Another approval:
For your adult patients with newly diagnosed, transplant-ineligible multiple myeloma

DARZALEX® (daratumumab) + Rd*

REDEFINING APPROACHES IN EARLY LINES OF MULTIPLE MYELOMA

For a strong start to their treatment journey

***Rd=lenalidomide (R) + dexamethasone (d).**

DARZALEX® is a CD38-directed cytolytic antibody indicated for the treatment of adult patients with multiple myeloma:

- in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® (daratumumab) is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion Reactions – DARZALEX® can cause severe and/or serious infusion reactions, including anaphylactic reactions. In clinical trials, approximately half of all patients experienced an infusion reaction. Most infusion reactions occurred during the first infusion and were Grade 1-2. Infusion reactions can also occur with subsequent infusions. Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Prior to the introduction of post-infusion medication in clinical trials, infusion reactions occurred up to 48 hours after infusion. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, laryngeal edema, and pulmonary edema. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, and hypotension.

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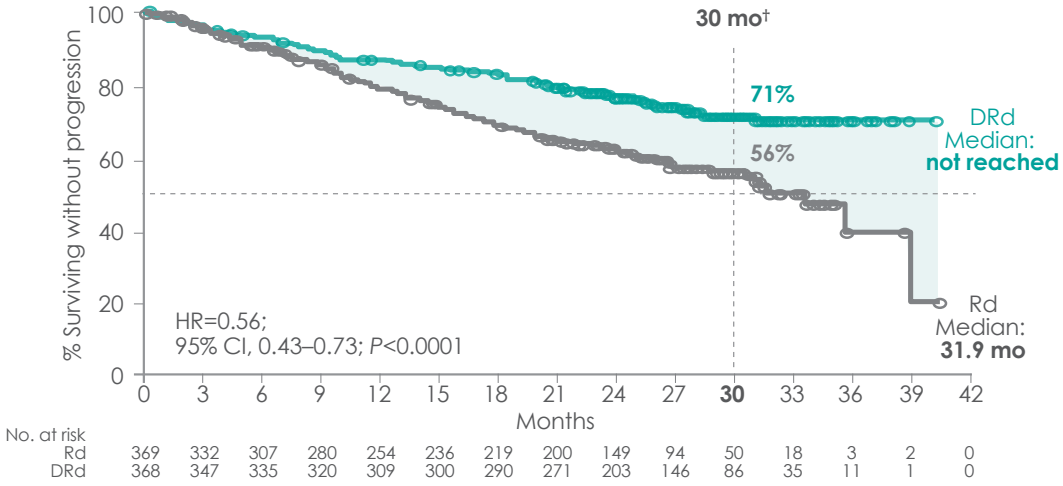
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL
DARE TO DREAM

Median PFS still not reached with DARZALEX® (daratumumab) + Rd after 28 months of follow-up* vs 31.9 months for Rd alone[1,2]



44% REDUCTION

in the risk of disease progression or death with DARZALEX® + Rd vs Rd alone in newly diagnosed, transplant-ineligible MM

DRd=DARZALEX® (D) + lenalidomide (R) + dexamethasone (d); HR=hazard ratio; MM=multiple myeloma; PFS=progression-free survival.
*Range: 0.0–41.4.
†Kaplan-Meier estimate.

At 30 months: 70.6% of patients had not progressed with DRd vs 55.6% of patients in the Rd group (DRd: 95% CI, 65.0–75.4; Rd: 95% CI, 49.5–61.3).[2]

Study Design: MAIA, an open-label, randomized, phase 3 study, compared treatment with DARZALEX® + lenalidomide + dexamethasone (DRd) (n=368) to Rd (n=369) in adult patients with newly diagnosed, transplant-ineligible MM. Treatment was continued until disease progression or unacceptable toxicity. The primary efficacy endpoint was PFS. *See CLINICAL STUDIES (14.1) section of the full Prescribing Information for more information.*

Select Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS

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To reduce the risk of delayed infusion reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications.

Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

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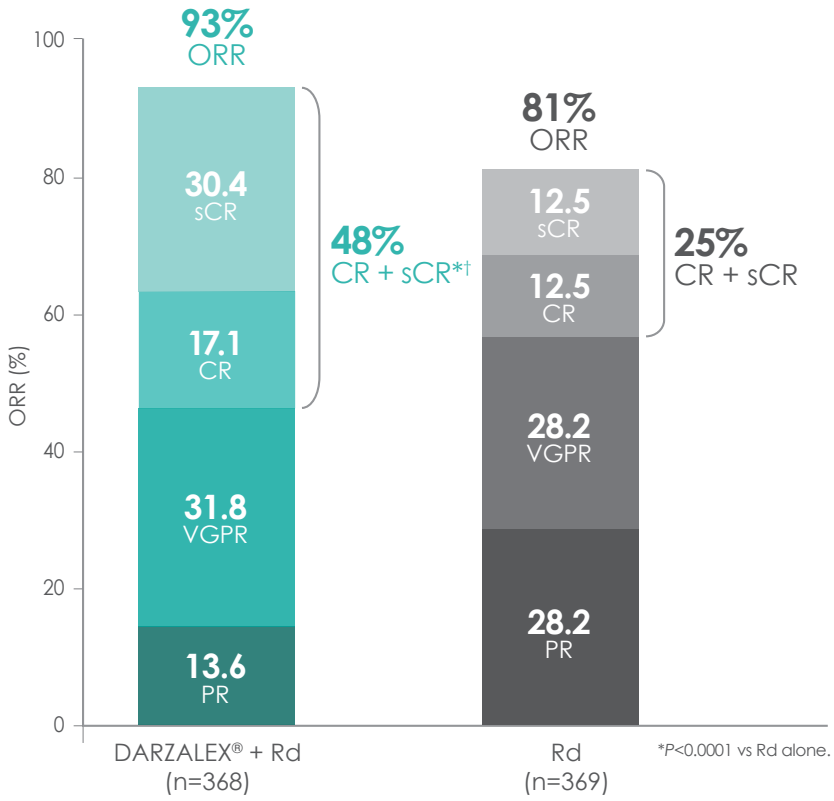
93% ORR was achieved with DARZALEX® (daratumumab) + Rd[1*]



CR=complete response; ORR=overall response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response.
†sCR is CR plus normal free light chain ratio, and the absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence.[2]

Select Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS

Interference With Serological Testing – Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Neutropenia and Thrombocytopenia – DARZALEX® may increase neutropenia and/or thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to the manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. DARZALEX® dose delay may be required to allow recovery of neutrophils and/or platelets. No dose reduction of DARZALEX® is recommended. Consider supportive care with growth factors for neutropenia or transfusions for thrombocytopenia.

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Choose DARZALEX® (daratumumab) + Rd to treat newly diagnosed, transplant-ineligible MM

Deep and durable responses[1]

- DRd nearly doubled the number of patients who achieved CR or better vs Rd alone[1]
  - More than doubled sCR: 30% with DRd vs 13% with Rd alone
- Median duration of response has not yet been reached with DRd vs 34.7 months (95% CI: 30.8, not estimable) for Rd alone[1]
- MRD negativity rates* more than tripled vs Rd alone (*P*<0.0001)[1]
  - 24% of patients were MRD negative with DRd (95% CI: 19.9%, 28.9%)
  - 7% of patients were MRD negative with Rd (95% CI: 4.9%, 10.5%)

MRD was based on a sensitivity threshold of 10^{-5} using a next-generation sequencing assay (ClonoSEQ) and was associated with a lower risk of progression or death.[1,2]

Demonstrated safety profile when combined with Rd in the MAIA Study[1]

- The most frequent (≥20%) adverse reactions were infusion reactions, diarrhea, constipation, nausea, peripheral edema, fatigue, back pain, asthenia, pyrexia, upper respiratory tract infection, bronchitis, pneumonia, decreased appetite, muscle spasms, peripheral sensory neuropathy, dyspnea, and cough
- Serious adverse reactions with at least a 2% greater incidence in the DRd arm compared to the Rd arm were pneumonia (DRd 15% vs Rd 8%), bronchitis (DRd 4% vs Rd 2%) and dehydration (DRd 2% vs Rd <1%)

MRD=minimal residual disease.

*MRD negativity was defined as undetectable levels of MM cells by bone marrow aspirate at any time point after the randomization and before disease progression or start of subsequent therapy, and in the trial was assessed by means of next-generation sequencing assay at a sensitivity threshold of 10^{-5} via bone marrow aspirate, collected at initial trial screening, at the time of confirmation of CR or sCR, and thereafter at 12, 18, 24, and 30 months.[2]

Select Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS

Interference With Determination of Complete Response – Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

Adverse Reactions – The most frequently reported adverse reactions (incidence ≥20%) were: infusion reactions, neutropenia, thrombocytopenia, fatigue, asthenia, nausea, diarrhea, constipation, decreased appetite, vomiting, muscle spasms, arthralgia, back pain, pyrexia, chills, dizziness, insomnia, cough, dyspnea, peripheral edema, peripheral sensory neuropathy, bronchitis, pneumonia and upper respiratory tract infection.

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DARZALEX® in combination with lenalidomide and dexamethasone (DRd): The most frequent (≥20%) adverse reactions for newly diagnosed or relapsed refractory patients were, respectively, infusion reactions (41%, 48%), diarrhea (57%, 43%), nausea (32%, 24%), fatigue (40%, 35%), pyrexia (23%, 20%), upper respiratory tract infection (52%, 65%), muscle spasms (29%, 26%), dyspnea (32%, 21%), and cough (30%, 30%). In newly diagnosed patients, constipation (41%), peripheral edema (41%), back pain (34%), asthenia (32%), bronchitis (29%), pneumonia (26%), decreased appetite (22%), and peripheral sensory neuropathy (24%) were also reported. In newly diagnosed patients, serious adverse reactions (≥2% compared to Rd) were dehydration (2%), bronchitis (4%), and pneumonia (15%), and treatment-emergent Grade 3-4 hematology laboratory abnormalities (≥20%) were leukopenia (35%), neutropenia (56%), and lymphopenia (52%). In relapsed/refractory patients, serious adverse reactions (≥2% compared to Rd) were pneumonia (12%), upper respiratory tract infection (7%), influenza (3%), and pyrexia (3%), and treatment-emergent Grade 3-4 hematology laboratory abnormalities (≥20%) were neutropenia (53%) and lymphopenia (52%).

cp-76663v2

References: 1. DARZALEX® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Facon T, Kumar S, Plesner T, et al; the MAIA Trial Investigators. Daratumumab plus lenalidomide and dexamethasone for untreated myeloma. *N Engl J Med*. 2019;308(22):2104-2115.

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