



## 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 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/ $\mu$ l: very high (>41%)
- Anemia Hb below 8g/dl: moderate (6-15%)
- Diarrhea: CTC AE  $\circ$ 3-4: 4%
- Hypertension: CTC AE  $\circ$ 3-4: 7%
- Dyspnea: CTC AE  $\circ$ 3-4: 4%
- Fatigue: CTC AE  $\circ$ 3-4: 5%
- Neuropathy: CTC AE  $\circ$ 3-4: 5%
- Pneumonia: CTC AE  $\circ$ 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	<b>Dexamethasone</b>	20 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d1)
1	<b>Dimetinden</b>	4 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d1)
1	<b>Paracetamol</b>	1000 mg		p.o.		60 min before Daratumumab (d1)
1	<b>Montelukast</b>	10 mg		p.o.		60 min before Daratumumab (d1)
8	<b>Dexamethasone</b>	20 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d8)
8	<b>Dimetinden</b>	4 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d8)
8	<b>Paracetamol</b>	1000 mg		p.o.		60 min before Daratumumab (d8)
15	<b>Dexamethasone</b>	20 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d15)
15	<b>Dimetinden</b>	4 mg	NaCl 0.9% 50 ml	i.v.	5 min	60 min before Daratumumab (d15)
15	<b>Paracetamol</b>	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	<b>Bortezomib</b>	1.3 mg/m <sup>2</sup> BSA	none	subc	Bolus	Sequence
1	<b>Daratumumab</b>	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	<b>Daratumumab</b>	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	<b>Daratumumab</b>	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	<b>Dexamethasone</b>	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 &lt; 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	<b>Filgrastim</b>	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 <sup>2</sup> , 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	<b>Aciclovir</b>	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.

## 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/m<sup>2</sup>, then increased to 1 mg/m<sup>2</sup> or further dose reduction to 0.5 mg/m<sup>2</sup> 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

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## References

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## Recommendations

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

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