The role of bortezomib, thalidomide, and lenalidomide in the management of multiple myeloma: an overview of clinical and economic information

Running title: novel agents for multiple myeloma

Word count (exclusive of title, abstract, references, tables): 6327

Andrea Messori*, Dario Maratea*, Chiara Nozzoli**, Alberto Bosi**

*Laboratorio di Farmacoeconomia, c/o Area Vasta Centro, Servizio Sanitario Regionale, Firenze and
**Cattedra di Ematologia, Università di Firenze, Firenze, Italy

Address correspondence to:
Dr. Andrea Messori
ESTAV Centro
Via Guimaraes 5-7
59100 Prato
ITALY

Email: andreamessori@interfree.it
Fax: +39-0574-527501
Phone: +39-347-6053933
Table of contents

ABSTRACT

1. INTRODUCTION

2. OVERVIEW OF THE CLINICAL LITERATURE
2.1. The role of bortezomib, thalidomide, and lenalidomide in the management of newly diagnosed patients eligible for transplantation
2.2. Magnitude of the survival benefit in newly diagnosed patients eligible for transplantation
2.3. The role of bortezomib, thalidomide, and lenalidomide for newly diagnosed patients ineligible for autologous transplantation
2.4. Magnitude of the survival benefit in newly diagnosed patients ineligible for transplantation
2.5. The role of bortezomib, thalidomide, and lenalidomide in the management of relapsed and/or refractory disease
2.6 Magnitude of the survival benefit in relapsed and/or refractory disease
2.7. Technical details of the literature search

3. CONTRASTING COSTS AND BENEFITS OF THE THREE NOVEL AGENTS
3.2 Overview of the survival gain information for the three novel agents
3.3 Cost of the novel anti-myeloma agents and preliminary assessment of the cost-effectiveness ratio

4. CONCLUSIONS
ABSTRACT

Bortezomib, thalidomide, and lenalidomide can be aimed at treating newly diagnosed patients with multiple myeloma (both eligible and ineligible for transplantation) as well as patients with relapsed or refractory disease. In the first part of this review we analyzed the information published on these three drugs (particularly phase III trials) in order the determine their impact on progression-free survival and overall survival. In the case of newly diagnosed patients eligible for transplantation, a total of 10 trials were examined (thalidomide, n=7; lenalidomide, n=2; bortezomib, n=1). There were 7 trials in the case of patients ineligible for transplantation (thalidomide, n=4; lenalidomide, n=1; bortezomib, n=2) and 7 in the treatment of relapsed or refractory disease (thalidomide, n=1; lenalidomide, n=3; bortezomib, n=3).

Irrespective of which of the three agents is considered, the magnitude of the benefit in newly diagnosed cases (transplanted or non-transplanted) tends to be between 10 and 20 months per patient in terms of progression-free survival or survival; the survival benefit is smaller in relapsed or refractory disease. In addition, a single-institution observational analysis has evaluated the outcomes in nearly 3,000 consecutive patients examined from 1971 to 2006. The survival in patients diagnosed between 2001 and 2006 was longer than that observed in patients diagnosed between 1994 and 2000. This finding supports the conclusion that novel agents have determined a survival improvement, the magnitude of which is in keeping with that derived from our literature analysis.

Formal cost-effectiveness studies on these three agents are still lacking, and a MEDLINE search in fact retrieved only 4 short papers or letters and no full-length analysis. Hence, determining the cost-effectiveness of these agents still needs further investigations with separate assessments of the different therapeutic settings.
In a simplified analysis, we tried to contrast the average cost of treatment for each of the novel agents versus their respective benefit expressed in quality-adjusted survival. Despite its preliminary nature, our assessment indicates that the cost-effectiveness of these three agents is likely to be within commonly accepted pharmacoeconomic thresholds.