

2. SYNOPSIS

Name of Sponsor/Company: Celgene Corporation	Individual Study Table Referring to Part of the Dossier Volume: Page:	<i>(For National Authority Use Only)</i>
Name of Finished Product: Revlimid® Capsules		
Name of Active Ingredient: Lenalidomide (CC-5013)		
Title of study: A Multicenter, Randomized, Parallel-group, Double-blind, Placebo-controlled Study of CC-5013 Plus Dexamethasone Versus Dexamethasone Alone in Previously Treated Subjects With Multiple Myeloma		
Coordinating principal investigator: [REDACTED]		
Investigators: Refer to Appendix 16.1.4 .		
Study centers: This study is being conducted at 55 sites in Australia, Europe, and Israel. Subjects were randomized in 50 sites (6 in Australia; 1 in Austria; 2 in Belgium; 5 in France; 6 in Germany; 1 in Greece; 3 in Israel; 6 in Italy; 3 in Poland; 6 in Spain; 2 in Switzerland; 5 in Ukraine; and 4 in the United Kingdom).		
Publication (reference): Dimopoulos M, Spencer A, Attal M, Prince HM, Harousseau J-L, Dmoszynska A, et al. Lenalidomide plus dexamethasone for relapsed or refractory multiple myeloma. <i>N Eng J Med</i> 2007;357:2123-32.		
Studied period (years): Date first patient enrolled: 22 Sep 2003 Date last patient completed: Ongoing study	Phase of development: 3	
Objectives: Primary: To compare the efficacy of oral lenalidomide in combination with oral pulse high-dose dexamethasone with that of placebo and oral pulse high-dose dexamethasone as treatment for subjects with relapsed or refractory multiple myeloma. Secondary: To compare the safety of oral lenalidomide in combination with oral pulse high-dose dexamethasone with that of placebo and oral pulse high-dose dexamethasone as treatment for subjects with relapsed or refractory multiple myeloma.		
Methodology: This study is phase 3, multicenter, double-blind, placebo-controlled, parallel-group study of the efficacy and safety of lenalidomide plus oral pulse high-dose dexamethasone and oral pulse high-dose dexamethasone therapy alone in subjects with relapsed or refractory multiple myeloma. The study was unblinded after a prespecified interim analysis demonstrated a highly significant treatment benefit in favor of the lenalidomide/dexamethasone combination. Eligible subjects were randomized in a 1:1 ratio to 1 of 2 treatment groups: <ul style="list-style-type: none"> • Lenalidomide plus oral pulse high-dose dexamethasone • Placebo plus oral pulse high-dose dexamethasone Subjects in the lenalidomide/dexamethasone group took 25 mg of lenalidomide orally once daily on Days 1 to 21 and a matching placebo capsule once daily on Days 22 to 28 of each 28-day cycle. Subjects in the placebo/dexamethasone group took 1 placebo capsule on Days 1 to 28 of each 28-day cycle. Subjects in both treatment groups took 40 mg of dexamethasone orally once daily on Days 1 to 4, 9 to 12, and 17 to 20 of each 28-day cycle for the first 4 cycles of therapy. Beginning with Cycle 5, the dose of dexamethasone was reduced to 40 mg orally once daily on Days 1 to 4 every 28 days for the remaining cycles. To maintain balance between the 2 treatment groups in the allocation of subjects with differing prognoses for the time to progression (TTP) and survival analyses, randomization was stratified by the following prognostic features: 1) baseline serum beta2 (β ₂)-microglobulin level (≤ 2.5 mg/L versus > 2.5 mg/L); 2) prior therapy with high-dose chemotherapy (HDT) and supported by stem cell transplant (SCT) versus no prior treatment with HDT or SCT; and 3) number of prior antimyeloma regimens (1 versus 2 or more). Treatment continued until disease progression occurred or until treatment was discontinued for another reason. Adjustments were made in the lenalidomide and/or dexamethasone dose for each subject based on tolerability. The lowest-allowable dose of lenalidomide was 5 mg daily (or 1 matching placebo capsule) on Days 1 to 21 of each 28-day cycle, and the lowest-allowable dose of dexamethasone was 20 mg daily for 4 days every 4 weeks. Subjects who could not tolerate these doses were discontinued from the study unless they had achieved a plateau phase of response to therapy. Subjects who achieved a plateau		

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<p>phase of response to therapy continued to adhere to the schedule of study assessments until disease progression occurred even though one or both of the study drugs had been discontinued.</p> <p>The primary efficacy endpoint was TTP, calculated as the time from randomization to the first occurrence of disease progression as determined by a detailed review of all the myeloma response assessment data using the Bladé criteria (Bladé, 1998). If disease progression was based on increasing M-paraprotein levels, then the Bladé criteria required that the increasing M-paraprotein level be documented on two consecutive occasions at least 1 week apart. Disease progression based on bone marrow findings, worsening lytic bone disease, progressively enlarging extramedullary plasmacytomas, or hypercalcemia did not require a second confirmatory measurement. TTP based on the investigators' assessment of response was performed as a sensitivity analysis. Two additional supportive analyses, progression-free survival (PFS) and time to treatment failure (TTF), were conducted to confirm the robustness of the results of the primary endpoint TTP. Progression-free survival was calculated as the time from randomization to documented progression or death due to any cause on study or within 2 months of the last adequate assessment, whichever occurred first. Except for the manner in which deaths were counted in the analysis, the definition PFS was identical to the TTP. Time to treatment failure was defined as the time from randomization to treatment failure.</p> <p>The secondary efficacy endpoints were overall survival (OS); the myeloma response rate; the time to the first symptomatic skeletal-related event (SRE) (not actually analyzed due to limited data); and the time to the first worsening in the Eastern Cooperative Oncology Group (ECOG) performance status. Also, a post hoc analysis was performed for determining duration of response. The safety endpoints were treatment-emergent adverse events and clinical laboratory measures, which are graded according to the National Cancer Institute (NCI) Common Toxicity Criteria (CTC), Version 2.0; electrocardiograms (ECGs); vital signs; and physical examinations.</p> <p>An interim analysis was included in the study plan and was to be performed after 50% of the progressions required for full power for the comparison of TTP over both treatment groups had occurred (i.e., when approximately 111 subjects over both treatment arms total had progressed). The interim analysis was intended to determine if the study should be stopped for superiority, futility, or unfavorable toxicity. At the time of this interim analysis, the predetermined stopping criteria for superiority in the primary efficacy endpoint, TTP, had been surpassed, with $p < 0.001$ in favor of the lenalidomide/dexamethasone treatment group. The data also demonstrated that lenalidomide/dexamethasone was well tolerated, with an acceptable safety profile. After the interim analysis results were reviewed by the Independent Data Monitoring Committee (IDMC) on 28 Feb 2005, the investigators' assessments of disease progression were confirmed in an independent review by an external panel of myeloma experts who were blinded to the subjects' treatment assignments. The results of the external panel's review confirmed the significant differences that were observed in the interim analysis. Based on the results of the preplanned interim analysis, which surpassed the prespecified O'Brien-Fleming boundary for superior efficacy in favor of the lenalidomide/dexamethasone treatment arm, the decision was made to unblind all subjects remaining in the treatment phase of the study.</p> <p>Unblinding was initiated in 03 Aug 2005 and the primary analyses were based on this data cutoff date. Analyses including all the data up to the extended follow-up cutoff date (02 Mar 2008) were primarily for the survival update, but analyses for other efficacy and safety endpoints were performed as well. As of 02 Mar 2008, 21 patients were still ongoing.</p>		
<p>Number of patients (planned and analyzed): Planned: 302 subjects, randomized in a 1:1 ratio to 1 of the 2 treatment groups Enrolled: 351 subjects Analyzed: 351 subjects – 176 in the lenalidomide/dexamethasone group and 175 in the placebo/dexamethasone group</p>		
<p>Diagnosis and main criteria for inclusion: Prior or current diagnosis of Durie-Salmon stage II or III multiple myeloma and considered to have disease progression after at least 2 cycles of antimyeloma treatment or to have relapsed with progressive disease after treatment; measurable levels of myeloma paraprotein (M-paraprotein) in serum (≥ 0.5 g/dL) or urine (≥ 0.2 g excreted in a 24-hour collection sample); and an ECOG performance status of 0, 1, or 2.</p>		
<p>Test product, dose and mode of administration, batch number: Lenalidomide was supplied by Celgene as 25-mg or 5-mg (for dosage reductions) capsules. The lenalidomide capsules were supplied in 28-day blister packs; each blister pack contained 21 capsules of lenalidomide (for administration on Days 1 to 21 of each cycle) and 7 matching placebo capsules (for administration on Days 22 to 28 of each cycle). The double-blind lenalidomide capsules packaged in blister cards were from the following batch/lot numbers: 0033U, 0264U, 0067W, 0068W, and 0216X for the 25-mg dosage; and 0180U, 0151W, 0380W, 0095X, 0104X, and 0106X, for the 5-mg dosage.</p>		

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<p>The open-label lenalidomide supply used after unblinding were packaged in 21-count bottles in either 25-mg or 5-mg dosage. The open-label lenalidomide was taken from the following batch numbers: 0216X, 0251X, 425075, 432877, and 432878 for the 25-mg lenalidomide capsules; and 0380W, 0095X, 430488, and 434011 for the 5-mg lenalidomide capsules.</p> <p>The dexamethasone tablets for the combination therapy were obtained commercially by the subjects using prescriptions provided by the investigators.</p>		
<p>Duration of treatment: Treatment continued until disease progression or until the subject withdrew from the study for another reason.</p>		
<p>Reference therapy, dose and mode of administration, batch number: Placebo capsules were identical in appearance to the 25- and 5-mg lenalidomide capsules and contained the inactive ingredients of the lenalidomide formulation. The placebo capsules were supplied by Celgene in 28-day blister packs that were identical in appearance to the lenalidomide blister packs; each blister pack of placebo contained 28 placebo capsules (for administration on Days 1-28 of the 28-day cycle). The double blind placebo capsules packaged in blister cards were from the following batch numbers: 0179U, 0373U, and 0089X for the matching 25-mg capsules; and 0181U, 0374U, and 0088X for the matching 5-mg capsules.</p> <p>The dexamethasone tablets for the combination therapy were obtained commercially by the subjects using prescriptions provided by the investigators.</p>		
<p>Criteria for evaluation:</p> <p>Efficacy: <u>Primary.</u> TTP based on reviewer’s assessment; TTP based on the investigators’ assessment was analyzed as a sensitivity analysis; PFS and TTF were also analyzed as additional supportive analyses. <u>Secondary.</u> OS, myeloma response rate, and time to first worsening of ECOG performance status. An additional post hoc analysis was also performed for duration of response.</p> <p>Safety: Incidence of treatment-emergent adverse events and change from baseline in clinical laboratory tests, ECGs, and vital signs.</p>		
<p>Statistical methods: Kaplan-Meier product limit methods were used to estimate the survivorship functions for the time-to-event endpoints (e.g., TTP, PFS, TTF, OS, duration of response, and time to first worsening of ECOG performance status). An unstratified log-rank test was used as the primary analytic method to compare survivorship functions for time-to-event variables in the 2 treatment groups. The time to first SRE was not analyzed due to the limited data available for this endpoint.</p> <p>Two-sided 95% confidence intervals (CI) for the median time-to-event in each treatment arm, the event rates at specific time-points, and the hazard rate (risk) ratio were computed for each time-to-event variable. To account for the stratified randomization, a log-rank test, stratified by the 3 strata used in the randomization (i.e., baseline serum β_2-microglobulin level, prior treatment with HDT and SCT or not, and the number of prior antimyeloma regimens) was performed for the primary efficacy endpoint, TTP, in addition to the unstratified analysis described above.</p> <p>Because of the crossover of placebo/dexamethasone subjects to receive lenalidomide or other treatment options, the assumption of proportional hazards for death events at all times may not be valid, and converging hazards was likely for events (i.e., deaths) in the overall survival analysis. Pepe and Fleming demonstrated Wilcoxon test and the weighted Kaplan-Meier test would be more sensitive than the log-rank test in this situation. P-values from all three tests (i.e., Pepe-Fleming, Wilcoxon, and log rank) were presented.</p> <p>Exact test procedures for proportions were used to compare response rates. Analyses were performed both to compare the distribution of responses over all response categories (complete response [CR], partial response [PR], stable disease [SD], progressive disease [PD], not evaluable [NE]), which resulted in a 2-by-5 table, and to compare the proportions of subjects who showed at least a confirmed PR (PR + CR), which resulted in a 2-by-2 table. The 2-by-5 table was analyzed using the Wilcoxon rank sum test, excluding the NE category, with ranks of 1 to 4 for CR through PD, respectively, and the 2-by-2 table was analyzed using the continuity corrected Pearson’s chi-square test. The number and percentage for each response category were provided for response data.</p> <p>Adverse events, clinical laboratory information, concomitant medications, and ECG interpretations, and vital signs were tabulated. All adverse events were summarized by frequency and severity grade, based on the NCI CTC (Version 2.0), and by the relationship to study drug. Serious adverse events, adverse events leading to discontinuation, and adverse events leading to dose reductions were summarized separately. Deaths were listed.</p>		

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SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

Time to Progression

The primary efficacy endpoint is TTP based on the reviewer’s assessment. A total of 74.3% (130/175) of the subjects in the placebo/dexamethasone group, compared with 38.6% (68/176) of subjects in the lenalidomide/dexamethasone group, had progressed as of the 03 Aug 2005 data cutoff date. The median TTP was 52.1 weeks (12.0 months) in the lenalidomide/dexamethasone group and 20.1 weeks (4.6 months) in the placebo/dexamethasone group.

Summary of Time to Progression (Based on Reviewer’s Assessment) Up to Unblinding (03 Aug 2005) (ITT Population)

	Statistic	Lenalidomide/Dexamethasone	Placebo/Dexamethasone
TTP	N	176	175
Progressed	n (%)	68 (38.6)	130 (74.3)
Censored	n (%)	108 (61.4)	45 (25.7)
Overall TTP (weeks)	Median	52.1	20.1
	[95% CI] [a]	[40.9, NE]	[16.6, 20.7]
	Mean	34.1	20.6
	SD	28.40	18.37
	Min, Max	0.1, 93.4	0.1, 86.1
Hazard Rate Ratio	HR [95% CI] [b]	0.324 [0.240, 0.438]	
Log-rank Test	p-value [c]	< 0.001	

CI = confidence interval; HR = hazard ratio; ITT = intent to treat; max = maximum; min = minimum; SD = standard deviation; TTP = time to progression.

Note: The median is based on Kaplan-Meier estimate and the mean is the univariate mean without adjusting for censoring.

[a] 95% confidence intervals about the median overall time to progression.

[b] Based on a proportional hazards model comparing the hazard functions associated with the treatment groups (lenalidomide/dexamethasone : placebo/dexamethasone).

[c] The p-value is based on an unstratified log rank test of survival curve differences between the treatment groups.

The TTP was significantly longer in the lenalidomide/dexamethasone group than in the placebo/dexamethasone group (p < 0.001, two-tailed unstratified log-rank test of survival curve difference between treatment groups). Based on the hazard ratio (0.324), subjects in the placebo/dexamethasone group were 3.1 times as likely to progress as those in the lenalidomide/dexamethasone group at any time during the treatment phase of the study. The results of the stratified log-rank test confirmed those of the unstratified analysis (primary analysis).

Subgroup analysis of TTP showed that lenalidomide/dexamethasone treatment was significantly more effective than placebo/dexamethasone treatment in all the subgroups analyzed (p < 0.001 including: male and female subjects; subjects ≤ 65 years and those > 65 years; subjects with a baseline serum β₂-microglobulin level of ≤ 2.5 mg/L and in those with a baseline level of > 2.5 mg/L [i.e., in those with a high tumor burden]; subjects who had been previously treated with HDT and SCT and those who had not; subjects who had 1 prior antimyeloma therapy and those who had 2 or more prior antimyeloma therapies; and subjects who had prior treatment with thalidomide) (p = 0.045 for subjects who had prior treatment with Velcade® [bortezomib]). The robustness of the TTP results based on the reviewer’s assessment was supported by analyses of TTP based on the investigators’ assessment, PFS and TTF.

Overall Survival

As of the 03 Aug 2005 data cutoff date, 48 (27.3%) of the 176 subjects in the lenalidomide/ dexamethasone group and 60 (34.3%) of the 175 subjects in the placebo/dexamethasone group had died (see next Table).

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Summary of Overall Survival Up to Unblinding (03 Aug 2005) (ITT Population)

	Statistic	Lenalidomide/Dexamethasone	Placebo/Dexamethasone
Overall Survival	N	176	175
Died	n (%)	48 (27.3)	60 (34.3)
Censored	n (%)	128 (72.7)	115 (65.7)
Overall survival time since randomization (weeks)	Median	NE [a]	NE
	[95% CI] [b]	NE	[71.6, NE]
	Mean	53.5	50.0
	SD	27.26	24.53
	Min, Max	2.0, 132.9	0.3, 92.7
Hazard Rate Ratio	HR [95% CI] [c]	0.730 [0.498, 1.070]	
Log-rank Test	p-value [d]	0.105	
Wilcoxon Test	p-value [e]	0.123	
Pepe-Fleming Test	p-value [f]	0.162	

CI = confidence interval; HR = hazard ratio; ITT = intent to treat; max = maximum; min = minimum; NE = not estimable; SD = standard deviation.

Note: The median is based on Kaplan-Meier estimate and the mean is the univariate mean without adjusting for censoring.

- [a] The Kaplan-Meier estimate drops from 65% to 0 at t = 133 weeks by default since the only subject at risk at this time point died. The median from the inverse Kaplan-Meier function is considered not materialized or estimable at this time point.
- [b] 95% confidence intervals about the median overall time to treatment failure.
- [c] Based on a proportional hazards model comparing the hazard functions associated with the treatment groups (lenalidomide/dexamethasone : placebo/dexamethasone).
- [d] The p-value is based on an unstratified log rank test of survival curve differences between the treatment groups.
- [e] The p-value is based on an unstratified Wilcoxon test of survival curve differences between the treatment groups.
- [f] Using the Pepe-Fleming test (Pepe, 1989).

Median OS in both the lenalidomide/dexamethasone group and the placebo/dexamethasone group had not yet been reached. Overall survival was not significantly different between the 2 treatment groups utilizing the log-rank (p = 0.105), Wilcoxon (p = 0.123), and Pepe-Fleming (p = 0.162) tests. Based on the hazard ratio of 0.730 (assuming proportional hazard ratio over time), the subjects in the placebo/dexamethasone group were 1.4 times as likely to die at any time as those in the lenalidomide/dexamethasone group.

Results of analysis of other efficacy analyses (i.e., myeloma response rate, TTF, and a post hoc analysis for duration of response) demonstrate significant differences supporting the effectiveness of the lenalidomide/dexamethasone treatment compared with placebo/dexamethasone treatment.

SAFETY RESULTS:

Adverse Events

All subjects reported at least 1 treatment-emergent adverse event during the study. Seventeen subjects in the lenalidomide/dexamethasone group and 18 in the placebo/dexamethasone group died during the study or within 30 days of the last dose of study drug. A higher percentage of subjects in the lenalidomide/dexamethasone group compared with the placebo/dexamethasone group had at least 1 serious adverse event (54.0% versus 41.1%); at least 1 adverse event leading to study drug discontinuation (21.6% versus 16.0%); at least 1 adverse event leading to study dose reduction or interruption (76.1% versus 57.1%); at least 1 drug-related serious adverse event (28.4% versus 14.9%); or at least 1 grade 4 adverse event (25.0% versus 16.6%).

Common adverse events (reported by ≥ 10% of subjects in either treatment group) were generally reported with higher frequencies in the lenalidomide/dexamethasone group than in the placebo/dexamethasone group. Constipation, neutropenia,

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asthenia, diarrhea NOS, muscle cramps, tremor, nausea, dizziness, thrombocytopenia, anorexia, vomiting NOS, abdominal pain upper, and rash NOS were notably reported more frequently in the lenalidomide/dexamethasone group.

Neutropenia was the primary reason for dose reductions or interruptions in the lenalidomide/dexamethasone group (25.6%), but the frequency of discontinuations of the study drug in this treatment group due to neutropenia was low (1.1%). Most cases of neutropenia were assessed by the investigator as drug-related and few cases (1.1%) in the lenalidomide/dexamethasone were serious. Grade 4 neutropenia was reported at a low frequency (4.0%) in the lenalidomide/dexamethasone group.

Deep vein thrombosis (DVT) was reported with the same frequency by subjects in the lenalidomide/dexamethasone group and the placebo/dexamethasone group (5.1%) while pulmonary embolism (PE) was reported more frequently by subjects in the lenalidomide/ dexamethasone group (4.5%) compared with those in the placebo/dexamethasone group (1.1%). The majority of the incidences of DVT and PE were grade 3/4 in both groups.

Thromboembolic events other than DVT and PE were reported as follows: venous thrombosis NOS limb (1.7% versus 0.6%), thrombosis (1.1% versus 0%), thrombophlebitis (0.6% versus 0%), and thrombophlebitis superficial (0.6% versus 0%).

The proportion of subjects who reported peripheral neuropathy NOS, peripheral sensory neuropathy, and neuropathy NOS was comparable between the treatment groups. No grade 4 peripheral sensory neuropathy, peripheral neuropathy NOS, or neuropathy NOS was reported in either treatment group.

Rash NOS was reported in approximately 3 times as many subjects in the lenalidomide/dexamethasone group (12.5%) compared with those in the placebo/dexamethasone group (4.6%). No grade 4 rash NOS was reported in either treatment group.

The proportion of subjects who reported cardiac disorders (of interest due to the advanced age of the study population) of any kind was comparable between treatment groups. The frequencies of individual cardiac-related adverse events were generally low (i.e., < 3%) in both treatment groups. The cardiac disorder with the highest incidence was palpitations, which occurred in 2.3% of the subjects in each group. One (0.6%) case of palpitations in the lenalidomide/dexamethasone group was considered to have a suspected relationship to study drug. There were no grade 4 palpitations.

Arrhythmia NOS was reported by 2 subjects in the lenalidomide/dexamethasone group, of which 1 was related to study drug; and 1 subject in the placebo/dexamethasone group, which was not related to study drug.

In the lenalidomide/dexamethasone group, the following grade 4 cardiac events were reported: atrial fibrillation, acute myocardial infarction, bradycardia NOS, extrasystoles NOS, and myocardial infarction in 1 (0.6%) subject each. In the placebo/dexamethasone group, the following grade 4 cardiac events were reported: pulmonary edema NOS (2.3%); and atrial fibrillation, myocardial infarction, cardiac failure acute, cardiac failure NOS, cardiorespiratory arrest, and cardiovascular disorder NOS (0.6% each).

The proportion of subjects who reported upper respiratory tract infection NOS in the lenalidomide/dexamethasone group was higher than that in the placebo/dexamethasone group. The proportion of subjects who reported pneumonia NOS, sinusitis NOS, oral candidiasis, urinary tract infection NOS, and herpes simplex was comparable between treatment groups. Herpes zoster was reported by 8 (4.5%) subjects in the lenalidomide/dexamethasone group, of which, 2 (1.1%) cases were considered to have a suspected relationship to study drug; and 6 (3.4%) in the placebo/dexamethasone group, of which, 1 (0.6%) case was considered to have a suspected relationship to study drug. One (0.6%) subject in each treatment group reported grade 4 pneumonia NOS. Few deaths occurred due to infection-related causes; 2 deaths in the lenalidomide/ dexamethasone group (brain hypoxia/pneumonia and multiorgan failure/pneumonia) and 3 deaths in the placebo/dexamethasone group (multiple myeloma/pneumonia, sepsis NOS, and septic shock).

Overall, the addition of lenalidomide to dexamethasone had a favorable safety profile; the adverse events were easily monitored and managed clinically.

Clinical Laboratory, ECG, and Vital Signs Assessments

A higher percentage of subjects in the lenalidomide/dexamethasone group compared with the placebo/dexamethasone group had shifts from baseline values of grade 0, 1, or 2 to a worst postbaseline value of grade 3 in absolute neutrophil count (ANC) (31.3% versus 4.2%) and white blood cell (WBC) count (18.4% versus 4.8%).

A higher percentage of subjects in the lenalidomide/dexamethasone group compared with the placebo/dexamethasone group had shifts from baseline values of grade 0, 1, or 2 to a worst postbaseline value of grade 3 in phosphorus (14.0% versus 8.4%)

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<p>and potassium (5.3% versus 3.0%). Conversely, more subjects in the placebo/dexamethasone group compared with the lenalidomide/dexamethasone had similar shifts in albumin (5.4% versus 2.9%) and sodium (7.8% versus 4.7%).</p> <p>Few shifts from baseline were seen in any value for any urinalysis parameter. For TSH, most subjects had normal values at baseline and the worst postbaseline values remained within the normal range. The proportion of subjects who had a worsening in TSH during treatment was low and comparable between the treatment groups.</p> <p>Little variation was observed in vital signs, ECGs, or weight in either treatment group during the study; abnormalities were observed in low and comparable proportions of subjects in each treatment group.</p> <p>CONCLUSION:</p> <p>Overall, the results of this study showed that the extended use of lenalidomide in combination with dexamethasone demonstrated a highly favorable benefit-to-risk ratio for multiple myeloma subjects who have received at least 1 prior antimyeloma therapy.</p> <p>Date of the report: 09 Dec 2008</p>		

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