Cost-effectiveness of Daratumumab-based Triplet Therapies in Patients With Relapsed or Refractory Multiple Myeloma

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ABSTRACT

Purpose: The prominent efficacy of the addition of daratumumab to lenalidomide and dexamethasone (DRd) or the addition to bortezomib and dexamethasone (DVd) was proven previously for patients with relapsed or refractory multiple myeloma (RRMM). However, the cost-effectiveness of adding daratumumab to traditional doublet regimens versus doublet regimens alone (DRd vs Rd; DVd vs Vd) was unknown.

Methods: We developed a semi-Markov model by using a US payer perspective and 10-year time horizon to estimate the cost and quality-adjusted life years (QALYs) for treatments. Clinical data were obtained from the POLLUX (Phase 3 Study Comparing DRd Versus Rd in Subjects with Relapsed or Refractory Multiple Myeloma [RRMM]) and CASTOR (Phase 3 Study Comparing DVd Versus Vd in Subjects with RRMM) trials. Deterministic and probabilistic sensitivity analyses were conducted to evaluate model uncertainty.

Findings: The incremental cost-effectiveness ratio (ICER) for DVd compared with Vd was $284,180 per QALY; the ICER for DRd compared with Rd was $1,369,062 per QALY. Only when the price of daratumumab was reduced to 37% (US $702/vial) of the current price could the addition of daratumumab to Vd be cost-effective under the US willingness-to-pay (WTP) of $50,000/QALY. However, under no discount level of the daratumumab price is the addition of daratumumab to Rd acceptable. When the WTP increased to $300,000/QALY, the addition of DVd had a 56.7% probability of being cost-effective compared with the Vd regimen.

Implications: Due to the high price of daratumumab, neither the addition of daratumumab to Rd nor Vd proved to be cost-effective under US WTP. However, if the daratumumab price fell to a certain discount level, the DVd regimen might be cost-effective. (*Clin Ther*. 2018;■:1–18) © 2018 Published by Elsevier Inc.

Key words: daratumumab, relapsed or refractory, multiple myeloma, cost-effectiveness.

INTRODUCTION

Multiple myeloma (MM) is characterized by the disorder of plasma cells in the bone marrow. MM is the second most common hematologic cancer. In the United States, MM accounts for 1.8% and 17.5% of all new cancers and hematologic malignancies, respectively. There were ~30,280 new diagnosed cases of MM and 12,590 MM-related deaths in 2017 in the United States.[1] Most of the patients with MM experience relapses after first-line treatment.[2]

Up to now, although relapsed or refractory MM (RRMM) remains incurable, patient survival was

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Table I. Triplet preferred regimens anchored with novel drugs approved by the US Food and Drug Administration for relapsed or refractory multiple myeloma.

Novel Agent	Brand Name	Triplet Regimen	Indications	Trial Name
Carfilzomib	Kyprolis	KRd	Received 1 to 3 prior therapies	ASPIRE[52]
Elotuzumab	Empliciti	ERd		ELOQUENT-2[53]
Ixazomib	Ninlaro	IRd	Received at least	TOURMALINE-MM1[54]
Daratumumab	Darzalex	DRd	1 prior therapy	POLLUX[10]
		DVd		CASTOR[11]
		DPod	Received at least	NCT01998971[55]
Panobinostat	Farydak	PVd	2 prior therapies	PANORAMA-1[56]

ASPIRE = A Randomized, Multicenter, Phase 3 Study Comparing Carfilzomib, Lenalidomide, and Dexamethasone Versus Lenalidomide and Dexamethasone in Subjects With Relapsed Multiple Myeloma; CASTOR = Phase 3 Study Comparing DVd Versus Vd in Subjects with RRMM; D = daratumumab; E = elotuzumab; ELOQUENT-2 = Phase 3, Randomized, Open Label Trial of Lenalidomide/Dexamethasone With or Without Elotuzumab in Relapsed or Refractory Multiple Myeloma; I = ixazomib; K = carfilzomib; P = panobinostat; PANORAMA-1 = A Multicenter, Randomized, Double Blind, Placebo Controlled Phase III Study of Panobinostat in Combination With Bortezomib and Dexamethasone in Patients With Relapsed Multiple Myeloma; Pod = pomalidomide and dexamethasone; POLLUX = Phase 3 Study Comparing DRd Versus Rd in Subjects with Relapsed or Refractory Multiple Myeloma (RRMM); Rd = lenalidomide and dexamethasone; TOURMALINE-MM1 = A Phase 3, Randomized, Double-Blind, Multicenter Study Comparing Oral Ixazomib (MLN9708) Plus Lenalidomide and Dexamethasone Versus Placebo Plus Lenalidomide and Dexamethasone in Adult Patients With Relapsed and/or Refractory Multiple Myeloma; Vd = bortezomib and dexamethasone.

prolonged significantly due to novel regimens recently approved by the US Food and Drug Administration. In virtue of the outstanding survival outcomes,[3] triplet regimens anchored with these novel agents plus traditional regimens are now recommended for RRMM in clinical practice guidelines as standard therapies. According to the latest guidelines, except for elderly or frail patients, almost all patients with RRMM who had received at least 1 or 1 to 3 prior therapies were recommended for the triplet regimens (Table I).[4]

Daratumumab is a humanized IgG1κ monoclonal antibody that kills MM cells, targeting the CD38 protein, a cell surface protein that is prominently expressed on myeloma cells and plays numerous roles in myeloma tumorigenesis.[5] It is approved in combination with lenalidomide, bortezomib plus dexamethasone (DRd, DVd) for patients with RRMM who have received at least 1 prior therapy. Recently, 4 articles compared the efficacy of the medications for RRMM; the results indicate that DRd and DVd have a higher probability of providing the longest progression-free survival (PFS) among patients who have received at least 1 prior therapy.[6–9]

Conversely, against the remarkable efficacy, a heavy economic burden became evident as well as negative issues due to the high expenditure for long-term use of daratumumab-based triplet regimens. In addition to information regarding efficacy, evidence concerning the cost-effectiveness of the DRd and DVd regimens is also an essential consideration when making clinical and health insurance policy decisions.

In the present study, we developed a decision analysis model to determine the cost-effectiveness from a US health care payer perspective of the addition of daratumumab to traditional doublet regimens (DRd and DVd) compared with doublet regimens (Rd or Vd) alone for patients with RRMM who received at least 1 prior therapy.

MATERIALS AND METHODS

The present analysis was conducted on the basis of 2 randomized clinical trials (RCTs): POLLUX (Phase 3 Study Comparing DRd Versus Rd in Subjects with Relapsed or Refractory Multiple Myeloma [RRMM]) and CASTOR (Phase 3 Study Comparing DVd Versus Vd in Subjects with RRMM).[10,11] The 2 RCTs were multicenter, randomized, open-label, active-controlled, Phase III trials. In addition, POLLUX compared the efficacy between the DRd and Rd regimens and