A phase 2 safety study of accelerated elotuzumab infusion, over less than 1 h, in combination with lenalidomide and dexamethasone, in patients with multiple myeloma

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Funding information
Bristol-Myers Squibb; AbbVie

Biotherapeutics

Abstract
Elotuzumab, an immunostimulatory SLAMF7-targeting monoclonal antibody, induces myeloma cell death with minimal effects on normal tissue. In a previous phase 3 study in patients with relapsed/refractory multiple myeloma (RRMM), elotuzumab (10 mg/kg, ~3-h infusion), combined with lenalidomide and dexamethasone, demonstrated durable efficacy and acceptable safety; 10% (33/321) of patients had infusion reactions (IRs; Grade 1/2: 29; Grade 3: 4). This phase 2 study (NCT02159365) investigated an accelerated infusion schedule in 70 patients with newly diagnosed multiple myeloma or RRMM. The primary endpoint was cumulative incidence of Grade 3/4 IRs by completion of treatment Cycle 2. Dosing comprised elotuzumab 10 mg/kg intravenously (weekly, Cycles 1-2; biweekly, Cycles 3+), lenalidomide 25 mg (daily, Days 1-21), and dexamethasone (28 mg orally and 8 mg intravenously, weekly, Cycles 1-2; 40 mg orally, weekly, Cycles 3+), in 28-day cycles. Premedication with diphenhydramine, acetaminophen, and ranitidine (or their equivalents) was given as in previous studies. If no IRs occurred, infusion rate was increased in Cycle 1 from 0.5 to 2 mL/min during dose 1 (~2 h 50 min duration) to 5 mL/min for the entire infusion by dose 3 and also during all subsequent infusions (~1-h duration). Median number of treatment cycles was six. No Grade 3/4 IRs occurred; only one Grade 1 and one Grade 2 IR occurred, both during the first infusion. These data support the safety of a faster infusion of elotuzumab administered over ~1 h by the third dose, providing a more convenient alternative dosing option for patients.

1 INTRODUCTION

Multiple myeloma (MM) is a progressive hematological bone marrow-based malignancy of terminally differentiated B lymphocytes (plasma cells) characterized by the aberrant accumulation of M protein, a monoclonal antibody (mAb). In recent years, several new therapeutic agents have been introduced. Current treatment guidelines recommend autologous stem cell transplantation (when eligible), chemotherapy (melphalan, cyclophosphamide, or pegylated liposomal doxorubicin), proteasome inhibitor (PI)-based regimens (bortezomib, carfilzomib, or ixazomib), and immunomodulatory drug (IMiD)-based regimens (thalidomide, lenalidomide, or pomalidomide), often coupled with a corticosteroid (eg, dexamethasone). Combined treatments (usually three agents; triplets) have been notably effective in improving patient outcomes. Unfortunately, long-term prognosis remains poor despite recent advances, with relapse and subsequent development of refractory disease being almost inevitable. Additionally, treatment with intravenous agents can involve frequent and/or time-consuming

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outpatient visits. New treatments with novel mechanisms of action and more convenient administration protocols, which would allow patients to fully benefit from available therapies, are needed. Recently, daratumumab (a humanized immunoglobulin [Ig]G1 mAb that targets the CD38 protein on plasma cells) and elotuzumab became the first two mAbs to have been approved for the treatment of patients with relapsed/refractory MM (RRMM).4,5,10,11

Elotuzumab is a humanized IgG1 immunostimulatory mAb that selectively targets signaling lymphocytic activation molecule family member 7 (SLAMF7) via a novel immunotherapeutic dual mechanism of action.12,13 SLAMF7 is expressed on natural killer cells and myeloma cells. Binding of elotuzumab to SLAMF7 on natural killer cells and myeloma cells directly activates these immune cells and indirectly enhances their anti-myeloma activity through antibody-dependent cell-mediated cytotoxicity (ADCC) via the CD16 pathway, resulting in increased targeted cell death of elotuzumab-bound myeloma cells that also express SLAMF7 and undergo apoptosis.14

In preclinical myeloma xenograft models involving mice, elotuzumab demonstrated dose-dependent antitumor activity via ADCC.15 Furthermore, elotuzumab in combination with lenalidomide (an IMiD) and bortezomib (a PI) enhanced ADCC in vitro, potentially mediated through enhancement of natural killer cell activity.16,17

On November 30, 2015, the US Food and Drug Administration approved the three-drug combination of elotuzumab plus lenalidomide and dexamethasone for use in patients with MM who had received 1-3 prior therapies, based on the positive results of the ELOQUENT-2 study (NCT01239797).4,18 Approval by the European Medicines Agency followed in May 2016 for adult patients with MM who had received one or more therapies.10

In a phase 1b/2 dose-escalation study of elotuzumab plus lenalidomide and dexamethasone for patients with RRMM (study 1703 [NCT07424560]) and a phase 2 study of elotuzumab in combination with bortezomib and dexamethasone (study 009 [NCT01478048]), this mAb was initially administered at 0.5 μL/min and then increased to 2 μL/min. If an infusion reaction (IR) did not occur, the infusion rate could be increased to 5 μL/min (duration ~1 h) after Cycle 4.19,20 In study 1703, patients with RRMM receiving elotuzumab plus lenalidomide and dexamethasone demonstrated an overall response rate (ORR) of 84% and a median progression-free survival of 28.6 months.19 The most common Grade 3/4 adverse events (AEs) were lymphopenia (21%) and neutropenia (19%). As a result of previous trials, elotuzumab was studied in combination with lenalidomide in the phase 3 ELOQUENT-2 study, in which patients receiving elotuzumab plus lenalidomide and dexamethasone showed a 30% relative reduction in the risk of disease progression or death when compared with patients receiving lenalidomide and dexamethasone alone, with minimal incremental toxicity.18 Common Grade 3/4 AEs were lymphopenia, neutropenia, fatigue, and pneumonia.

Administration of mAbs is known to carry a risk of IRs, most often independent of infusion rate. These hypersensitivity reactions can manifest as coughing, shortness of breath, changes in heart rate, nausea/vomiting, flushing, pruritus, fever, and chills. Premedication regimens including antihistamines, acetaminophen, and corticosteroids are commonly used in clinical practice to mitigate the incidence and severity of such reactions.21 The premedication regimens were adopted because of the known risk of IRs associated with mAb therapy. During study 1703, a premedication regimen that included dexamethasone, diphenhydramine, ranitidine, and acetaminophen was established as effective at limiting potential IRs due to elotuzumab administration. Specifically, IRs occurred in 11% of patients; most IRs observed were Grade 1/2, with one Grade 3 IR (rash). When the infusion rate was increased to >2 μL/min, one Grade 1/2 IR (nausea) and no Grade 3/4 IRs were observed. Thirty-one patients had the infusion rate escalated to 5 μL/min; 33% of all infusions given during the study were at 5 μL/min, and one patient experienced an IR (Grade 1 nausea) at this rate.19 In study 009 of elotuzumab plus bortezomib/dexamethasone, the rate of IRs was 5%; all were Grade 1/2. One IR was reported among the 27 patients who had received the 5 μL/min infusion.20

The premedication regimen and administration schedule of these medications implemented in studies 1703 and 009 were shown to successfully reduce the number and severity of IRs associated with elotuzumab.19,22 As a result, this premedication regimen, or an appropriate equivalent, is currently required for all patients prior to infusion of elotuzumab. In the ELOQUENT-2 study, patients received the premedication regimen that had been developed during study 1703.18 Premedication consisted of oral dexamethasone 28 mg 3-24 h prior to each elotuzumab infusion and then an additional 8 mg administered intravenously 30-90 min before the infusion along with diphenhydramine (25-50 mg), ranitidine (50 mg), and acetaminophen (650-1000 mg), or their equivalents.18,19 In the ELOQUENT-2 study, IRs occurred in 33/321 patients (10%) in the elotuzumab arm and were mostly Grade 1/2 (29 patients [9%]), with 1% (4 patients) at Grade 3. Two patients (1%) discontinued treatment because of an IR.

The current prescribing information for elotuzumab states that the infusion rate can be increased to 5 μL/min after four treatment cycles (ie, 12 doses).4 Based on previous studies that demonstrated low levels of IRs at 5 μL/min,18,20 we conducted a study to determine whether infusing this mAb at the rate of 5 μL/min could be achieved safely within the first cycle, rather than after four treatment cycles, thus increasing convenience for patients and reducing resource use during the administration of elotuzumab mAb therapy. This study aimed to assess the safety and tolerability of elotuzumab administered at the rate of 5 μL/min (~1-h infusion time) by the third dose (dose 3 of treatment Cycle 1), in combination with lenalidomide and dexamethasone, for patients with newly diagnosed MM or RRMM who had received 1-3 prior regimens.

2 | METHODS

2.1 | Trial design

This phase 2, open-label, single-arm safety study (NCT02159365) was carried out at multiple sites across the United States. Treatment was administered in 28-day cycles until disease progression or unacceptable toxicity, as follows: elotuzumab was administered intravenously at a
dose of 10 mg/kg on Days 1, 8, 15, and 22 during Cycles 1 and 2, and on Days 1 and 15 from Cycle 3 onward; lenalidomide 25 mg was taken orally once daily on Days 1-21; and dexamethasone was administered 3-24 h (28 mg orally) and 45-90 min (8 mg intravenously) prior to each elotuzumab infusion and, starting with Cycle 3, once weekly (40 mg orally) on the non-elotuzumab dosing weeks (Supporting Information, Fig. 1). As previously described, the premedication regimen was compulsory for all patients. In addition to dexamethasone, it consisted of an H1 blocker (diphenhydramine 25-50 mg orally or intravenously, or equivalent), an H2 blocker (ranitidine 50 mg intravenously or equivalent), and acetaminophen (650-1000 mg orally) administered 45-90 min prior to the initiation of the elotuzumab infusion. No postinfusion corticosteroids were administered.

The accelerated infusion schedule is detailed in Table 1. Briefly, during Cycle 1, the elotuzumab infusion rate was increased, in the absence of IRs at each step, from 0.5 to 2 mL/min during dose 1 (duration $\approx$2 h 50 min), from 3 to 4 mL/min during dose 2 (duration $\approx$1 h 13 min), and to 5 mL/min for all subsequent doses (duration <1 h). The times for each infusion as specified above were based on a patient of average weight (80 kg). From Cycle 1, dose 3 onward, elotuzumab was administered at 5 mL/min. If an IR occurred during infusion at any rate, the following responses were required: for Grade 1 IR, no intervention (but increased monitoring recommended); for Grade 2/3, infusion interrupted and treatment given as clinically indicated; once resolved to Grade $\leq$1, infusion was restarted at 0.5 mL/min; if no recurrence, acceleration was continued as per the previous schedule; for Grade 4 IR, discontinuation from the study.

2.2 | Patients

Key inclusion criteria included age $\geq$18 years, documented evidence of active, newly diagnosed MM (stem cell transplantation-ineligible) or RRMM (with up to three prior lines of therapy), and Eastern Cooperative Oncology Group performance status $\leq$2. Prior lenalidomide exposure was permitted provided that patients were not refractory and did not discontinue lenalidomide due to related Grade $\geq$3 AEs.

The study protocol was approved by the Institutional Review Board/Independent Ethics Committee prior to initiation of the study at each site, and the study was conducted in accordance with Good Clinical Practice and the Declaration of Helsinki. Informed written consent was obtained from each study participant.

2.3 | Endpoints and assessments

The primary endpoint was the incidence of Grade 3/4 IRs by the end of treatment Cycle 2. The secondary endpoints were the overall incidence of IRs of any grade and specifically Grade 3/4 IRs. An IR was defined as any relevant sign or symptom occurring during or after elotuzumab infusion that was considered by the investigator to be an IR.

Exploratory endpoints included safety and efficacy, determined by ORR (partial response or better), as assessed using International Myeloma Working Group criteria. Response and progression assessment were investigator-based.

2.4 | Statistical analysis

Information on overall safety was reported for all treated patients (safety analysis set: patients who had received at least one elotuzumab infusion). The IRs observed overall, as well as the incidence of Grade 3/4 IRs, were reported throughout the study. The cumulative incidence rate of investigator-reported IRs by the completion of the second cycle of infusions and its 95% confidence interval (CI) were estimated. The efficacy analysis set included the subset of the safety analysis set that also had at least one efficacy assessment completed. Descriptive statistics—including number of patients with recorded values, mean, median, minimum, and maximum—are reported for all patients and analysis sets. Data cutoff for the analyses reported herein was September 21, 2015.

3 | RESULTS

3.1 | Patients and dosing

Seventy patients (median age 67.5 years) were enrolled, of whom 33 (47%) had received prior MM therapy. Prior therapy included

| Infusion rate (mL/min) | Duration of infusion (min) | Volume delivered (mL) | Volume remaining (mL) |
|-----------------------|---------------------------|----------------------|----------------------|
| Cycle 1, dose 1. Approximate total duration: 2 h 50 min | 0.5 | 30 | 15 | 262a |
| | 1 | 30 | 30 | 247 |
| | 2 | 110 | 217 | 0 |
| Cycle 1, dose 2. Approximate total duration: 1 h 13 min | 3 | 30 | 90 | 262a |
| | 4 | 43 | 172 | 0 |
| Cycle 1, doses 3 and 4. Approximate total duration: 53 min | 5 | 53 | 262 | 262a |
| | | 0 | 0 |
| Cycle 2+. Approximate total duration: 53 min | 5 | 53 | 262 | 262a |
| | | 0 | 0 |

*aVolume for patient weighing 80 kg. Total volume varies according to patient weight. Increase of infusion rate to the next (higher) level was permitted only if no infusion reactions were encountered.*
bortezomib, dexamethasone, carfilzomib, and lenalidomide in 41%, 37%, 17%, and 13% of patients, respectively. Baseline demographics and disease characteristics are summarized in Table 2.

At data cutoff, 48 patients (69%) remained on treatment. The main reason for discontinuation of study treatment was disease progression, in 11 patients (16%; Supporting Information, Fig. 2).

The median number of study treatment cycles was 6 (range 1-13) and 49 patients (70%) received ≥90% of the relative intended dose of elotuzumab. Of the 1,113 elotuzumab infusions given, 87% (968) were given at the maximum 5 mL/min rate; of the remaining 13% (145), 144 infusions were given during the dose acceleration phase in Cycle 1, doses 1 and 2, as per protocol, whereas the rate for one infusion was not reported (Tables 1 and 3). Of the 70 patients enrolled, 65 patients received two or more full cycles (the primary endpoint for analysis). Five patients, none of whom experienced an IR, had only one cycle of treatment. Four of these patients discontinued treatment due to AEs unrelated to any of the study drugs, including a severe AE (SAE) of spinal cord compression, Grade 2 neutropenia, fatal ischemic colitis with SAEs of metabolic acidosis and septic shock, and death from respiratory failure due to chronic obstructive pulmonary disease. A fifth patient discontinued treatment following withdrawal of consent. Relative dose intensity of ≥90% was achieved in 19 (27%) and 12 (17%) patients for lenalidomide and dexamethasone, respectively. For lenalidomide, the initial dose (25 mg) received was reduced during treatment in 39 (56%) patients. The main reason for reduction in dose was nonhematological toxicity, in 19 (27%) patients. For dexamethasone, dose reduction was also carried out in 19 (27%) patients; the main reason given, in 11 (16%) patients, was nonhematological toxicity. All dexamethasone dose reductions were for the orally administered dose. Reduction in elotuzumab dose was not permitted in this study.

### 3.2 | Safety

The primary endpoint analysis showed that there were no Grade 3/4 IRs by the end of treatment Cycle 2 (exact 95% CI: 0%-5.1%). As of September 2015, only two patients had experienced an IR, both while receiving their first dose of elotuzumab, and both at the 2 mL/min rate (Table 3). The patient experiencing a Grade 2 IR was reported as having a nonspecific “infusion-related reaction,” and infusion was interrupted, followed by administration of diphenhydramine and hydrocortisone. The IR was considered resolved after 10 min and the infusion was restarted without further problems. Specifically, the patient had a total of nine treatment cycles and a treatment duration of 7.9 months. A second patient experienced a Grade 1 IR described as pyrexia, 6.5 h and 24 h after elotuzumab dose 1 during Cycle 1 and was treated with ibuprofen. Infusion was not interrupted because of this reaction. This patient had six cycles of elotuzumab and five cycles of lenalidomide and dexamethasone (treatment durations of 4.8, 3.9, and 4.4 months, respectively). None of the IRs observed led to discontinuation of treatment; both patients were still on study at data cutoff.

### TABLE 2 Baseline demographics and disease characteristics

| Characteristic                  | Patients (N = 70) |
|--------------------------------|-------------------|
| Age categorization, years      |                   |
| <65                            | 26 (37)           |
| 65-74                          | 23 (33)           |
| ≥75                            | 21 (30)           |
| Male                           | 35 (50)           |
| White                          | 57 (81)           |
| Myeloma type                   |                   |
| IgG                            | 41 (59)           |
| IgA                            | 11 (16)           |
| IgM                            | 1 (1)             |
| IgD                            | 1 (1)             |
| Light chain disease            |                   |
| Nonsecretory                   | 0 (0)             |
| Not classified/not reported    | 3 (4)             |
| Median (range) M protein in serum, g/L | 14 (0–73) |
| Performance status (ECOG), n (%) |     |
| 0                              | 34 (49)           |
| 1                              | 32 (46)           |
| 2                              | 4 (6)             |
| Prior lines of therapy         |                   |
| None                           | 37 (53)           |
| 1                              | 13 (19)           |
| 2                              | 13 (19)           |
| 3                              | 7 (10)            |
| Prior drugs (in >10% of patients) |               |
| Bortezomib                     | 29 (41)           |
| Dexamethasone                  | 26 (37)           |
| Carfilzomib                    | 12 (17)           |
| Cyclophosphamide               | 11 (16)           |
| Lenalidomide                   | 9 (13)            |
| Doxorubicin hydrochloride (liposome) | 9 (13) |

Values shown as n (%) of patients unless indicated otherwise.
ECOG, Eastern Cooperative Oncology Group; Ig, immunoglobulin.

### TABLE 3 Infusion reactions by infusion rate

| Elotuzumab infusion rate, mL/min | Total number of infusions (N = 1113) | Grade 1-2 n (%) | Grade 3-4 n (%) |
|----------------------------------|--------------------------------------|-----------------|-----------------|
| <2                               | 0                                    | 0               | 0               |
| 2                                | 72                                   | 2 (2.8)         | 0               |
| 3                                | 0                                    | 0               | 0               |
| 4                                | 71                                   | 0               | 0               |
| >4-5                             | 1                                    | 0               | 0               |
| Not reported                     | 1                                    | 0               | 0               |

*aCommon Terminology Criteria for Adverse Events version 3.0. Percentages based on the total number of infusions.*

*bPercentages based on the number of infusions at the specified infusion rate.*
The most common any grade AEs overall were infection (n = 42, 60%), fatigue (n = 35, 50%), and diarrhea (n = 22, 31%); any AEs that were observed in \( \geq 15\% \) of patients are detailed in Table 4. Eight patients experienced Grade 4 AEs. AEs led to discontinuation of one or more study drug in 13 patients (19%), in whom the most common events (\( \geq 1 \) patient) were infection (n = 3), spinal cord compression (n = 2), and neutropenia (n = 2). SAEs were observed in 27 patients (39%), most commonly pneumonia and atrial fibrillation, both in three patients (4%). Three patients experienced an AE of pulmonary embolism (all Grade 4), two of which were considered SAEs and related to lenalidomide and dexamethasone but not elotuzumab. Four patients had a deep vein thrombosis AE (two Grade 1 and two Grade 2); one of these patients had a history of deep vein thrombosis and suffered a Grade 2 SAE of deep vein thrombosis, in both legs, which was associated with lenalidomide and dexamethasone treatment only. No second primary malignancies were reported.

Five deaths occurred during the study (or within 60 days of the last dose) and were due to MM progression (n = 1), ischemic bowel syndrome (n = 1), fatal bleeding (n = 1), and respiratory failure (n = 2); none of these deaths were attributed to study treatment. One case of respiratory failure was accompanied by atrial fibrillation and hypotension, whereas the other case resulted from advanced chronic obstructive pulmonary disease.

### 3.3 Responses

ORR for all patients was 70% (95% CI: 58%-80%), with responses achieved in 49/70 patients. ORR was 78% (95% CI: 62%-90%; 29/37) for newly diagnosed patients and 61% (95% CI: 42%-77%; 20/33) for patients with RRMM. Overall, complete response was achieved by four patients (6%), very good partial response by 19 (27%), partial response by 26 (37%), minimal response by four (6%), and stable disease by 13 (19%). The median time to first response was 1.7 months (range: 0.5-5.6 months).

### DISCUSSION

This phase 2 study evaluated the implementation of a faster infusion rate of 5 mL/min of elotuzumab beginning with the third dose of Cycle 1, for both previously untreated and treated patients with MM. Herein, the 5 mL/min infusion rate, achieved at the earlier time point of Cycle 1, dose 3 through acceleration from 0.5 mL/min during the first two doses of Cycle 1, led to an acceptable IR profile. Using this faster infusion, there were no Grade 3/4 IRs or discontinuations due to an IR and the overall rate of IRs was very low (0.2% of infusions); therefore, the safety of this 5 mL/min (\( \leq 1 \) h infusion time) rate compared favorably with the standard 2 mL/min (\( \geq 3 \) h infusion time) rate in previous clinical studies.\(^{18}\)

Only two reported Grade IRs, one Grade 1 and one Grade 2, occurred following administration of the first dose of the first treatment cycle at the 2 mL/min rate and did not result in discontinuation of elotuzumab; subsequent infusions at the accelerated 5 mL/min rate did not lead to any additional IRs. Overall, the types of AEs (including IRs) observed were similar to those reported in the ELOQUENT-2 study,\(^{18}\) with no new safety signals observed. Notably, the rate of IRs

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**TABLE 4** AEs in \( \geq 15\% \) of patients

| AE\(^a\)                  | Grade 1 n (%) | Grade 2 n (%) | Grade 3 n (%) | Any grade n (%) |
|--------------------------|--------------|--------------|--------------|----------------|
| Total number of patients with an AE | 8 (11)       | 22 (31)      | 28 (40)      | 70 (100)       |
| Fatigue                  | 14 (20)      | 16 (23)      | 5 (7)        | 35 (50)        |
| Diarrhea                 | 13 (19)      | 8 (11)       | 1 (1)        | 22 (31)        |
| Muscle spasms            | 15 (21)      | 1 (1)        | 1 (1)        | 17 (24)        |
| Constipation             | 11 (16)      | 4 (6)        | 1 (1)        | 16 (23)        |
| Pyrexia                  | 13 (19)      | 2 (3)        | 0            | 15 (21)        |
| Pruritus                 | 13 (19)      | 2 (3)        | 0            | 15 (21)        |
| Insomnia                 | 9 (13)       | 5 (7)        | 1 (1)        | 15 (21)        |
| Renal and urinary disorders | 7 (10)      | 5 (7)        | 1 (1)        | 15 (21)        |
| Anemia                   | 2 (3)        | 5 (7)        | 7 (10)       | 14 (20)        |
| Dyspnea                  | 9 (13)       | 3 (4)        | 1 (1)        | 13 (19)        |
| Nausea                   | 9 (13)       | 4 (6)        | 0            | 13 (19)        |
| Neutropenia              | 1 (1)        | 5 (7)        | 6 (9)        | 13 (19)        |
| Upper respiratory tract infection | 8 (11) | 3 (4)    | 0            | 11 (16)        |
| Rash                     | 11 (16)      | 0            | 0            | 11 (16)        |
| Injury, poisoning, and procedural complications | 5 (7) | 4 (6) | 1 (1) | 11 (16) |

AE, adverse event.

\(^a\)As defined in the Medical Dictionary for Regulatory Activities, Version 18.0, and the Common Terminology Criteria for Adverse Events, Version 3.0.
was lower than that reported in ELOQUENT-2, in which elotuzumab was infused at a maximum rate of 2 mL/min (~3 h infusion time). In ELOQUENT-2, IRs were observed in 10% of patients, the majority being either Grade 1 or 2, and resolved without discontinuation.\(^\text{18}\) The rates of AEs in our study were lower than those observed in study 1703, in which elotuzumab was infused at a maximum rate of 2 mL/min in Cycles 1–4 and could be escalated to a maximum rate of 5 mL/min thereafter, where only one Grade 1/2 IR was observed at >2 mL/min.\(^\text{19}\)

In addition, exploratory efficacy results demonstrated a partial response or better in 70% of patients. While bearing in mind that cross-trial comparisons should be done with caution, a number of factors may account for the ORR being slightly lower than that reported, for instance, in the phase 2 portion of study 1703 \((n = 73, \text{ORR } 84\%)\).\(^\text{19}\) These include the small sample size and disparate patient demographics, frequent dose reductions of lenalidomide and dexamethasone, and, notably, the inclusion of patients with prior exposure to lenalidomide in this study, as well as the higher proportion of patients aged >75 years \((30\% \text{ herein vs } 8\% \text{ in study 1703})\).\(^\text{19}\) The interpretation of efficacy is also limited by enrollment of both newly diagnosed patients with MM and patients with RRMM but no measurable disease. Treatment and patient follow-up are ongoing, with further analyses planned.

As the use of mAbs is increasing for the treatment of cancer, understanding how to administer them more safely and efficiently is becoming increasingly important. With daratumumab, another intravenous mAb recently approved in the United States and Europe for treating patients with RRMM, IRs occur in nearly half of the patients despite a longer, less convenient infusion time. The dosing schedule involves a first infusion using a dilution volume of 1000 mL \((\text{escalated to a maximum rate of } 200 \text{ mL/h})\) and, in the absence of Grade >1 IRs, a dilution volume of 500 mL is used at a maximum of 200 mL/h for the second and subsequent infusions.\(^\text{5}\) Premedication, including antihistamines, acetaminophen, and corticosteroids, as well as administration of corticosteroids for several days after infusion—also recommended when this mAb is given.\(^\text{5}\) The infusion time averages more than 7 h during the first infusion, and remains longer than 3 h for all subsequent infusions.\(^\text{5}\)

The use of faster infusion times with other mAbs has also been shown to reduce overall time spent receiving treatment, increase nursing satisfaction and, similarly, increase patient satisfaction.\(^\text{24–25}\) Decreasing infusion time, therefore, has the potential to improve delivery of the drug and reduce resource utilization, while increasing patient convenience and adherence, with a low risk of IRs.

In the present study, only two (3%) patients experienced an IR (one Grade 1 and one Grade 2) while receiving the drug at 2 mL/min, and none occurred at the faster 5 mL/min (~1 h) infusion rate, suggesting that the premedication regimen implemented in earlier elotuzumab trials\(^\text{18,19}\) was successful in mitigating IRs, even with an accelerated infusion schedule. Implementation of this infusion schedule reduces the time required to receive treatment with elotuzumab from the currently indicated ~3 h to ~1 h, with no reduction in efficacy or safety observed.

This study demonstrates that elotuzumab infusion can be safely accelerated to 5 mL/min by treatment Cycle 1, dose 3 (infused over ~1 h), with no increase in the incidence or severity of IRs. In fact, no IRs were observed during the infusion of elotuzumab at 5 mL/min in this study. Elotuzumab represents a new treatment option with a novel mechanism of action and clinically relevant outcomes for patients with MM, which can be administered at a more convenient accelerated infusion rate resulting in reduced time spent receiving treatment, providing patients with an alternative to the current dosing schedule.

ACKNOWLEDGMENTS

The authors would like to thank all the physicians and patients who took part in this study. This study was funded by Bristol-Myers Squibb (Princeton, NJ, USA) in collaboration with AbbVie Biopharmaceuticals (Redwood City, CA, USA). Medical writing assistance was provided by Kate Rees (Caudex, Oxford, UK) and editorial assistance by Hannah Lederman (Caudex, New York, NY, USA), and were funded by Bristol-Myers Squibb.

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**SUPPORTING INFORMATION**

Additional Supporting Information may be found in the online version of this article.

**How to cite this article:** Berenson J, Manges R, Badarinath S, et al. A phase 2 safety study of accelerated elotuzumab infusion, over less than 1 h, in combination with lenalidomide and dexamethasone, in patients with multiple myeloma. *Am J Hematol.* 2017;92:460–466. https://doi.org/10.1002/ajh.24687