Nursing Implications for Patients with Relapsed and Refractory Multiple Myeloma Receiving Combination Therapy with Daratumumab (Darzalex™)

Donna Catamero, ANP-BC, OCN, CCRC; Erika Florendo, RN, ANP-BC; Gillian Morgan, RN, CCRC

The Mount Sinai Medical Center

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/dexamethasone and bortezomib/dexamethasone.

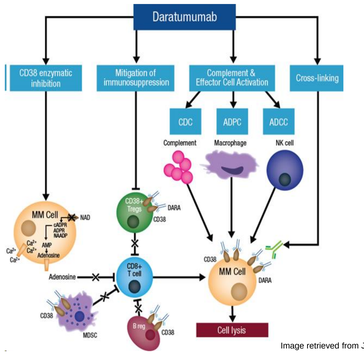
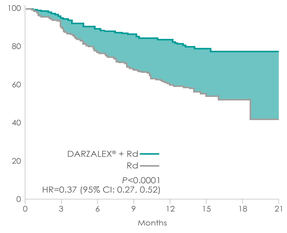
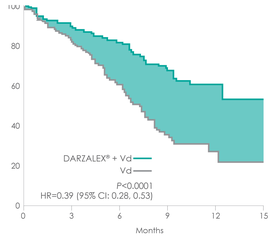


Image retrieved from Janssen, 2016

Significance and Background

November 16, 2016, the FDA granted approval to DARA in combination with lenalidomide/dexamethasone (DRd) and bortezomib/dexamethasone (DVd) for patients who have received one or more prior therapies. DRd had an overall response rate (ORR) of 93% and a complete response (CR) rate of 42%. Progression free survival (PFS) with DRd was 72%. DVd had an ORR of 79% with a complete response of 18%. DVd had a PFS of 61% vs 27% in Vd.





Images retrieved from Janssen, 2016

Evaluation

Prior to initiation: Prior to receiving the first dose of DARA, patients must have their blood typed and cross-matched for associated false-positive indirect Coombs tests.

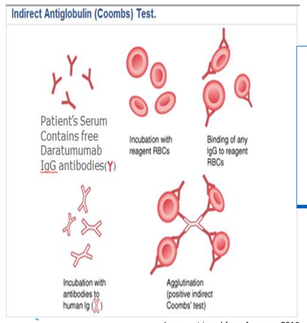
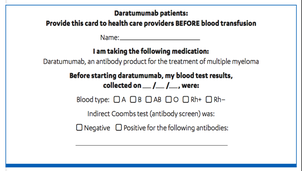


Image retrieved from Janssen, 2016



Patients on DARA are at an increased risk of infusion reactions. The majority of infusion reactions occur during the first infusion or within 4 hours of starting. Approximately half of all patients will experience a reaction. There is no increased incidence of a reaction when given in combination therapy. The most common type of infusion reactions are respiratory symptoms such as cough, wheeze, larynx and throat tightness or irritation, laryngeal edema, nasal congestion, and allergic rhinitis. Patients must be pre-medicated with an antihistamine, antipyretic, and corticosteroid. Chari et al. (2016) demonstrated that premedicating with montelukast reduces respiratory reactions by one third.

All patients should have shingles prophylaxis. For patients receiving lenalidomide, an anticoagulant must be added for blood clot prophylaxis.

DARA is a monoclonal IgG Kappa antibody; its presence can be seen in SPEP and IFE. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein. There is a DARA interference reflex assay (DIRA) that can be utilized to abrogate interference.

Administration

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 PO weekly.

DVd: DARA 16mg/kg IV weekly x 3 cycles, Day 1 of Cycles 4-9, every 4 weeks thereafter; bortezomib 1.3mg/m^2 SC Days 1, 4, 8, and 11 of each 21-day cycle; dexamethasone 80mg PO weekly. Bortezomib dosing should be discontinued after 8 cycles. Dexamethasone is continued as a pre-infusion medication.

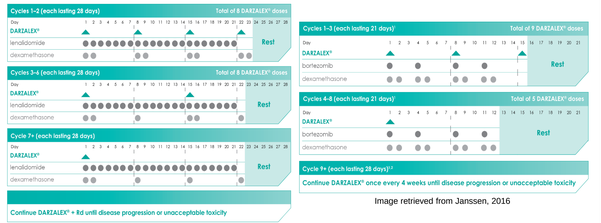


Image retrieved from Janssen, 2016

Monitoring

Higher incidence of neutropenia, diarrhea, fatigue, upper respiratory infection, constipation, cough and muscle spasms were seen in DRd. Higher incidence of thrombocytopenia, neuropathy, and diarrhea were seen in patients receiving DVd.

DRd:

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[a]	30	0	0	15	0	0
Dyspnea[a]	21	3	< 1	12	1	0

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

Image retrieved from Dimopoulos, M.A., et al. NEJM 2016.

DVd:

Event	Daratumumab Group (N=243)		Control Group (N=237)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients (percent)			
Common hematologic adverse event				
Thrombocytopenia	143 (58.8)	110 (45.3)	104 (43.9)	78 (32.9)
Anemia	64 (26.3)	35 (14.4)	74 (31.2)	38 (16.0)
Neutropenia	43 (17.7)	31 (12.8)	22 (9.3)	10 (4.2)
Lymphopenia	32 (13.2)	23 (9.5)	9 (3.8)	6 (2.5)
Common nonhematologic adverse events				
Peripheral sensory neuropathy	115 (47.3)	11 (4.5)	89 (37.6)	16 (6.8)
Diarrhea	77 (31.7)	9 (3.7)	53 (22.4)	3 (1.3)
Upper respiratory tract infection	60 (24.7)	4 (1.6)	43 (18.1)	2 (0.8)
Fatigue	52 (21.4)	11 (4.5)	58 (24.5)	8 (3.4)
Cough	58 (23.9)	0	30 (12.7)	0
Constipation	48 (19.8)	0	37 (15.6)	2 (0.8)
Dyspnea	45 (18.5)	9 (3.7)	21 (8.9)	2 (0.8)
Insomnia	41 (16.9)	0	35 (14.8)	3 (1.3)
Peripheral edema	40 (16.5)	1 (0.4)	19 (8.0)	0
Asthenia	21 (8.6)	2 (0.8)	37 (15.6)	5 (2.1)
Pyrexia	38 (15.6)	3 (1.2)	27 (11.4)	3 (1.3)
Pneumonia	29 (11.9)	20 (8.2)	28 (11.8)	23 (9.7)
Hypertension	21 (8.6)	16 (6.6)	8 (3.4)	2 (0.8)
Secondary primary cancer†	6 (2.5)	NA	1 (0.4)	NA

Image retrieved from Palumbo, A., et al. NEJM 2016.

Education

Patient counseling should include discussion of the most common adverse events. Nurses should instruct patients to inform the care team if fevers, chills, rigors, chest pain, shortness of breath, or a cough develop. Understanding DIRA interference will allow nurses to explain to patients the meaning of their lab results. DIRA positive means that serum IFE is positive for endogenous protein, thus the patient still has disease and is in VGPR. DIRA negative means that serum IFE is negative for endogenous protein and it is DARA causing an interference, thus the patient is in CR and should have a bone marrow biopsy to confirm remission.

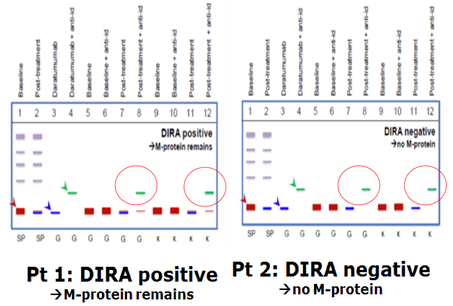


Image retrieved from McCudden C, et al. ASCO. 2015.

Discussion

Because nurses are involved in administration, assessment, management of side effects, and patient education, it is imperative that oncology nurses are knowledgeable of current and emerging MM therapies.

References

1. Chari, A., Mark,T.M., Krishnan, A., Stockerl-Goldstein, K., Usmani, S.Z., Londhe, A.,Etheredge, D., Parros, H., Fleming, S., Liu, B., Freeman, S., Ukropec, J., Lin, T., Nooka, A.K. (2016). *Use of Montelukast to Reduce Infusion Reaction in an Early Access Program(EAP) of Daratumumab in united states Patients with Relapse or Refractory Multiple Myeloma* . Poster session presented at the American Society of Hematology.
2. Catamero, D., Morgan, G., Imran, K. (2016) *Assay Interference and Blood Transfusion Safety in Patients With Relapsed or Refractory Multiple Myeloma (MM) Treated With Daratumumab.* Poster session presented at Oncology Nursing Society, San Antonio, TX.
3. Dimopoulos, M. A., Oriol, A., Nahi, H., San-Miguel, J., Bahlis, N. J., Usmani, S. Z., ... & Plesner, T. (2016). Daratumumab, lenalidomide, and dexamethasone for multiple myeloma. *New England Journal of Medicine*, *375*(14), 1319-1331.
4. Palumbo, A., Chanan-Khan, A., Weisel, K., Nooka, A.K., Masszi, T., Beksac, M., ...& Sonneveld, P. (2016). Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma. *New England Journal of Medicine,* 375(8):754-766.
5. Janssen Biotec Inc. (2016). *Highlights of prescribing information.* Horsham, PA

printed by MegaPrint Inc. www.postersession.com