616 PHARMACOKINETICS AND SAFETY OF A SUBCUTANEOUS FORMULATION OF NIVOLUMAB (NIVO SC) MONOTHERAPY: UPDATED RESULTS FROM THE PHASE 1/2 CHECKMATE 8KX STUDY

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Background NIVO administered via intravenous (IV) infusion is a transformative immuno-oncology therapy across multiple tumor types. However, there remains an unmet need to decrease the burden of oncology treatment for patients, healthcare facilities, and healthcare professionals (HCPs). SC administration may alleviate these challenges, is typically preferred over IV infusions by patients and HCPs, and improves healthcare resource utilization by decreasing preparation and chair time and reducing administrative burden.[1] Previously reported results from CheckMate 8KX had <17 months follow-up.[2] We present analyses with extended follow-up from CheckMate 8KX (NCT03656718), a phase 1/2 study investigating NIVO SC ± the permeation enzyme recombinant human hyaluronidase PH20 (rHuPH20).

Methods Enrolled patients were immune checkpoint inhibitor-naïve, eligible for NIVO monotherapy, and had advanced solid tumors, including non-small cell lung cancer (NSCLC), melanoma, renal cell carcinoma, and colorectal cancer. Study design is shown in figure 1. The primary endpoint was to describe the pharmacokinetics of NIVO SC ± rHuPH20 by non-compartmental analyses. Secondary endpoints included the safety and immunogenicity of NIVO SC. Exploratory endpoints included patient-reported outcomes and efficacy.

Results A total of 139 patients were treated. Median (range) age was 66 (24–93) years, 33.8% of patients were female, and patients had an ECOG performance status of 0 (38.1%) or 1 (61.9%). The most common tumor type was NSCLC (27.3%), and most patients (56.1%) had one prior line of therapy. Minimum follow-up is shown in figure 1. Pharmacokinetic data are shown in table 1. Most treatment-related adverse events were low-grade (table 2). Few patients developed anti-drug antibodies (ADAs), and no patients developed neutralizing ADAs (table 1). ORR data across all parts will be presented. Responding to an experience and preference questionnaire, most patients reported high satisfaction with SC administration, preferring it over IV administration, and noted limited pain associated with SC injection (table 3).

Conclusions The pharmacokinetics of NIVO SC was well characterized. NIVO SC was well tolerated, with a safety and ADA profile consistent with NIVO IV. Patients were highly satisfied with SC administration and preferred it over IV infusion. These data support the evaluation of NIVO SC + rHuPH20 in the ongoing phase 3 randomized noninferiority study, CheckMate 67T (NCT04810078).

Trial Registration NCT03656718

REFERENCES

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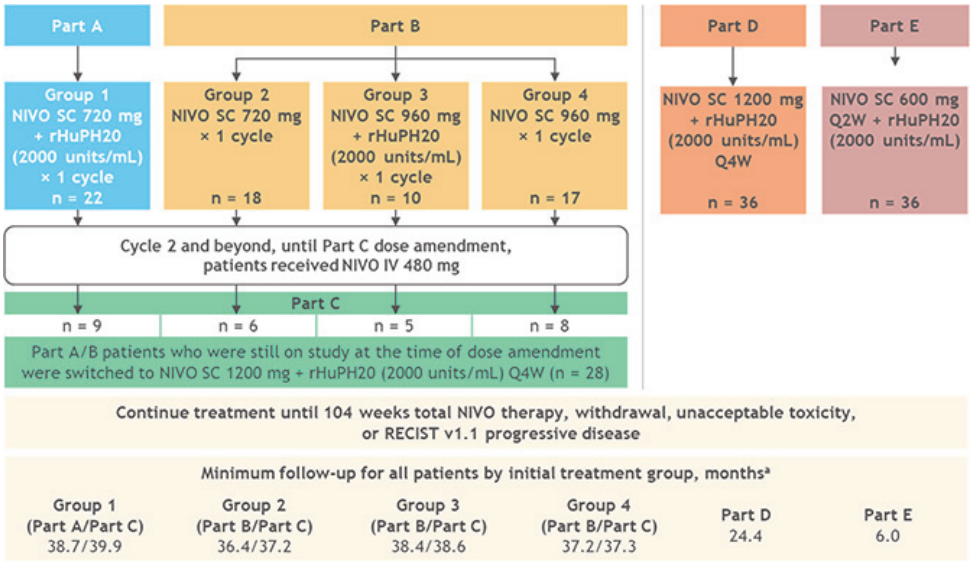
2. Lonardi S, Ługowska I, Jackson C *et al*. CheckMate 8KX: phase 1/2 multi-tumor preliminary analyses of a subcutaneous formulation of nivolumab (± rHuPH20). Poster presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting, June 4–8, 2021.

Ethics Approval This study was conducted in accordance with the Declaration of Helsinki and the international guidelines for Good Clinical Practice. The independent ethics committee or institutional review board of each participating study centre approved the protocol and all amendments.

Consent Written informed consent was obtained from all patients.



Abstract 616 Figure 1 Study design

Abstract 616 Table 1 Summary of pharmacokinetic and ADA data

	Part A	Part B			Part D	Part E
	Group 1 (n = 22)	Group 2 (n = 18)	Group 3 (n = 10)	Group 4 (n = 17)	(n = 36)	(n = 36)[a]
C_{max} geo. mean, µg/mL	54.8	56.6	81.4	63.9	106	57.8
N (geo. %CV)	22 (51)	18 (34)	10 (41)	17 (30)	34 (46)	36 (31)
Median T_{max}, h	167	167	141	168	130	130
N (range)	22 (47.0–357)	18 (50.1–339)	10 (47.2–333)	17 (139–355)	34 (44.5–317)	36 (45.2–337)
AUC_{tau} geo. mean, h × µg/mL	24,908	27,909	40,264	32,702	53,561	15,857
N (geo. %CV)	20 (53)	16 (36)	10 (45)	13 (31)	33 (40)	35 (30)
C_{tau} geo. mean, µg/mL	22.2	26.9	39.2	34.8	54.4	43.6
N (geo. %CV)	20 (86)	16 (65)	10 (67)	13 (41)	33 (49)	35 (36)
Baseline ADA-positive, n (%)[b]	2 (9.5)	0	2 (20.0)	0	1 (2.8)	1 (2.9)
ADA-positive, n (%)[b]	7 (33.3)	5 (27.8)	3 (30.0)	0	4 (11.1)	10 (28.6)
Persistent positive	1 (4.8)	0	0	0	1 (2.8)	0
Not persistent positive: last sample positive	0	3 (16.7)	0	0	1 (2.8)	2 (5.7)
Other positive	6 (28.6)	2 (11.1)	3 (30.0)	0	2 (5.6)	8 (22.9)
ADA-negative, n (%)[b]	14 (66.7)	13 (72.2)	7 (70.0)	17 (100.0)	32 (89.9)	25 (71.4)

[a]n = 35 patients were included in the ADA analysis for Part E; [b]Immunogenicity data pertain specifically to nivolumab.
ADA, anti-drug antibody; AUC_{tau}, area under the curve at the end of the first dosing interval; C_{max}, maximum concentration after the first dose; C_{tau}, concentration at the end of the first dosing interval; CV, coefficient of variation; geo. mean, geometric mean; T_{max}, time to C_{max}.

Abstract 616 Table 2 Safety summary

	Part A	Part B			Part C				Part D	Part E
n (%)	Group 1	Group 2	Group 3	Group 4	Group 1	Group 2	Group 3	Group 4		
TRAE										
SC										
N	22	18	10	17	9	6	5	8	36	36
Any grade	8 (36.4)	4 (22.2)	5 (50.0)	6 (35.5)	5 (55.6)	5 (83.3)	3 (60.0)	3 (37.5)	27 (75.0)	28 (77.8)
Grade 3/4	0	1 (5.6)	0	1 (5.9)	0	0	0	0	6 (16.7)	4 (11.1)
IV										
N	19	16	10	14	–	–	–	–	–	–
Any grade	9 (47.4)	9 (56.3)	5 (50.0)	6 (42.9)	–	–	–	–	–	–
Grade 3/4	1 (5.3)	1 (6.3)	0	1 (7.1)	–	–	–	–	–	–
TRAE leading to discontinuation										
SC										
N	22	18	10	17	9	6	5	8	36	36
Any grade	0	0	0	1 (5.9)	0	0	0	0	4 (11.1)	1 (2.8)
Grade 3/4	0	0	0	1 (5.9)	0	0	0	0	3 (8.3)	1 (2.8)
IV										
N	19	16	10	14	–	–	–	–	–	–
Any grade	2 (10.5)	1 (6.3)	1 (10.0)	1 (7.1)	–	–	–	–	–	–
Grade 3/4	1 (5.3)	1 (6.3)	0	1 (7.1)	–	–	–	–	–	–
Injection-site TRAE										
SC										
N	22	18	10	17	9	6	5	8	36	36
Any grade	5 (22.7)	1 (5.6)	4 (40.0)	3 (17.6)	3 (33.3)	1 (16.7)	3 (60.0)	1 (12.5)	10 (27.8)	12 (33.3)
Grade 3/4	0	0	0	0	0	0	0	0	0	0
IV										
N	19	16	10	14	–	–	–	–	–	–
Any grade	0	0	1 (10.0)	1 (7.1)	–	–	–	–	–	–
Grade 3/4	0	0	0	0	–	–	–	–	–	–

IV, intravenous; N, number of patients; SC, subcutaneous; TRAE, treatment-related adverse event.

Abstract 616 Table 3 Patient-reported outcomes

	Part A			Part B									Part D	Part E
	Group 1			Group 2			Group 3			Group 4			(n = 36)	(n = 36)
	C1D1 (n = 22)	C2D1 (n = 19)	Part C C1D1 (n = 9)	C1D1 (n = 18)	C2D1 (n = 16)	Part C C1D1 (n = 6)	C1D1 (n = 10)	C2D1 (n=10)	Part C C1D1 (n = 5)	C1D1 (n = 17)	C2D1 (n = 14)	Part C C1D1 (n = 8)		
Patient preference, n (%)														
IV	0	1 (5.3)	1 (11.1)	1 (5.6)	4 (25.0)	0	0	2 (20.0)	1 (20.0)	1 (5.9)	2 (14.3)	0	2 (5.6)	2 (5.6)
SC	10 (45.5)	8 (42.1)	5 (55.6)	9 (50.0)	3 (18.8)	5 (83.3)	5 (50.0)	3 (30.0)	2 (40.0)	6 (35.3)	6 (42.9)	3 (37.5)	21 (58.3)	28 (77.8)
No preference	10 (45.5)	9 (47.4)	1 (11.1)	8 (44.4)	7 (43.8)	1 (16.7)	5 (50.0)	3 (30.0)	0	9 (52.9)	3 (21.4)	2 (25.0)	7 (19.4)	2 (5.6)
No response	2 (9.1)	1 (5.3)	2 (22.2)	0	2 (12.5)	0	0	2 (20.0)	2 (40.0)	1 (5.9)	3 (21.4)	3 (37.5)	6 (16.7)	4 (11.1)
Patient satisfaction, n (%)														
Very satisfied	20 (90.9)	17 (89.5)	7 (77.8)	15 (83.3)	11 (68.8)	6 (100.0)	9 (90.0)	8 (80.0)	3 (60.0)	15 (88.2)	10 (71.4)	5 (62.5)	28 (77.8)	31 (86.1)
Somewhat satisfied	1 (4.5)	1 (5.3)	0	3 (16.7)	2 (12.5)	0	0	0	0	0	1 (7.1)	0	2 (5.6)	0
Neither	0	0	0	0	1 (6.3)	0	1 (10.0)	0	0	0	0	0	0	1 (2.8)
Somewhat dissatisfied	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Very dissatisfied	0	0	0	0	0	0	0	0	0	1 (5.9)	0	0	0	0
No response	1 (4.5)	1 (5.3)	2 (22.2)	0	2 (12.5)	0	0	2 (20.0)	2 (40.0)	1 (5.9)	3 (21.4)	3 (37.5)	6 (16.7)	4 (11.1)
Pain associated with SC injection (scale of 0–10)[a]														
N	21	18	7	18	14	6	10	8	3	16	11	5	30	32
Mean (SD)	0.6 (0.7)	0.3 (0.5)	0.4 (0.5)	0.1 (0.2)	0.3 (0.6)	0.8 (1.3)	0.3 (0.5)	0.0 (0.0)	2.0 (1.0)	0.1 (0.3)	0.3 (0.9)	0.8 (0.4)	1.5 (1.7)	0.7 (0.9)

[a]0 = no pain or discomfort at all, 10 = pain or discomfort as bad as you can imagine. C, cycles; D, dose; IV, intravenous; SC, subcutaneous; SD, standard deviation.

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