Potential Therapeutic and Economic Value of Risk-Stratified Treatment as Initial Treatment of Multiple Myeloma in Europe

Jennifer G. Gaultney1, Therese W. Ng1, Carin A. Uyl-de Groot2, Pieter Sonneveld4, Erik H. van Beers4, Martin H. van Vliet4, William K. Redekop2

1Mapi Group, London, UK, 2Erasmus School of Health Policy & Management, Institute for Medical Technology Assessment, Erasmus University Rotterdam, Rotterdam, Netherlands, 3Department of Haematology, Erasmus MC Cancer Institute, The Netherlands, 4SkylineDx BV, Rotterdam Science Tower, The Netherlands

Introduction

Background

- Despite a general trend for increasing survival, the outcome of multiple myeloma (MM) remains highly variable. Some of this variability may be captured by prognostic biomarkers such as International Staging System (ISS), fluorescence in situ hybridization (FISH) testing and gene expression profiling (GEP). The best prognostic biomarker thus far reported is the SKY92 GEP signature (1).

- In this cost-effectiveness analysis, using an economic model, we examined scenarios in which all newly diagnosed MM patients are treated the same (uniform treatment (UT)) or via a risk-stratified treatment (RST) approach based on one or more risk biomarkers (2).

- The health economic impact of UT compared with RST may be influenced by the cost of treatment, the expected clinical outcome and health related quality of life.

- No study has ever examined the potential health economic value of RST in MM within the European Union (EU).

Methods

Target patient population

- HOVON 65/MMGHD4 clinical trial: A total of 815 newly diagnosed transplant eligible patients were randomised to either bortezomib-based induction, high-dose melphalan (HDMP), autologous stem cell transplantation (ASCT), then bortezomib maintenance (bortezomib, doxorubicin and dexamethasone (PAD-D)) or chemotherapy-based induction, HDMP and ASCT, thalidomide maintenance (vinorelbine, doxorubicin and dexamethasone (VAD-T)).

Decision analytic model

- A decision analytic model simulated the total costs and health benefits for UT versus RST (Figure 1). Three risk categories were distinguished: 1) high-risk, 2) standard-risk patients and 3) unknown-risk patients for which data was not available for one or more prognostic factors. High-risk disease was defined by 1) RST-FISH+iSS92, 2) RST-SKY92 and 3) RST-FISH+iSS92.

- In RST, only standard risk patients receive treatment with the standard of care, whilst high and unknown-risk patient receive bortezomib-based therapy.

Markov structure

- An early Markov model was used with one-month cycles and a lifetime horizon (Figure 2).

- 408 patients enter the first cycle in the progression-free state and are at risk of two events (death before progression or progressive disease). The patients who become progressive are then at risk of death.

- The probability of the first event type being progression or death was estimated using a logistic regression with ‘event type’ as the dependent variable and treatment arm, risk group, and time as event as the independent variables.

- For progression free survival and OS survival model development and extrapolation, various distributions were assessed for model fit.

Analytic specifications

- A cost-utility analysis (CUA) from the Dutch, German, French, Spanish and United Kingdom (UK) health care payer’s perspective was performed. Only direct medical costs associated with the interventions were included (Supplementary Table 1 on hand-out).

Data sources and sensitivity analyses

- Input data originated from the HOVON 65/MMGHD4 clinical trial, literature reviews, observational studies and national tariffs (Supplementary Table 1 on hand-out).

- Uncivariate sensitivity analyses on the difference in total costs and quality adjusted life years (QALYs) between comparators were performed.

Results

- Across all country perspectives, all RST scenarios dominated UT (Table 1). RST-SKY92 produced maximum health gains followed by RST-FISH+iSS92 and RST-FISH+iSS92 compared to UT.

- RST produced cost-savings due to lower costs of induction treatment, maintenance treatment and grade 3/4 peripheral neuropathy. RST-FISH+iSS92 generated the greatest cost-savings followed by RST-SKY92 and RST-FISH+iSS92 compared to UT.

- The cost effectiveness plane (Figure 3) shows that the greatest benefits of RST compared to UT were demonstrated in Germany and France.

- In sensitivity analyses, the top 4 key parameters of cost influence were the duration of maintenance therapy, cost of bortezomib maintenance therapy per month and the cost of relapsed refractory multiple myeloma per month. Varying the cost maintenance therapy, cost of cycle administration, the cost of bortezomib maintenance therapy and the utility of progression-free state and the duration of grade 3 PN occurring with VAD-T therapy.

Conclusions

- A health economic evaluation demonstrated the potential transferability for the therapeutic and health economic benefits for RST in MM from the European perspective.

- Across all markets (the Netherlands, Germany, France, Spain and the UK), all RST scenarios dominated UT, i.e. RST is potentially cost-saving and health generating compared to UT.

- RST approached with the SKY92 signature (i.e. RST-SKY92 and RST-FISH+ISS92) led to the greatest health gain.

- Early modelling made it feasible to assess the circumstances under which RST would be promising, providing early evidence which should encourage stakeholders to support the adoption of RST approaches in MM.

References