



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

Protocol-ID: 817 V2.1 (Short), 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 therapy
- Therapy 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/ μ l: very high (>41%)
- Anemia Hb below 8g/dl: moderate (6-15%)
- Diarrhea: CTC AE \geq 3-4: 4%
- Hypertension: CTC AE \geq 3-4: 7%
- Dyspnea: CTC AE \geq 3-4: 4%
- Fatigue: CTC AE \geq 3-4: 5%
- Neuropathy: CTC AE \geq 3-4: 5%
- Pneumonia: CTC AE \geq 3-4: 8%

Therapy

Hydration: Balanced Crystalloid Solution

HYD

Access: peripheral venous

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

AP

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)

CTX

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/m ² 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. Maximum 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. Maximum 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 below 18.5 or over 75 years of age received 20mg of dexamethasone 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/μl 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/μl						

Infection prophylaxis: Herpes prophylaxis

IP

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

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.

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](#)]
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- 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](#)]

Links

- Daratumumab: Risiko der Reaktivierung von Hepatitis B [[BfARM Risikoinf. Rote Hand etc.](#)]

Recommendations

- 07/2017: [European Society for Medical Oncology](#)
- 05/2020: [National Comprehensive Cancer Network](#)



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