Cost per Median Overall Month of Survival in Multiple Myeloma Patients With ≥3 Lines of Therapy or Double Refractory

E.M. Maiese,[1] M. Dimova,[2] C. Makin[2]

[1]HECOR, Janssen Scientific Affairs, LLC, Horsham, PA, USA; [2]Mapi, Boston, MA, USA

Background

- Multiple myeloma (MM) is a neoplastic plasma cell disorder, the second most common hematologic malignancy, with 30,330 new patients diagnosed and 12,650 deaths in US estimated for 2016[1,2]
- MM has no cure, and has a median overall survival of about 6 years[3,4]
- Daratumumab, a first-in-class fully human monoclonal antibody that binds to CD38, was recently approved by the FDA for the treatment of patients with MM who have received at least 3 prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent, or who are double refractory to a PI and immunomodulatory agent (IMiD)[5]

Objective

- The aim of this study was to evaluate the cost per median month of overall survival (mOS) for daratumumab and other novel treatments among MM patients with at least three prior lines of therapy including a PI and an IMiD, and/or patients who are double refractory to a PI and an IMiD

Methods

Model Design

Structure

- A cost calculator was developed in Microsoft Excel® 2010
  - Population: MM patients who either:
    1) Received ≥3 prior lines of therapy or were double refractory (DR) to a PI and an IMiD;
    2) Received ≥3 prior lines of therapy regardless of DR status; or
    3) Were DR to a PI and an IMiD regardless of number of prior lines of therapy
  - Comparators: daratumumab, carfilzomib, and pomalidomide plus dexamethasone
  - Time horizon: duration of overall survival of each therapy
  - Discounting: not applied

Analysis Inputs

- Treatment duration was assumed to be the median progression-free survival (mPFS), as treatment duration was not consistently reported and treatment is typically continued until progression. Median progression-free survival (mPFS) and median overall survival (mOS), both reported in months, were obtained from the Sirius (daratumumab)[6], FOCUS (carfilzomib)[7], PX-171-003-A1 (carfilzomib)[8], and MM-003 (pomalidomide plus dexamethasone)[9] trials. (Table 1)
  - Only daratumumab, carfilzomib (double refractory subgroup), and pomalidomide plus dexamethasone (double refractory subgroup) were included in the analysis since these treatments had published data in the populations of interest needed for the analysis

Table 1. Inputs: Survival and Drug Costs Data

Treatment	Treatment Duration Based on Median Progression-Free Survival (months)	Median Overall Survival (months)	Drug Cost per Administration ($)
Daratumumab (Sirius)[6]	3.7	17.5	$5,850
Carfilzomib (FOCUS)[7]	3.7	10.2	$1,862
Carfilzomib (PX-171-003-A1)[8]	3.7	11.9	$1,862
Pomalidomide plus Dexamethasone (MM-003)[9]	3.7	11.1	$633.03

- Only direct costs were included: drug, pre- and post-medication, administration, monitoring, auxiliary, and adverse events (AEs) costs. All costs were inflated to 2015 values using the Consumer Price Index for the USA, as needed.
  - All drug costs were based on Wholesale Acquisition Cost (WAC) published in the RedBook[10] by Truven Health Analytics as of May 2016
  - Pre-and post-medication costs included the costs of any medications administered before and after the treatment of interest. Medications were included based on the prescribing information for each treatment of interest.
    - Daratumumab required both pre- and post-medication with methylprednisolone (pre- and post-), acetaminophen and diphenhydramine HCL (pre-medication)[5]
    - Carfilzomib required pre-medication with normal saline IV[11] and
    - Pomalidomide plus dexamethasone did not require any pre- or post-medication
  - Administration costs were only incurred by IV treatments, i.e. daratumumab and carfilzomib, with costs varying by infusion number due to shorter length of infusions (first, second, third or more) and by the infusion hour (first or subsequent hours) for daratumumab. Administration costs were based on Medicare Physician Fee Schedule (MPFS).[12]
  - Monitoring and auxiliary items included in the model were obtained from the FDA labels[5,11,13] and the corresponding costs were based on the Medicare Fee Schedules[12] (Table 2)
  - The frequency of occurring AEs were obtained from the FDA labels[9,15,17] and the corresponding costs were based on publications[14,15] (Table 2)

Table 2. Cost and Frequency of Monitoring/Auxiliary Items and Adverse Events

Item/Event	Cost Per Item/Event (USD)	Frequency: Daratumumab (Sirius)[6]	Frequency: Carfilzomib (FOCUS)[7]	Frequency: Carfilzomib (PX-171-003-A1 DR Subgroup)[8]	Frequency: Pomalidomide + Dexamethasone (MM-003 DR Subgroup)[9]
Monitoring/Auxiliary (frequency per month)					
Physician visit	51.38	1	1	1	1
Complete blood count test	10.58	0	1	1	2.5
Liver enzyme test	11.11	0	1	1	1
Blood chemistry/electrolyte test	14.37	0	1	1	0
Electrocardiogram	17.25	0	1	1	0
Prophylactic therapy for herpes zoster (weekly)	5.34	4	4	4	0
Prophylactic therapy for renal toxicity, tumor lysis syndrome (weekly)	2.20	0	4	4	0
Prophylactic antithrombotics (acetylsalicylic acid 325 mg)	0.01	0	0	0	28
Adverse Events (frequency during trial)					
Urinary tract infections	12,895				8%
Renal failure	17,645				6%
Fatigue/asthenia	11,508		8%	8%	13%
Hypertension	162	5%			
Back pain	1,106				9%

Calculations

- Total costs were obtained by summing-up the drug costs, the pre- and post-medication costs, the administration, monitoring and auxiliary costs and the adverse event costs for each regimen according to its treatment duration. The cost per mOS was then calculated by dividing the total cost by the median month of OS reported in the clinical trials. (Figure 1 and Figure 2)

Figure 1. Calculation of Cost per Treatment

Drug Costs =	Number of Drug Administrations X Cost per Drug Administration
Pre-medication Costs =	Number of Pre-medication Administrations X Cost per Pre-medication Administration
Post-medication Costs =	Number of Post-medication Administrations X Cost per Pre-medication Administration
Administration Costs =	Number of Administrations X Cost per Administration
Monitoring and Auxiliary Costs =	Frequency per Month of Monitoring Visits/Auxiliary Item X Cost per Monitoring Visit/Auxiliary Item X Treatment Duration
Adverse Event Costs =	Proportion of Patients with Adverse Events (for whole treatment duration) X Cost per Adverse Event

Figure 2. Calculation of Cost per Month of Median OS (mOS)

$$\text{Cost per Month of Median OS} = \frac{\text{Drug Costs + Pre- and Post-Medication Costs + Administration Costs + Monitoring and Auxiliary Costs + Adverse Event Costs}}{\text{Median OS Months}}$$

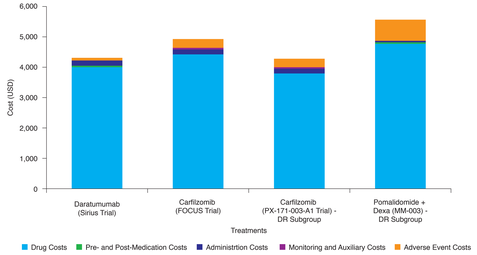
Results

- The average cost per mOS was (Table 3 and Figure 3):
  - $4,264 for daratumumab
  - $4,884 for carfilzomib (FOCUS)
  - $4,213 for carfilzomib (PX-171-003-A1 DR subgroup), and
  - $5,536 for pomalidomide plus dexamethasone (MM-003 DR subgroup)
- Drug costs had the highest contribution to the mOS costs, followed by either the AEs costs or the administration costs, depending on the regimen considered
  - Drug costs per month of mOS were lowest for carfilzomib in the PX-171-003-A1 study by $3,755, followed by daratumumab at $4,011, carfilzomib in the FOCUS trial at $4,381 and pomalidomide plus dexamethasone at $4,783
- Daratumumab had the lowest monitoring and auxiliary costs per month of mOS – $15, compared to $49 for carfilzomib (FOCUS), $42 for carfilzomib (PX-171-003-A1 DR subgroup), and $30 for pomalidomide plus dexamethasone
- Daratumumab was associated with the lowest AEs costs per month of mOS ($67), while the highest AEs costs were estimated for pomalidomide ($724)

Table 3. Median Cost per OS Month

Cost Category	Daratumumab (Sirius)[6]	Carfilzomib (FOCUS)[7]	Carfilzomib (PX-171-003-A1 DR subgroup)[8]	Pomalidomide + Dexamethasone (MM-003 DR Subgroup)[9]
Drug cost	$4,011	$4,381	$3,755	$4,783
Pre- and post-medication cost	$13	$2	$2	$0
Administration cost	$158	$186	$186	$0
Monitoring and auxiliary cost	$15	$49	$42	$30
Adverse events cost	$67	$265	$228	$724
Total average cost per mOS	**$4,264**	**$4,884**	**$4,213**	**$5,536**

Figure 3. Summary of Results for Cost per mOS



Limitations

- No prospective, randomized controlled trial (i.e. head-to-head) comparisons of daratumumab, carfilzomib and pomalidomide or indirect comparison of these therapies were available. The clinical evidence used in the analysis was derived from separate publications on individual treatments.
- mPFS was not available for the carfilzomib DR subgroup in the PX-171-003-A1 trial, therefore, the mPFS for the whole study population was assumed
- Costs like those related to post-progression were not included in this analysis, potentially leading to underestimation of the costs occurred during treatment
- The analysis did not account for contracting or pricing discounts or for different pricing conventions that may be used by commercial or Medicare/government payers, which may result in an overestimation of the drug costs

Conclusions

- In this analysis, cost per mOS was lowest for daratumumab and carfilzomib, and highest for pomalidomide plus dexamethasone
  - Adverse events costs were lowest for daratumumab and highest for pomalidomide plus dexamethasone
- This analysis provides background and a framework for future economic analyses of MM treatments and can support comprehensive healthcare decision-making considering the efficacy and safety benefits of MM treatments

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Acknowledgements

Dr. Gianluca Baio, PhD (Department of Statistical Science, University College London, London, UK and Mapi) for his input during developing the cost calculator

This study was supported by Janssen Scientific Affairs, LLC.

Please contact Eric Maiese (emaiese@ITS.JNJ.COM) for additional information or questions regarding the poster.