

# Bortezomib 1.3 / Daratumumab 16 / Dexamethasone (20/20), Multiple Myeloma, Cycle 1

Protocol-ID: 817 V2.1 (Standard), BORT1.3/DRTM16/DEXA(20/20), MM, C1

## Indication(s)

• Multiple Myeloma; ICD-10 C90.-, C90.0-

#### **Protocol classification**

· Classification: current standard

· Intensity: Standard dose

Therapy mode: Relapse therapyTherapy intention: disease control

## **Cycles**

Cycle length 21 days, recommended cycles: 1

# **Protocol sequences**

• CASTOR: BORT1.3/DRTM16/DEXA(20/20), MM, C1 (PID817) -|- C2-3 (PID818) -|- C4-8 (PID819) -|- C9+ (PID820)

#### **Risks**

• Emetogenicity (MASCC/ESMO): minimal (<10%)

• Neutropenia: moderate (11-20%)

• Thrombocytopenia below 50 000/µl: very high (>41%)

• Anemia Hb below 8g/dl: moderate (6-15%)

Diarrhea: CTC AE °3-4: 4%
Hypertension: CTC AE °3-4: 7%
Dyspnea: CTC AE °3-4: 4%
Fatigue: CTC AE °3-4: 5%
Neuropathy: CTC AE °3-4: 5%
Pneumonia: CTC AE °3-4: 8%

## **Therapy**

Hydration: Balanced Crystalloid Solution								
Access: peripheral venous								
Hydr	Hydration before, during, or after antitumor therapy							
Day	Substance	Dosage	Solution	Appl.	Inf. time	Procedure		
1	Balanced Crystalloid Solution	500 ml		i.v.	60 min	60 min before Daratumumab (d1)		
8	Balanced Crystalloid Solution	500 ml		i.v.	60 min	60 min before Daratumumab (d8)		
15	Balanced Crystalloid Solution	500 ml		i.v.	60 min	60 min before Daratumumab (d15)		

## Allergy prophylaxis: Daratumumab allergy prophylaxis with dexamethasone

Access: peripheral venous

Preinfusion Medication: To reduce the risk of IRRs, premedication should be given to all patients approximately 1 hour before each infusion.

Day	Substance	Dosage	Solution	Appl.	Inf. time	Procedure
1	Dexamethasone	20 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d1)
1	Dimetinden	4 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d1)
1	Paracetamol	1000 mg		p.o.		60 min before Daratumumab (d1)
1	Montelukast	10 mg		p.o.		60 min before Daratumumab (d1)
8	Dexamethasone	20 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d8)
8	Dimetinden	4 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d8)
8	Paracetamol	1000 mg		p.o.		60 min before Daratumumab (d8)
15	Dexamethasone	20 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d15)
15	Dimetinden	4 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d15)
15	Paracetamol	1000 mg		p.o.		60 min before Daratumumab (d15)

#### Antineoplastic therapy: BORT1,3/DRTM16/DEXA(20/20)

ANTX

ΑP

Access: peripheral venous

Bortezomib, daratumumab, and dexamethasone in multiple myeloma

Day	Substance	Dosage	Solution	Appl.	Inf. time	Procedure			
1,4,8,11	Bortezomib	1.3 mg/m² BSA	none	subc	Bolus	Sequence			
1	Daratumumab	16 mg/kg bw	NaCl 0.9% 1000 ml	i.v.	6.5h	Sequence			
Initial rate 50 ml/h,	increase infusion rate by 50	ml/h every 60 minutes. M	aximum infusion rate: 200 ml/h						
8	Daratumumab	16 mg/kg bw	NaCl 0.9% 500 ml	i.v.	4 h	Sequence			
Initial rate 50 ml/h,	increase infusion rate by 50	ml/h every 60 minutes. M	aximum infusion rate: 200 ml/h						
15	Daratumumab	16 mg/kg bw	NaCl 0.9% 500 ml	i.v.	3.25h	Sequence			
Initial rate 100 ml/h, increase infusion rate by 50 ml/h every 60 minutes. Maximum infusion rate: 200 ml/h									
2,4-5,9,11-12	Dexamethasone	20 mg		p.o.		1-0-0-0			
Patients with BMI to	pelow 18.5 or over 75 years of	of age received 20mg of d	lexamethasone per week.						

## Hematopoietic growth factors: G-CSF prophylaxis MM, low/intermediate risk

HW

Access: - none -

Neutrophils < 1000/μl at start of therapy + 1 additional risk factor (Palumbo et al. 2012)

Day	Substance	Dosage	Solution	Appl.	Inf. time	Procedure
2-3,5-7,9-10,12-14,16-19	Filgrastim	5 μg/kg bw		subc	Bolus	1-0-0-0

Neutrophils below  $1000/\mu l$  at start of therapy + 1 additional risk factor: age > 65 yrs, female gender, comorbidities, decreased immune function, body surface area less than  $2m^2$ , low performance status; daily until neutrophils >  $1000/\mu l$ 

## Infection prophylaxis: Herpes prophylaxis

ΙP

Access: - none -

Aciclovir administration for herpes prophylaxis under proteasome inhibitor therapy. DGHO recommendation 07/2015

Day	Substance	Dosage	Solution	Appl.	Inf. time	Procedure
1-21	Aciclovir	400 mg		p.o.		1-0-1-0

# **Substance links**

Links to substances are found here.

## **Concomitant therapy supplements**

Dexamethasone for antitumor therapy is covered by dexamethasone of allergy prophylaxis on days 1,8 and 15. The use of methylprednisolone p.o. at a low dose (less than 20 mg) or equivalent should be considered on day 3 after infusion of daratumumab.

Montelukast in allergy prophylaxis is optional starting on day 8.

Levofloxacin infection prophylaxis (2 x 250mg/day) is recommended for the first 3 months after initiation of therapy in patients at high risk of infection (ESMO Guideline 02/2020).

In obstructive lung disease, the use of short- and long-acting bronchodilators and inhaled corticosteroids should be considered after daratumumab infusion. If no significant IRRs occur, inhaled agents may be discontinued after the first four infusions.

#### **Controls:**

- Blood count: on day 1 and subsequently weekly
- Day 1: IgG
- Coombs test Before starting treatment with daratumumab, patients should be typed and screened. Interference with indirect antiglobulin test (indirect Coombs test): Daratumumab binds to CD38, which is also found on erythrocytes. This may result in a positive indirect Coombs test up to 6 months after therapy. It should be noted that daratumumab bound to erythrocytes may mask the detection of antibodies against minor antigens in the serum of patients (risk of hemolysis).
- · Blood group Blood grouping before the 1st cycle
- Hepatitis (B) screening Risk of hepatitis B reactivation under daratumumab.
- X-ray thorax Bortezomib: as a baseline finding before possible pulmonary changes with therapy (pneumonitis, interstitial pneumonia, ARDS).
- Echocardiography, ECG Bortezomib: Occurrence/worsening of heart failure possible with therapy. Decrease in LVEF possible. Isolated cases of QT prolongation. Monitoring of LVEF and ECG during therapy.
- Blood pressure regular control under therapy
- Day 1: GOT, GPT, GGT, Bilirubin, AP, Cholinesterase Bortezomib: Patients with moderate or severe hepatic impairment should be treated with 0.7 mg/m², then increased to 1 mg/m² or further dose reduction to 0.5 mg/m² if necessary. Monitor liver enzymes during therapy.
- Day 1: Creatinine, glomerular filtration rate (GFR) Bortezomib: close monitoring of renal values in patients with renal impairment.
- Day 1-3,8-10,15-17: Infusion reactions Signs of nasal congestion, cough, chills, allergic rhinitis, throat irritation, dyspnea, nausea, bronchospasm, hypertension, and hypoxia

#### **Original author**

Palumbo A (2016)

## **Origin**

Department of Hematology, University of Turin, Italy, CASTOR

#### References

- Palumbo A, Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma. N Engl J Med 2016 Aug 25;375(8):754-66. doi: 10.1056/NEJMoa1606038. PMID: 27557302. [PMID]
- Richardson PG, A phase 2 study of bortezomib in relapsed, refractory myeloma. N Engl J Med 2003 Jun 26;348(26):2609-17. doi: 10.1056/NEJMoa030288. PMID: 12826635. [PMID]
- Nooka AK, Managing Infusion Reactions to New Monoclonal Antibodies in Multiple Myeloma: Daratumumab and Elotuzumab. J Oncol Pract 2018 Jul;14(7):414-422. doi: 10.1200/JOP.18.00143. PMID: 29996069. [PMID]
- Spencer A, Daratumumab plus bortezomib and dexamethasone versus bortezomib and dexamethasone in relapsed or refractory multiple myeloma: updated analysis of CASTOR. Haematologica 2018 Dec;103(12):2079-2087. doi: 10.3324/haematol.2018.194118. PMID: 30237264. [PMID]
- Palumbo A, How to manage neutropenia in multiple myeloma. Clin Lymphoma Myeloma Leuk 2012 Feb;12(1):5-11. doi: 10.1016/j.clml.2011.11.001. PMID: 22178143. [PMID]

#### Recommendations

- 07/2017: European Society for Medical Oncology
- 05/2020: National Comprehensive Cancer Network

#### BORT1.3/DRTM16/DEXA(20/20), MM, C1 PID 817 V2.1

## Important notice

The copyrighted protocols are treatment recommendations. The information contained in this compilation on cytostatic drugs, concomitant medication and other therapeutic procedures, as well as dosage and application information, is continuously reviewed with all due care by the authors and editors involved. Nevertheless, the publishers and authors do not assume any liability for the correctness - also with regard to possible printing errors.

The protocols may not be changed in terms of content.

Diagnosis, indication for therapy and treatment of malignant diseases must be carried out in each individual case by the hematologist and oncologist on his or her own responsibility. The treating physician is obligated to this personal responsibility to weigh in each case before a diagnostic or therapeutic measure, indication, contraindications, dosage and application under consideration of the specialized information or other documents of the manufacturers. This applies in particular to rarely used preparations or preparations that are new to the market.



The publishers and authors assume no liability for the accuracy of the contents. The application is at the own responsibility of the treating physician. ©Onkopti.