ORIGINAL ARTICLE

Primary Results from IMscin002: A Study to Evaluate Patient Preferences and Perceptions of Health Care Professionals for Atezolizumab Subcutaneous Versus Intravenous for the Treatment of NSCLC

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Received 21 November 2024; revised 28 January 2025; accepted 11 February 2025
Available online - 19 February 2025

ABSTRACT

Introduction: Subcutaneous (SC) atezolizumab, a co-formulation containing atezolizumab and recombinant human hyaluronidase PH20), has been approved for use in more than 50 countries for the same indications as intravenous (IV) atezolizumab. IMscin002 (NCT05171777), a phase 2, randomized, open-label, crossover trial, investigated patient preferences and health care professionals' (HCPs') perceptions of atezolizumab SC versus IV for the treatment of NSCLC; we report the primary results of IMscin002.

Methods: Patients with programmed death-ligand 1-positive resected NSCLC who had completed adjuvant chemotherapy without evidence of recurrence, and chemotherapy-naive patients with programmed death-ligand 1–high metastatic NSCLC were randomized 1:1 to arm A (atezolizumab SC then atezolizumab IV) or arm B (atezolizumab IV then atezolizumab SC). After cycle 3, patients switched administration routes. After cycle 6, the patients chose the route of administration for the continuation period. The primary end point was patient preference for SC or IV atezolizumab, and the secondary end points were patient- and HCP-reported outcomes and safety.

Results: A total of 179 patients were included in this study. Most patients (70.7%; n = 87 of 123) preferred SC atezolizumab over IV, with 79.4% (n = 85 of 107) choosing SC atezolizumab during the continuation period. Among the HCPs, 75.2% (n = 76 of 101) indicated that atezolizumab SC

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Data from this study were presented at the ELCC 2024 in Prague, Czech Republic, March 20-23, 2024. Full citation at: Cappuzzo, F. et al. Primary results from IMscin002: A study evaluating patient- and health care professional-reported preferences for subcutaneous versus intravenous atezolizumab for the treatment of NSCLC. Presentation number: 244MO.

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Cite this article as: Cappuzzo F, Zvirbule Z, Korbenfeld E, et al. Primary results from IMscin002: a study to evaluate patient preferences and perceptions of health care professionals regarding subcutaneous versus intravenous atezolizumab for the treatment of NSCLC. *JTO Clin Res Rep*. 2025;6:100815.

ISSN: 2666-3643

https://doi.org/10.1016/j.jtocrr.2025.100815

was more convenient than IV, and 77.8% (n = 77 of 99) strongly agreed or agreed that it would allow patients to spend less time in care units. No new or unexpected safety findings were identified, and switching between administration routes was well tolerated and managed.

Conclusions: Most patients preferred SC atezolizumab over IV. There were no new safety findings, and switching between the administration routes was well tolerated. These results support the preference for SC formulations to reduce the treatment burden.

Keywords: IMscin002; Atezolizumab; Subcutaneous; Intravenous; Patient preferences

Introduction

Atezolizumab intravenous (IV) has been approved for for the treatment of various solid tumors, including NSCLC, SCLC, triple-negative breast cancer, and urothelial carcinoma.[1,2] Ateozlizumab subcutaneous (SC), a coformulation containing atezolizumab and recombinant human hyaluronidase PH20, has been approved for use in more than 50 countries and regions, including the European Union and Great Britain, for the same indications for which atezolizumab IV was previously approved.[3–5] The primary results of the phase 1b/3 IMscin001 study (NCT03735121) reported that atezolizumab SC had noninferior drug exposure in cycle 1 compared with atezolizumab IV,[6] and that the efficacy (including overall survival), safety, and immunogenicity were similar between the SC and IV arms.[6,7]

Studies investigating SC formulations of other anticancer therapies have shown that SC administration is associated with time and cost savings for health care centers compared with IV administration.[8–10] Atezolizumab SC administration had shorter median treatment times than IV administration (7.1 minutes versus 40.0 minutes, respectively), with most patients (75.7%) reporting an average SC injection time of four to eight minutes in the IMscin001 study.[7] In addition, health care professionals' (HCPs') perceptions of atezolizumab SC were positive; most HCPs were satisfied with atezolizumab SC, they found it convenient, easy to administer, and thought it could save time compared with IV infusion.[7] Importantly, previous studies have shown that patients prefer SC administration of anticancer therapies over IV administration owing to reduced pain and discomfort, shorter administration time, and reduced time in the clinic.[11–13]

To date, patient preference for atezolizumab SC or IV has not been investigated. Although there is evidence that other SC formulations are preferred by patients,[11–13] preference for atezolizumab SC and the reasons for this preference need to be confirmed. The safety of switching from IV to SC or vice versa also remains to be determined. We report the results of the primary analysis of the IMscin002 study (NCT05171777): patient preferences for atezolizumab SC versus IV, HCP perceptions of atezolizumab SC (including perceptions of time- and resource-saving benefits), and the safety of switching routes of administration.

Materials and Methods

IMscin002 is a phase 2 randomized multicenter open-label crossover study of SC versus IV atezolizumab in patients with programmed death-ligand 1-positive (PD-L1-positive) NSCLC (Fig. 1). Patients with PD-L1+ resected NSCLC (stage II, IIIA, or selected IIIB according to the American Joint Committee on Cancer eighth edition) who had completed adjuvant platinum-based chemotherapy without evidence of recurrence and chemotherapy-naive patients with PD-L1–high stage IV NSCLC were screened. Eligible patients were aged 18 years or older, had an Eastern Cooperative Oncology performance status of 0 to 1, and were *EGFR* or *ALK* wild-type. PD-L1 positivity, in patients with early-stage NSCLC only, was defined as minimum tumor cell (TC) expression of 1% or higher by VENTANA PD-L1 (SP263) immunohistochemistry (IHC) assay (Ventana Medical Systems, Tucson, AZ) or a tumor proportion score of 1% or higher by Dako PD-L1 IHC 22C3 pharmDx assay (Agilent Technologies, Santa Clara, CA). PD-L1-high, in patients with stage IV NSCLC only, was defined as a minimum TC expression of 50% or higher by VENTANA PD-L1 (SP263) IHC assay, a minimum tumor proportion score of 50% or higher by Dako PD-L1 IHC 22C3 pharmDx assay, or TC3 or immune cell 3 by VENTANA PD-L1 (SP142) IHC assay (Ventana Medical Systems, Tucson, AZ). PD-L1 testing was performed at both local and central laboratories.

The patients were randomized 1:1 to arm A (atezolizumab SC followed by atezolizumab IV) or arm B (atezolizumab IV followed by atezolizumab SC). Atezolizumab SC 1875 mg plus 30,000 U (recombinant human hyaluronidase PH20) or IV (1200 mg) was administered every 3 weeks, and patients were stratified according to disease stage (II versus III versus IV) and type of surgery (no surgery versus pneumonectomy versus any other surgery). Further details related to the preparation and administration of atezolizumab SC have previously been published.[6] The crossover period comprised cycles 1 through 6. Patients received either atezolizumab SC or IV for the first three cycles and then switched over to the

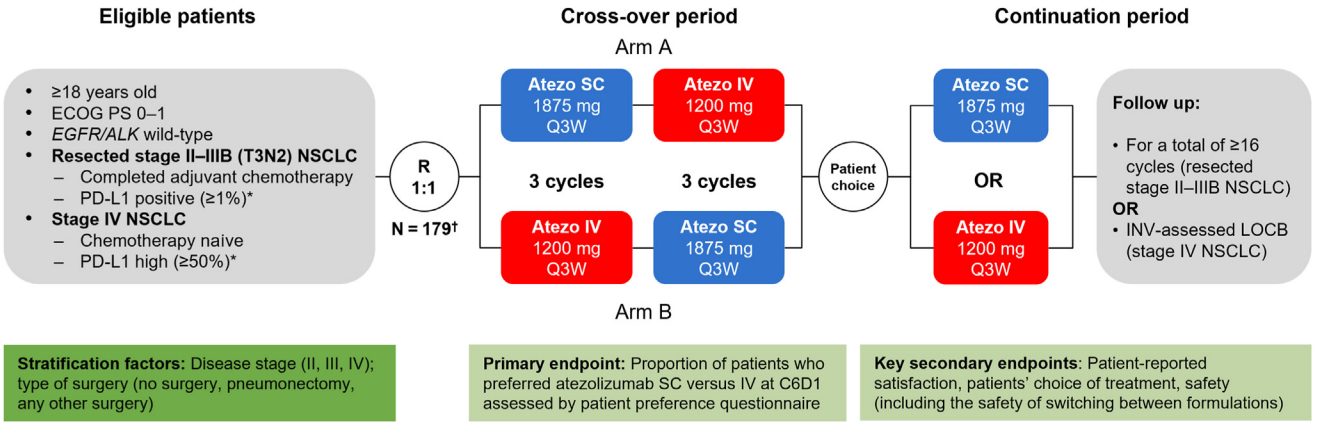


Figure 1. IMscin002 study design. *PD-L1 expression was assessed by a local or central laboratory using VENTANA PD-L1 (SP263) or Dako PD-L1 IHC 22C3 pharmDx assay. †On the basis of a 70% preference rate with plus or minus 8% precision for the 95% confidence interval and 28% missing questionnaire response rate. Atezo, atezolizumab; ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; INV, investigator; IV, intravenous; LOCB, loss of clinical benefit; PD-L1, programmed death-ligand 1; SC, subcutaneous.

alternative route of administration for the following three cycles. After cycle 6, the patients selected their administration route for the continuation period. Patients with resected NSCLC continued treatment for up to 16 cycles, whereas those with metastatic NSCLC continued treatment until the investigator-determined loss of clinical benefit.

The primary end point of the IMscin002 study was the proportion of patients who preferred SC to IV atezolizumab. Key secondary end points included patients' choice of administration route for the continuation period, patient-reported satisfaction with treatment administration, health-related quality of life (HRQoL), perception of time and resource use and convenience, and safety (including the safety of switching between formulations). Patient preference was assessed using question 1 of the Patient Preference Questionnaire (PPQ), in which all patients still receiving the study treatment were asked to complete cycle 6 day 1. Patients who discontinued treatment before cycle 6 day 1 were eligible to state their preferred administration route at the time of discontinuation if they received two or more consecutive doses of atezolizumab SC and IV. The PPQ used in this study was developed and used in clinical trials designed to assess patient preferences for the SC administration of monoclonal antibodies.[13–15] PPQ is a generic preference questionnaire designed to ask patients questions about which form of administration they preferred after receiving atezolizumab in two forms (SC and IV). The PPQ was composed of three questions: the first asked patients whether they preferred SC or IV, or had no preference; the second asked patients if they had a preference, to list the strength of their preference; and the third asked patients to state the reasons for their preference. The frequency with which individuals preferred one or the other was calculated, and frequency distributions were provided for the strength and reasons for the preference. Treatment satisfaction was assessed using the SC and IV Therapy Administration Satisfaction Questionnaire (TASQ), that all eligible patients were asked to complete following treatment on day 1 of cycles 3 and 6 during the cross-over period. The TASQ contained 12 questions investigating five factors: treatment satisfaction, convenience, physical impact, psychological impact, and impact on activities of daily living. Ten of these questions had five response options (response options were: very satisfied to very dissatisfied; none to very severe; not at all to very much; very convenient to very inconvenient; not at all bothered to very bothered; lost a lot of time to gained a lot of time; definitely yes to definitely not; yes, I had more than enough time to talk to my nurse and doctor to no, I did not talk to my nurse or doctor at all), one question required a "yes or no" answer and one question asked patients for their treatment preference. Two almost identical versions of the TASQ were used: one for patients receiving atezolizumab SC, and one for patients receiving atezolizumab IV.[16] HCP perception of time and resource and convenience was assessed using the Healthcare Professional Questionnaire; HCPs' perception of time and resource was assessed during the crossover period, and perception of convenience was assessed after administration of each patient's treatment at cycle 6.

HRQoL was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30) during the cross-over period (cycles 1, 3, and 6), treatment continuation period (cycles 7, 10, 13, and 16), and at the end of the study treatment. The EORTC QLQ-C30 consists of 30 questions that assess patient functioning, global health

Table 1. Patient Demographics and Baseline Characteristics

Patient Baseline Demographics and Disease Characteristics	Arm A: Atezolizumab SC Then IV (n = 90)	Arm B: Atezolizumab IV Then SC (n = 89)	All Patients (N = 179)
Median age, y (range)	68.5 (39-91)	66.0 (39-87)	67.0 (39-91)
Sex: male/female, n (%)	58 (64.4)/32 (35.6)	61 (68.5)/28 (31.5)	119 (66.5)/60 (33.3)
Race: White/Asian/American Indian or Alaska Native Native Hawaiian or Other Pacific/unknown, n (%)	74 (82.2)/8 (8.9)/2 (2.2) 0/6 (6.7)	75 (84.3)/5 (5.6)/1 (1.1) 1 (1.1)/7 (7.9)	149 (83.2)/13 (7.3)/3 (1.7) 1 (0.6)/13 (7.3)
ECOG PS: 0/1, n (%)	40 (44.4)/50 (55.6)	41 (46.1)/48 (53.9)	81 (45.3)/98 (54.7)
Tobacco use: Never/current/former, n (%)	11 (12.2)/22 (24.4)/57 (63.3)	5 (5.6)/27 (30.3)/57 (64.0)	16 (8.9)/49 (27.4)/114 (63.7)
Prior systemic cancer therapy: yes/no, n (%)	36 (40.0)/54 (60.0)	36 (40.4)/53 (59.6)	72 (40.2)/107 (59.8)
Disease stage at enrolment II/III/IV, n (%)	15 (16.7)/17 (18.9)/58 (64.4)	13 (14.6)/17 (19.1)/59 (66.3)	28 (15.6)/34 (19.0)/117 (65.4)
Nonsquamous/squamous NSCLC at initial diagnosis, n (%)	45 (50.0)/45 (50.0)	68 (76.4)/21 (23.6)	113 (63.1)/66 (36.9)
Type of surgery No surgery/pneumonectomy/other surgery, n (%)	51 (56.7)/9 (10.0)/30 (33.3)	52 (58.4)/9 (10.1)/28 (31.5)	103 (57.5)/18 (10.1)/58 (32.4)

ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; SC, subcutaneous.

status, and quality of life, three symptom scales (fatigue, nausea, vomiting, and pain), and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties).[17]

This study was conducted in accordance with the Declaration of Helsinki and the Good Clinical Practice Guidelines. Written informed consent was obtained from all the patients. The protocols were approved by the relevant institutional review boards of each study site.

Results

Study Population

From April 4, 2022, to July 28, 2023, 179 patients were randomized to arm A (atezolizumab SC followed by IV; n = 90) or arm B (atezolizumab IV followed by SC; n = 89), and four patients were randomized by error to arm A (atezolizumab SC followed by IV) and were removed from the study before receiving any treatment. At the data cutoff (November 9, 2023), the median treatment duration across the study was 6.0 months (range: 0.2–18.0 mo). In total, 59.8% of the patients (n = 107 of 179) completed the crossover period, 5.0% (n = nine of 179) were still receiving treatment in the crossover period, and 35.2% (n = 63 of 179) discontinued treatment (including the four patients in arm A who were randomized in error and did not receive treatment). Of the patients randomized to arm A, 21.1% (n = 19 of 90) discontinued atezolizumab SC before switching to atezolizumab IV, and 22.5% of those randomized to arm B (n = 20 of 89) discontinued atezolizumab IV before switching to atezolizumab SC. In total, 82.6% of the patients (n = 71 of 86) were randomized to arm A, received atezolizumab SC, and crossover to atezolizumab IV, and 77.5% of the patients (n = 69 of 89) were randomized to arm B, received atezolizumab IV, and crossover to atezolizumab SC. Among all the patients treated during the crossover period, 69.1% (n = 121 of 175) completed six cycles of atezolizumab.

Baseline characteristics were generally similar between the treatment groups (Table 1). The median age of all patients was 67 years (range: 39–91 y), over half of all patients (n = 98 of 179, 54.7%) had an Eastern Cooperative Oncology performance status of 1, and 63.7% of patients (n = 114 of 179) were former smokers. At initial diagnosis, a higher proportion of patients had nonsquamous NSCLC: 63.1% (n = 113 of 179) versus 36.9% (n = 66 of 179).

Patient-Reported Outcomes

A total of 126 patients (65 in arm A [atezolizumab SC followed by IV] and 61 in arm B [atezolizumab IV followed by SC]) were eligible to complete the PPQ; the PPQ completion rate was 97.6% (123 of 126). Three patients did not complete the questionnaire for the following reasons (n = 1 each): withdrawn consent, treatment at another hospital without returning to the site, or accidental omission. Most patients (70.7%, n = 87 of 123; 95% confidence interval: 61.9–78.6) preferred atezolizumab SC, 21.1% of patients (n = 26 of 123) preferred atezolizumab IV, and 8.1% of patients (n = 10 of 123) had no preference (Fig. 2*A*). Patients could choose up to two reasons for preferring atezolizumab SC: the patients' main reasons were that it reduced the time spent in the clinic (64.4%, n = 56 of 87), was a more comfortable route of administration (46.0%, n = 40 of 87), and they felt less emotional distress (29.9%, n = 26

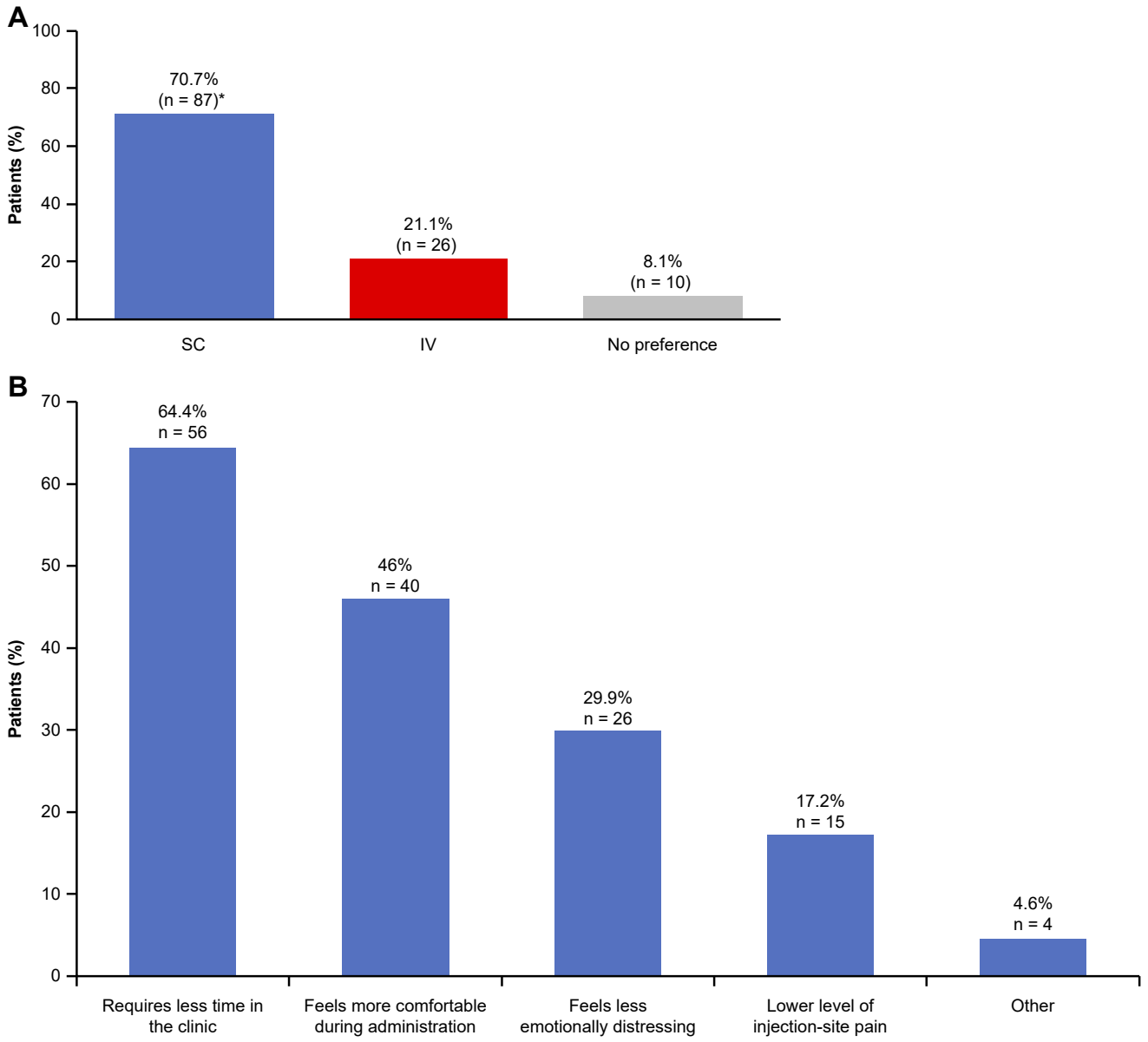
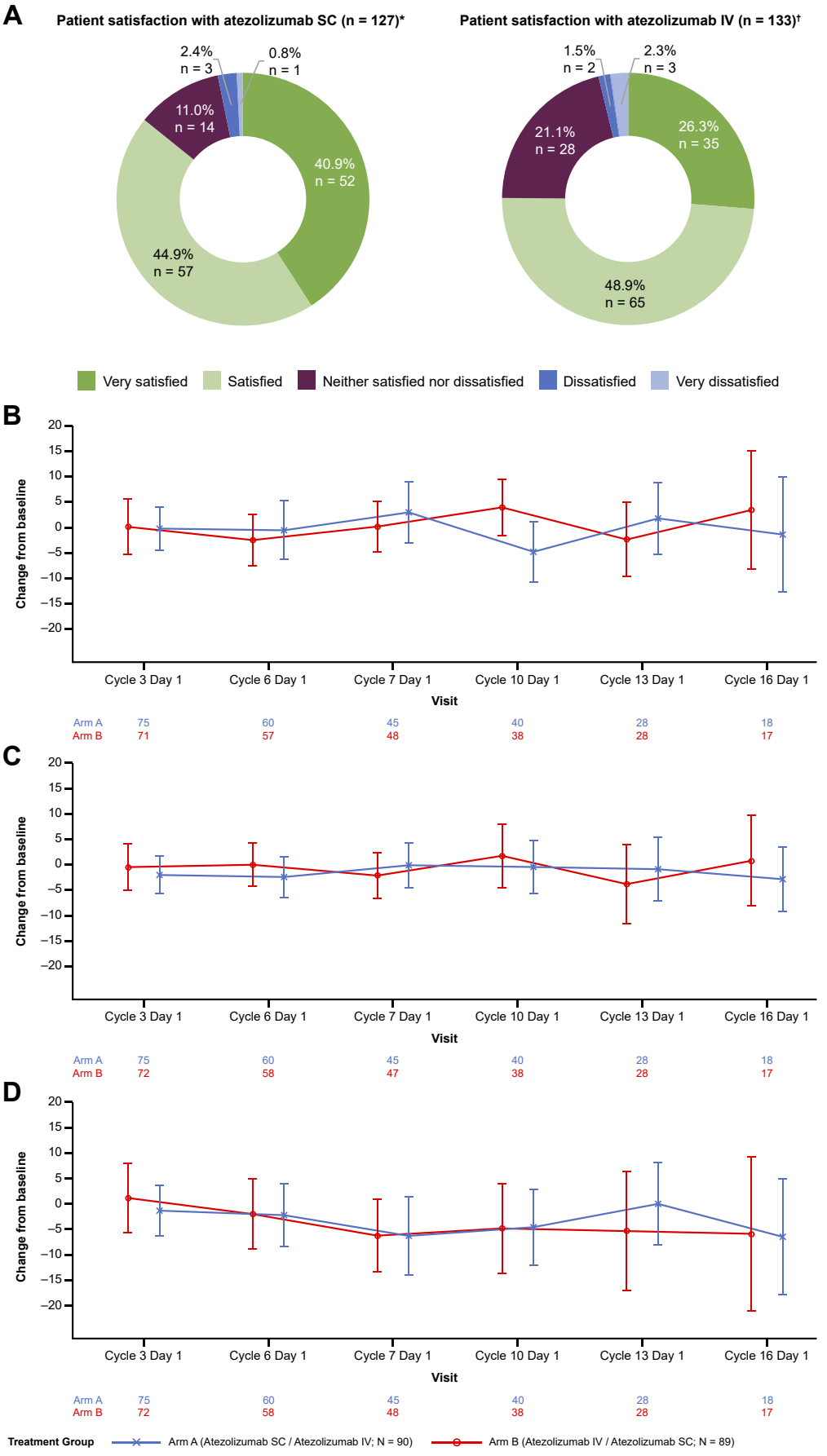


Figure 2. Patients' *(A)* preferred administration method and *(B)* reasons for preferring atezolizumab SC over IV. *95% confidence interval: 61.8 to 78.6. The patient preference questionnaire completion rate was 98% (n = 123 of 126); 126 patients completed cycle 5 of treatment and were alive on cycle 6 on day 1. *(A)* Question 1 of the patient preference questionnaire: "All things considered, which route of administration did you prefer?" *(B)* Question 2 of the patient preference questionnaire had responses from 87 patients: "If you have a preference for one of the administration routes, what are the two main reasons for your preference?" IV, intravenous; SC, subcutaneous.

of 87; Fig. 2*B*). Of the patients who stated their preferred administration route and entered the continuation period, 79.4% (n = 85 of 107) chose atezolizumab SC and 20.6% (n = 22 of 107) chose atezolizumab IV for the rest of the study duration. All patients who preferred atezolizumab SC chose SC for the continuation period; one patient who stated that atezolizumab IV was their preferred route of administration chose SC for the continuation period. Among the patients who indicated that they had no preference, five chose SC atezolizumab and three chose IV atezolizumab for the continuation period.

On the basis of the TASQ-SC and TASQ-IV, patients reported higher satisfaction rates with atezolizumab SC: 85.8% of patients (n = 109 of 127) were satisfied or very satisfied with atezolizumab SC, compared with 75.2% of patients (n = 100 of 133) with atezolizumab IV (Fig 3*A*). In addition, the median satisfaction score for the TASQ-SC was 87.5 (range: 0.0–100), whereas for the TASQ-IV it was 75.0 (range: 0.0–100). Furthermore, most patients (74.8%, n = 92 of 123) indicated that they would definitely or probably recommend atezolizumab SC to another patient, whereas 62.8% (n = 81 of 129)


A
Patient satisfaction with atezolizumab SC (n = 127)*
2.4% n = 3
0.8% n = 1
11.0% n = 14
40.9% n = 52
44.9% n = 57
Patient satisfaction with atezolizumab IV (n = 133)†
1.5% n = 2
2.3% n = 3
21.1% n = 28
26.3% n = 35
48.9% n = 65
Very satisfied
Satisfied
Neither satisfied nor dissatisfied
Dissatisfied
Very dissatisfied
B
Change from baseline
20
15
10
5
0
−5
−10
−15
−20
Cycle 3 Day 1
Cycle 6 Day 1
Cycle 7 Day 1
Cycle 10 Day 1
Cycle 13 Day 1
Cycle 16 Day 1
Visit
Arm A 75 60 45 40 28 18
Arm B 71 57 48 38 28 17
C
Change from baseline
Visit
Arm A 75 60 45 40 28 18
Arm B 72 58 47 38 28 17
D
Change from baseline
Visit
Arm A 75 60 45 40 28 18
Arm B 72 58 48 38 28 17
Treatment Group
Arm A (Atezolizumab SC / Atezolizumab IV; N = 90)
Arm B (Atezolizumab IV / Atezolizumab SC; N = 89)

stated that they would definitely or probably recommend atezolizumab IV to another patient.

Other assessed areas included the psychological impact (perception of restriction), convenience, impact on daily living, and physical impact. In terms of the psychological impact, most patients (74.6%, n = 94 of 126) did not feel restricted when receiving atezolizumab SC, whereas a lower proportion of patients (65.4%, n = 87 of 133) did not feel restricted when receiving atezolizumab IV. Patients also found atezolizumab SC to be more convenient than atezolizumab IV: the median convenience domain scores were 87.5 (range: 12.5–100) versus 75.0 (range: 0.0–100), respectively. A small proportion of patients reported that atezolizumab SC and IV affected their activities of daily living, but there was no difference between the administration methods; 3.3% of patients (four of 123) receiving atezolizumab SC and 3.0% of patients (four of 133) receiving atezolizumab IV said they lost a lot of time during treatment. Nevertheless, more patients felt that they lost time (some or a lot of time) because of the IV infusion (27.8%, n = 37 of 133) versus the SC injection (8.9%, n = 11 of 123), and more patients indicated that they gained time (some or a lot of time) with atezolizumab SC (30.9%, n = 38 of 123) versus IV (9.8%, n = 13 of 133). No meaningful difference in physical impact was reported with atezolizumab SC and IV: median physical impact domain score was 100 (range: 33.3–100) for atezolizumab SC and 91.7 (range: 33.3–100) for atezolizumab IV.

Most patients (>98%) completed at least one question on the EORTC QLQ-30 throughout the crossover period (baseline, n = 173 of 176; cycle 3, n = 148 of 153; cycle 6, n = 119 of 121), and the completion rates were comparable between the treatment arms. Throughout the study, the mean changes in baseline scores were similar between the treatment arms, with overlapping 95% confidence intervals at each visit (global health status, physical functioning, and role functioning; Fig. 3*B–D*). No meaningful deterioration relative to baseline was observed in either arm during treatment visits.

HCP-Reported Outcomes

During the first six cycles, atezolizumab SC and IV formulations were prepared by pharmacists or pharmacy technicians in 59.9% of the cases, nurses in 38.6%, and other HCPs in 1.5%. Atezolizumab SC was prepared approximately three times quicker by nurses on the ward (median: 3.0 min, interquartile range: 1.0–5.0 min) compared with pharmacists or pharmacy technicians in the pharmacy (median: 8.0 min, interquartile range: 3.0–20.0 min) (Supplementary Fig. 1).

Most HCPs (76.8%, n = 76 of 99 responders) indicated that SC atezolizumab was quicker to administer (from the start of preparation to the completion of administration) than IV atezolizumab (Supplementary Fig. 2*A*). In terms of perceptions of the benefits of atezolizumab SC for patients, most HCPs (77.8%, n = 77 of 99 responders) indicated that patients would spend less time in the care unit with atezolizumab SC, 75.2% (n = 76 of 101 responders) agreed that SC administration was more convenient than IV administration, and 68.3% (n = 69 of 101 responders) believed that SC administration would be preferred by patients over IV administration (Supplementary Fig. 2*B–D*). In terms of HCP perceptions of the benefits of atezolizumab SC for health care systems, most HCPs (73.7%, n = 73 of 99 responders) responded that atezolizumab SC used fewer resources for preparation and administration than atezolizumab IV (Supplementary Fig. 2*E*).

Safety

The safety-evaluable population included 175 patients (excluding four patients who were randomized to the study in error and did not receive any treatment). The overall safety profiles of all patients during both the crossover and continuation periods were consistent with previous findings, and no new safety findings were identified (Table 2). Overall, 76.6% of patients (n = 134 of 175) experienced at least one adverse event (AE) with 52.0% (n = 91 of 175) experiencing at least one treatment-related AE. Grade 3 to 4 AEs occurred in 22.3% of the patients (n = 39 of 175). Six (3.4%) deaths due to AE occurred in this study, with one death considered by the investigator to be owing to respiratory failure (treatment-related AE). The rates of AEs leading to treatment discontinuation and interruption were 10.3% (n = 18 of 175) and 21.1% (n = 37 of 175), respectively.

Switching between SC and IV atezolizumab, regardless of the sequence, was well tolerated (Table 3). Higher numbers of AEs were reported in cycles 1 to 3 than in cycles 4 to 6 (Table 3). In arm A (atezolizumab SC followed by IV), 15.1% of the patients (n = 13 of 86) experienced grade 3 to 4 AE in cycles 1 to 3 compared with 9.9% (n = seven of 71) in cycles 4 to 6. Similarly, in

Figure 3. *(A)* Patient satisfaction with atezolizumab SC and IV, and patient-reported outcomes from the EORTC QLQ-C30 for *(B)* global health status, *(C)* physical functioning, and *(D)* role functioning. *Assessed by Q1 of TASQ-SC: "How satisfied or dissatisfied were you with the SC injection?" †Assessed by Q1 of TASQ-IV: "How satisfied or dissatisfied were you with the IV infusion?" EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30; IV, intravenous; SC, subcutaneous; TASQ, therapy administration satisfaction questionnaire.

Table 2. Overall Safety in All Patients

Patients, n (%)	Safety-Evaluable Patients (N = 175)
≥1 AE	134 (76.6)
Related AE	91 (52.0)
AE with fatal outcome	6 (3.4)
Related AE with fatal outcome	1 (0.6)
Serious AE	35 (20.0)
Related serious AE	14 (8.0)
Highest grade 3-4 AE	39 (22.3)
Related highest grade 3-4 AE	15 (8.6)
AE leading to treatment discontinuation	18 (10.3)
AE leading to treatment interruption	37 (21.1)

Combined data from the crossover and continuation period.
AE, adverse event.

arm B (atezolizumab IV followed by SC), 16.9% of the patients (n = 15 of 89) experienced grade 3 to 4 AE in cycles 1 to 3, whereas no grade 3 to 4 AEs occurred in cycles 4 to 6. In arm A (atezolizumab SC followed by IV), serious AEs (SAEs) occurred in 12.8% of patients (n = 11 of 86) during cycles 1 to 3 and 5.6% of patients (n = four of 71) during cycles 4 to 6. In arm B (atezolizumab IV followed by SC), SAEs occurred in 12.4% of the patients (n = 11 of 89) during cycles 1 to 3 and 2.9% (n = two of 69) during cycles 4 to 6.

Injection site reactions occurred in 10.3% of patients (n = 18 of 175). During the crossover period, injection site reactions occurred in 8.6% of patients (n = 15 of 175): 11.6% of patients (n = 10 of 86) in arm A (atezolizumab SC followed by IV) experienced an injection site reaction during cycles 1 to 3 and 7.2% of patients (n = five of 69) in arm B (atezolizumab IV followed by SC) experienced an injection site reaction during cycles 4 to 6. Overall, 2.9% of patients (n = five of 175) experienced an infusion-related reaction. During the crossover period, all infusion-related reactions were due to atezolizumab IV: in cycles 1 to 3 in arm B (atezolizumab IV followed by SC), 4.5% of patients (n = four of 89) experienced an infusion-related reaction, and in cycles 4 to 6 in arm A (atezolizumab SC followed by IV), 1.4% of patients (n = one of 71) experienced an infusion-related reaction (Table 3). The likelihood of a patient experiencing an injection site reaction or infusion-related reaction event did not increase when switching from atezolizumab SC to IV or vice versa.

Discussion

Primary analysis of the IMscin002 study found that more patients preferred atezolizumab SC to IV (70.7% and 21.1%, respectively). In addition, atezolizumab SC was the route of administration chosen by most patients during the continuation period (79.4% chose atezolizumab SC and 20.6% chose atezolizumab IV), and the rates of treatment satisfaction were higher with atezolizumab SC (85.8%) than with atezolizumab IV (75.2%).

These results are in line with those of previous studies that have shown that patients prefer SC administration of anticancer therapies over IV administration.[11–13,15] The reasons given by patients for preferring SC administration over IV in the current study were similar to those in previous reports.[11–13,15] In areas assessed in the TASQs, patient perspectives on atezolizumab SC were positive: atezolizumab SC had a lower negative psychological impact than IV, and patients found atezolizumab SC more convenient than IV and were more likely to recommend atezolizumab SC than IV to another patient. Furthermore, patient-reported outcomes reported using the EORTC QLQ-C30 found that the global health status, physical functioning, and role functioning over the duration of the study were similar between the atezolizumab SC and IV groups. These results are similar to those reported in the IMscin001

Table 3. Safety of Switching Between Formulations of Atezolizumab During the Crossover Period (C1-6)

	Crossover Arm A: Atezolizumab SC Then IV		Crossover Arm B: Atezolizumab IV Then SC		All Patients
Patients, n (%)	C1-C3 (n = 86)	C4-C6 (n = 71)	C1-C3 (n = 89)	C4-C6 (n = 69)	C1-C6 (n = 175)
≥1 AE	47 (54.7)	38 (53.5)	56 (62.9)	27 (39.1)	121 (69.1)
Injection site reactions	10 (11.6)	0	0	5 (7.2)	15 (8.6)
Infusion-related reaction	0	1 (1.4)	4 (4.5)	0	5 (2.9)
Related AE	31 (36.0)	22 (31.0)	28 (31.5)	21 (30.4)	81 (46.3)
AE with fatal outcome	3 (3.5)	0	1 (1.1)	1 (1.4)	5 (2.9)
Related AE with fatal outcome	1 (1.2)	0	0	0	1 (0.6)
Serious AE	11 (12.8)	4 (5.6)	11 (12.4)	2 (2.9)	28 (16.0)
Related serious AE	4 (4.7)	2 (2.8)	4 (4.5)	2 (2.9)	12 (6.9)
Highest grade 3-4 AE	13 (15.1)	7 (9.9)	15 (16.9)	0	34 (19.4)
Higher grade 3-4 related AE	5 (5.8)	1 (1.4)	6 (6.7)	0	12 (6.9)
AE leading to treatment discontinuation	5 (5.8)	2 (2.8)	7 (7.9)	2 (2.9)	16 (9.1)
AE leading to treatment interruption	9 (10.5)	7 (9.9)	7 (7.9)	2 (2.9)	24 (13.7)

AE, adverse event; C, cycle; IV, intravenous; SC, subcutaneous.

trial, which assessed HRQoL using another questionnaire (European Organization for Research and Treatment of Cancer Item Library 57).[7]

In addition to patients' perspectives on atezolizumab SC, the IMscin002 study also collected HCP perspectives on atezolizumab SC, which were positive overall. HCP perceptions of atezolizumab SC were that it was more convenient for patients and required fewer health care resources. When preparing atezolizumab IV in a pharmacy, pharmacists or pharmacy technicians are required to follow standard operating procedures to maintain sterile conditions, which affect preparation times. An advantage of SC atezolizumab over IV is that it does not need to be prepared under sterile conditions and can be prepared by nurses in wards (where local legislation allows). In the current study, nurses were able to prepare atezolizumab SC approximately three times faster than pharmacists. In addition, this study did not consider hospital transportation times or pharmacy preparation queues; thus, further improvements may be observed in real-world settings. Importantly, a reduction in treatment times with SC formulations has been shown to yield meaningful health care time and cost savings.[8,10] The PrefHer study (NCT01401166) reported that trastuzumab SC in patients with *HER2*-positive early breast cancer can lead to substantial reductions in patient "chair time" and active HCP time compared with trastuzumab IV.[9] Similarly, in the PHranceSCa trial (NCT03674112), HCPs indicated that SC injections of a fixed-dose combination of pertuzumab and trastuzumab reduced the overall time that patients spent in the treatment room compared with IV administration.[11]

Overall, the safety profile of atezolizumab SC was consistent with previous reports, with no new safety findings.[1,2,7,18] As expected, because of the route of administration, injection site reactions were more common with atezolizumab SC; nevertheless, all injection site reactions were low-grade and nonserious and did not result in any changes to atezolizumab treatment. Switching between SC and IV atezolizumab, regardless of the sequence, was well tolerated. A greater number of AEs, including grade 3 to 4 AEs and SAEs, occurred during the earlier treatment cycles (cycles 1–3).

A limitation of this study is that it was powered to determine patient preference for SC or IV atezolizumab; therefore, additional analyses, such as patient satisfaction and HCP-reported outcomes, should be interpreted with caution.

The IMscin002 study is ongoing and updated safety data, and additional results on patient-reported outcomes are expected in the final analysis. These data on the benefits of SC administration will help guide future research and clinical practice by helping to implement new strategies to reduce the burden on hospitals and patients with NSCLC.

In conclusion, atezolizumab SC was the preferred route of administration and route of choice for the continuation period compared with atezolizumab IV, and satisfaction rates with atezolizumab SC were high. In addition, the HCP perspectives of atezolizumab SC were positive overall: HCPs agreed that SC administration was more convenient, quicker to administer from the start of preparation to completing administration, would be preferred by patients, and would allow patients to spend less time in the cancer clinic than IV. Similarly, the preparation time of atezolizumab SC was approximately three times quicker when prepared by nurses in the ward than when prepared by pharmacists in the pharmacy. The overall safety profile was consistent with that of atezolizumab. No new safety concerns were identified in relation to switching between the formulations. These results support previous findings that atezolizumab SC is a convenient option preferred by patients and HCPs compared with IV, and has the potential to reduce the burden on hospitals and for all patients who are eligible for treatment with atezolizumab, including lung cancer and other approved indications.

CRediT Authorship Contribution Statement

Federico Cappuzzo: Writing - original draft, Writing - review & editing, Investigation.

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Ernesto Korbenfeld: Writing - original draft, Writing the review & editing, Investigation.

Jaroslaw Kolb-Sielecki: Writing - original draft, Writing - review & editing, Investigation.

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Alberto Bustillos: Writing - original draft, Writing - review & editing, Formal analysis.

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Disclosure

Dr. Cappuzzo reports receiving consultancy fees from Hoffmann-La Roche Ltd., AstraZeneca, Bristol-Myers

Squibb, Pfizer, Takeda, Eli Lilly, Bayer, Amgen, Sanofi, Pharmamar, Novocure, Mirati, Galecto, OSE, ILLUMINA, Thermofisher, BeiGene, and Merck Sharp & Dohme; received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Hoffmann-La Roche Ltd., AstraZeneca, Bristol-Myers Squibb, Pfizer, Takeda, Eli Lilly, Bayer, Amgen, Sanofi, Pharmamar, Novocure, Mirati, Galecto, OSE, ILLUMINA, Thermofisher, Beigene, and Merck Sharp & Dohme; participation on a data safety monitoring board or advisory board for F. Hoffmann-La Roche Ltd., AstraZeneca, Bristol-Myers Squibb, Pfizer, Takeda Pharmaceuticals, Eli Lilly and Company, Bayer AG, Amgen Inc., Sanofi S.A., PharmaMar, Novocure, Mirati Therapeutics, Inc., Galecto Biotech, OSE Immunotherapeutics, Illumina, Inc., Thermofisher, and Merck Sharp & Dohme. Dr. Zvirbule reports receiving honoraria from AstraZeneca and travel support for attending meetings from F. Hoffmann-La Roche Ltd., Merck Sharp & Dohme, and Astra. Dr. Korbenfeld reports being a principal investigator and has shares in Centro Oncologico Korben; providing consultancy or advisory roles for Pfizer; and honoraria from AstraZeneca. Dr. Kolb-Sielecki reports receiving travel support for attending congresses from AstraZeneca and F. Hoffmann-La Roche Ltd.; primary investigator for AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, F. Hoffmann-La Roche Ltd., and Merck Sharp & Dohme. Dr. Isla reports being a speaker bureau for Pfizer, Merck Sharp & Dohme, AstraZeneca, F. Hoffmann-La Roche Ltd., Sanofi, Bristol-Myers Squibb, Janssen, Eli Lilly, Merck, and Novartis; having an advisory role for Sanofi, AstraZeneca, Merck Sharp & Dohme, Bristol-Myers Squibb, Janssen, GlaxoSmithKline, and Amgen; and receiving travel, accommodation, or expenses from AstraZeneca, Merck Sharp & Dohme, Pfizer, and Genentech, Inc./F. Hoffmann-La Roche Ltd.; received honoraria from Merck Sharp & Dohme Oncology, AstraZeneca, Sanofi, Bristol-Myers Squibb, Amgen, Pfizer, Merck, Novartis, and Genentech, Inc., F. Hoffmann-La Roche Ltd. Dr. Sanchez is employed full-time at F. Hoffmann-La Roche Ltd. and has stocks/shares in F. Hoffmann-La Roche Ltd. Dr. Bustillos is employed full-time at F. Hoffmann-La Roche Ltd. Dr. Liu is employed full-time at Genentech, Inc., and has stocks/shares in F. Hoffmann-La Roche Ltd. Dr. Young is employed full-time at F. Hoffmann-La Roche Ltd. and has stocks/shares at F. Hoffmann-La Roche Ltd. Dr. Tosti is employed full-time at F. Hoffmann-La Roche Ltd. and has stocks/shares in F. Hoffmann-La Roche Ltd. Dr. Monteiro is employed full-time at F. Hoffmann-La Roche Ltd. and has stocks/shares in F. Hoffmann-La Roche Ltd. Dr. Majem reports receiving grants or contracts from any entity from Hoffmann-La Roche Ltd. and AstraZeneca; received consulting fees from Merck Sharp & Dohme, Pfizer, Boehringer Ingleheim, Novartis, Helsinn Therapeutics, Takeda, Janssen Oncology, Pierre Fabre, Pfizer, Beigene, Bristol-Myers Squibb, AstraZeneca, and F. Hoffmann-La Roche Ltd.; invited speaker for F. Hoffmann-La Roche Ltd., Merck Sharp & Dohme, Pfizer, AstraZeneca, and Helsinn Therapeutics; support for attending meetings or travel from AstraZeneca, Merck Sharp & Dohme Oncology, Pfizer and F. Hoffmann-La Roche Ltd.; research funding from AstraZeneca, Bristol-Myers Squibb, Merck Sharp & Dohme Oncology, and F. Hoffmann-La Roche Ltd. The remaining authors declare no conflict of interest.

Acknowledgments

This work was supported and funded by F. Hoffmann-La Roche Ltd. The authors would like to thank the patients and their families, study investigators, clinical site staff, and past and present study teams who supported the IMscin002 trial. Third-party medical writing assistance, under the direction of the authors, was provided by Neave Baldwin (BSc) of Ashfield MedComms, an Initio company, and funded by F. Hoffmann-La Roche Ltd.

Data Availability Statement

For eligible studies, qualified researchers may request access to individual patient-level clinical data through a data request platform. At the time the manuscript was written, the request platform was VivLi (https://vivli.org/ourmember/roche/). For updated details on Roche's Global Policy on the Sharing of Clinical Information and on how to request access to related clinical study documents, see https://go.roche.com/data_sharing. Anonymized records for individual patients across more than one data source external to Roche cannot, and should not, be linked owing to a potential increase in the risk of patient reidentification.

Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *JTO Clinical and Research Reports* at www.jtocrr.org and at https://doi.org/10.1016/j.jtocrr.2025.100815.

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