Study Results Synopsis for Public Disclosure

Name of product: QEQ278

Protocol identification number: Protocol no. CQEQ278A12101, EU CT number. 2022- 500540-38-00, ClinicalTrials.gov number NCT05462873

Title of study: A phase I/Ib, open-label, multi-center, study of QEQ278 in patients with advanced solid tumors

Study centers: 11 centers in 9 countries: Japan (1 sites; 2 patients); France (1 site; 5 patients); Singapore (1 site; 3 patients); United States (3 sites, 3 patients); Belgium (1 site, 2 patients); Germany (1 site, 3 patients); Italy (1 site, 4 patients); Spain (1 site, 4 patients); Taiwan (1 site, 4 patients)

Publication (reference): None

Study period:

Study initiation date: 04-Apr-2023 (first patient first visit)

Early termination date: 26-Jan-2026 (last patient last visit)

Phase of development (phase of this clinical study): I/Ib

Objectives: The purpose of this synopsis is to provide key results of the final analysis, based on all available data up to last patient last visit (LPLV) date of 26-Jan-2026, after the study was terminated early as per the Sponsor's decision. There were no safety related reasons for the early termination.

The primary and secondary study objectives with the corresponding endpoints for which data are provided for patients treated with QEQ278 single agent (Q2W) schedule in this report are summarized in Table 2-1.

Table 2-1 Objectives and related endpoints

Objectives	Endpoints
Primary Objective(s) **Dose escalation part:** • To characterize the safety and tolerability and identify the maximum tolerated dose (MTD)/recommended dose (RD) for expansion of single-agent QEQ278	**Endpoint(s) for primary objective(s)** **Dose escalation part:** • Safety: Incidence and nature of dose-limiting toxicities (DLTs) during the DLT evaluation period for single agent QEQ278. Incidence and severity of adverse events (AEs) and serious adverse events (SAEs), including changes in laboratory values, vital signs, and electrocardiograms (ECGs) • Tolerability: Dose interruptions, reductions, and dose intensity

Objectives	Endpoints
Dose expansion part: • To further evaluate the safety and tolerability of single agent QEQ278 in the expansion group(s)	**Dose expansion part:** • Safety: Incidence and nature of DLT(s) during the DLT evaluation period. Incidence and severity of AEs and SAEs, including changes in laboratory values, vital signs, and ECGs • Tolerability: Dose interruptions, reductions, and dose intensity
Secondary Objective(s)	**Endpoint(s) for secondary objective(s)**
Dose escalation and expansion part: • To assess the preliminary anti-tumor activity of single agent QEQ278	**Dose escalation and expansion part:** • Overall response rate (ORR), disease control rate (DCR), duration of response (DOR), and progression-free survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
• To characterize pharmacokinetics (PK) of single agent QEQ278	• Pharmacokinetics: Serum QEQ278 concentration versus time profiles and PK parameters
• To evaluate immunogenicity of single agent QEQ278	• Immunogenicity: incidence of anti-drug antibodies

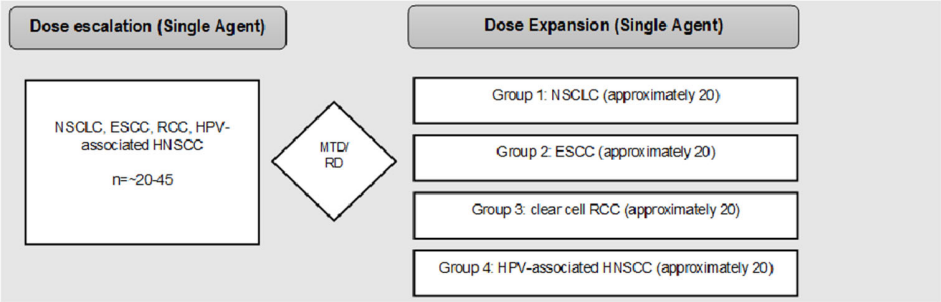
Study design and methodology: This was a first-in-human (FIH), open-label, phase I/Ib, multi-center study of QEQ278 as a single agent in patients with advanced or metastatic non-small cell lung cancer (NSCLC), esophageal squamous cell carcinoma (ESCC), renal cell carcinoma (RCC), and human papilloma virus (HPV)-associated head and neck squamous cell carcinoma (HNSCC). The study plan consisted of a dose-escalation part followed by a dose-expansion part.

During the dose escalation part of the study, the plan was to treat up to approximately 45 patients with NSCLC, ESCC, RCC, or HPV-associated HNSCC with QEQ278 as a single agent. Cohorts consisting of 3 to 6 evaluable patients were planned to receive QEQ278 until either the maximum tolerated dose (MTD) was reached or a lower recommended dose (RD) was established. The study design is summarized in Figure 2-1.

A total of 30 patients were enrolled in the study (in four dose escalation cohorts) and were treated with QEQ278 single agent using every two weeks (Q2W) schedule.

The study was planned to enter the dose expansion phase after the MTD and/or RD was declared during dose escalation, however, due to premature termination of the study, the expansion phase was not performed.

Figure 2-1 Study design



This figure depicts every two weeks (Q2W)

Duration of treatment: Study treatment was continued until the patient experienced unacceptable toxicity, disease progression as per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, and/or treatment was discontinued at the discretion of the investigator or the patient, or withdrawal of consent.

Diagnosis and main criteria for inclusion: This study enrolled adult patients (≥ 18 years) with histologically confirmed advanced malignancies (locally advanced and non-curable by surgery or radiotherapy, or metastatic disease). Eligible malignancies included NSCLC, ESCC, RCC, or HPV-associated HNSCC. Patients were required to have had measurable disease per RECIST v1.1 with at least one measurable lesion. Patients were required to have received but not benefited from standard therapies, be intolerant or ineligible for such therapies, or have no standard therapy option.

Patients with active or unstable central nervous system (CNS) metastases; prior allogeneic transplant; recent anti-cancer therapy, major surgery, or unresolved toxicities; active previously documented or suspected autoimmune disease, patients with a history of or current interstitial lung disease (ILD) or pneumonitis ≥ grade 2; clinically significant cardiac disease or risk factors at screening; prior discontinuation of programmed death (ligand) (PD-(L)1) therapy or target-specific agents due to toxicity; severe hypersensitivity to study drug ingredients; inadequate marrow, hepatic, or renal function; concurrent active malignancies other than target disease (with defined exceptions); inability to stop prohibited medications; serious medical/psychiatric illness; active infections (HIV, HBV, HCV, COVID-19, TB, or uncontrolled bacterial/viral/fungal infections); recent live vaccination; participation in other investigational studies; ongoing systemic immunosuppression (> 10 mg prednisone equivalent); pregnancy or breastfeeding; and any prior therapy targeting natural killer group 2 member D (NKG2D) or NKG2D-ligands were excluded from the study.

Test and reference therapies, dose and mode of administration:

QEQ278 was administered as an intravenous (i.v.) infusion over approximately one hour, with flexibility to extend the infusion time if clinically indicated. The starting dose was 70 mg, and four dose levels (70 mg, 210 mg, 700 mg and 1400 mg) were explored during the dose escalation phase. The treatment dosing schedule was every two weeks (Q2W).

All dosages prescribed, administered, and any dose changes were recorded in the corresponding electronic case report form (eCRF).

Protocol amendments and other changes to study conduct: The study protocol was amended 3 times. This synopsis describes the conduct of the study according to protocol amendment 3, dated 28-Jun-2023 (Table 2-2).

Table 2-2 Protocol amendments

Version and date	Summary of key changes
Amendment 3 28-Jun-2023	The primary purpose of this amendment was to add a new exclusion criterion to prevent enrollment of patients who have already received NKG2D or NKG2D-L targeting therapies as the number of these types of therapies has increased and the impact of prior treatment targeting the same biological pathway is unknown. Additionally, circulating free DNA (cfDNA) biomarker was added as an exploratory endpoint to explore the relationship of tumor mutations and mutation burden with clinical response to QEQ278. The reference to PD marker UL16 binding protein 2 (ULBP2) had been replaced with NKG2D-L to allow for investigation of any other ligand(s) if required or necessary. Already collected samples were repurposed for this new assay. Finally, biomarker samples were consolidated across all regimens. Other minor changes were made for consistency, clarification, and correction of typographical errors.
Amendment 2 08-Nov-2022	The protocol had been amended to address Health Authority feedback regarding frequency of urinalysis and coagulation labs, safety labs and vital signs at the safety follow up visit, and data used to support decision RD were provided to Health Authorities where required.
Amendment 1 27-Jun-2022	The protocol had been amended to address Health Authority feedback regarding eligibility criteria, rationale for patients selected based on historic PD-L1 ≥1% expression, the DLT definition and criteria, the usage of male contraception and associated female partner of a male patient language, dose modifications and reductions, reporting guidance for drug-induced liver injury, treatment beyond disease progression criteria, PK sampling schedule, monitoring requirements following QEQ278 infusions, intra-patient dose escalations, caution with substrates of cytochrome P450 (CYP450) enzymes, study stopping rules for dose expansion, and references.

Criteria for evaluation:

Efficacy: Tumor response was assessed locally by the investigator based on RECIST v1.1. Imaging assessments were performed at screening/baseline within 28 days of start of treatment (Day - 28 to Day -1 prior to Cycle 1 Day 1). Post baseline imaging assessments for response evaluation were performed every 8 weeks (+/- 7 days) during the first year, and every 12 weeks (+/- 7 days) thereafter until disease progression, death, lost to follow-up or withdrawal of consent using the same imaging modality used at baseline.

The primary analysis was the best overall response (BOR). Based on the patients' BOR during the study, the following rates were then calculated: overall response rate (ORR), disease control rate (DCR). ORR and DCR were summarized with exact confidence intervals (CIs). Time-to-event endpoints such as duration of response (DOR) and progression-free survival (PFS) were analyzed using Kaplan–Meier methods, with median estimates and confidence intervals presented, where applicable.

Pharmacokinetics: The following pharmacokinetic (PK) parameters were determined using the actual recorded sampling times and non-compartmental methods with Phoenix WinNonlin (Version 8.3 or higher): Cmax, Tmax, AUClast, AUCinf, T1/2, Vz and CL from the serum concentration-time data.

Immunogenicity assessments: Immunogenicity of QEQ278 was evaluated using a validated three-tier antidrug antibody (ADA) testing approach. ADA responses were characterized at the sample and patient level using predefined criteria, excluding samples collected more than 90 days after the last dose. Serum samples were screened for anti-QEQ278 antibodies, and the titer of confirmed positive samples were reported.

Safety: Safety analyses included incidence of DLTs during the first treatment cycle, frequency and severity of adverse events (AEs) and serious adverse events (SAEs) (Medical Dictionary for Regulatory Activities (MedDRA), Common Terminology Criteria for Adverse Events (CTCAE) v5.0), laboratory abnormalities, electrocardiograms (ECG) changes, and vital signs and tolerability (dose interruptions, reductions, and dose intensity).

Statistical methods: Study data was analyzed by Novartis personnel using the most updated SAS® version in the GPS environment.

The analysis set has been defined as:

- The Full analysis set (FAS) and safety set included all patients who received at least one dose of study treatment.
- The dose-determining set included all FAS patients, who met the minimum exposure criteria and have sufficient safety evaluations (as determined by Novartis and Investigators) or experienced a dose-limiting toxicity (DLT) during the DLT-evaluation period.
- The pharmacokinetic analysis set included all patients who provided an evaluable PK profile
- The immunogenicity prevalence set included all patients in the safety set with a non-missing baseline ADA sample or at least one non-missing post-baseline ADA sample.
- The immunogenicity incidence set included all patients in the immunogenicity prevalence set with a non-missing baseline ADA sample and at least one non-missing post-baseline ADA sample.
- The post-treatment analysis set included all patients that did not die in the on-treatment period and were not loss to follow-up.

Patients without a DLT during cycle 1 were considered to have sufficient safety evaluations if observed for ≥ 28 days for Q2W following the first dose and both sponsor and investigators concluded sufficient safety data existed to determine no DLT occurred. Patients in the dose-determining set were summarized according to the lowest dose level received between Day 1 and the end of the DLT evaluation period, DLT onset, or treatment discontinuation, whichever occurred first.

Primary endpoints focused on safety and tolerability (DLTs, AEs, lab changes, dose modifications). Dose escalation followed a Bayesian Logistic Regression Model (BLRM) under escalation with overdose control (EWOC) principles. Secondary endpoints (BOR, ORR, DCR, DOR, PFS) were analyzed using Bayesian methods and Kaplan-Meier estimates. PK and immunogenicity were summarized descriptively. No formal interim analyses were planned; dose decisions were based on ongoing safety and efficacy review.

Summary – Results

Disposition: A total of 30 patients were treated with QEQ278, and all treated patients discontinued the study treatment. Progressive disease (23 patients, 76.7%) was the most common reason for discontinuation from the study treatment. Three patients (10%) discontinued due to death, 2 patients (6.7%) discontinued due to adverse events, and 1 patient (3.3%) each discontinued due to physician decision and study termination by sponsor.

Twenty-one patients (70%) discontinued the post-treatment follow-up period, of which 13 patients (43.3%) completed the follow-up period, 6 patients (20%) died, and 1 patient (3.3%) each discontinued due to new therapy (alternate anti-neoplastic therapy) for study indication and subject decision (Table 2-3).

Table 2-3 Patient disposition (Full analysis set)

Disposition/Reason	QEQ278 70 mg Q2W N=5 n (%)	QEQ278 210 mg Q2W N=7 n (%)	QEQ278 700 mg Q2W N=6 n (%)	QEQ278 1400 mg Q2W N=12 n (%)	All patients N=30 n (%)
Patients treated					
Discontinued from treatment	5 (100)	7 (100)	6 (100)	12 (100)	30 (100)
Reasons for discontinuation					
Adverse event	0	0	1 (16.7)	1 (8.3)	2 (6.7)
Death	0	0	1 (16.7)	2 (16.7)	3 (10.0)
Physician decision	0	1 (14.3)	0	0	1 (3.3)
Progressive disease	5 (100)	6 (85.7)	4 (66.7)	8 (66.7)	23 (76.7)
Study terminated by sponsor	0	0	0	1 (8.3)	1 (3.3)
Post-treatment follow-up for patients who discontinued treatment					
Discontinued from post-treatment follow-up	4 (80.0)	6 (85.7)	3 (50.0)	8 (66.7)	21 (70.0)
Reasons for discontinuation					
Completed*	3 (60.0)	5 (71.4)	1 (16.7)	4 (33.3)	13 (43.3)
Death	1 (20.0)	1 (14.3)	1 (16.7)	3 (25.0)	6 (20.0)
New therapy for study indication	0	0	1 (16.7)	0	1 (3.3)
Subject decision	0	0	0	1 (8.3)	1 (3.3)

Source: Table 14.1-1

*Completed referred to completion of the post-treatment follow-up period.

Analysis sets: Analysis sets used in this study are shown in Table 2-4 below. Definitions of analysis sets are provided in the statistical methods section above.

Table 2-4 Analysis sets (Full analysis set)

Analysis set	QEQ278 70 mg Q2W N=5 n (%)	QEQ278 210 mg Q2W N=7 n (%)	QEQ278 700 mg Q2W N=6 n (%)	QEQ278 1400 mg Q2W N=12 n (%)	All patients N=30 n (%)
Full analysis set	5 (100)	7 (100)	6 (100)	12 (100)	30 (100)
Safety set	5 (100)	7 (100)	6 (100)	12 (100)	30 (100)
Dose determining set	5 (100)	6 (85.7)	5 (83.3)	11 (91.7)	27 (90.0)
Post-treatment analysis set	5 (100)	6 (85.7)	2 (33.3)	7 (58.3)	20 (66.7)
Pharmacokinetic analysis set	5 (100)	7 (100)	6 (100)	12 (100)	30 (100)
Immunogenicity prevalence set	5 (100)	7 (100)	6 (100)	12 (100)	30 (100)
Immunogenicity incidence set	5 (100)	7 (100)	4 (66.7)	11 (91.7)	27 (90.0)

N is the number of patients in Full analysis set (FAS).
Source: Table 14.1-3

Demographic and background characteristics: The study included 22 males (73.3%) and 8 females (26.7%) with a mean (SD) age of 63.8 years (11.78); 16 patients (53.3%) were 18-<65 years and 14 patients (46.7%) were 65-<85 years (Table 2-5).

Table 2-5 Patient demographics (Full analysis set)

Characteristic Categories/Statistics	QEQ278 70mg Q2W N=5	QEQ278 210 mg Q2W N=7	QEQ278 700 mg Q2W N=6	QEQ278 1400 mg Q2W N=12	All patients N=30
Age (years)					
n	5	7	6	12	30
Mean (SD)	69.8 (6.46)	62.6 (17.93)	61.0 (12.54)	63.4 (9.06)	63.8 (11.78)
Median	70.0	67.0	62.0	61.0	63.0
Min-Max	61 - 79	27 - 82	39 - 76	53 - 78	27 - 82
Age group -n (%)					
18 - <65 years	1 (20.0)	3 (42.9)	4 (66.7)	8 (66.7)	16 (53.3)
65 - <85 years	4 (80.0)	4 (57.1)	2 (33.3)	4 (33.3)	14 (46.7)
Sex -n (%)					
Male	4 (80.0)	6 (85.7)	4 (66.7)	8 (66.7)	22 (73.3)
Female	1 (20.0)	1 (14.3)	2 (33.3)	4 (33.3)	8 (26.7)
Race -n (%)					
Asian	1 (20.0)	2 (28.6)	3 (50.0)	4 (33.3)	10 (33.3)
White	4 (80.0)	4 (57.1)	1 (16.7)	4 (33.3)	13 (43.3)
Not Reported	0	1 (14.3)	2 (33.3)	3 (25.0)	6 (20.0)
Unknown	0	0	0	1 (8.3)	1 (3.3)
Ethnicity -n (%)					
Hispanic or Latino	1 (20.0)	0	1 (16.7)	1 (8.3)	3 (10.0)
Not Hispanic or Latino	4 (80.0)	7 (100)	4 (66.7)	8 (66.7)	23 (76.7)
Not reported	0	0	0	3 (25.0)	3 (10.0)
Unknown	0	0	1 (16.7)	0	1 (3.3)

Characteristic Categories/Statistics	QEQ278 70mg Q2W N=5	QEQ278 210 mg Q2W N=7	QEQ278 700 mg Q2W N=6	QEQ278 1400 mg Q2W N=12	All patients N=30
ECOG at baseline - n (%)					
0	3 (60.0)	3 (42.9)	2 (33.3)	3 (25.0)	11 (36.7)
1	2 (40.0)	4 (57.1)	4 (66.7)	9 (75.0)	19 (63.3)
Smoking history -n (%)					
Current	1 (20.0)	0	0	1 (8.3)	2 (6.7)
Former	2 (40.0)	6 (85.7)	5 (83.3)	5 (41.7)	18 (60.0)
Missing	2 (40.0)	1 (14.3)	1 (16.7)	6 (50.0)	10 (33.3)

Source: Table 14.1-2

Protocol deviations: Protocol deviations by individual patients are provided in Listing 14.8-1.

Exposure: The mean (SD) duration of exposure to the study drug was 14 weeks (16.29). Overall, 8 patients (26.7%) were exposed to > 16 weeks of treatment (Table 2-6).

The mean values were 5654.48 mg (SD 10547.137) for cumulative dose, 751.41 mg/2weeks (SD 560.994) for dose intensity, and 0.996 (SD 0.0155) for relative dose intensity (Table 2-7).

Table 2-6 Duration of exposure to QEQ278 (Safety set)

	QEQ278 70 mg Q2W N=5	QEQ278 210 mg Q2W N=7	QEQ278 700 mg Q2W N=6	QEQ278 1400 mg Q2W N=12	All patients N=30
Duration of exposure (weeks)					
Mean (SD)	16.5 (13.76)	9.6 (5.62)	15.1 (17.89)	15.0 (21.23)	14.0 (16.29)
Median	12.3	8.3	7.1	7.9	8.0
Q1-Q3	8.1 - 16.1	4.0 - 14.9	1.7 - 27.4	5.0 - 16.4	6.0 - 16.1
Min-Max	6 - 40	2 - 17	2 - 46	2 - 80	2 - 80
Duration of exposure categories - n (%)					
≤ 4 weeks	0	2 (28.6)	2 (33.3)	3 (25.0)	7 (23.3)
> 4 and ≤ 8 weeks	1 (20.0)	1 (14.3)	2 (33.3)	5 (41.7)	9 (30.0)
> 8 and ≤ 12 weeks	1 (20.0)	1 (14.3)	0	0	2 (6.7)
> 12 and ≤ 16 weeks	1 (20.0)	2 (28.6)	0	1 (8.3)	4 (13.3)
> 16 weeks	2 (40.0)	1 (14.3)	2 (33.3)	3 (25.0)	8 (26.7)

Source: Table 14.1-4

Table 2-7 Dose of QEQ278 received (Safety set)

	QEQ278 70 mg Q2W N=5	QEQ278 210 mg Q2W N=7	QEQ278 700 mg Q2W N=6	QEQ278 1400 mg Q2W N=12	All patients N=30
Average Dose (mg)					

	QEQ278 70 mg Q2W N=5	QEQ278 210 mg Q2W N=7	QEQ278 700 mg Q2W N=6	QEQ278 1400 mg Q2W N=12	All patients N=30
Mean (SD)	80.3* (23.07)	209.2 (1.44)	720.3 (49.70)	1390.3 (33.77)	762.4 (564.35)
Median	70.0	210.0	700.0	1400.0	700.0
Q1-Q3	70.0 - 70.0	208.3 - 210.0	700.0 - 700.0	1400.0 - 1400.0	210.0 - 1400.0
Min-Max	70 - 122	206 - 210	700 - 822	1283 - 1400	70 - 1400
Cumulative dose (mg)					
Mean (SD)	756.00 (879.051)	926.90 (527.147)	5833.33 (7243.112)	10363.83 (14820.734)	5654.48 (10547.137)
Median	420.00	833.00	2450.00	5600.00	2205.00
Q1-Q3	280.00 - 560.00	420.00 - 1470.00	700.00 - 9800.00	3500.00 - 11200.00	700.00 - 5600.00
Min-Max	210.0 - 2310.0	210.0 - 1680.0	700.0 - 18900.0	1400.0 - 56000.0	210.0 - 56000.0
Dose intensity (mg/2weeks)					
Mean (SD)	78.32 (20.562)	197.29 (18.193)	713.55 (53.974)	1374.03 (55.179)	751.41 (560.994)
Median	69.38	199.21	700.00	1400.00	700.00
Q1-Q3	68.77 - 70.00	197.65 - 210.00	683.72 - 700.00	1364.41 - 1400.00	197.88 - 1400.00
Min-Max	68.4 - 115.1	158.1 - 210.0	675.9 - 821.7	1251.1 - 1425.5	68.4 - 1425.5
Relative dose intensity					
Mean (SD)	1.000 (0.0000)	0.996 (0.0068)	1.000 (0.0000)	0.993 (0.0241)	0.996 (0.0155)
Median	1.000	1.000	1.000	1.000	1.000
Q1-Q3	1.000 - 1.000	0.992 - 1.000	1.000 - 1.000	1.000 - 1.000	1.000 - 1.000
Min-Max	1.00 - 1.00	0.98 - 1.00	1.00 - 1.00	0.92 - 1.00	0.92 - 1.00
Relative dose intensity categories - n (%)					
≥0.9 - < 1.1	5 (100)	7 (100)	6 (100)	12 (100)	30 (100)

Average dose did not consider drug free days, whereas dose intensity and relative dose intensity included days of zero dose in the calculation.

* For the mean dose, the observed mean for 70 mg Q2W exceeds the nominal cohort dose due to intra-patient dose escalation in one patient.
Source: Table 14.1-5

Twenty-four patients (80%) had neither dose change nor interruption and 6 patients (20%) had at least one dose change or interruption. Five patients had (16.7%) dose reduction. All dose

changes are dose reductions because there were no dose increases in the study as defined in protocol (Table 2-8).

Table 2-8 Dose adjustments and discontinuation of QEQ278 (Safety Set)

	QEQ278 70 mg Q2W N=5	QEQ278 210 mg Q2W N=7	QEQ278 700 mg Q2W N=6	QEQ278 1400 mg Q2W N=12	All patients N=30
Number of patients-n (%)					
With neither dose change nor interruption	4 (80.0)	4 (57.1)	5 (83.3)	11 (91.7)	24 (80.0)
With at least one dose change or interruption	1 (20.0)	3 (42.9)	1 (16.7)	1 (8.3)	6 (20.0)
Only one dose change or interruption	0	3 (42.9)	1 (16.7)	1 (8.3)	5 (16.7)
More than one dose changes or interruptions	1 (20.0)	0	0	0	1 (3.3)
Dose change number of patients-n (%)					
With no dose change	4 (80.0)	5 (71.4)	5 (83.3)	11 (91.7)	25 (83.3)
With at least one dose change	1 (20.0)	2 (28.6)	1 (16.7)	1 (8.3)	5 (16.7)
Only one dose change	1 (20.0)	2 (28.6)	1 (16.7)	1 (8.3)	5 (16.7)
Number of patients with at least one dose change by reason-n (%)					
Adverse event	0	2 (28.6)	0	1 (8.3)	3 (10.0)
Physician decision	1 (20.0)	0	1 (16.7)	0	2 (6.7)
Dose interruptions number of patients -n (%)					
With no dose interruption	4 (80.0)	6 (85.7)	6 (100)	12 (100)	28 (93.3)
With at least one dose interruption	1 (20.0)	1 (14.3)	0	0	2 (6.7)
Only one dose interruption	1 (20.0)	1 (14.3)	0	0	2 (6.7)
Number of patients with at least one dose interruption by reason-n (%)					
Adverse event	0	1 (14.3)	0	0	1 (3.3)
Physician decision	1 (20.0)	0	0	0	1 (3.3)
Permanent discontinuation number of patients-n (%)	5 (100)	7 (100)	6 (100)	12 (100)	30 (100)
Reason for permanent discontinuation-n (%)					
Adverse event	0	0	1 (16.7)	1 (8.3)	2 (6.7)
Death	0	0	1 (16.7)	2 (16.7)	3 (10.0)
Physician decision	0	1 (14.3)	0	0	1 (3.3)
Progressive disease	5 (100)	6 (85.7)	4 (66.7)	8 (66.7)	23 (76.7)
Study terminated by sponsor	0	0	0	1 (8.3)	1 (3.3)

Source: Table 14.1-6

Efficacy results:

Best overall response and disease control rate: No patient achieved a complete response (CR) or partial response (PR) per RECIST 1.1, hence, duration of response (DoR) could not be determined. Seven patients (23.3%) had stable disease (SD) and 18 patients (60.0 %) had progressive disease (PD) as their BOR. Five patients (16.7%) were not evaluable for response. The ORR was 0.0% (90% CI: 0.0, 9.5) and the DCR was 23.3% (90% CI: 11.5, 39.4) (Table 2-9)

Table 2-9 Best overall response based on local investigator review as per RECIST v1.1 (Full analysis set)

	QEQ278 70 mg Q2W N=5 n (%)	QEQ278 210 mg Q2W N=7 n (%)	QEQ278 700 mg Q2W N=6 n (%)	QEQ278 1400 mg Q2W N=12 n (%)	All patients N=30 n (%)
Best overall response					
Stable disease (SD)	1 (20.0)	1 (14.3)	2 (33.3)	3 (25.0)	7 (23.3)
Progressive disease (PD)	4 (80.0)	5 (71.4)	2 (33.3)	7 (58.3)	18 (60.0)
Not evaluable (NE)	0	1 (14.3)	2 (33.3)	2 (16.7)	5 (16.7)
Overall Response Rate (ORR: CR+PR)	0	0	0	0	0
90% CI	(0.0, 45.1)	(0.0, 34.8)	(0.0, 39.3)	(0.0, 22.1)	(0.0, 9.5)
Disease Control Rate (DCR: CR+PR+SD)	1 (20.0)	1 (14.3)	2 (33.3)	3 (25.0)	7 (23.3)
90% CI	(1.0, 65.7)	(0.7, 52.1)	(6.3, 72.9)	(7.2, 52.7)	(11.5, 39.4)

Source: Table 14.2-1

Progression-free survival: Disease progression was reported in 23 patients (76.7%) and 4 patients (13.3%) died. The median PFS was 1.7 months (95% CI: 1.6, 1.8) and the Kaplan-Meier estimated PFS rates at 3 months, 6 months and 12 months were 25% (95% CI: 11.1, 41.8), 10.7% (95% CI: 2.7, 25.1) and 3.6% (95% CI: 0.3, 15.4), respectively (Table 2-10).

Table 2-10 PFS based on local investigator review as per RECIST v1.1 using the Kaplan-Meier method (Full analysis set)

	QEQ278 70 mg Q2W N=5	QEQ278 210 mg Q2W N=7	QEQ278 700 mg Q2W N=6	QEQ278 1400 mg Q2W N=12	All patients N=30
Number of events - n (%)	5 (100)	6 (85.7)	5 (83.3)	11 (91.7)	27 (90.0)
Progression	5 (100)	6 (85.7)	4 (66.7)	8 (66.7)	23 (76.7)
Death [$]	0	0	1 (16.7)	3 (25.0)	4 (13.3)
Number of censored - n (%)	**0**	**1 (14.3)**	**1 (16.7)**	**1 (8.3)**	**3 (10.0)**
Kaplan-Meier estimate (%) (95% CI)					
1 months	NA	NA	NA	83.3 (48.2, 95.6)	85.7 (66.3, 94.4)

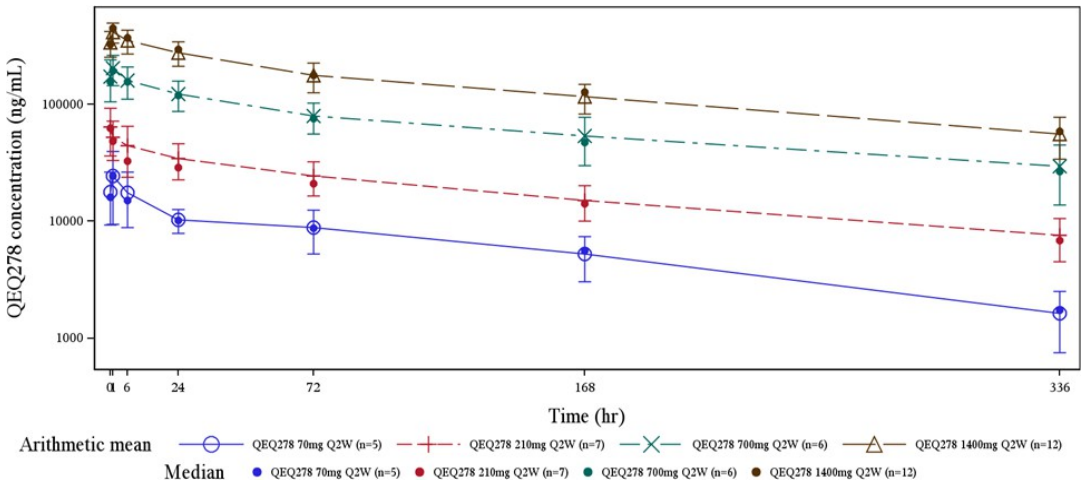
	QEQ278 70 mg Q2W N=5	QEQ278 210 mg Q2W N=7	QEQ278 700 mg Q2W N=6	QEQ278 1400 mg Q2W N=12	All patients N=30
3 months	NA	NA	NA	25.0 (6.0, 50.5)	25.0 (11.1, 41.8)
6 months	NA	NA	NA	8.3 (0.5, 31.1)	10.7(2.7, 25.1)
12 months	NA	NA	NA	8.3 (0.5, 31.1)	3.6 (0.3, 15.4)
18 months	NA	NA	NA	NE	NE
24 months	NA	NA	NA	NE	NE
Percentiles (95% CI)					
25th	NA	NA	NA	1.5 (0.5, 1.7)	1.5 (0.5, 1.6)
50th, median	NA	NA	NA	1.7 (0.8, 3.7)	1.7 (1.6, 1.8)
75th	NA	NA	NA	3.2 (1.7, NE)	3.2 (1.7, 6.2)

NE=not estimable.
$ Death before progression.
Ongoing patients were treated as censored at last assessment before data cut-off date 2026-01-26.
Source: Table 14.2-2

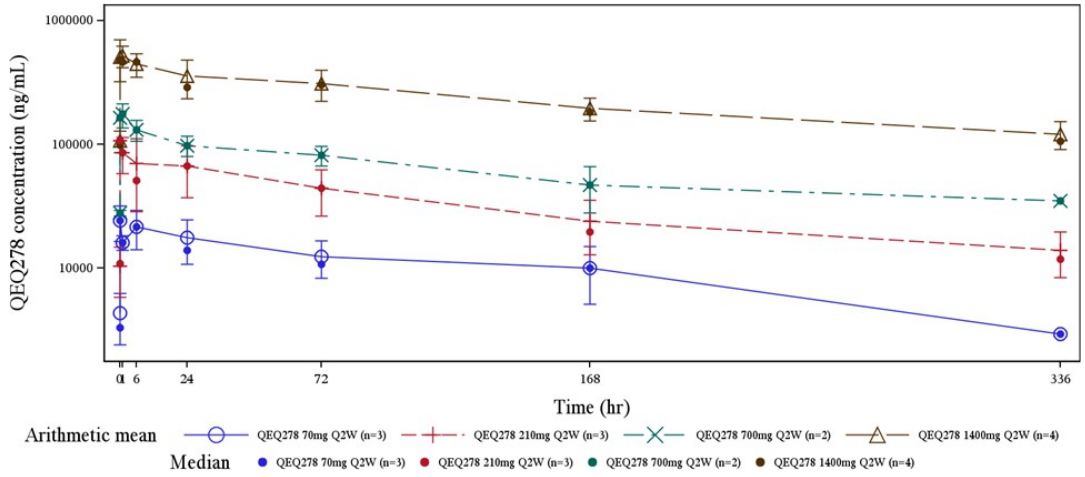
Pharmacokinetic results: The median time to reach maximum concentration (Tmax) was at end of infusion or 1 hour post infusion and ranged from 1.16 to 2.17 hours across all cycles and dose groups. Drug exposure increased proportionally with dose escalation, demonstrating dose proportionality across dose groups. Following multiple dosing, both the area under curve (AUC) and Cmax exhibited less than a two-fold increase (Cycle 3/Cycle 1), with maximum increases of 1.7-fold and 1.3-fold, respectively, indicating low to moderate drug accumulation. The steady-state half-life was approximately 6 to 9 days. Inter-subject variability remained below 50% (Figure 2-2 and Table 2-11).

Figure 2-2 **Median and arithmetic mean (SD) serum concentration-time profiles for QEQ278 by treatment/visit over time (Pharmacokinetic analysis set)**

Dose profile: Cycle 1 Day 1- Semi-logarithmic view



Dose profile: Cycle 3 Day 1- Semi-logarithmic view



Source: Figure 14.5-1

Table 2-11 **Summary of PK parameters for QEQ278 (Pharmacokinetic analysis set)**

Visit	Parameter	Statistics	QEQ278 70mg Q2W N=5	QEQ278 210mg Q2W N=7	QEQ278 700mg Q2W N=6	QEQ278 1400mg Q2W N=12
Cycle 1 Day1	**AUC(0-336) (h*µg/mL)**	**n**	**5**	**4**	**4**	**11**
		Geo-mean	2050	6610	20700	44200

Visit	Parameter	Statistics	QEQ278 70mg Q2W N=5	QEQ278 210mg Q2W N=7	QEQ278 700mg Q2W N=6	QEQ278 1400mg Q2W N=12
		Geo-CV%	43.3	35.2	41.2	35.9
	Cmax (µg/mL)	**n**	**5**	**4**	**4**	**11**
		Geo-mean	18.2	55.7	213	389
		Geo-CV%	44.2	42.1	28.9	23.6
	Tmax (h)	**n**	**5**	**4**	**4**	**11**
		Median	2.17	1.61	1.7	1.53
		Min; Max	1.12; 3.07	1.08; 18.5	1.08; 2.50	1.08; 3.83
Cycle 3 Day1	**AUC(0-336) (h*µg/mL)**	**n**	**2**	**3**	**2**	**4**
		Geo-mean	3570	9360	19300	75400
		Geo-CV%	46.9	49.3	27.2	20.7
	Cmax (µg/mL)	**n**	**2**	**3**	**2**	**4**
		Geo-mean	23.6	72.5	182	511
		Geo-CV%	33.6	47.3	15.2	28.2
	Tmax (h)	**n**	**2**	**3**	**2**	**4**
		Median	1.16	1.95	1.76	1.83
		Min; Max	1.08; 1.23	1.00; 7.00	1.38; 2.13	1.08; 2.20

n=number of patients with corresponding evaluable PK parameters.

CV% = coefficient of variation (%) = sd/mean*100, Geo-CV% = sqrt (exp (variance for log transformed data)-1)*100.
Source: Table 14.2-3

Immunogenicity results: No patients reported positive anti-drug antibody results at any post-baseline timepoint after administration of QEQ278 (Table 14.2-4).

Safety results:

Estimation of MTD/RD: Dose escalation was guided using a BLRM incorporating the EWOC principle. However, due to the early termination of the study during the dose-escalation phase, the MTD or RD was not determined. All evaluated dose levels were considered safe and tolerable within the explored range, In the last and fifth dose escalation meeting, all doses including 2100 mg Q2W achieved lower than 0.25 probability of target toxicity.

Dose limiting toxicities: A total of 2 DLTs occurred in 2 patients (7.4%), overall; both were grade 3. One patient experienced a DLT of cytokine release syndrome in QEQ278 700 mg Q2W and another patient experienced infusion-related reaction in QEQ278 1400 mg Q2W dose group. No DLTs were reported in patients treated with QEQ278 70 mg Q2W or 210 mg Q2W dose groups (Table 2-12 and Listing 16.3-1).

Table 2-12 Dose limiting toxicities by system organ class, preferred term and maximum grade (Dose determining set)

	QEQ278 70 mg Q2W N=5		QEQ278 210 mg Q2W N=6		QEQ278 700 mg Q2W N=5		QEQ278 1400 mg Q2W N=11		All patients N=27	
Primary system organ class	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**
Preferred term	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Number of patients with at least one event	**0**	**0**	**0**	**0**	**1 (20.0)**	**1 (20.0)**	**1 (9.1)**	**1 (9.1)**	**2 (7.4)**	**2 (7.4)**
Immune system disorders	0	0	0	0	1 (20.0)	1 (20.0)	0	0	1 (3.7)	1 (3.7)
Cytokine release syndrome	0	0	0	0	1 (20.0)	1 (20.0)	0	0	1 (3.7)	1 (3.7)
Injury, poisoning and procedural complications	0	0	0	0	0	0	1 (9.1)	1 (9.1)	1 (3.7)	1 (3.7)
Infusion related reaction	0	0	0	0	0	0	1 (9.1)	1 (9.1)	1 (3.7)	1 (3.7)

Numbers (n) represent counts of patients.
A patient with multiple severity grades for an AE was only counted under the maximum grade.
MedDRA version 28.1, CTCAE version V5.0.
Source: Table 14.3-5

Adverse events regardless of study drug relationship by system organ class (SOC): Overall, 28 patients (93.3%) had at least one AE, including 15 patients (50%) with at least one grade ≥ 3 AE (Table 2-13).

The most frequently reported SOCs for patients reporting grade ≥ 3 AEs (≥ 10% of all patients) regardless of study drug relationship were:

- Metabolism and nutrition disorders (4 patients, 13.3%)
- Respiratory, thoracic and mediastinal disorders (4 patients, 13.3%)
- Vascular disorders (4 patients, 13.3%)
- Blood and lymphatic system disorders (3 patients, 10%)

Table 2-13 AEs regardless of study drug relationship by system organ class, preferred term and maximum grade (≥10% SOC/ PT; All grades; All patients) (Safety Set)

	QEQ278 70 mg Q2W N=5		QEQ278 210 mg Q2W N=7		QEQ278 700 mg Q2W N=6		QEQ278 1400 mg Q2W N=12		All patients N=30	
Primary system organ class / **Preferred term**	**All Grades n (%)**	**Grade ≥3 n (%)**	**All Grades n (%)**	**Grade ≥3 n (%)**	**All Grades n (%)**	**Grade ≥3 n (%)**	**All Grades n (%)**	**Grade ≥3 n (%)**	**All Grades n (%)**	**Grade ≥3 n (%)**
Number of patients with at least one event	**4 (80.0)**	**2 (40.0)**	**7 (100)**	**2 (28.6)**	**6 (100)**	**4 (66.7)**	**11 (91.7)**	**7 (58.3)**	**28 (93.3)**	**15 (50.0)**
General disorders and administration site conditions	2 (40.0)	0	3 (42.9)	0	2 (33.3)	0	7 (58.3)	0	14 (46.7)	0
Chills	0	0	0	0	1 (16.7)	0	2 (16.7)	0	3 (10.0)	0
Fatigue	0	0	0	0	1 (16.7)	0	2 (16.7)	0	3 (10.0)	0
Pyrexia	0	0	0	0	0	0	3 (25.0)	0	3 (10.0)	0
Respiratory, thoracic and mediastinal disorders	1 (20.0)	0	3 (42.9)	0	3 (50.0)	2 (33.3)	5 (41.7)	2 (16.7)	12 (40.0)	4 (13.3)
Dyspnea	0	0	2 (28.6)	0	2 (33.3)	2 (33.3)	1 (8.3)	1 (8.3)	5 (16.7)	3 (10.0)
Cough	1 (20.0)	0	2 (28.6)	0	1 (16.7)	0	0	0	4 (13.3)	0
Injury, poisoning and procedural complications	2 (40.0)	0	2 (28.6)	0	1 (16.7)	0	5 (41.7)	1 (8.3)	10 (33.3)	1 (3.3)
Infusion related reaction	2 (40.0)	0	2 (28.6)	0	0	0	5 (41.7)	1 (8.3)	9 (30.0)	1 (3.3)
Gastrointestinal disorders	1 (20.0)	0	2 (28.6)	0	2 (33.3)	0	4 (33.3)	1 (8.3)	9 (30.0)	1 (3.3)
Diarrhea	1 (20.0)	0	0	0	0	0	2 (16.7)	0	3 (10.0)	0
Investigations	1 (20.0)	0	4 (57.1)	0	2 (33.3)	0	2 (16.7)	1 (8.3)	9 (30.0)	1 (3.3)
Blood creatinine increased	0	0	2 (28.6)	0	1 (16.7)	0	0	0	3 (10.0)	0
Gamma-glutamyl transferase increased	1 (20.0)	0	1 (14.3)	0	1 (16.7)	0	0	0	3 (10.0)	0
Metabolism and nutrition disorders	2 (40.0)	0	2 (28.6)	1 (14.3)	3 (50.0)	2 (33.3)	2 (16.7)	1 (8.3)	9 (30.0)	4 (13.3)
Decreased appetite	1 (20.0)	0	1 (14.3)	0	1 (16.7)	0	1 (8.3)	1 (8.3)	4 (13.3)	1 (3.3)

	QEQ278 70 mg Q2W N=5		QEQ278 210 mg Q2W N=7		QEQ278 700 mg Q2W N=6		QEQ278 1400 mg Q2W N=12		All patients N=30	
Primary system organ class	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**
Preferred term	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Blood and lymphatic system disorders	2 (40.0)	1 (20.0)	1 (14.3)	0	2 (33.3)	1 (16.7)	2 (16.7)	1 (8.3)	7 (23.3)	3 (10.0)
Anemia	2 (40.0)	1 (20.0)	1 (14.3)	0	1 (16.7)	1 (16.7)	2 (16.7)	1 (8.3)	6 (20.0)	3 (10.0)
Musculoskeletal and connective tissue disorders	1 (20.0)	0	2 (28.6)	1 (14.3)	1 (16.7)	0	3 (25.0)	1 (8.3)	7 (23.3)	2 (6.7)
Infections and infestations	1 (20.0)	1 (20.0)	2 (28.6)	0	0	0	3 (25.0)	1 (8.3)	6 (20.0)	2 (6.7)
Vascular disorders	0	0	0	0	2 (33.3)	1 (16.7)	4 (33.3)	3 (25.0)	6 (20.0)	4 (13.3)
Nervous system disorders	0	0	2 (28.6)	0	0	0	3 (25.0)	1 (8.3)	5 (16.7)	1 (3.3)
Skin and subcutaneous tissue disorders	1 (20.0)	0	1 (14.3)	0	1 (16.7)	0	2 (16.7)	0	5 (16.7)	0
Psychiatric disorders	0	0	1 (14.3)	0	2 (33.3)	0	0	0	3 (10.0)	0

Numbers (n) represent counts of patients.

AEs occurring during treatment or within 30 days of the last study medication are summarized.

A patient with multiple severity grades for an AE was only counted under the maximum grade.

MedDRA version 28.1, CTCAE version V5.0.
Source: Table 14.3-1

Adverse events regardless of study drug relationship by PT (≥ 10% of all patients) are summarized in (Table 2-14). The most commonly reported PTs for patients reporting all grade AEs (≥ 10% of all patients) were infusion-related reaction (9 patients, 30%), anemia (6 patients, 20%), and dyspnea (5 patients, 16.7%).

The most frequently reported PTs for patients reporting grade ≥ 3 AEs (≥ 10% of all patients) were anemia and dyspnea, each reported in 3 patients (10%).

Table 2-14 AEs regardless of study drug relationship by preferred term and maximum grade (≥10% all grades, all patients) (Safety Set)

	QEQ278 70 mg Q2W N=5		QEQ278 210 mg Q2W N=7		QEQ278 700 mg Q2W N=6		QEQ278 1400 mg Q2W N=12		All patients N=30	
	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number of patients with at least one event	**4 (80.0)**	**2 (40.0)**	**7 (100)**	**2 (28.6)**	**6 (100)**	**4 (66.7)**	**11 (91.7)**	**7 (58.3)**	**28 (93.3)**	**15 (50.0)**
Infusion related reaction	2 (40.0)	0	2 (28.6)	0	0	0	5 (41.7)	1 (8.3)	9 (30.0)	1 (3.3)
Anemia	2 (40.0)	1 (20.0)	1 (14.3)	0	1 (16.7)	1 (16.7)	2 (16.7)	1 (8.3)	6 (20.0)	3 (10.0)
Dyspnea	0	0	2 (28.6)	0	2 (33.3)	2 (33.3)	1 (8.3)	1 (8.3)	5 (16.7)	3 (10.0)
Cough	1 (20.0)	0	2 (28.6)	0	1 (16.7)	0	0	0	4 (13.3)	0
Decreased appetite	1 (20.0)	0	1 (14.3)	0	1 (16.7)	0	1 (8.3)	1 (8.3)	4 (13.3)	1 (3.3)
Blood creatinine increased	0	0	2 (28.6)	0	1 (16.7)	0	0	0	3 (10.0)	0
Chills	0	0	0	0	1 (16.7)	0	2 (16.7)	0	3 (10.0)	0
Diarrhea	1 (20.0)	0	0	0	0	0	2 (16.7)	0	3 (10.0)	0
Fatigue	0	0	0	0	1 (16.7)	0	2 (16.7)	0	3 (10.0)	0
Gamma-glutamyl transferase increased	1 (20.0)	0	1 (14.3)	0	1 (16.7)	0	0	0	3 (10.0)	0
Pyrexia	0	0	0	0	0	0	3 (25.0)	0	3 (10.0)	0

Numbers (n) represent counts of patients.
AEs occurring during treatment or within 30 days of the last study medication are summarized.
A patient with multiple severity grades for an AE is only counted under the maximum grade.
MedDRA version 28.1, CTCAE version V5.0.
Source: Table 14.3-2

Adverse events leading to discontinuation: Overall, AEs leading to discontinuation were reported in 2 patients (6.7%). These included cytokine release syndrome and infusion-related reaction, reported in 1 patient each (3.3%). Both the events were grade 3 and were considered to be treatment related. (Table 2-12 and Table 2-15).

Table 2-15 AEs leading to discontinuation regardless of study drug relationship by preferred term and maximum grade (Safety set)

	QEQ278 70 mg Q2W N=5		QEQ278 210 mg Q2W N=7		QEQ278 700 mg Q2W N=6		QEQ278 1400 mg Q2W N=12		All patients N=30	
	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number of patients with at least one event	**0**	**0**	**0**	**0**	**1 (16.7)**	**1 (16.7)**	**1 (8.3)**	**1 (8.3)**	**2 (6.7)**	**2 (6.7)**
Cytokine release syndrome	0	0	0	0	1 (16.7)	1 (16.7)	0	0	1 (3.3)	1 (3.3)
Infusion related reaction	0	0	0	0	0	0	1 (8.3)	1 (8.3)	1 (3.3)	1 (3.3)

Numbers (n) represent counts of patients.
AEs occurring during treatment or within 30 days of the last study medication are summarized.
A patient with multiple severity grades for an AE was only counted under the maximum grade.
MedDRA version 28.1, CTCAE version V5.0.
Source: Table 14.3-3

Deaths: Overall, 13 patients (43.3%) died, of these 3 deaths were reported during the on-treatment period, and 10 deaths were reported after on-treatment period (Listing 16.3- 2). The primary reason for death was study indication (12 patients, 40%); the other one patient died due to an AE (pancreatitis acute) in the QEQ278 1400 mg Q2W dose group, which was not related to study drug (Table 2-16 and Listing 16.3-1).

Table 2-16 All deaths by system organ class and preferred term (Safety set)

Primary system organ class Primary reason (preferred term)	QEQ278 70 mg Q2W N=5 n (%)	QEQ278 210 mg Q2W N=7 n (%)	QEQ278 700 mg Q2W N=6 n (%)	QEQ278 1400 mg Q2W N=12 n (%)	All patients N=30 n (%)
Number of patients who died	**3 (60.0)**	**3 (42.9)**	**2 (33.3)**	**5 (41.7)**	**13 (43.3)**
Adverse event	0	0	0	1 (8.3)	1 (3.3)
Study indication	3 (60.0)	3 (42.9)	2 (33.3)	4 (33.3)	12 (40.0)
Gastrointestinal disorders	0	0	0	1 (8.3)	1 (3.3)
Pancreatitis acute	0	0	0	1 (8.3)	1 (3.3)

Includes all deaths occurring during treatment and post-treatment period.
MedDRA version 28.1.
Source: Table 14.3-6

Serious adverse events: Overall, SAEs regardless of study drug causal relationship were reported in 12 patients (40%) and grade ≥ 3 SAEs were reported in 9 (30%). Grade ≥ 3 SAEs by PT (regardless of study drug relationship) were dyspnea (2 patients, 6.7%); and bronchospasm, cytokine release syndrome, gastric hemorrhage, hypercalcemia, infusion-related reaction, nerve compression, pancreatitis acute, and sepsis (each 1 patient, 3.3%). Of these grade ≥ 3 SAEs, 3 patients had study drug-related SAEs (bronchospasm, cytokine release syndrome, infusion-related reaction) (Table 2-17 and Listing 16.3- 1).

Table 2-17 SAEs regardless of study drug relationship by preferred term and maximum grade (Safety set)

	QEQ278 70 mg Q2W N=5		QEQ278 210 mg Q2W N=7		QEQ278 700 mg Q2W N=6		QEQ278 1400 mg Q2W N=12		All patients N=30	
	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number of patients with at least one event	**1 (20.0)**	**1 (20.0)**	**1 (14.3)**	**1 (14.3)**	**3 (50.0)**	**2 (33.3)**	**7 (58.3)**	**5 (41.7)**	**12 (40.0)**	**9 (30.0)**
Bronchospasm	0	0	0	0	0	0	1 (8.3)	1 (8.3)	1 (3.3)	1 (3.3)
Cytokine release syndrome	0	0	0	0	1 (16.7)	1 (16.7)	0	0	1 (3.3)	1 (3.3)
dyspnea	0	0	0	0	1 (16.7)	1 (16.7)	1 (8.3)	1 (8.3)	2 (6.7)	2 (6.7)
Gastric hemorrhage	0	0	0	0	0	0	1 (8.3)	1 (8.3)	1 (3.3)	1 (3.3)
Hypercalcemia	0	0	1 (14.3)	1 (14.3)	0	0	0	0	1 (3.3)	1 (3.3)
Infusion related reaction	0	0	0	0	0	0	1 (8.3)	1 (8.3)	1 (3.3)	1 (3.3)
Malaise	0	0	0	0	0	0	1 (8.3)	0	1 (3.3)	0
Nerve compression	0	0	0	0	0	0	1 (8.3)	1 (8.3)	1 (3.3)	1 (3.3)
Overdose	0	0	0	0	1 (16.7)	0	0	0	1 (3.3)	0
Pain in extremity	0	0	0	0	1 (16.7)	0	0	0	1 (3.3)	0
Pancreatitis acute	0	0	0	0	0	0	1 (8.3)	1 (8.3)	1 (3.3)	1 (3.3)
Pulmonary hemorrhage	0	0	0	0	0	0	1 (8.3)	0	1 (3.3)	0
Sepsis	1 (20.0)	1 (20.0)	0	0	0	0	1 (8.3)	0	2 (6.7)	1 (3.3)
Tracheo-oesophageal fistula	0	0	0	0	1 (16.7)	0	0	0	1 (3.3)	0

Numbers (n) represent counts of patients.
SAEs occurring during treatment or within 30 days of the last study medication are summarized.
A patient with multiple severity grades for an AE is only counted under the maximum grade.
MedDRA version 28.1, CTCAE version V5.0.
Source: Table 14.3-4

Laboratory values, vital signs, and ECGs:

No clinically meaningful trend in laboratory parameters, vital signs, or ECGs was observed in the study. Any individual abnormalities were captured in the AE listings (Listing 16.3-1).

Conclusions:

This first-in-human, dose-escalation study evaluated the safety, pharmacokinetics, immunogenicity, and preliminary efficacy of QEQ278 administered intravenously every two weeks at increasing doses of 70 mg to 1400 mg (four dose cohorts in the dose escalation phase) in patients with advanced malignancies.

QEQ278 was generally tolerable. Adverse events were observed in the majority of patients, consistent with an advanced oncology setting. Dose-limiting toxicities occurred in two patients (cytokine release syndrome and infusion-related reaction at higher doses). Serious adverse events were reported in 40% of patients. Deaths were largely attributable to disease progression; one death was attributed to acute pancreatitis. No deaths were considered casually related to QEQ278.

All 30 treated patients discontinued study treatment, predominantly due to disease progression (76.7%). Median duration of treatment exposure was 8.0 weeks. Dose compliance was high, with relative dose intensity close to 100% across cohorts.

QEQ278 showed limited clinical benefits with 7 patients having stable disease, as BOR while none of the patients achieved complete or partial response (ORR 0.0%). All administered doses in the study were safe and tolerable, but MTD and/or RD could not be determined due to early study termination.

Pharmacokinetic data for QEQ278 showed dose-proportional exposure, expected time to maximum concentration (median Tmax ~1–2 hours), low to moderate accumulation as expected for a terminal half-life of approximately 6- 9 days, all supporting exploring the bi-weekly dosing schedule. No treatment-emergent anti-drug antibodies were detected, indicating no evidence of immunogenicity.

Overall, QEQ278 demonstrated an acceptable safety profile and predictable pharmacokinetics without evidence of immunogenicity and showed limited clinical activity up to the maximum administered dose of 1400 mg Q2W.