NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

MIK665 / S64315

Trial Indication(s)

Lymphoma and multiple myeloma

Protocol Number

CMIK665X2101

Protocol Title

Phase I open label, multi-center study to characterize the safety, tolerability and pharmacokinetics of intravenously administered MIK665, a Mcl-1 inhibitor, in patients with refractory or relapsed lymphoma or multiple myeloma

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase 1

Study Start/End Dates

Study Start Date: July 2017 (Actual)
Primary Completion Date: June 2019 (Actual)

Study Completion Date: June 2019 (Actual)

Reason for Termination

After careful evaluation of the enrollment situation due to the current competitive landscape for anticancer therapies and given the limited clinical activity currently observed with the study treatment, Novartis has decided on 8-Jul-2020 to terminate the study CMIK665X2101. This is an early termination following a temporary halt of the trial, which occurred on 26-Aug-2019. Global last subject last visit (LSLV) was on 07-Jun-2019. Importantly, this recruitment halt was not a consequence of any safety concerns.

Study Design/Methodology

This was a Phase I, open label, multi-center study including subjects with refractory or relapsed lymphoma or multiple myeloma (r/r lymphoma and r/r MM) that evaluated the safety, efficacy, and pharmacokinetics (PK) of MIK665.

This study had two parts: dose escalation and dose expansion.

In the dose escalation part, MIK665 was administered via intravenous (i.v.) infusion over 30 minutes once every week (21-day cycle) to identify the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE).

The dose expansion part was designed to further explore the safety and assess the preliminary anti-tumor activity of MTD(s) and/or RDE(s) in two groups of subjects, r/r MM and MYC positive diffuse large B-cell lymphoma (DLBCL). However, dose expansion was not opened to either group of subjects, as the study was terminated early, before determination of the MTD(s)/RDE(s).

Centers

8 centers in 7 countries: Japan(1), Spain(1), Italy(1), Australia(1), United States(1), Germany(2), France(1)

Objectives:

The primary objective of the trial was to characterize the safety and tolerability of MIK665 and identify the MTD and/or RDE of MIK665 in selected indications. The following related endpoints were assessed:

- Incidence of adverse events (AEs) and serious adverse events (SAEs)
- Incidence of Dose Limiting Toxicities (DLTs) during the first cycle of treatment
- Number of participants with dose reductions or dose interruptions
- Dose intensity

The secondary objectives were:

- To assess the preliminary anti-tumor activity of MIK665 per the International Myeloma Working Group (IMWG) criteria for Myeloma and per the revised criteria for staging of the International Working Group (IWG) guidelines for Lymphoma in terms of:
  - Number of participants with Best Overall Response (BOR)
  - Duration of response (DOR)
  - Progression-free survival (PFS) rate
- To characterize the pharmacokinetic (PK) profile of MIK665

Test Product (s), Dose(s), and Mode(s) of Administration

MIK665 was administered via intravenous (i.v.) infusion over 30 minutes once every week (21-day cycle). A total of 6 dose levels of MIK665 were assessed: 50 mg, 100 mg, 150 mg, 200 mg, 250 mg and 300 mg.

Subjects continued on treatment with MIK665 until the subject experienced unacceptable toxicity that precluded any further treatment or disease progression. Treatment could also be discontinued at the discretion of the Investigator or by the subject's request.

Statistical Methods

The dose escalation part of this study was guided by a Bayesian analysis of Cycle 1 DLT data for MIK665. The relationship between dose and the probability of dose limiting toxicity (DLT) was modelled using a Bayesian hierarchical model (BHM) for each of the two indications (r/r MM and r/r lymphoma). The BHM was designed to assess the level of similarity in the rate of DLT across dose levels of MIK665 across the different indications. The model and design also allowed for the determination of separate MTD(s)/RDE(s) for the different indications. Dosing decisions were guided by the escalation with overdose control principal.

BOR, overall response rate (ORR) and DOR were computed and summarized by treatment group and by indication in the dose escalation part of the study. Kaplan-Meier estimated probabilities (PFS rate) with corresponding 95% CIs at several time points were presented.

DOR was summarized using descriptive analysis only. No statistical analysis was performed for DOR.

The assessment of safety was based mainly on the frequency of DLTs, adverse events (AEs) and on the assessment of laboratory values that fell outside of pre-determined ranges. Other safety events of interest (troponin AEs and cardiac-related AEs) were also summarized.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria

- Age ≥ 18 years.
- Histologically confirmed lymphoma (WHO classification), or confirmed MM (IMWG), that is relapsed and/or refractory.

Exclusion Criteria
- Known history of chronic liver disease
- History of chronic pancreatitis.
- Prior treatment with Mcl-1 inhibitor.

Participant Flow Table

Overall Study

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg	Total
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)	
Started	5	4	5	9	5	3	31
Completed	0	0	0	0	0	0	0
Not Completed	5	4	5	9	5	3	31
Progressive disease	5	2	3	6	5	3	24
Adverse Event	0	2	0	2	0	0	4
Subject/guardian decision	0	0	1	1	0	0	2
Physician Decision	0	0	1	0	0	0	1

Baseline Characteristics

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg	Total
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)	
Number of Participants [units: participants]	5	4	5	9	5	3	31
Age Continuous (units: years) Mean ± Standard Deviation							
	67.4±9.10	67.8±9.74	55.0±8.66	57.1±16.59	59.2±8.58	62.7±6.43	60.7±11.86
Sex: Female, Male (units: participants) Count of Participants (Not Applicable)							
Female	1	3	1	3	1	0	9
Male	4	1	4	6	4	3	22
Race/Ethnicity, Customized (units: participants) Count of Participants (Not Applicable)							
Caucasian	3	3	4	8	4	1	23
Asian	2	1	0	1	0	1	5
Other	0	0	1	0	1	1	3

Primary Outcome Result(s)

Incidence of AEs and SAEs

(Time Frame: From the day of the first dose of MIK665 up to 30 days after the last dose, up to maximum duration of 94 weeks)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5	4	5	9	5	3
Incidence of AEs and SAEs (units: participants) Count of Participants (Not Applicable)						
AEs	5 (100%)	4 (100%)	5 (100%)	9 (100%)	5 (100%)	3 (100%)
Treatment-related AEs	3 (60%)	4 (100%)	5 (100%)	8 (88.89%)	5 (100%)	3 (100%)
SAEs	2 (40%)	1 (25%)	2 (40%)	2 (22.22%)	2 (40%)	0 (%)
Treatment-related SAEs	0 (%)	0 (%)	1 (20%)	1 (11.11%)	1 (20%)	0 (%)
AEs leading to discontinuation	1 (20%)	2 (50%)	0 (%)	2 (22.22%)	0 (%)	0 (%)
Treatment-related AEs leading to discontinuation	0 (%)	1 (25%)	0 (%)	2 (22.22%)	0 (%)	0 (%)
AEs leading to dose adjustment/interruption	1 (20%)	3 (75%)	2 (40%)	5 (55.56%)	3 (60%)	3 (100%)
AEs requiring additional therapy	5 (100%)	4 (100%)	5 (100%)	8 (88.89%)	5 (100%)	3 (100%)

Incidence of Dose Limiting Toxicities (DLTs) during the first cycle of treatment

(Time Frame: 21 days)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5	4	5	9	5	3
Incidence of Dose Limiting Toxicities (DLTs) during the first cycle of treatment (units: participants) Count of Participants (Not Applicable)						
	0 (%)	0 (%)	1 (20%)	2 (22.22%)	1 (20%)	2 (66.67%)

Number of participants with dose reductions or dose interruptions

(Time Frame: A median of 7 weeks, up to maximum duration of 90 weeks)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5	4	5	9	5	3
Number of participants with dose reductions or dose interruptions (units: participants) Count of Participants (Not Applicable)						
At least one dose reduction	0 (%)	0 (%)	1 (20%)	0 (%)	0 (%)	2 (66.67%)
At least one dose interruption	3 (60%)	2 (50%)	1 (20%)	3 (33.33%)	2 (40%)	3 (100%)

Dose intensity
(Time Frame: A median of 7 weeks, up to maximum duration of 90 weeks)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5	4	5	9	5	3
Dose intensity (units: mg/day) Mean ± Standard Deviation						
	53.75 ± 17.984	94.34 ± 4.361	138.38 ± 29.220	185.93 ± 27.171	224.03 ± 37.868	192.13 ± 6.851

Secondary Outcome Result(s)

Number of participants with Best Overall Response (BOR) based on Multiple Myeloma criteria
(Time Frame: From the day of the first dose of MIK665 up to 30 days after the last dose, up to maximum duration of 94 weeks)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	1	2	5	3	5	0
Number of participants with Best Overall Response (BOR) based on Multiple Myeloma criteria (units: participants) Count of Participants (Not Applicable)						

Complete Response (CR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	(NaN%)
Partial Response (PR)	0 (%)	0 (%)	1 (20%)	0 (%)	0 (%)	(NaN%)
Stable Disease (SD)	0 (%)	2 (100%)	2 (40%)	0 (%)	2 (40%)	(NaN%)
Progressive Disease (PD)	0 (%)	0 (%)	1 (20%)	1 (33.33%)	3 (60%)	(NaN%)
Unknown	1 (100%)	0 (%)	1 (20%)	2 (66.67%)	0 (%)	(NaN%)

Number of participants with Best Overall Response (BOR) based on Lymphoma criteria

(Time Frame: From the day of the first dose of MIK665 up to 30 days after the last dose, up to maximum duration of 94 weeks)

	MIK665 QW 50 mg	**MIK665 QW 100 mg**	**MIK665 QW 150 mg**	**MIK665 QW 200 mg**	**MIK665 QW 250 mg**	**MIK665 QW 300 mg**
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	4	2	0	6	0	3
Number of participants with Best Overall Response (BOR) based on Lymphoma criteria (units: participants) Count of Participants (Not Applicable)						
Complete Response (CR)	0 (%)	0 (%)	(NaN%)	0 (%)	(NaN%)	0 (%)
Partial Response (PR)	2 (50%)	1 (50%)	(NaN%)	0 (%)	(NaN%)	0 (%)
Stable Disease (SD)	1 (25%)	0 (%)	(NaN%)	1 (16.67%)	(NaN%)	0 (%)
Progressive Disease (PD	1 (25%)	0 (%)	(NaN%)	5 (83.33%)	(NaN%)	3 (100%)

Unknown	0 (%)	1 (50%)	(NaN%)	0 (%)	(NaN%)	0 (%)

Duration of Response (DOR) based on Multiple Myeloma criteria

(Time Frame: From the day of the first dose of MIK665 up to 30 days after the last dose, up to maximum duration of 94 weeks)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	0	0	1	0	0	0
Duration of Response (DOR) based on Multiple Myeloma criteria (units: weeks) Median (Full Range)			16.0 (16.0 to 16.0)			

Duration of Response (DOR) based on Lymphoma criteria

(Time Frame: From the day of the first dose of MIK665 up to 30 days after the last dose, up to maximum duration of 94 weeks)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	2	1	0	0	0	0
Duration of Response (DOR) based on Lymphoma criteria (units: weeks) Median (Full Range)						

26.43 (4.7 to 48.1)	28.14 (28.14 to 28.14)

Progression-Free Survival (PFS) rate based on Multiple Myeloma criteria

(Time Frame: From the day of the first dose of MIK665 up to 30 days after the last dose, up to maximum duration of 94 weeks)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	1	2	5	3	5	0
Progression-Free Survival (PFS) rate based on Multiple Myeloma criteria (units: percentage of participants) Number (95% Confidence Interval)						
3 months	NA (NA to NA)	NA (NA to NA)	53.3 (6.8 to 86.3)	NA (NA to NA)	NA (NA to NA)	

NA: Not applicable - insufficient number of participants with events

Progression-Free Survival (PFS) rate based on Lymphoma criteria

(Time Frame: From the day of the first dose of MIK665 up to 30 days after the last dose, up to maximum duration of 94 weeks)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	4	2	0	6	0	3
Progression-Free Survival (PFS) rate based on Lymphoma criteria (units: percentage of participants) Number (95% Confidence Interval)						

3 months	50.0 (5.8 to 84.5)	100 (100 to 100)	16.7 (0.8 to 51.7)	NA (NA to NA)
6 months	25.0 (0.9 to 66.5)	100 (100 to 100)	NA (NA to NA)	NA (NA to NA)
9 months	25.0 (0.9 to 66.5)	100 (100 to 100)	NA (NA to NA)	NA (NA to NA)
12 months	25.0 (0.9 to 66.5)	NA (NA to NA)	NA (NA to NA)	NA (NA to NA)
15 months	25.0 (0.9 to 66.5)	NA (NA to NA)	NA (NA to NA)	NA (NA to NA)

NA: Not applicable - insufficient number of participants with events

Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of MIK665

(Time Frame: pre dose, end of infusion, 0.25, 0.5, 1, 1.5, 2, 4, 6, 8 and 24 hours after end of infusion on Cycle 1 Day 1 and Cycle 1 Day 15. The duration of each cycle was 21 days)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5 (C1D1) 5 (C1D15)	4 (C1D1) 4 (C1D15)	3 (C1D1) 3 (C1D15)	9 (C1D1) 7 (C1D15)	5 (C1D1) 2 (C1D15)	3 (C1D1) 1 (C1D15)
Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of MIK665 (units: h*ng/mL) Geometric Mean (Geometric Coefficient of Variation)						
Cycle 1 Day 1 (C1D1)	1240 (48.9%)	3530 (54.9%)	3730 (23.7%)	9710 (72.6%)	10500 (72.2%)	20300 (68.1%)
Cycle 1 Day 15 (C1D15)	1490 (42.1%)	3190 (90.5%)	2790 (98.4%)	8720 (39.0%)	10800 (28.4%)	20100

Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of MIK665

(Time Frame: pre dose, end of infusion, 0.25, 0.5, 1, 1.5, 2, 4, 6, 8 and 24 hours after end of infusion on Cycle 1 Day 1 and Cycle 1 Day 15. The duration of each cycle was 21 days)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5 (C1D1) 5 (C1D15)	4 (C1D1) 2 (C1D15)	3 (C1D1) 3 (C1D15)	8 (C1D1) 7 (C1D15)	5 (C1D1) 2 (C1D15)	3 (C1D1) 1 (C1D15)
Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of MIK665 (units: h*ng/mL) Geometric Mean (Geometric Coefficient of Variation)						
Cycle 1 Day 1 (C1D1)	1250 (48.9%)	3550 (55.0%)	3740 (23.6%)	10800 (66.4%)	10500 (72.4%)	20400 (68.5%)
Cycle 1 Day 15 (C1D15)	1500 (42.3%)	3810 (159.7%)	2800 (97.9%)	8780 (38.5%)	10800 (28.7%)	20100

Maximum observed plasma concentration (Cmax) of MIK665

(Time Frame: pre dose, end of infusion, 0.25, 0.5, 1, 1.5, 2, 4, 6, 8 and 24 hours after end of infusion on Cycle 1 Day 1 and Cycle 1 Day 15. The duration of each cycle was 21 days)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5 (C1D1) 5 (C1D15)	4 (C1D1) 4 (C1D15)	3 (C1D1) 3 (C1D15)	9 (C1D1) 7 (C1D15)	5 (C1D1) 2 (C1D15)	3 (C1D1) 1 (C1D15)
Maximum observed plasma concentration (Cmax) of MIK665 (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)						
Cycle 1 Day 1 (C1D1)	2250 (62.3%)	6370 (35.2%)	7780 (27.3%)	16700 (70.7%)	15400 (47.3%)	27600 (51.3%)

Cycle 1 Day 15 (C1D15)	3020 (38.1%)	5060 (76.5%)	5390 (126.9%)	16700 (40.1%)	19800 (12.5%)	25900

Time to reach maximum plasma concentration (Tmax) of MIK665

(Time Frame: pre dose, end of infusion, 0.25, 0.5, 1, 1.5, 2, 4, 6, 8 and 24 hours after end of infusion on Cycle 1 Day 1 and Cycle 1 Day 15. The duration of each cycle was 21 days)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5 (C1D1) 5 (C1D15)	4 (C1D1) 4 (C1D15)	3 (C1D1) 3 (C1D15)	9 (C1D1) 7 (C1D15)	5 (C1D1) 2 (C1D15)	3 (C1D1) 1 (C1D15)
Time to reach maximum plasma concentration (Tmax) of MIK665 (units: hours) Median (Full Range)						
Cycle 1 Day 1 (C1D1)	0.583 (0.55 to 0.7)	0.592 (0.55 to 0.667)	0.5 (0.5 to 0.583)	0.55 (0.5 to 0.8)	0.55 (0.5 to 0.583)	0.583 (0.533 to 0.7)
Cycle 1 Day 15 (C1D15)	0.567 (0.5 to 0.65)	0.567 (0.55 to 0.783)	0.567 (0.5 to 0.667)	0.567 (0.55 to 0.833)	0.508 (0.5 to 0.517)	0.65 (0.65 to 0.65)

Plasma clearance (CL) of MIK665

(Time Frame: pre dose, end of infusion, 0.25, 0.5, 1, 1.5, 2, 4, 6, 8 and 24 hours after end of infusion on Cycle 1 Day 1 and Cycle 1 Day 15. The duration of each cycle was 21 days)

	MIK665 QW 50 mg	MIK665 QW 100 mg	MIK665 QW 150 mg	MIK665 QW 200 mg	MIK665 QW 250 mg	MIK665 QW 300 mg
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5 (C1D1) 5 (C1D15)	4 (C1D1) 2 (C1D15)	3 (C1D1) 3 (C1D15)	8 (C1D1) 7 (C1D15)	5 (C1D1) 2 (C1D15)	3 (C1D1) 1 (C1D15)

Plasma clearance (CL) of MIK665 (units: L/h) Geometric Mean (Geometric Coefficient of Variation)						
Cycle 1 Day 1 (C1D1)	40 (48.9%)	28.2 (55.0%)	40.1 (23.6%)	18.5 (66.4%)	23.7 (72.4%)	14.7 (68.5%)
Cycle 1 Day 15 (C1D15)	33.2 (41.9%)	26.2 (159.7%)	46.8 (64.6%)	22.8 (38.5%)	23.1 (28.7%)	9.94

Volume of distribution during the terminal elimination phase (Vz) of MIK665

(Time Frame: pre dose, end of infusion, 0.25, 0.5, 1, 1.5, 2, 4, 6, 8 and 24 hours after end of infusion on Cycle 1 Day 1 and Cycle 1 Day 15. The duration of each cycle was 21 days)

	MIK665 QW 50 mg	**MIK665 QW 100 mg**	**MIK665 QW 150 mg**	**MIK665 QW 200 mg**	**MIK665 QW 250 mg**	**MIK665 QW 300 mg**
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)
Number of Participants Analyzed [units: participants]	5 (C1D1) 5 (C1D15)	4 (C1D1) 2 (C1D15)	3 (C1D1) 3 (C1D15)	8 (C1D1) 7 (C1D15)	5 (C1D1) 2 (C1D15)	3 (C1D1) 1 (C1D15)
Volume of distribution during the terminal elimination phase (Vz) of MIK665 (units: Liters) Geometric Mean (Geometric Coefficient of Variation)						
Cycle 1 Day 1 (C1D1)	255 (69.4%)	324 (58.8%)	422 (40.3%)	182 (69.6%)	248 (59.4%)	149 (97.4%)
Cycle 1 Day 15 (C1D15)	233 (47.9%)	282 (201.6%)	515 (72.9%)	235 (73.3%)	245 (12.0%)	63.7

Terminal elimination half-life (T1/2) of MIK665

(Time Frame: pre dose, end of infusion, 0.25, 0.5, 1, 1.5, 2, 4, 6, 8 and 24 hours after end of infusion on Cycle 1 Day 1 and Cycle 1 Day 15. The duration of each cycle was 21 days)

	MIK665 QW 50 mg	**MIK665 QW 100 mg**	**MIK665 QW 150 mg**	**MIK665 QW 200 mg**	**MIK665 QW 250 mg**	**MIK665 QW 300 mg**
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)

Number of Participants Analyzed [units: participants]	5 (C1D1) 5 (C1D15)	4 (C1D1) 2 (C1D15)	3 (C1D1) 3 (C1D15)	8 (C1D1) 7 (C1D15)	5 (C1D1) 2 (C1D15)	3 (C1D1) 1 (C1D15)
Terminal elimination half-life (T1/2) of MIK665 (units: hours) Median (Full Range)						
Cycle 1 Day 1 (C1D1)	7.32 (1.64 to 9.23)	7.98 (6.82 to 9.35)	7.53 (6.14 to 8.41)	6.63 (5.73 to 8.53)	7.21 (6.17 to 8.11)	8.98 (3.94 to 9.76)
Cycle 1 Day 15 (C1D15)	6.74 (1.54 to 9.83)	7.48 (6.7 to 8.26)	8.36 (6.26 to 8.49)	7.65 (3.03 to 12.6)	7.42 (6.57 to 8.26)	4.44 (4.44 to 4.44)

Safety Results

All-Cause Mortality

	MIK665 QW 50 mg N = 5	**MIK665 QW 100 mg N = 4**	**MIK665 QW 150 mg N = 5**	**MIK665 QW 200 mg N = 9**	**MIK665 QW 250 mg N = 5**	**MIK665 QW 300 mg N = 3**	**All Subjects N = 31**
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)	All Subjects
Total participants affected	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	2 (6.45%)

Serious Adverse Events by System Organ Class

Time Frame	From the day of the first dose of MIK665 up to 30 days after the last dose, with a maximum duration of 94 weeks.
Source Vocabulary for Table Default	MedDRA (23.0)
Assessment Type for Table Default	Systematic Assessment

	MIK665 QW 50 mg N = 5	MIK665 QW 100 mg N = 4	MIK665 QW 150 mg N = 5	MIK665 QW 200 mg N = 9	MIK665 QW 250 mg N = 5	MIK665 QW 300 mg N = 3	All Subjects N = 31
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)	All Subjects
Total participants affected	2 (40.00%)	1 (25.00%)	2 (40.00%)	2 (22.22%)	2 (40.00%)	0 (0.00%)	9 (29.03%)
Cardiac disorders							
Angina pectoris	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	2 (6.45%)
Bradycardia	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Gastrointestinal disorders							
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Hepatobiliary disorders							
Hepatocellular injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Infections and infestations							
Pneumonia	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Sepsis	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)

Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Investigations							
Electrocardiogram T wave inversion	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
N-terminal prohormone brain natriuretic peptide increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Troponin I increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Troponin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Troponin T increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Metabolism and nutrition disorders							
Hypercalcaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Musculoskeletal and connective tissue disorders							
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Rotator cuff syndrome	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Gastrointestinal stromal tumour	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Nervous system disorders							
Epilepsy	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Renal and urinary disorders							
Renal failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)

Respiratory, thoracic and mediastinal disorders							
Pleural effusion	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Pneumonitis	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)

Other Adverse Events by System Organ Class

Time Frame	From the day of the first dose of MIK665 up to 30 days after the last, with a maximum duration of 94 weeks.
Source Vocabulary for Table Default	MedDRA (23.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	0%

	MIK665 QW 50 mg N = 5	**MIK665 QW 100 mg N = 4**	**MIK665 QW 150 mg N = 5**	**MIK665 QW 200 mg N = 9**	**MIK665 QW 250 mg N = 5**	**MIK665 QW 300 mg N = 3**	**All Subjects N = 31**
Arm/Group Description	MIK665 50 mg administered once every week (QW)	MIK665 100 mg administered once every week (QW)	MIK665 150 mg administered once every week (QW)	MIK665 200 mg administered once every week (QW)	MIK665 250 mg administered once every week (QW)	MIK665 300 mg administered once every week (QW)	All Subjects
Total participants affected	5 (100.00%)	4 (100.00%)	5 (100.00%)	9 (100.00%)	5 (100.00%)	3 (100.00%)	31 (100.00%)
Blood and lymphatic system disorders							
Anaemia	2 (40.00%)	1 (25.00%)	1 (20.00%)	4 (44.44%)	2 (40.00%)	1 (33.33%)	11 (35.48%)
Eosinophilia	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Febrile neutropenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (3.23%)
Leukopenia	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	2 (6.45%)

Lymphopenia	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (11.11%)	1 (20.00%)	0 (0.00%)	3 (9.68%)
Neutropenia	1 (20.00%)	2 (50.00%)	1 (20.00%)	6 (66.67%)	1 (20.00%)	2 (66.67%)	13 (41.94%)
Pancytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Thrombocytopenia	2 (40.00%)	2 (50.00%)	1 (20.00%)	1 (11.11%)	0 (0.00%)	1 (33.33%)	7 (22.58%)
Cardiac disorders							
Bundle branch block right	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (3.23%)
Eye disorders							
Dry eye	0 (0.00%)	1 (25.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)
Gastrointestinal disorders							
Abdominal distension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (3.23%)
Abdominal pain	0 (0.00%)	1 (25.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	3 (9.68%)
Abdominal pain upper	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Constipation	1 (20.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	2 (40.00%)	0 (0.00%)	5 (16.13%)
Dental caries	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Diarrhoea	2 (40.00%)	3 (75.00%)	2 (40.00%)	3 (33.33%)	2 (40.00%)	2 (66.67%)	14 (45.16%)
Gastritis	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Gingival bleeding	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Gingival pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Hypoaesthesia oral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Mucous stools	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Nausea	2 (40.00%)	3 (75.00%)	4 (80.00%)	2 (22.22%)	1 (20.00%)	1 (33.33%)	13 (41.94%)
Stomatitis	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	2 (6.45%)
Vomiting	1 (20.00%)	1 (25.00%)	2 (40.00%)	4 (44.44%)	3 (60.00%)	1 (33.33%)	12 (38.71%)

General disorders and administration site conditions							
Asthenia	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (6.45%)
Catheter site pain	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Fatigue	1 (20.00%)	1 (25.00%)	1 (20.00%)	3 (33.33%)	1 (20.00%)	0 (0.00%)	7 (22.58%)
Gait disturbance	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Malaise	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (33.33%)	2 (6.45%)
Non-cardiac chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	2 (6.45%)
Oedema peripheral	2 (40.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (33.33%)	4 (12.90%)
Pain	1 (20.00%)	0 (0.00%)	0 (0.00%)	3 (33.33%)	0 (0.00%)	0 (0.00%)	4 (12.90%)
Pyrexia	1 (20.00%)	0 (0.00%)	1 (20.00%)	2 (22.22%)	1 (20.00%)	1 (33.33%)	6 (19.35%)
Infections and infestations							
Bronchitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (3.23%)
Cytomegalovirus infection reactivation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (3.23%)
Genital candidiasis	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Rash pustular	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Rhinitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Upper respiratory tract infection	1 (20.00%)	1 (25.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (9.68%)
Urinary tract infection fungal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Injury, poisoning and procedural complications							
Contusion	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Fall	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)

Infusion related reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Procedural pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Thermal burn	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Investigations							
Alanine aminotransferase increased	2 (40.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	2 (66.67%)	6 (19.35%)
Amylase increased	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Aspartate aminotransferase increased	3 (60.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	2 (66.67%)	7 (22.58%)
Blood alkaline phosphatase increased	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (6.45%)
Blood bilirubin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Blood creatine phosphokinase increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	2 (22.22%)	2 (40.00%)	0 (0.00%)	5 (16.13%)
Blood creatine phosphokinase MB increased	1 (20.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (33.33%)	4 (12.90%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Blood uric acid increased	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Ejection fraction decreased	1 (20.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	3 (9.68%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (33.33%)	2 (6.45%)
Electrocardiogram T wave abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (3.23%)

Gamma-glutamyltransferase increased	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (6.45%)
Lipase increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Lymphocyte count decreased	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Neutrophil count decreased	2 (40.00%)	2 (50.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (33.33%)	6 (19.35%)
Oxygen saturation decreased	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Platelet count decreased	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (33.33%)	3 (9.68%)
Troponin I increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (33.33%)	1 (20.00%)	0 (0.00%)	4 (12.90%)
Troponin increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (66.67%)	3 (9.68%)
Troponin T increased	2 (40.00%)	0 (0.00%)	1 (20.00%)	1 (11.11%)	2 (40.00%)	1 (33.33%)	7 (22.58%)
White blood cell count decreased	2 (40.00%)	0 (0.00%)	1 (20.00%)	1 (11.11%)	1 (20.00%)	1 (33.33%)	6 (19.35%)
White blood cell count increased	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Metabolism and nutrition disorders							
Decreased appetite	0 (0.00%)	0 (0.00%)	2 (40.00%)	1 (11.11%)	1 (20.00%)	2 (66.67%)	6 (19.35%)
Hypercalcaemia	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Hyperkalaemia	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Hypertriglyceridaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (3.23%)
Hyperuricaemia	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	2 (6.45%)
Hypoalbuminaemia	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Hypocalcaemia	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)
Hypokalaemia	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	3 (9.68%)
Hypomagnesaemia	2 (40.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	4 (12.90%)

Hyponatraemia	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)
Hypophosphataemia	1 (20.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)
Tumour lysis syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (3.23%)
Musculoskeletal and connective tissue disorders							
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (20.00%)	1 (33.33%)	3 (9.68%)
Bone pain	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Musculoskeletal pain	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	2 (40.00%)	0 (0.00%)	4 (12.90%)
Myalgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Neck pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Pain in extremity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Tendonitis	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Tumour pain	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (6.45%)
Nervous system disorders							
Depressed level of consciousness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (3.23%)
Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Headache	1 (20.00%)	1 (25.00%)	1 (20.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	4 (12.90%)
Neuropathy peripheral	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	2 (6.45%)
Paraesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Presyncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Syncope	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)

Tremor	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Psychiatric disorders							
Anxiety	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Insomnia	1 (20.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)
Renal and urinary disorders							
Urinary tract pain	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Respiratory, thoracic and mediastinal disorders							
Dyspnoea	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)
Hiccups	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Hypoventilation	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Oropharyngeal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Skin and subcutaneous tissue disorders							
Ecchymosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Pruritus	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Rash	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)
Skin exfoliation	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)
Vascular disorders							
Hypotension	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (6.45%)

Conclusion:

In this study, preliminary data showed MIK665-related, dose-dependent increases in troponin. An association between the increases in troponin and the occurrence of specific cardiac adverse events could not be identified from the data currently available.

No other significant safety findings were observed at the dose levels explored during dose escalation and before study termination.

Amongst the subjects treated during dose escalation who were evaluable for response, evidence of limited efficacy (4 partial responses in both multiple myeloma and lymphoma) was observed. However, as the study was terminated early after six dose levels were tested and before determination of the MTD(s)/RDE(s), conclusions about the efficacy of treatment are limited.

Date of Clinical Trial Report

21-Jun-2021