Epidemiological Modelling to Estimate the Number of US Patients With Multiple Myeloma at Different Lines of Treatment

Poster No. MM-138

Andreas Nikolaou,[1] Cosmina Hogea,[2] Feng Wang,[2] Yevgeniy Samyshkin,[3] Nedra Joseph,[2†] Mustafa Oguz,[4] Javier Cid Ruzafa[4]

[1]Modelling and Simulation, Evidera, London, UK; [2]GlaxoSmithKline, Upper Providence, PA, USA; [3]GlaxoSmithKline, Brentford, Middlesex, UK; [4]Real-World Evidence, Evidera, London, UK. [†]At the time of the study

Aims

To estimate the current (2020) number of patients with relapsed or refractory MM (RRMM) in the US on different lines of treatment (LOTs).

To quantify a subgroup of heavily pre-treated patients with a high unmet need (e.g. those with ≥3 prior LOTs, including a proteasome inhibitor (PI), an immunomodulatory agent, and/or an anti-CD38 monoclonal antibodies (mAbs, represented by daratumumab [DAR)]).

Background

Multiple myeloma (MM) is the second most common hematologic malignancy in the US.[1] It accounts for 1.8% of all cancer cases, with 32,110 new cases in 2019 and 131,392 patients living with MM estimated for 2017.[2] Incidence rates of MM have increased over time; concurrently, new treatments have reduced mortality rates, therefore larger numbers of people are living with MM in the US.[1]

In recent years, new therapies have expanded treatment options and increased survival rates.[1]

- Options, alone or in combination, now include PIs, immunomodulatory agents, anti-CD38 mAbs (such as DAR).[1,3]
- Despite these advances, relapse is usually inevitable, with the disease becoming increasingly refractory to treatment and remissions becoming shorter.[4–7]

Given the number of patients with MM, the evolving treatment landscape, and the propensity of patients to relapse, it is important to have a contemporary view of the patient estimates across different LOTs.

Publicly available estimates of the number of patients with MM in different LOTs are sparse and outdated. We employed an epidemiological modelling approach to estimate the current number of patients with MM in the US.

Methods

A compartmental model based on differential equations was developed, modelling population group moves between treatment statuses over time.[8]

Patients transition through four main compartments representing different LOT: first (LOT1), second (LOT2), third (LOT3) and after third (LOT4+).

- Transition to next LOT is defined as a change in therapy due to progression, toxicity or any other reason.
- Patients in LOTs 1–3 included patients who could transition to the next LOT or die.
- Patients in LOT 4+ could remain in that compartment or die.

Four further sub-compartments for each LOT were created based on stem cell transplant (SCT; SCT eligible or SCT ineligible), and treatment type (DAR, as a representative anti-CD38 mAb, or others). Patients could change treatment type when they transitioned to the next LOT (**Figure 1**).

For SCT eligible patients, the first LOT was represented by induction, SCT, and maintenance therapy post-SCT.

The model estimated patient numbers in 4 strata based on combinations of age group (≥65 or <65 years) and cytogenetic risk (high or standard) and aggregated the results to provide overall patient numbers by LOT.

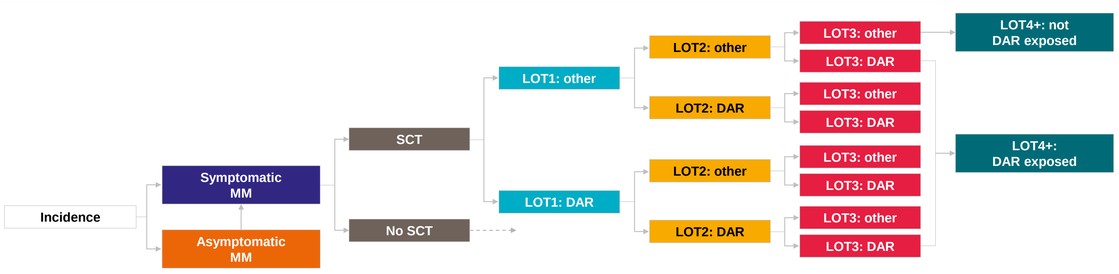
Mortality and time to next treatment (TTNT; defined as time from initiation of treatment in current LOT until initiation of treatment in the next LOT) depended on LOT, SCT, age, and cytogenetic risk. These inputs were informed from published median outcomes from epidemiological and real-world studies assuming that they follow an exponential distribution.

The proportion of patients receiving DAR at each LOT was based on 2019 market-share data[9] (LOT1, 6%; LOT2, 22%; LOT3, 20%; LOT4+, 33%), and was assumed to be independent of SCT status. Mortality and TTNT for DAR were based on relative treatment effects of DAR from publications of randomized-controlled-trials.

The model was simulated until steady-state conditions were reached (i.e. the number of patients at each compartment did not vary further over time).

Probabilistic and deterministic sensitivity analyses were conducted to quantify the variability of model projections due to uncertainty in the model parameters.

Figure 1. Modelled patient flow from diagnosis to LOT4



Patients could change treatment type when they transitioned to the next LOT, with the following assumptions: for SCT-eligible patients, the first LOT represents induction, SCT, and maintenance therapy post-SCT; patients initiating treatment after third LOT are assumed to have been exposed at least once to a proteasome inhibitor and an immunomodulatory agents; neither retreatment with with DAR between subsequent LOTs nor DAR retreatment in two sequential LOTs is allowed. DAR, daratumumab; LOT, line of treatment; SCT, stem cell transplant.

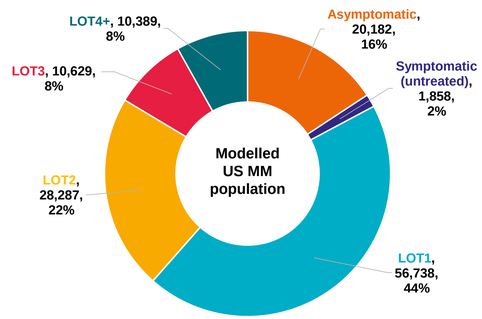
Results

Overall distribution of patients with MM in the US

At steady-state conditions, the model projected an overall MM prevalence of 128,083 patients in the US (**Figure 2**). Of these, 20,182 were asymptomatic and 1,858 symptomatic (untreated), with 106,043 receiving treatment (of whom, LOT1: 54% [n=56,738]; LOT2: 27% [n=28,287]; LOT3: 10% [n=10,629]; LOT4+: 10% [n=10,389]).

The estimate of 128,083 patients compares well with an estimate derived from the Surveillance, Epidemiology, and End Results program (SEER) 2016 data of 131,392 (based on a population size of 327,167,434 and implied incidence of 9.81 per patient-year).[2,9,10]

Figure 2. Model prediction of the US MM population size by LOT



GSK data on file 2020. LOT, line of treatment; MM, multiple myeloma.

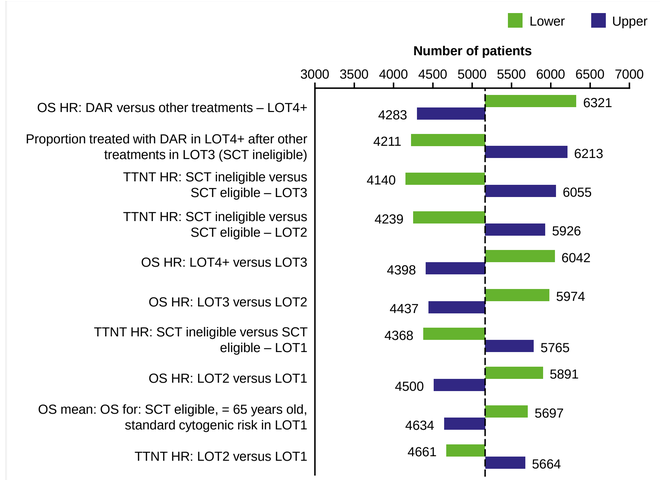
Patients with prior exposure to a PI, an immunomodulatory agent and/or an anti-CD38 antibody (represented by DAR)

An estimated 50% (5156/10,389) of patients in LOT4+ (standard deviation [SD] by probabilistic sensitivity analysis=1361); 26% had prior exposure to a PI, an immunomodulatory agent, and/or an anti-CD38 mAb as represented by DAR.

Sensitivity analyses

Model estimates of the number of US patients with MM at LOT4+ with prior PI, immunomodulatory agents, and DAR exposure were most sensitive to mortality, TTNT, and the proportion of patients receiving DAR in LOT4+ (**Figure 3**).

Figure 3. OWSA for predicted prevalence of MM in the US



The maximum variation of the target population size was between 6321 and 4140 patients and was associated with variations in the OS HR of DAR versus other treatments in LOT4+; thus mortality and number of patients receiving DAR were heavily influential. The TTNT HR of SCT ineligible versus eligible patients was the next most influential parameter.
DAR, daratumumab; HR, hazard ratio; LOT, line of treatment; MM< multiple myeloma; OS, overall survival; OWSA, one-way sensitivity analysis, SCT, stem cell transplant; TTNT, time to next treatment.

Conclusions

This study is among the first to estimate the current number of patients with MM in the US by LOT, accounting for recent changes in the treatment landscape. Our up-to-date estimate can be used as a basis for understanding patient treatment experience and need in this difficult-to-treat population.

The epidemiological model allows for projections of the number of patients by LOT with certain treatment exposure characteristics (e.g., patients in LOT4+ whose prior treatments include PIs, immunomodulatory agents, and anti-CD38 mAb). This modelling framework can be adapted to other settings outside the US.

Study limitations include: input derivation for TTNT and OS was based on exponential distribution; target population prediction is based on steady-state while in the real world the target population evolves in response to treatment changes; model inputs were based on multiple real-world effectiveness studies potentially biasing results due to heterogeneity across studies; DAR market shares are expected to evolve.

Disclosures
AN, **MO** and **JCR** are employees of Evidera; **CH**, **FW** and **YS** are employees of and hold stocks and shares in GlaxoSmithKline.
NJ was an employee of GlaxoSmithKline at the time of the study.

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Author email address: Andreas.Nikolaou@evidera.com

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