Patient preference for subcutaneous vs intravenous nivolumab in participants with resected melanoma: primary endpoint analysis of a phase 2 open-label study (CA224-1044)

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Objectives

- The primary objective of the CA224-1044 study was to evaluate patient preference for route of administration after switching from nivolumab (NIVO) IV to NIVO subcutaneous (SC) (cohort 2) in participants with resected melanoma
- A secondary objective was to evaluate safety after switching from NIVO IV to NIVO SC

Conclusions and discussion

- A total of 96% of participants successfully completed the primary endpoint assessment
  - Among those, 71% (34 participants) expressed a preference for NIVO SC over the IV formulation, and 10% (5 participants) indicated a preference for IV administration
  - However, 19% (9 participants) reported no preference between the 2 administration routes
- The safety profile reported following the transition from IV to SC administration of NIVO was consistent with the established safety profiles of both formulations, with no new safety signals identified
- These results support the use of NIVO SC as a patient-preferred alternative to IV administration
- Results from cohort 1, ie, participants with metastatic melanoma treated with NIVO + relatlimab (RELA) fixed-dose combination (FDC) IV or NIVO + RELA FDC + recombinant human hyaluronidase PH20 (rHuPH20) SC, are pending

Background

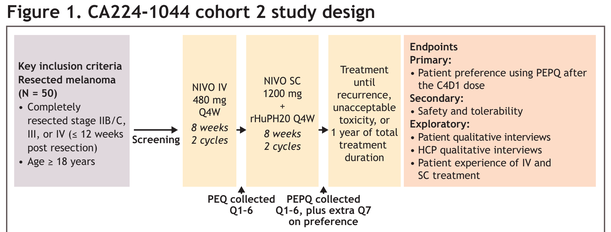
- The SC administration of NIVO + rHuPH20 was approved by the FDA and EMA based on pharmacokinetics, safety, and efficacy vs IV NIVO administration in CheckMate 67T[1-3]
- This approval represents a meaningful advancement in immuno-oncology, offering potential advantages in terms of patient convenience, reduced chair time, and optimization of healthcare delivery as seen with other SC therapies[4-10]
- Alongside these potential benefits and the demonstrated noninferior efficacy and comparable safety of NIVO SC vs IV, data on patient experience and preference in switching from IV to SC treatment remain an important gap to inform real-world use of NIVO SC
  - Understanding patient-reported outcomes, preferences, and safety is therefore essential to inform clinical practice
- CA224-1044 (NCT06101134) is a 2-cohort, phase 2 study in participants with either metastatic (cohort 1) or resected (cohort 2) melanoma[11]
- Here, we report results from cohort 2, which was designed to specifically evaluate the patient experience, preference, and safety associated with switching from NIVO IV to NIVO + rHuPH20 SC in participants with resected melanoma[11]
  - Cohort 1 evaluated participant experience and safety associated with switching from NIVO + RELA FDC IV or NIVO + RELA FDC + rHuPH20 SC

Methods

Study design and population

- CA224-1044 is an ongoing 2-cohort, multicenter, open-label study
  - Reported here are details for cohort 2 (**Figure 1**)
- Participants aged ≥ 18 years with completely resected stage IIB/IV melanoma and no evidence of disease at baseline (≤ 12 weeks post-surgery), Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 1, and who were eligible for adjuvant therapy were enrolled (**Figure 1**)
- Participants initially received adjuvant treatment with NIVO IV 480 mg every 4 weeks (Q4W) for 2 cycles, followed by a switch to NIVO SC 1200 mg coformulated with rHuPH20, also administered Q4W
- Treatment continued for up to 1 year or until disease recurrence or unacceptable toxicity

Figure 1. CA224-1044 cohort 2 study design



C4D1, cycle 4, day 1; HCP, healthcare provider; PEQ, Patient Experience Questionnaire; PEPQ, Patient Experience and Preference Questionnaire; Q, question.

Objectives and endpoints

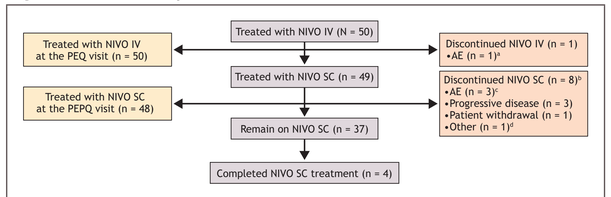
- The primary objective was to assess patient preference between NIVO IV and SC after 2 doses of each using the PEPQ
  - The PEPQ is a modification of the 6-question PEQ that includes an additional question on patient preference (Q7)
  - The primary endpoint was the proportion of evaluable participants who preferred NIVO SC using PEPQ (Q7)
- A secondary objective was to evaluate safety after switching from NIVO IV to SC
  - The secondary safety endpoints were the incidence of adverse events (AEs) during administration cycles 1 and 2 (NIVO IV), cycles 3 and 4 (NIVO SC), and overall (between the first dose and 30 days after the last dose of study therapy)
- Exploratory endpoints included a summary of the PEQ and PEPQ Q1-6, and a summary of HCP and patient qualitative interviews
- This was a descriptive study with no formal hypothesis testing

Results

Patient disposition

- Fifty participants were enrolled, with 48 evaluable for the primary endpoint (**Figure 2**)
- Median (range) duration of time on study was 7.44 (5.5-12.9) months

Figure 2. Patient disposition



[a]Hypertransaminasemia. [b]n = 4 discontinued during cycle 3 or 4, n = 4 discontinued after cycle 4. [c]Immune-mediated hepatitis (n = 1), diabetes mellitus (n = 1), and musculoskeletal chest pain (n = 1). [d]Death due to respiratory failure, not considered treatment related.

Baseline demographics

- The median (range) age was 66 (23-85) years and 28 (56%) participants were female
- Most participants had stage II (n = 16, 32%) or III (n = 29, 58%) disease, and 46 (92%) had an ECOG performance status of 0

Patient preference

- Of the 48 evaluable participants, 34 (70.8%, 95% CI, 55.9-83.0) preferred NIVO SC to NIVO IV, 9 (18.8%, 95% CI, 8.9-32.6) reported no preference, and 5 (10.4%, 95% CI, 3.5-22.7) preferred NIVO IV (**Figure 3**)

Perceived pain

- Using a scale from 0 to 10, where 0 represents "no pain or discomfort at all," 75% of participants rated their pain between 0 and 2 after NIVO SC administration and between 0 and 1 post IV administration

Perceptions on time to administer NIVO IV or SC

- Perceptions on time to administer NIVO were similar after IV and SC administration
  - The majority of participants responded that it was either less time than expected or an acceptable amount of time to administer either the IV (98%) or SC (96%) formulation (**Figure 4**)
  - Most participants (81%) thought that NIVO IV and SC administration had no impact at all on the amount of time they had to speak with the nurse or doctor (**Table 1**)
  - However, it appeared that more participants thought IV administration impacted their ability to socialize/interact with individuals other than the HCP compared with SC administration (25.5% vs 8.5%; **Table 1**)

Figure 3. Patient preference for NIVO SC or NIVO IV

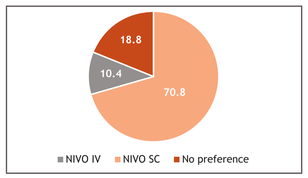


Figure 4. Perceptions on time to administer NIVO

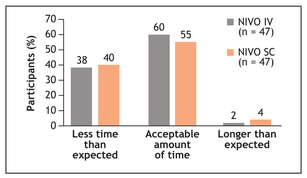


Table 1. Impact of time to administer NIVO IV or SC

Question		Not at all	A little bit	Somewhat	Quite a bit	Very much	Not applicable
Impact on time to speak to the nurse or doctor	NIVO SC, %	80.9	6.4	8.5	2.1	0	2.1
	NIVO IV, %	80.9	4.3	8.5	6.4	0	0
Impact on ability to socialize/interact with other individuals besides the HCP	NIVO SC, %	89.4	6.4	0	2.1	0	2.1
	NIVO IV, %	74.5	6.4	8.5	10.6	0	0
Level of bother on time for medication administration	NIVO SC, %	87.2	10.6	0.0	2.1	0	0
	NIVO IV, %	83.0	10.6	2.1	4.3	0	0

Patient satisfaction

- The majority of participants were very satisfied with IV (89.4%) or SC (80.9%) administration of NIVO
- Two participants (4.3%) responded that they were "somewhat dissatisfied/very dissatisfied" after SC administration of NIVO
- Results from the patient qualitative interviews showed that more participants found IV treatment more concerning/worrying than SC treatment, mainly due to the length of administration time, the discomfort of receiving IV treatment, and that the needle/catheter remained in the administration site for longer

Safety

- Treatment-emergent adverse events (TEAEs) of any grade were reported in 64.0% and 71.4% of participants during the 8-week NIVO IV (cycles 1 and 2) and SC (cycles 3 and 4) treatment periods
  - Grade 3/4 TEAEs were reported by 6.0% and 4.1% of participants during NIVO IV and SC administration, respectively
- The incidence of treatment-related adverse events (TRAEs) during NIVO IV and the first 2 cycles of NIVO SC treatment were 42.0% and 38.8%, respectively (**Table 2**)

Table 2. Overall incidence and most frequently reported (≥ 10% overall) TRAEs

	IV period (8 weeks) (N = 50)		SC period (8 weeks) (N = 49)[a]		Overall[b] (N = 50)	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Total patients with a TRAE, n (%)	21 (42.0)	1 (2.0)	19 (38.8)	1 (2.0)	36 (72.0)	3 (6.0)
Fatigue	5 (10.0)	0	1 (2.0)	0	6 (12.0)	0
Asthenia	3 (6.0)	0	2 (4.1)	0	5 (10.0)	0
Pruritus	3 (6.0)	0	3 (6.1)	0	6 (12.0)	0
Diarrhea	3 (6.0)	0	1 (2.0)	0	5 (10.0)	0
Arthralgia	1 (2.0)	0	0	0	6 (12.0)	0

[a]One patient discontinued treatment during the NIVO IV phase because of treatment-related hypertransaminasemia and did not receive subsequent NIVO SC. [b]Overall period includes events reported between the first dose and 30 days after the last dose of study therapy.

- The most frequently reported TRAEs over the duration of the study were fatigue, pruritus, arthralgia, asthenia, and diarrhea
- No treatment-related mortality was reported
- Injection-site reactions with NIVO SC (cycles 3 and 4) were reported in 3/49 (6%) participants and were all low grade (**Table 3**), consistent with what was reported in the CheckMate 67T phase 3 study (7%; all low grade)[3]

Table 3. Injection-site or infusion-related reactions

	IV period (8 weeks) (N = 50)		SC period (8 weeks) (N = 49)[a]		Overall[b] (N = 50)	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Total patients with an event, n (%)	1 (2.0)	0	3 (6.1)	0	6 (12.0)	0
Injection-site erythema	0	0	2 (4.1)	0	4 (8.0)	0
Injection-site pruritus	0	0	2 (4.1)	0	2 (4.0)	0
Administration-site pain	0	0	1 (2.0)	0	1 (2.0)	0
Infusion-related reaction	1 (2.0)	0	0	0	1 (2.0)	0
Injection-site edema	0	0	0	0	1 (2.0)	0
Injection-site reaction	0	0	0	0	1 (2.0)	0
Injection-site swelling	0	0	1 (2.0)	0	1 (2.0)	0
Injection-site warmth	0	0	0	0	1 (2.0)	0

[a]One patient discontinued treatment during the NIVO IV phase because of treatment-related hypertransaminasemia and did not receive subsequent NIVO SC. [b]Overall period includes events reported between the first dose and 30 days after the last dose of study therapy.

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Declaration of interests

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