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Treatment With Velcade (Bortezomib) Plus Dexamethasone (VD) or VD Plus Cyclophosphamide or VD Plus Lenalidomide in Patients With Multiple Myeloma Stabilized After 4 Cycles of VD (SEQUENTIAL)

This study has been completed.

Sponsor:
Janssen-Cilag International NV

Information provided by (Responsible Party):
Janssen-Cilag International NV

ClinicalTrials.gov Identifier:
NCT00908232

First received: May 21, 2009
Last updated: January 14, 2015
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History of Changes

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Results First Received: May 4, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Multiple Myeloma
Interventions:	Drug: Cyclophosphamide Drug: Bortezomib Drug: Dexamethasone Drug: Lenalidomide

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
190 patients screened, 163 enrolled and received Bortezomib-Dexamethasone (VD) . Participants that completed cycles 1 to 4 were assessed for Response. Complete or Partial Responders were not randomized and continued on VD for cycles 5-8. Participants with Stable Disease (SD) were randomized to either VD, VDC, or VDR for cycles 5-8.

Reporting Groups

	Description
Cycle 1 to 4: Bortezomib + Dexamethasone (VD)	bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for 4 cycles
Stable Disease: Bortezomib + Dexamethasone (VD)	Stable disease after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 5 to 8
SD: Bortezomib+Dexamethasone+Cyclophosphamide (VDC)	Stable disease after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 and cyclophosphamide 500 mg, orally daily, days 1, 8 and 15 for cycle 5 to 8
SD: Bortezomib+Dexamethasone+Lenalidomide (VDR)	Stable disease after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8 and 11 in combination with dexamethasone 20 mg

	orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 and lenalidomide 10 mg orally daily from day 1 to day 14 for cycle 5 to 8

Participant Flow for 2 periods

Period 1: Cycle 1 to 4

	Cycle 1 to 4: Bortezomib + Dexamethasone (VD)	Stable Disease: Bortezomib + Dexamethasone (VD)	SD: Bortezomib+Dexamethasone+Cyclophosphamide (VDC)	SD: Bortezomib+Dexamethasone+Lenalidomide (VDR)
STARTED	163 [1]	0	0	0
COMPLETED	135 [2]	0	0	0
NOT COMPLETED	28	0	0	0
Death	5	0	0	0
Withdrawal by Subject	4	0	0	0
Progressive Disease	6	0	0	0
Adverse Event	12	0	0	0
not specified	1	0	0	0

[1] All participants started VD treatment for 4 cycles prior to local site response assessments
[2] Of those completed, 120 subjects were assessed for response, 117 w/ Response or SD continued.

Period 2: Randomization (Cycle 5) to Cycle 8

	Cycle 1 to 4: Bortezomib + Dexamethasone (VD)	Stable Disease: Bortezomib + Dexamethasone (VD)	SD: Bortezomib+Dexamethasone+Cyclophosphamide (VDC)	SD: Bortezomib+Dexamethasone+Lenalidomi (VDR)
STARTED	98 [1]	7	8	4
COMPLETED	63	4	7	4
NOT COMPLETED	35	3	1	0
Complete Response/Partial Response	1	0	0	0
Progressive Disease	5	0	0	0
Death	2	0	0	0
Withdrawal by Subject	4	0	1	0
Adverse Event	17	2	0	0
Physician Decision	2	0	0	0
Unknown	3	1	0	0
Protocol Violation	1	0	0	0

[1] Responding patients (not randomized) who received 4 more cycles of VD

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
modified Intent to Treat Population consisting of all 163 participants with at least 1 dose and 1 post baseline efficacy assessment.: Complete and Partial Responders (non-randomized), n=144. Stable Disease (randomized to VD, VDC, and VDL), n=19.

Reporting Groups

	Description
All Study Participants	bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for 4 cycles

Baseline Measures

	All Study Participants
Number of Participants [units: participants]	**163**
Age [units: years] Mean (Standard Deviation)	**63.7 (11.04)**
Gender [units: participants]	
Female	**77**
Male	**86**
Region of Enrollment [units: participants]	
France	**20**
Germany	**15**
Greece	**23**
Hungary	**2**
Lithuania	**9**
Poland	**19**
Serbia	**15**
Spain	**20**
Turkey	**19**
United Kingdom	**21**

Outcome Measures

Hide All Outcome Measures

1. Primary: Overall Best Confirmed Response [Time Frame: Prior to treatment at day 1 of each cycle and at the end of treatment (day 21 of cycle 8), up to 168 days]

Measure Type	Primary
Measure Title	Overall Best Confirmed Response
Measure Description	Overall Best Confirmed Response is the best Overall Response Rate with borezomib-dexamathasone (+/- cyclophosphamide or lenalidomide) recorded between baseline and end of treatment. Response was assessed using the International Myeloma working Group (IMWG) Uniform Response Criteria and validated by an Independent Monitoring Committee.
Time Frame	Prior to treatment at day 1 of each cycle and at the end of treatment (day 21 of cycle 8), up to 168 days
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
mITT: All patients with at least 1 dose and 1 post baseline assessment. Low powered study because necessary sample size for the randomized part could not be reached. Thus, data were analyzed and reported by combining the randomized groups with SD, (n=19). Data are missing for 21 patients in the non-randomized CR/PR group, n=123.

Reporting Groups

	Description
Complete to Partial Response: Bortezomib + Dexamethasone	Complete, very good partial or partial response after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 5 to 8
Stable Disease After 4 Cycles: VD, VDC, VDL	Patients were treated with bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally on days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 1 to 4. Patients with stable disease after these 4 cycles, were randomized at the start of cycle 5 and received either bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally, on days 1, 2, 4, 5, 8, 9, 11, 12 alone or in combination with cyclophosphamide 500 mg orally on days 1, 8 and 15 or lenalidomide 10 mg orally daily from day 1 to day 14 for cycle 5 to 8

Measured Values

	Complete to Partial Response: Bortezomib + Dexamethasone	**Stable Disease After 4 Cycles: VD, VDC, VDL**
Number of Participants Analyzed [units: participants]	**123**	**19**
Overall Best Confirmed Response [units: number of participants]	**101**	**6**

No statistical analysis provided for Overall Best Confirmed Response

2. Secondary: Median Time to First Confirmed Response [Time Frame: At Day 1 of each treatment cycle, at the End of Treatment visit until there is evidence of Progressive Disease or relapse from Complete Response (CR), up to 168 days]

Measure Type	Secondary
Measure Title	Median Time to First Confirmed Response
Measure Description	Time from start of treatment to the date of the first documentation of a confirmed response. Estimated using the Kaplan-Meier method. Response was assessed using the International Myeloma Working Group (IMWG) Uniform Response Criteria and validated by an Independent Monitoring Committee.
Time Frame	At Day 1 of each treatment cycle, at the End of Treatment visit until there is evidence of Progressive Disease or relapse from Complete Response (CR), up to 168 days
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
mITT: All patients with at least 1 dose and 1 post baseline assessment. The non- randomized CR/PR group, n=144 for Time to First confirmed Response. Low powered study because necessary sample size for the randomized part could not be reached. Thus, data were analyzed and reported by combining the randomized groups with SD, (n=19).

Reporting Groups

	Description
Complete to Partial Response: Bortezomib + Dexamethasone	Complete, very good partial or partial response after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 5 to 8

Stable Disease After 4 Cycles: VD, VDC, VDL	Patients were treated with bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally on days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 1 to 4. Patients with stable disease after these 4 cycles, were randomized at the start of cycle 5 and received either bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally, on days 1, 2, 4, 5, 8, 9, 11, 12 alone or in combination with cyclophosphamide 500 mg orally on days 1, 8 and 15 or lenalidomide 10 mg orally daily from day 1 to day 14 for cycle 5 to 8

Measured Values

	Complete to Partial Response: Bortezomib + Dexamethasone	**Stable Disease After 4 Cycles: VD, VDC, VDL**
Number of Participants Analyzed [units: participants]	**144**	**19**
Median Time to First Confirmed Response [units: days] Median (95% Confidence Interval)	**43.0 (43.0 to 58.0)**	**NA** [1]

[1] It is not possible to estimate the median time to first response or upper limit for the CI. This is because of the 19 subjects only 6 have an event, the majority is censored.

No statistical analysis provided for Median Time to First Confirmed Response

3. Secondary: Progression Free Survival [Time Frame: At Day 1 of each treatment cycle, at the End of Treatment visit until there is evidence of Progressive Disease or relapse from Complete Response (CR). Median Follow-Up of 16.9 months]

Measure Type	Secondary
Measure Title	Progression Free Survival
Measure Description	Time from start of treatment to date of disease progression, relapse from CR or death. Estimated using the kaplan-meier method. Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.0), as a 20% increase in the sum of the longest diameter of target lesions, or a measurable increase in a non-target lesion, or the appearance of new lesions", or similar definition as accurate and appropriate.
Time Frame	At Day 1 of each treatment cycle, at the End of Treatment visit until there is evidence of Progressive Disease or relapse from Complete Response (CR). Median Follow-Up of 16.9 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
mITT: All patients with at least 1 dose and 1 post baseline assessment. The non-randomized CR/PR group, n=144. Low powered study because necessary sample size for the randomized part could not be reached. Thus, data were analyzed and reported by combining the randomized groups with SD, (n=19).

Reporting Groups

	Description
Complete to Partial Response: Bortezomib + Dexamethasone	Complete, very good partial or partial response after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 5 to 8
Stable Disease After 4 Cycles: VD, VDC, VDL	Patients were treated with bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally on days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 1 to 4. Patients with stable disease after these 4 cycles, were randomized at the start of cycle 5 and received either bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally, on days 1, 2, 4, 5, 8, 9, 11, 12 alone or in combination with cyclophosphamide 500 mg orally on days 1, 8 and 15 or lenalidomide 10 mg orally daily from day 1 to day 14 for cycle 5 to 8

Measured Values

	Complete to Partial Response: Bortezomib + Dexamethasone	Stable Disease After 4 Cycles: VD, VDC, VDL
Number of Participants Analyzed [units: participants]	**144**	**19**
Progression Free Survival [units: days] Median (95% Confidence Interval)	**311.0 (224.0 to 424.0)**	**214.0 (198.0 to 234.0)**

No statistical analysis provided for Progression Free Survival

4. Secondary: Time to Progression [Time Frame: At Day 1 of each treatment cycle, at the End of Treatment visit until there is evidence of Progressive Disease or relapse from Complete Response (CR), Median Follow-up of 16.9 months]

Measure Type	Secondary
Measure Title	Time to Progression
Measure Description	Is calculated as the time from start of treatment to the date of the first observation of disease progression or relapse from CR. Deaths owing to causes other than progression not counted, but censored. Subjects who withdraw from the study or die will be censored at the time of last disease assessment. Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.0).
Time Frame	At Day 1 of each treatment cycle, at the End of Treatment visit until there is evidence of Progressive Disease or relapse from Complete Response (CR), Median Follow-up of 16.9 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
mITT: All patients with at least 1 dose and 1 post baseline assessment. The non-randomized CR/PR group, n=144 for Time to First confirmed Response. Low powered study because necessary sample size for the randomized part could not be reached. Thus, data were analyzed and reported by combining the randomized groups with SD, (n=19).

Reporting Groups

	Description
Complete to Partial Response: Bortezomib + Dexamethasone	Complete, very good partial or partial response after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 5 to 8
Stable Disease After 4 Cycles: VD, VDC, VDL	Patients were treated with bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally on days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 1 to 4. Patients with stable disease after these 4 cycles, were randomized at the start of cycle 5 and received either bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally, on days 1, 2, 4, 5, 8, 9, 11, 12 alone or in combination with cyclophosphamide 500 mg orally on days 1, 8 and 15 or lenalidomide 10 mg orally daily from day 1 to day 14 for cycle 5 to 8

Measured Values

	Complete to Partial Response: Bortezomib + Dexamethasone	Stable Disease After 4 Cycles: VD, VDC, VDL
Number of Participants Analyzed [units: participants]	**144**	**19**
Time to Progression [units: days] Median (95% Confidence Interval)	**366.0 (281.0 to 475.0)**	**214.0 (198.0 to 234.0)**

No statistical analysis provided for Time to Progression

5. Secondary: One Year Survival [Time Frame: At each visit from baseline to end of treatment. After treatment, monthly visit until progression or relapse or until the start of alternative MMY therapy, up to 1 year]

Measure Type	Secondary
Measure Title	One Year Survival
Measure Description	Percent Probability of Survival at 1 year from the start of treatment, estimated using Kaplan-Meier analysis.
Time Frame	At each visit from baseline to end of treatment. After treatment, monthly visit until progression or relapse or until the start of alternative MMY therapy, up to 1 year
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
mITT: All patients with at least 1 dose and 1 post baseline assessment. The non- randomized CR/PR group, n=144 for Time to First confirmed Response. Low powered study because necessary sample size for the randomized part could not be reached. Thus, data were analyzed and reported by combining the randomized groups with SD, (n=19).

Reporting Groups

	Description
Complete to Partial Response: Bortezomib + Dexamethasone	Complete, very good partial or partial response after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 5 to 8
Stable Disease After 4 Cycles: VD, VDC, VDL	Patients were treated with bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally on days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 1 to 4. Patients with stable disease after these 4 cycles, were randomized at the start of cycle 5 and received either bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally, on days 1, 2, 4, 5, 8, 9, 11, 12 alone or in combination with cyclophosphamide 500 mg orally on days 1, 8 and 15 or lenalidomide 10 mg orally daily from day 1 to day 14 for cycle 5 to 8

Measured Values

	Complete to Partial Response: Bortezomib + Dexamethasone	**Stable Disease After 4 Cycles: VD, VDC, VDL**
Number of Participants Analyzed [units: participants]	**144**	**19**
One Year Survival [units: percent probability] Number (95% Confidence Interval)	**80 (73 to 87)**	**89 (62 to 97)**

No statistical analysis provided for One Year Survival

6. Secondary: Overall Survival [Time Frame: At each visit from baseline to end of treatment. After treatment, monthly visit until progression or relapse or until the start of alternative MMY therapy. Further follow up by monthly phone call until the last patient was treated and followed for 1 year]

Measure Type	Secondary
Measure Title	Overall Survival
Measure Description	Is defined as the time interval from start of treatment to the date of death due to any cause. In the absence of confirmation of death (including subjects lost to follow-up), survival time will be censored at the last date the subject is known to be alive
Time Frame	At each visit from baseline to end of treatment. After treatment, monthly visit until progression or relapse or until the start of alternative MMY therapy. Further follow up by monthly phone call until the last patient was treated and followed for 1 year

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
mITT: All patients with at least 1 dose and 1 post baseline assessment. The non-randomized CR/PR group, n=144 for Time to First confirmed Response. Low powered study because necessary sample size for the randomized part could not be reached. Thus, data were analyzed and reported by combining the randomized groups with SD, (n=19).

Reporting Groups

	Description
Complete to Partial Response: Bortezomib + Dexamethasone	Complete, very good partial or partial response after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 5 to 8
Stable Disease After 4 Cycles: VD, VDC, VDL	Patients were treated with bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally on days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 1 to 4. Patients with stable disease after these 4 cycles, were randomized at the start of cycle 5 and received either bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally, on days 1, 2, 4, 5, 8, 9, 11, 12 alone or in combination with cyclophosphamide 500 mg orally on days 1, 8 and 15 or lenalidomide 10 mg orally daily from day 1 to day 14 for cycle 5 to 8

Measured Values

	Complete to Partial Response: Bortezomib + Dexamethasone	Stable Disease After 4 Cycles: VD, VDC, VDL
Number of Participants Analyzed [units: participants]	**144**	**19**
Overall Survival [units: days] Median (95% Confidence Interval)	**NA** [1]	**NA** [1]

[1] this value could not be calculated due to the limited number of events

No statistical analysis provided for Overall Survival

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	From signing of informed consent until 30 days after the last dose of study medication (approximately 7 months) or longer if considered related to study medication.
Additional Description	Due to the high response rate of the bortezomib-dexmathasone (VD) in the first four cycles, not enough patients could be randomized to the sequential therapies in cycles 5-8 to allow us to evaluate safety data according randomization or intervention. Thus, adverse events were analyzed by combining (randomized) participants with SD After 4 Cycles.

Reporting Groups

	Description
Complete to Partial Response: Bortezomib + Dexamethasone	Complete, very good partial or partial response after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 5 to 8
Stable Disease After 4 Cycles: VD, VDC, VDL	Patients were treated with bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally on days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 1 to 4. Patients with stable disease after these 4 cycles, were randomized at the start of cycle 5 and received either bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally, on

	days 1, 2, 4, 5, 8, 9, 11, 12 alone or in combination with cyclophosphamide 500 mg orally on days 1, 8 and 15 or lenalidomide 10 mg orally daily from day 1 to day 14 for cycle 5 to 8

Serious Adverse Events

	Complete to Partial Response: Bortezomib + Dexamethasone	Stable Disease After 4 Cycles: VD, VDC, VDL
Total, serious adverse events		
# participants affected / at risk	**59/144 (40.97%)**	**6/19 (31.58%)**
Blood and lymphatic system disorders		
Thrombocytopenia [*1]		
# participants affected / at risk	**6/144 (4.17%)**	**0/19 (0.00%)**
# events	**7**	**0**
Anaemia [*1]		
# participants affected / at risk	**1/144 (0.69%)**	**0/19 (0.00%)**
# events	**2**	**0**
Cardiac disorders		
Cardiac Failure [*1]		
# participants affected / at risk	**3/144 (2.08%)**	**1/19 (5.26%)**
# events	**3**	**3**
Myocardial Infarction [*1]		
# participants affected / at risk	**3/144 (2.08%)**	**0/19 (0.00%)**
# events	**3**	**0**
Atrial Fibrilation [*1]		
# participants affected / at risk	**3/144 (2.08%)**	**0/19 (0.00%)**
# events	**3**	**0**
Agina pectoris [*1]		
# participants affected / at risk	**1/144 (0.69%)**	**0/19 (0.00%)**
# events	**1**	**0**
Cardiac Failure Congestive [*1]		
# participants affected / at risk	**1/144 (0.69%)**	**0/19 (0.00%)**
# events	**1**	**0**
Cardio-Respiratory Arrest [*1]		
# participants affected / at risk	**1/144 (0.69%)**	**0/19 (0.00%)**
# events	**1**	**0**
Gastrointestinal disorders		
Diarrhoea [*1]		
# participants affected / at risk	**4/144 (2.78%)**	**0/19 (0.00%)**
# events	**4**	**0**
Colitis [*1]		
# participants affected / at risk	**2/144 (1.39%)**	**0/19 (0.00%)**
# events	**2**	**0**
Constipation [*1]		
# participants affected / at risk	**2/144 (1.39%)**	**0/19 (0.00%)**
# events	**2**	**0**
Dyspepsia [*1]		
# participants affected / at risk	**2/144 (1.39%)**	**0/19 (0.00%)**
# events	**2**	**0**
Abdominal Discomfort [*1]		
# participants affected / at risk	**1/144 (0.69%)**	**0/19 (0.00%)**
# events	**1**	**0**
Abdominal Mass [*1]		
# participants affected / at risk	**1/144 (0.69%)**	**0/19 (0.00%)**

# events	1	0
Abdominal Pain [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Colitis Ischaemic [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Gastritis [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Ileus [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Nausea [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	2	0
Pancreatitis [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Small Intestinal Obstruction [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Vomiting [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
General disorders		
Pyrexia [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	3	1
Oedema Peripheral [*1]		
# participants affected / at risk	2/144 (1.39%)	1/19 (5.26%)
# events	2	1
Asthenia [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Hepatobiliary disorders		
Cholelithiasis [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Infections and infestations		
Pneumonia [*1]		
# participants affected / at risk	9/144 (6.25%)	0/19 (0.00%)
# events	10	0
Lower Respiratory Tract Infection [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	3	1
Bronchitis [*1]		
# participants affected / at risk	3/144 (2.08%)	0/19 (0.00%)
# events	4	0
Bronchopneumonia [*1]		
# participants affected / at risk	1/144 (0.69%)	1/19 (5.26%)
# events	1	1
Influenza [*1]		

# participants affected / at risk	2/144 (1.39%)	0/19 (0.00%)
# events	2	0
Subcutaneous Abscess [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Cellulitis [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	2	0
Clostridium Difficile Colitis [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Gastroenteritis Rotavirus [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Hepatitis B [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Herpes Zoster [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Peritonsillar Abscess [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Pneumomonia Pneumococcal [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Respiratory Tract Infection [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Sepsis [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Septic Shock [*1]		
# participants affected / at risk	2/144 (1.39%)	0/19 (0.00%)
# events	2	0
Staphylococcal Infection [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Upper Respiratory Tract Infection [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Urinary Tract Infection [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Viral Infection [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Chest Wall Abscess [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Injury, poisoning and procedural complications		
Cervical Vertebral Fraction [*1]		

# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Facial Bones Fracture [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	3	0
Femoral Neck Fracture [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Femur Fracture [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Fracture [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Ligament Injury [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Investigations		
Liver Function Test Abnormal [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Metabolism and nutrition disorders		
Dehydration [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Hypokalaemia [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Hyponatraemia [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Hypovolaemia [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Musculoskeletal and connective tissue disorders		
Back Pain [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Osteolysis [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Nervous system disorders		
Cerebellar Infarction [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Convulsion [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Paraesthesia [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Polyneuropathy [*1]		

# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Syncope [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Transient Ischemic Attack [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Psychiatric disorders		
Depression [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Renal and urinary disorders		
Renal failure acute [*1]		
# participants affected / at risk	2/144 (1.39%)	0/19 (0.00%)
# events	2	0
Renal failure [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Urinary Retention [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Renal Impairment [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Oliguria [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Respiratory, thoracic and mediastinal disorders		
Dyspnoea [*1]		
# participants affected / at risk	1/144 (0.69%)	1/19 (5.26%)
# events	1	1
Pulmonary Oedema [*1]		
# participants affected / at risk	2/144 (1.39%)	0/19 (0.00%)
# events	2	0
Acute Pulmonary Oedema [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Acute Respiratory Failure [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Dyspnoea exertional [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Hypoxia [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Pulmonary fibrosis [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Sleep Apnoea Syndrome [*1]		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)

# events	1	0
Upper Respiratory Tract Inflammation * 1		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Acute Respiratory Distress Syndrome * 1		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Skin and subcutaneous tissue disorders		
Urticaria * 1		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	2	0
Vascular disorders		
Hypotension * 1		
# participants affected / at risk	3/144 (2.08%)	0/19 (0.00%)
# events	3	0
Orthostatic Hypotension * 1		
# participants affected / at risk	2/144 (1.39%)	0/19 (0.00%)
# events	3	0
Aortic Aneurysm * 1		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Aortic Stenosis * 1		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Arterial Rupture * 1		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0
Deep Vein Thrombosis * 1		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Shock Haemorrhagic * 1		
# participants affected / at risk	1/144 (0.69%)	0/19 (0.00%)
# events	1	0

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA (11.0)

Other Adverse Events

Hide Other Adverse Events

Time Frame	From signing of informed consent until 30 days after the last dose of study medication (approximately 7 months) or longer if considered related to study medication.
Additional Description	Due to the high response rate of the bortezomib-dexmathasone (VD) in the first four cycles, not enough patients could be randomized to the sequential therapies in cycles 5-8 to allow us to evaluate safety data according randomization or intervention. Thus, adverse events were analyzed by combining (randomized) participants with SD After 4 Cycles.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Complete to Partial Response: Bortezomib + Dexamethasone	Complete, very good partial or partial response after 4 cycles bortezomib + dexamethasone: bortezomib 1.3 mg/m2 IV bolus on Day 1, 4, 8, 11 in

	combination with dexamethasone 20 mg orally daily, on Days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 5 to 8
Stable Disease After 4 Cycles: VD, VDC, VDL	Patients were treated with bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally on days 1, 2, 4, 5, 8, 9, 11, 12 for cycle 1 to 4. Patients with stable disease after these 4 cycles, were randomized at the start of cycle 5 and received either bortezomib 1.3 mg/m2 IV bolus on day 1, 4, 8 and 11 in combination with dexamethasone 20 mg orally, on days 1, 2, 4, 5, 8, 9, 11, 12 alone or in combination with cyclophosphamide 500 mg orally on days 1, 8 and 15 or lenalidomide 10 mg orally daily from day 1 to day 14 for cycle 5 to 8

Other Adverse Events

	Complete to Partial Response: Bortezomib + Dexamethasone	Stable Disease After 4 Cycles: VD, VDC, VDL
Total, other (not including serious) adverse events		
# participants affected / at risk	**137/144 (95.14%)**	**19/19 (100.00%)**
Blood and lymphatic system disorders		
Thrombocytopenia [*1]		
# participants affected / at risk	**52/144 (36.11%)**	**8/19 (42.11%)**
# events	**216**	**22**
Anaemia [*1]		
# participants affected / at risk	**29/144 (20.14%)**	**6/19 (31.58%)**
# events	**79**	**14**
Neutropenia [*1]		
# participants affected / at risk	**10/144 (6.94%)**	**2/19 (10.53%)**
# events	**20**	**7**
Leukopenia [*1]		
# participants affected / at risk	**8/144 (5.56%)**	**1/19 (5.26%)**
# events	**37**	**1**
Leukocytosis [*1]		
# participants affected / at risk	**8/144 (5.56%)**	**0/19 (0.00%)**
# events	**11**	**0**
Lymphocytosis [*1]		
# participants affected / at risk	**0/144 (0.00%)**	**1/19 (5.26%)**
# events	**0**	**1**
Cardiac disorders		
Atrial fibrillation [*1]		
# participants affected / at risk	**3/144 (2.08%)**	**2/19 (10.53%)**
# events	**3**	**3**
Tachycardia [*1]		
# participants affected / at risk	**2/144 (1.39%)**	**1/19 (5.26%)**
# events	**2**	**1**
Sinus tachycardia [*1]		
# participants affected / at risk	**1/144 (0.69%)**	**1/19 (5.26%)**
# events	**1**	**1**
Palpitations [*1]		
# participants affected / at risk	**0/144 (0.00%)**	**1/19 (5.26%)**
# events	**0**	**1**
Eye disorders		
Conjunctivitis [*1]		
# participants affected / at risk	**8/144 (5.56%)**	**2/19 (10.53%)**
# events	**10**	**3**
Lacrimation increased [*1]		
# participants affected / at risk	**1/144 (0.69%)**	**1/19 (5.26%)**

# events	1	1
Gastrointestinal disorders		
Constipation [*1]		
# participants affected / at risk	45/144 (31.25%)	5/19 (26.32%)
# events	81	6
Diarrhoea [*1]		
# participants affected / at risk	45/144 (31.25%)	5/19 (26.32%)
# events	66	5
Nausea [*1]		
# participants affected / at risk	16/144 (11.11%)	3/19 (15.79%)
# events	23	5
Abdominal Pain [*1]		
# participants affected / at risk	8/144 (5.56%)	2/19 (10.53%)
# events	8	2
Dyspepsia [*1]		
# participants affected / at risk	11/144 (7.64%)	1/19 (5.26%)
# events	15	2
Vomiting [*1]		
# participants affected / at risk	10/144 (6.94%)	1/19 (5.26%)
# events	11	1
Flatulence [*1]		
# participants affected / at risk	4/144 (2.78%)	1/19 (5.26%)
# events	4	1
Abdominal distension [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	3	1
Toothache [*1]		
# participants affected / at risk	1/144 (0.69%)	2/19 (10.53%)
# events	1	2
Stomach discomfort [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
General disorders		
Oedema Peripheral [*1]		
# participants affected / at risk	38/144 (26.39%)	5/19 (26.32%)
# events	49	11
Fatigue [*1]		
# participants affected / at risk	37/144 (25.69%)	0/19 (0.00%)
# events	62	0
Asthenia [*1]		
# participants affected / at risk	29/144 (20.14%)	4/19 (21.05%)
# events	36	5
Pyrexia [*1]		
# participants affected / at risk	15/144 (10.42%)	4/19 (21.05%)
# events	15	12
Chest discomfort [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Generalised oedema [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Localised oedema [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)

# events	0	1
Hepatobiliary disorders		
Hepatic lesion [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Immune system disorders		
Seasonal allergy [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Infections and infestations		
Bronchitis [*1]		
# participants affected / at risk	13/144 (9.03%)	3/19 (15.79%)
# events	17	3
Herpes Zoster [*1]		
# participants affected / at risk	12/144 (8.33%)	3/19 (15.79%)
# events	12	3
Upper Respiratory Tract Infection [*1]		
# participants affected / at risk	12/144 (8.33%)	2/19 (10.53%)
# events	17	2
Nasopharyngitis [*1]		
# participants affected / at risk	9/144 (6.25%)	1/19 (5.26%)
# events	11	1
Oral Candidiasis [*1]		
# participants affected / at risk	8/144 (5.56%)	2/19 (10.53%)
# events	10	4
Urinary tract infection [*1]		
# participants affected / at risk	5/144 (3.47%)	1/19 (5.26%)
# events	5	3
Lower respiratory tract infection [*1]		
# participants affected / at risk	4/144 (2.78%)	1/19 (5.26%)
# events	4	1
Respiratory tract infection [*1]		
# participants affected / at risk	4/144 (2.78%)	1/19 (5.26%)
# events	4	1
Cellulitis [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	6	1
Oral herpes [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	3	1
Oral infection [*1]		
# participants affected / at risk	1/144 (0.69%)	1/19 (5.26%)
# events	1	1
Injury, poisoning and procedural complications		
Limb injury [*1]		
# participants affected / at risk	1/144 (0.69%)	1/19 (5.26%)
# events	1	1
Excoriation [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Injury [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)

# events	0	1
Investigations		
Platelet count decreased [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	3	1
Haemoglobin decreased [*1]		
# participants affected / at risk	1/144 (0.69%)	1/19 (5.26%)
# events	6	1
Metabolism and nutrition disorders		
Hyperglycaemia [*1]		
# participants affected / at risk	11/144 (7.64%)	3/19 (15.79%)
# events	11	4
Anorexia [*1]		
# participants affected / at risk	6/144 (4.17%)	1/19 (5.26%)
# events	6	1
Hypocalcaemia [*1]		
# participants affected / at risk	6/144 (4.17%)	1/19 (5.26%)
# events	8	1
Hypercalcaemia [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	3	1
Increased appetite [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Musculoskeletal and connective tissue disorders		
Back Pain [*1]		
# participants affected / at risk	21/144 (14.58%)	3/19 (15.79%)
# events	28	4
Arthralgia [*1]		
# participants affected / at risk	14/144 (9.72%)	0/19 (0.00%)
# events	15	0
Bone Pain [*1]		
# participants affected / at risk	11/144 (7.64%)	1/19 (5.26%)
# events	19	3
Pain in Extremity [*1]		
# participants affected / at risk	14/144 (9.72%)	2/19 (10.53%)
# events	25	3
Muscular Weakness [*1]		
# participants affected / at risk	11/144 (7.64%)	1/19 (5.26%)
# events	13	1
Muscle spasms [*1]		
# participants affected / at risk	5/144 (3.47%)	2/19 (10.53%)
# events	6	3
Myalgia [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	3	1
Sensation of heaviness [*1]		
# participants affected / at risk	2/144 (1.39%)	1/19 (5.26%)
# events	2	1
Monarthritis [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1

Osteonecrosis [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Nervous system disorders		
Peripheral Sensory Neuropathy [*1]		
# participants affected / at risk	29/144 (20.14%)	4/19 (21.05%)
# events	80	11
Polyneuropathy [*1]		
# participants affected / at risk	26/144 (18.06%)	2/19 (10.53%)
# events	40	5
Neuralgia [*1]		
# participants affected / at risk	22/144 (15.28%)	4/19 (21.05%)
# events	33	6
Neuropathy Peripheral [*1]		
# participants affected / at risk	21/144 (14.58%)	0/19 (0.00%)
# events	42	0
Paraesthesia [*1]		
# participants affected / at risk	19/144 (13.19%)	2/19 (10.53%)
# events	27	2
Hypoaesthesia [*1]		
# participants affected / at risk	13/144 (9.03%)	2/19 (10.53%)
# events	19	3
Dizziness [*1]		
# participants affected / at risk	13/144 (9.03%)	1/19 (5.26%)
# events	17	2
Headache [*1]		
# participants affected / at risk	9/144 (6.25%)	0/19 (0.00%)
# events	13	0
Balance disorder [*1]		
# participants affected / at risk	2/144 (1.39%)	1/19 (5.26%)
# events	3	1
Trigeminal Neuralgia [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Psychiatric disorders		
Insomnia [*1]		
# participants affected / at risk	15/144 (10.42%)	3/19 (15.79%)
# events	19	4
Confusional state [*1]		
# participants affected / at risk	5/144 (3.47%)	1/19 (5.26%)
# events	5	1
Anxiety [*1]		
# participants affected / at risk	1/144 (0.69%)	1/19 (5.26%)
# events	1	1
Nervousness [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Reproductive system and breast disorders		
Prostatitis [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Respiratory, thoracic and mediastinal disorders		

Cough [*1]		
# participants affected / at risk	22/144 (15.28%)	4/19 (21.05%)
# events	27	5
Dyspnoea [*1]		
# participants affected / at risk	9/144 (6.25%)	3/19 (15.79%)
# events	11	4
Dyspnoea Exertional [*1]		
# participants affected / at risk	9/144 (6.25%)	1/19 (5.26%)
# events	10	1
Oropharyngeal pain [*1]		
# participants affected / at risk	4/144 (2.78%)	4/19 (21.05%)
# events	4	4
Productive cough [*1]		
# participants affected / at risk	7/144 (4.86%)	1/19 (5.26%)
# events	10	1
Epistaxis [*1]		
# participants affected / at risk	2/144 (1.39%)	1/19 (5.26%)
# events	2	1
Obstructive airways disorder [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Skin and subcutaneous tissue disorders		
Rash [*1]		
# participants affected / at risk	6/144 (4.17%)	2/19 (10.53%)
# events	6	3
Night sweats [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	3	1
Dermatitis allergic [*1]		
# participants affected / at risk	1/144 (0.69%)	1/19 (5.26%)
# events	1	1
Pruritus generalised [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Vascular disorders		
Hypotension [*1]		
# participants affected / at risk	11/144 (7.64%)	1/19 (5.26%)
# events	17	1
Orthostatic Hypotension [*1]		
# participants affected / at risk	9/144 (6.25%)	0/19 (0.00%)
# events	15	0
Flushing [*1]		
# participants affected / at risk	2/144 (1.39%)	2/19 (10.53%)
# events	3	2
Haematoma [*1]		
# participants affected / at risk	1/144 (0.69%)	1/19 (5.26%)
# events	1	1
Aortic elongation [*1]		
# participants affected / at risk	0/144 (0.00%)	1/19 (5.26%)
# events	0	1
Hypertension [*1]		
# participants affected / at risk	3/144 (2.08%)	1/19 (5.26%)
# events	3	1

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA (11.0)

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
The response rate of bortezomib in combination with dexamethasone after 4 cycles was much higher than originally assumed. Therefore the sample size of the randomized groups is too small for further statistical analysis.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☑ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

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Responsible Party:	Janssen-Cilag International NV
ClinicalTrials.gov Identifier:	NCT00908232 History of Changes
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Study First Received:	May 21, 2009
Results First Received:	May 4, 2012
Last Updated:	January 14, 2015
Health Authority:	Belgium: Ministry of Social Affairs, Public Health and the Environment

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