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

Protocol-ID: 817 V2.1 (Complete), 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/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 **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) **ANTX**

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. 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 2m², 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

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.

Cycle diagram

Hydration: Balanced Crystalloid Solution

	Week 1 / d							Week 2 / d							Week 3 / d						
Substance	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**
Balanced Crystalloid Solution (i.v.)	■																				
Balanced Crystalloid Solution (i.v.)								■													
Balanced Crystalloid Solution (i.v.)															■						

Allergy prophylaxis: Daratumumab allergy prophylaxis with dexamethasone

	Week 1 / d							Week 2 / d							Week 3 / d						
Substance	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**
Dexamethasone (i.v.)	■																				
Dimetinden (i.v.)	■																				
Paracetamol (p.o.)	■																				
Montelukast (p.o.)	■																				
Dexamethasone (i.v.)								■													
Dimetinden (i.v.)								■													
Paracetamol (p.o.)								■													
Dexamethasone (i.v.)															■						
Dimetinden (i.v.)															■						
Paracetamol (p.o.)															■						

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

	Week 1 / d							Week 2 / d							Week 3 / d						
Substance	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**
Bortezomib (subc)	■			■				■			■										
Daratumumab (i.v.)	■																				
Daratumumab (i.v.)								■													
Daratumumab (i.v.)															■						
Dexamethasone (p.o.)		■		■	■				■		■	■									

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

	Week 1 / d							Week 2 / d							Week 3 / d						
Substance	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**
Filgrastim (subc)		■	■		■	■	■		■	■		■	■	■		■	■	■	■		

Infection prophylaxis: Herpes prophylaxis

	Week 1 / d							Week 2 / d							Week 3 / d						
Substance	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**
Aciclovir (p.o.)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

Cycles

Cycle length 21 days, recommended cycles: 1

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

Dose adjustment

- **Aciclovir**
  - **for Renal Failure**: **Glomerular Filtration Rate (GFR)**
    Depending on creatinine clearance or serum creatinine, the dose may need to be adjusted (due to renal elimination of Aciclovir) (from summary of product characteristics)

Original indication

recurrent or refractory multiple myeloma

Original author

Palumbo A (2016)

Origin

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References

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- 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

Status

Valid since 2021-04-15, Version 2.1, last updated 2021-06-17

Last modification: V2.1: Cato test done. Insertion of hematopoietic growth factors module according to Palumbo et al. 2012. V2.0: Cato test done Montelukast added at day 1, adjustment of durations of Daratumumab, Protocol name changed, added note on dexamethasone dosing, V1.0: Cato test done. V0.1: Duration Daratumumab according to the SmPC.

Important notice