Cost-effectiveness of Novel agent regimens for Transplant-Eligible Newly Diagnosed Multiple Myeloma patients in India

Health Technology Assessment in India (HTAIn)
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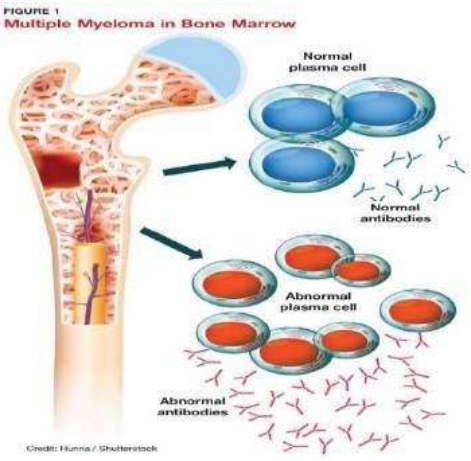
Policy Brief

Executive Summary:

Multiple myeloma (MM) is the second most frequent haematological malignancy (~15%), accounting for nearly 20% of all haematological cancer-related deaths [1–3]. The therapeutic landscape of MM has changed significantly over the past few years with the introduction of novel agents like bortezomib, lenalidomide and thalidomide. Due to these advanced therapeutic combinations and standard use of AHSCT, the cost of care of MM has increased significantly in the last two decades. Since the number of treatment options for NDMM have increased substantially, it is vital to compare the costs and consequences of different induction regimens.

In this analysis, we aimed to evaluate the cost-effectiveness of novel agent regimes with and without autologous haematopoietic stem cell transplantation (AHSCT). Using a Markov model, the clinical effectiveness and cost of bortezomib-based triplets or quadruplet drug regimens in isolation and followed by AHSCT for the treatment of newly diagnosed multiple myeloma (NDMM) in the Indian context were estimated. Incremental cost per QALY gained with a given treatment option was compared against the next best alternative, and assessed for cost-effectiveness.



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At the current WTP threshold, VRd plus AHSCT and VTd plus AHSCT has 6.9% and 3.7% probability to be cost-effective, respectively. Reduction in current reimbursement rates of novel drugs namely VRd, lenalidomide, pomalidomide plus dexamethasone under national insurance program and societal cost of transplant by 50%, would make VRd plus AHSCT and VTd plus AHSCT cost-effective at an incremental cost of ₹ 40,671 (US$ 534) and ₹ 97,639 (US$ 1,281) per QALY gained respectively.

Policy Recommendations

- From the societal perspective, we recommend a 50% reduction in the reimbursement rate of VRd, pomalidomide plus dexamethasone, lenalidomide and transplant to make it a cost-effective treatment option for Indian MM patients.
- We would further recommend the inclusion of carfilzomib drug regimen in the HBP 2.0 for the treatment of MM patients in India.
- Drugs like daratumumab may also be considered for inclusion under publicly financed health insurance schemes in order to further improve the survival as well as quality of life of MM patients in India.
- There is an urgent need to place certain price regulations in place so as to make these drugs more accessible and affordable to MM patients.

Background and Gap in Literature:

As per GLOBOCAN data from the International Agency for Research on Cancer (IARC), there were an estimated 114,000 new cases of Multiple myeloma globally in 2012 [4]. More recent estimates suggested 159,985 newly diagnosed MM worldwide (i.e. about 0.9% of all cancers and 1.1% of all cancer deaths) in 2018 [5]. Survival outcomes for multiple myeloma have improved dramatically since the introduction of novel therapeutic agents. While these drugs are highly effective in improving survival outcomes and quality of life in patients with multiple myeloma, they come at a significant cost. The therapeutic landscape of MM has changed significantly over the past few years with the introduction of novel agents like bortezomib, lenalidomide and thalidomide and are used in combinations to improve the outcomes among newly diagnosed multiple myeloma (NDMM) patients [6-7]. The improvements were marked when using the novel agents as induction therapy followed by autologous hematopoietic cell transplantation (AHSCT) [6, 8-9]. The initial therapy for transplant-eligible NDMM patients consists of 3-6 cycles of induction therapy followed by AHSCT and maintenance therapy [8-9]. Due tothese advanced therapeutic combinations and standard use of AHSCT, the cost of care of MM has increased significantly in the last two decades. Since the number of treatment options for NDMM have increased substantially. So, it is vital tocompare the costs and consequences of different induction regimens. According to a systematic review, few studies have evaluated the cost-effectiveness of regimens based on novel agents, including bortezomib, thalidomide and lenalidomide [10] but 3 of them have included only the transplant-ineligible MM population [11-13].

Aims and Objective

This policy brief addressed the policy question of cost-effectiveness of bortezomib-based triplets or quadruplet drug regimens in isolation and followed by AHSCT for the treatment of NDMM in the Indian context. It summarizes the results of a Economic evaluation study on various NDMM treatment regimens, conducted by the HTA Resource Hub, PGIMER, Chandigarh.

Treatment arms:

(1) Bortezomib, lenalidomide, dexamethasone (VRd) alone
(2) Bortezomib, thalidomide, dexamethasone (VTd) alone
(3) Bortezomib, cyclophosphamide, dexamethasone (VCd) alone
(4) VRd followed by AHSCT
(5) VTd followed by AHSCT
(6) VCd followed by AHSCT
(7) Daratumumab plus VRd (DVRd) followed by AHSCT

Methods and Approach

We undertook this cost-effectiveness analysis (CEA) using a societal perspective, which accounted for both health system and patients' costs and not indirect costs. We compared the bortezomib-based triplets or quadruplet drug regimens in isolation and followed by autologous hematopoietic stem cell transplantation (AHSCT) for the treatment of newly diagnosed multiple myeloma (NDMM). Our methodological principles are consistent with the Indian reference case for conducting economic evaluations used by the agency for Health Technology Assessment in India (HTAIn).

The analysis was performed under the following components:

1. **Markov model** was developed in Microsoft Excel to estimate health and economic outcomes (in terms of Quality Adjusted Life-years (QALYs)* and Life-years). The model consisted of three mutually exclusive health states: Progression-free survival (PFS), Progressive disease (PD) and death. (Figure 1).
2. Reimbursement rates under publicly financed national insurance program were used to estimate the treatment cost in each health stage. However, for drugs not included under insurance scheme, their market price was used from published literature. In order to obtain the Out-of-Pocket Expenditure (OOPE), the primary data collected based on the **CADCQoL** database was analysed [14].
3. Transition probabilities for treatment arms-VRd plus AHSCT, VTd plus AHSCT and VCd plus AHSCT were obtained from survival functions calculated from data obtained from published literature. However, for patients who did not undergo transplant stratified by the induction regimen, a gradient was calculated and used to derive the probability. For DVRd plus AHSCT arm, estimates reported in the **GRIFFIN trial** was used.
4. Stage wise utility scores were estimated from the **CADCQoL** primary data collected from 320 MM patients to measure the HRQoL. The Indian tariff values were used to calculate the index utility score.

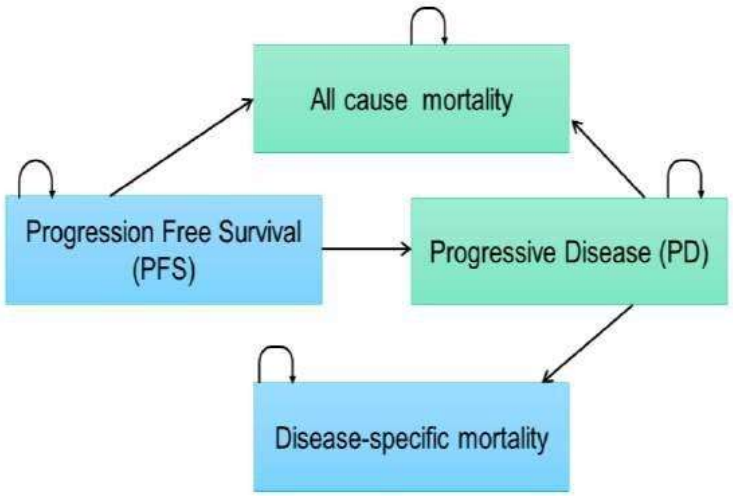

Figure 1: Schematic diagram for the Markov state transition model.

***Quality Adjusted Life-years:**

- QALY is a generic measure of health and is used to compare the health gains across different diseases and hence provide a uniform platform to compare effectiveness across all the different areas of healthcare.
- EQ5D is the most utilised tool worldwide to measure QoL.

Results:

- Among the seven treatment sequences, VCd alone arm has lowest cost and health benefits as compared to four treatment sequences namely VTd alone, VRd alone, VRd plus AHSCT and DVRd plus AHSCT
- VTd plus AHSCT and VCd plus AHSCT arm are extendedly dominated (ED) by combination of two alternative treatments.
- The ICER of DVRd plus AHSCT arm [₹ 824,969 (US$ 10,826)] is 5.6 times the per-capita GDP of India and hence not cost-effective at the currently recommended willingness to pay (WTP) threshold of per capita GDP.
- Among the five non-dominated strategies, VRd has an incremental cost of ₹ 2,20,093 (US$ 2,888) per QALY gained compared to VTd alone followed by VRd plus AHSCT, with an incremental cost of ₹ 3,14,530 (US$ 4,128) per QALY gained.

Price Threshold Analysis:

- At the current WTP threshold of one-time per capita GDP (₹ 146,890) of India, VRd alone and VRd plus AHSCT has 38.1% and 6.9% probability to be cost-effective, respectively.
- On reducing the current reimbursement rates under national insurance program by 50% i.e. from ₹ 17,800 to ₹ 8,900 for VRd, ₹ 7200 to ₹ 3600 for pomalidomide plus dexamethasone, ₹4800 to ₹ 2400 for lenalidomide and societal cost of transplant from ₹3,53,027 to ₹1,76,513, VRd plus AHSCT (against VTd plus AHSCT) becomes cost-effective at an ICER value of ₹ 40,671 (US$ 534) followed by VTd plus AHSCT treatment at an incremental cost of 97,639 (US$ 1281) per QALY gained (against VCd plus AHSCT) which is much below current WTP threshold of India.

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