Synopsis

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Effectiveness of Bortezomib Retreatment for Patients with Relapsed Multiple Myeloma

1. Background and Rationale:

For patients who have relapsed or are refractory to therapy, a standard of care is now bortezomib, based on the results of previous trials. However, there is currently no curative therapy for myeloma. When disease eventually recurs in patients who have received bortezomib for relapsed or refractory myeloma.In the 2006 ASH,#3531;of patients evaluable for response, a PR or better as achieved in 44 of 78 (56%) patients in response to initial therapy (26% achieved a VGPR or better)and #3532;Overall, the Velcade retreatment response rate was 50% (11/22).It is critical to obtain data on the value of retreatment with bortezomib to determine response rates and duration in patients receiving it for the second time.We think data from this study may further strengthen Velcade retreatment platform in relapsed and refractory MM in Korea.

2. Objectives:

Primary Objective;The primary objective of this study is to clarify the utility of Velcade as a repeat therapy for patients with multiple myeloma in Korean.

Secondary Objective;The secondary objectives of this study are to confirm the safety of Velcade retreatmentfor patients with multiple myeloma in Korean.

3. Primary Hypothesis:

The estimated overall response rate is more than 35%.

4. Study Design:

open-label, single arm, observational study

5. Study Population:

Relapsed and refractory patients who were previously treated with Velcad

6. Outcome measures-efficacy:

The primary end point of overall response rate will be assessed by investigators and according to percentage reduction in M-protein level.

7. Outcome measures-safety:

CTCAE V3.0

8. Critical selection criteria (inclusion & exclusion criteria):

8.1 Inclusion criteria

1. Patient was previously diagnosed with multiple myeloma and has measurable disease
2. Patient was previously treated with bortezomib alone or in combination with other agents.

3. It has been ≥ 6 months since the patient's last bortezomib dose and the patient has progressive disease or has relapsed
4. If female, the patient is either postmenopausal or surgically sterilised or willing to use an acceptable method of birth control for defined period, If male, the patient agrees to use an acceptable barrier method of contraception for defined period of time.
5. Subjects must have signed an informed consent document indicating that they understand the purpose of and procedures required for the study and are willing to participate in the study.

8.2. Exclusion criteria

1. patients who are hypersensitive to the study drug or any component of the study drug or with a history of the hypersensitivity.
2. Patients with severe hepatic impairment.
3. Female patient is pregnant or breast-feeding.
4. Younger than 18 years of age.

9. Number of subjects with justification (statistical power calculation):

The estimated overall response rate is more than 35%. Approximately 73 observations are required to estimate a rate of response of 35 % with a precision of 11 %. The values of N of patients were calculated with the following standard formula: N = (z1-a/2/w)2[p(1- p)],where a=0.05 (for a 95% CI), w=0.11(the width of the CI), and p=0.35(the expected rate of response) Taking into account a drop-out rate of about 20%, a sample of 92 patients would be required.

Sample size : 92 Pts.

Study variables :

1) Complete/partial response
2) Progression
3) Overall survival

Endpoints :

The primary end point of overall response rate will be assessed by investigators and according to percentage reduction in M-protein level.

10. Duration of study

Minimum follow-up 6 months

Enrollment duration: 6 months

Total study duration: 12 months (1 years)

11. Active treatment regimen:

Boretezomib 1.3 mg/m^2 twice weekly for 2 weeks(Day 1,4,8 and 11) per cycles
Cycles every 3 weeks for at least 4 cycles until disease progression.

12. Comparator / Dose (if applicable):

NA

13. Budget:

14. Publication plans:
TBD

15. References:

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2. Conner TM, QuynhChau DD, LeBlanc AL, et al. An observational, retrospective analysis of retreatment with bortezomib of multiple myeloma patients. Poster presented at: 48th ASH Annual Meeting December 9-12 2006. Blood 2006; 108(11): Abstract 3531
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