMD. Be Part of the Knowledge.

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