Nursing Implications for Patients with Myeloma Receiving Combination Therapy with Daratumumab (Darzalex™) and Lenalidomide

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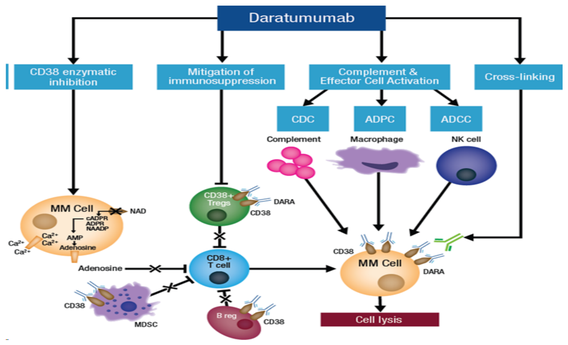
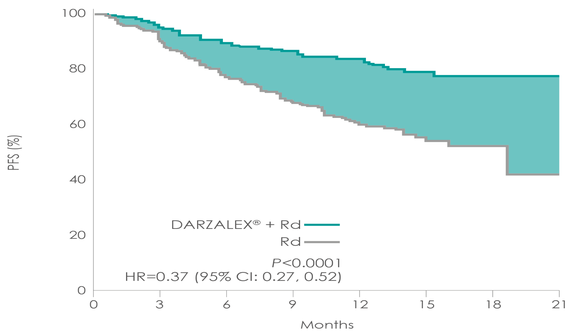
Introduction

Daratumumab (DARA) is a first-in-class, human IgG1 monoclonal antibody that targets CD38, a protein that is highly expressed on multiple myeloma (MM) cells. First approved as a monotherapy, DARA has now been shown to increase length and depth of response when added to lenalidomide and dexamethasone (Rd).

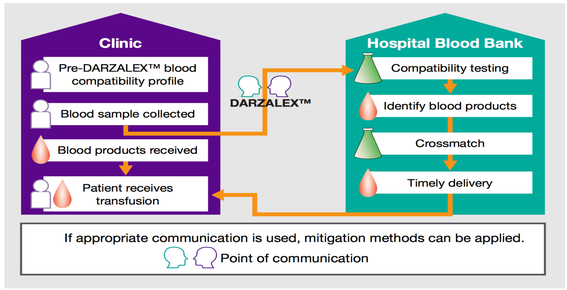


November 16, 2016, the United States Food and Drug Administration granted breakthrough therapy designation to DARA in combination with lenalidomide and dexamethasone (DRd) for patients who have received one or more prior therapies. DRd has shown an increase in overall response rate from 76% to 93% and a complete response rate from 19% to 43% versus Rd alone. Progression free survival (PFS) at 18 months with DRd was 72% versus 48% with Rd.



Evaluation

Prior to initiation: DARA administration creates false-positive indirect Coombs tests in 100% of DARA treated patients. DARA interferes with the test by binding to endogenous CD38 on RBCs, resulting in pan-agglutination. This can be solved by cross typing the patient's blood BEFORE initial DARA administration. The blood bank can then provide phenotypically matched blood despite incompatibility readings. If the patient has not had typing before DARA, the blood bank can use Dithiothreitol (DTT) denaturation of the CD38 to reverse the false incompatibility. Appropriate and timely transfusions can still be accomplished through communication between healthcare provider and the blood bank.



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Patients should be encouraged to carry ID cards for at least 6 months after their last DARA infusion.

Daratumumab patients:
Provide this card to health care providers BEFORE blood transfusion

Name:_____

I am taking the following medication:
Daratumumab, an antibody product for the treatment of multiple myeloma

Before starting daratumumab, my blood test results, collected on ___ /___ /___, were:

Blood type: ☐ A ☐ B ☐ AB ☐ O ☐ Rh+ ☐ Rh−

Indirect Coombs test (antibody screen) was:

☐ Negative ☐ Positive for the following antibodies:

_____

Figure 4. Identification card for patients receiving DARA.

Approximately half of DARA patients will have an infusion reaction during the first infusion; 2% will have an infusion reaction during the second infusion. Median time of onset of reaction is 1.5 hours. Reactions are usually respiratory in nature: cough, bronchospasm, rhinitis, or laryngeal edema.

Chari et al. (2016) demonstrated that premedicating with montelukast reduces respiratory reactions by one third. Other reactions include rash, fever, back pain, and/or rigors. There is no increase in incidences of infusion reaction when given in combination with lenalidomide.

Administration

Premedication: Diphenhydramine 25mg, acetaminophen 650mg, montelukast 4mg, and dexamethasone 20mg IV pre infusion, then 20mg oral the following day (40mg weekly)
DRd: DARA 16mg/kg IV weekly x 8, every 2 weeks x 16, every 4 weeks thereafter; lenalidomide 25mg PO Days 1-21 of each 28-day cycle; dexamethasone 40mg orally once on non infusion weeks.

	Dilution volume	Initial rate (first hour)	Rate increment[a]	Maximum rate
First infusion	1000 mL	50 mL/hour	50 mL/hour every hour	200 mL/hour
Second infusion[b]	500 mL	50 mL/hour	50 mL/hour every hour	200 mL/hour
Subsequent infusions[c]	500 mL	100 mL/hour	50 mL/hour every hour	200 mL/hour

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In the event of an infusion reaction: Stop infusion, medicate as necessary until reaction subsides, then restart at half the infusion rate and increase again as above.
Concomitant medications: Daily anticoagulation and antiviral prophylaxis

Monitoring

Higher incidences of diarrhea, nausea, vomiting, fatigue, upper respiratory infection, cough and muscle spasms were seen in DRd, as compared to Rd. A higher incidence of neutropenia was also seen (92% vs. 87%).

Table 4: Adverse reactions reported in ≥ 10% of patients and with at least a 5% frequency greater in the DRd arm in Study 3

Adverse Reaction	DRd (N=283) %			Rd (N=281) %		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
Infusion reactions[a]	48	5	0	0	0	0
Gastrointestinal disorders						
Diarrhea	43	5	0	25	3	0
Nausea	24	1	0	14	0	0
Vomiting	17	1	0	5	1	0
General disorders and administration site conditions						
Fatigue	35	6	< 1	28	2	0
Pyrexia	20	2	0	11	1	0
Infections and infestations						
Upper respiratory tract infection[b]	65	6	< 1	51	4	0
Musculoskeletal and connective tissue disorders						
Muscle spasms	26	1	0	19	2	0
Nervous system disorders						
Headache	13	0	0	7	0	0
Respiratory, thoracic and mediastinal disorders						
Cough[c]	30	0	0	15	0	0
Dyspnea[d]	21	3	< 1	12	1	0

Key: D=daratumumab, Rd=lenalidomide-dexamethasone.

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DARA is a human IgG kappa monoclonal antibody that can be detected in the serum protein electrophoresis, causing an interference in determination of complete response. This can make it hard to distinguish between a very good partial response and complete response.

Education

Patient counseling should include discussion of the possible infusion reactions, signs and symptoms of infection and prevention, DVT (asymmetric swelling, pain, redness), and pulmonary embolism (shortness of breath, dyspnea, chest pain). Patients must be educated on the importance of medication adherence, the risk of false positive antibody screen, and encouraged to carry an ID card when available. It may be important to discuss the possible M-spike discrepancy with the patient when evaluating labs to prevent unnecessary upset.

Conclusion

- DARA is a first-in-class, human IgG1 monoclonal antibody that targets CD38, a protein that is highly expressed on multiple myeloma (MM) cells
- DARA can cause false positive indirect Coombs tests. Proper steps are necessary to prevent transfusion delays
- Proper premedication and concomitant medications can minimize infusion reactions and toxicities
- DARA in combination with Rd has a higher incidence of GI symptoms, neutropenia, upper respiratory infections, muscle spasms, fatigue and dyspnea than Rd alone.
- Overall, DARA increases length and depth of response when added to Rd and is well tolerated.

References

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Acknowledgements

Sundar Jagannath, MD; Ajai Chari, MD; Hearn Cho, MD; Samir Parekh, MD; Bart Barlogie, MD; Deepu Madduri, MD; Daniel Verina, MSN, RN, ANP-BC; Melissa Cortes, RN, ANP-BC; Meredith Curtis, AGPCNP-BC; Donna Berizzi, RN, MSN, OCN; Mari Lynn Silverberg, RN, OCN, MPA; Nadege Stevens, RN; Chloe Spear, RN, OCN; Phoebe Shi, RN; Anne Steele, RN; Brittany Hartman, RN; Yu-Mee Song, LCSW.