NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

CGM097

Trial Indication(s)

Advanced solid tumors

Protocol Number

CCGM097X2101

Protocol Title

A Phase I, open-label, multi-center, dose escalation study of oral CGM097, a p53/HDM2-interaction inhibitor, in adult patients with selected advanced solid tumors

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase 1

Study Start/End Dates

Study Start Date: March 2013 (Actual)
Primary Completion Date: July 2020 (Actual)
Study Completion Date: July 2020 (Actual)

Reason for Termination (If applicable)

Based on the sponsor decision to terminate CGM097 program, recruitment into CGM097X2101 was halted on 06-Jun-2016. As the decision to halt the recruitment was not a consequence of any safety concern, the subjects enrolled in the study by the time of this decision were allowed to continue with treatment until discontinuation was warranted by the protocol.

Study Design/Methodology

This was a multi-center, open-label, dose-finding, Phase I study of oral single agent CGM097, administered on a three times weekly schedule in subjects with advanced solid tumors who had progressed despite standard therapy or for whom no standard therapy exists.

The patients included in the study had one of the following tumor types: melanoma, liposarcoma, osteosarcoma, renal cell carcinoma (RCC), or proximal colorectal cancer (CRC), with a tumor characterized by $p53^{wt}$ status. Patients with other solid tumors for which $p53^{wt}$ status was known were also included in the study after individual assessment.

For all patients, p53 status was determined on a tumor biopsy. It was assessed in molecular pre-screening unless the $p53^{wt}$ status was already known from a tumor biopsy collected no more than 36 months before start of Screening.

The study was planned to consist of both a dose escalation part and a dose expansion part.

Dose escalation consisted of cohorts of newly enrolled patients. The dose escalation was to be continued until the maximum tolerated dose (MTD) and or the recommended dose for expansion (RDE) was determined. The sponsor and the site Investigators jointly decided on each subsequent dose escalation step based on the recommendation from the adaptive Bayesian logistic regression model (BLRM). The dose escalation continued until the enrollment was prematurely halted. The MTD was unable to be determined in the study.

The dose expansion part was not initiated.

Centers

5 centers in 5 countries: United States(1), Singapore(1), France(1), Switzerland(1), Germany(1)

Objectives:

The primary objective of the trial was to estimate the MTD and/or to identify the RDE of CGM097. The following related endpoint was assessed:

- Incidence of Dose Limiting Toxicities (DLTs) in the first 28 days of dosing

The secondary objectives were:

- To characterize the safety and tolerability of CGM097 in terms of:
  - Incidence of adverse events (AEs) and serious adverse events (SAEs)
  - Number of participants with dose delays or dose reductions
- To characterize the pharmacokinetics (PK) properties of CGM097
- To assess the preliminary anti-tumor activity of CGM097 in solid tumors according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) in terms of:
  - Number of participants with Best Overall Response (BOR)
  - Duration of response (DOR)
  - Progression-free survival (PFS)
- To assess the pharmacodynamic (PD) effect of CGM097 by measuring the changes from baseline of PD biomarkers (GDF-15 in serum and p21 in tumor tissue)

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

CGM097 was used as an investigational product in this study. CGM097 was supplied as hard gelatin capsules of dosage strengths of 10 mg, 50 mg and 100 mg (expressed in mg of CGM097 free base).

Two dosing regimens (Regimen 1 and Regimen 3) of CGM097 administered orally at different dose-levels were explored in the 10 cohorts of the study.

- Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous. In Regimen 1 the following doses of CGM097 were assessed: 10 mg, 20 mg, 40 mg, 80 mg, 150 mg, 300 mg and 400 mg.
- Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment. In regimen 3 the following doses of CGM097 were assessed: 300 mg, 500 mg and 700 mg.

Subjects could continued treatment with the study drug until they experienced unacceptable toxicity, disease progression and/or treatment was discontinued at the discretion of the Investigator or withdrawal of consent.

Statistical Methods

The primary variable was the incidence of DLTs in the first 28 days of dosing. Estimation of the MTD was based upon the estimation of the probability of a DLT in the first 28 days of dosing.

The adaptive BLRM employing the escalation with overdose control (EWOC) principle guided the dose escalation of treatment with CGM097 to its MTD and/or RDE. The BLRM model estimated the relationship between the CGM097 doses and DLTs and utilized the down-weighted approach of adding a weight on Regimen 1 while keeping the full weight for Regimen 3 for estimating the posterior probabilities of DLT rates.

The PK parameters were determined by a non-compartmental approach based on CGM097 plasma concentrations.

Investigator read Computed tomography/Magnetic resonance imaging (CT/MRI) assessments evaluated under RECIST v1.1 were used for all preliminary tumor activity evaluations.

For all safety analyses, the safety set including all subjects who received at least one dose of CGM097 and had at least one valid post-baseline safety assessment was used.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Patient has advanced solid malignancy that has progressed despite standard therapy, or for which no effective standard therapy exists
- Tumor of the patient is p53wt
- Evaluable disease as determined by RECIST 1.1
- WHO performance status 0-2

Exclusion criteria:
- Prior treatment with CGM097 or other p53/HDM2-interaction inhibitor
- Patient with symptomatic or growing CNS metastatic lesions
- Concurrent other malignancy
- Clinically significant cardiac disease as defined in the protocol
- Diagnosis of acute or chronic pancreatitis
- Concomitant therapy that precludes enrollment, as defined in the protocol
- Women of child-bearing potential, unless they are using highly effective methods of contraception during dosing and for 2 weeks after study drug discontinuation
- Pregnant or nursing women

Participant Flow Table

Overall Study

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3	Total
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	
Started	3	4	4	4	4	7	5	8	6	6	51
Completed	0	0	0	0	0	0	0	0	0	0	0
Not Completed	3	4	4	4	4	7	5	8	6	6	51
Adverse Event	0	0	0	0	0	1	2	1	0	1	5
Subject withdrew consent	0	0	0	0	0	0	0	0	0	1	1
Administrative problems	0	0	0	0	0	1	0	0	0	0	1
Death	1	0	1	0	0	0	0	0	0	0	2
Disease progression	2	4	3	4	4	5	3	7	6	4	42

Baseline Characteristics

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3	Total
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	
Number of Participants [units: participants]	3	4	4	4	4	7	5	8	6	6	51
Age Continuous (units: years) Mean ± Standard Deviation											
	47.0±8.89	50.0±9.13	50.8±13.65	59.3±5.38	44.5±7.00	58.7±7.67	56.8±12.05	50.3±12.51	56.3±11.55	56.7±8.26	53.6±10.33
Sex: Female, Male (units: participants) Count of Participants (Not Applicable)											
Female	2	1	1	2	3	5	3	5	4	3	29
Male	1	3	3	2	1	2	2	3	2	3	22
Race/Ethnicity, Customized (units: participants) Count of Participants (Not Applicable)											

Caucasian	1	3	1	2	3	4	5	6	5	6	36
Asian	1	0	1	1	1	2	0	2	1	0	9
Other	0	0	2	0	0	1	0	0	0	0	3
Missing	1	1	0	1	0	0	0	0	0	0	3

Primary Outcome Result(s)

Incidence of Dose Limiting Toxicities (DLTs) in the first 28 days of dosing

(Time Frame: 28 days)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	3	4	4	4	4	7	5	8	6	6
Incidence of Dose Limiting Toxicities (DLTs) in the first 28 days of dosing (units: participants) Count of Participants (Not Applicable)										
	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Secondary Outcome Result(s)

Incidence of adverse events

(Time Frame: From the day of the first dose of CGM097 up to 30 days after the last dose, up to maximum duration of 329 weeks)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	3	4	4	4	4	7	5	8	6	6
Incidence of adverse events (units: participants) Count of Participants (Not Applicable)										
AEs	3 (100%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)	7 (100%)	5 (100%)	8 (100%)	6 (100%)	6 (100%)
Treatment-related AEs	2 (66.67%)	4 (100%)	2 (50%)	2 (50%)	2 (50%)	7 (100%)	5 (100%)	8 (100%)	6 (100%)	6 (100%)
AEs with grade ≥ 3	2 (66.67%)	1 (25%)	2 (50%)	3 (75%)	2 (50%)	7 (100%)	5 (100%)	6 (75%)	5 (83.33%)	4 (66.67%)
Treatment-related AEs with grade ≥ 3	1 (33.33%)	0 (%)	1 (25%)	0 (%)	0 (%)	6 (85.71%)	5 (100%)	3 (37.5%)	3 (50%)	3 (50%)
SAEs	1 (33.33%)	1 (25%)	1 (25%)	2 (50%)	4 (100%)	4 (57.14%)	2 (40%)	4 (50%)	1 (16.67%)	4 (66.67%)

Treatment-related SAEs	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	3 (42.86%)	1 (20%)	1 (12.5%)	0 (%)	3 (50%)
AEs leading to discontinuation	1 (33.33%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (14.29%)	2 (40%)	0 (%)	0 (%)	1 (16.67%)
Treatment-related AEs leading to discontinuation	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (14.29%)	2 (40%)	0 (%)	0 (%)	1 (16.67%)
AEs leading to dose adjustment/interruption	0 (%)	0 (%)	1 (25%)	1 (25%)	2 (50%)	4 (57.14%)	5 (100%)	5 (62.5%)	5 (83.33%)	5 (83.33%)
AEs requiring additional therapy	2 (66.67%)	3 (75%)	2 (50%)	4 (100%)	4 (100%)	7 (100%)	5 (100%)	8 (100%)	5 (83.33%)	6 (100%)

Number of participants with dose delays or dose reductions

(Time Frame: A median of 9.7 weeks, up to maximum duration of 325.1 weeks)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	3	4	4	4	4	7	5	8	6	6
Number of participants with dose delays or dose reductions (units: participants) Count of Participants (Not Applicable)										
At least one dose delay	0 (%)	0 (%)	1 (25%)	0 (%)	1 (25%)	1 (14.29%)	4 (80%)	7 (87.5%)	2 (33.33%)	4 (66.67%)
At least one dose reduction	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	3 (60%)	0 (%)	2 (33.33%)	3 (50%)

Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of CGM097 following Regimen 1

(Time Frame: pre dose, 0.5, 1, 2, 3, 4, 8 and 24 hours post dose on Cycle 1 Day 1. Samples were taken up to 8 hours post dose on Cycle 1 Day 8 and Cycle 2 Day 1. The duration of each cycle was 4 weeks.)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous
Number of Participants Analyzed [units: participants]	3 (C1D1) 3 (C1D8) 3 (C2D1)	4 (C1D1) 3 (C1D8) 2 (C2D1)	4 (C1D1) 1 (C1D8) 3 (C2D1)	4 (C1D1) 4 (C1D8) 3 (C2D1)	4 (C1D1) 4 (C1D8) 4 (C2D1)	6 (C1D1) 4 (C1D8) 4 (C2D1)	4 (C1D1) 3 (C1D8) 5 (C2D1)
Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of CGM097 following Regimen 1 (units: h*ng/mL) Geometric Mean (Geometric Coefficient of Variation)							
Cycle 1 Day 1 (C1D1)	1652.87 (39.75%)	3528.17 (27.92%)	8065.16 (44.29%)	24440.03 (39.99%)	26444.39 (49.69%)	68414.05 (45.84%)	79657.96 (34.40%)
Cycle 1 Day 8 (C1D8)	740.09 (19.52%)	1823.42 (35.41%)	4557.75	11814.93 (41.91%)	12890.76 (94.98%)	39470.71 (59.10%)	42506.96 (34.40%)
Cycle 2 Day 1 (C2D1)	741.57 (22.62%)	2300.08 (59.04%)	4390.96 (12.15%)	12818.71 (48.45%)	16987.70 (53.22%)	43575.02 (78.02%)	45342.10 (30.70%)

Maximum observed plasma concentration (Cmax) of CGM097 following Regimen 1

(Time Frame: pre dose, 0.5, 1, 2, 3, 4, 8 and 24 hours post dose on Cycle 1 Day 1. Samples were taken up to 8 hours post dose on Cycle 1 Day 8 and Cycle 2 Day 1. The duration of each cycle was 4 weeks.)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous
Number of Participants Analyzed [units: participants]	3 (C1D1) 3 (C1D8) 3 (C2D1)	4 (C1D1) 4 (C1D8) 2 (C2D1)	4 (C1D1) 2 (C1D8) 3 (C2D1)	4 (C1D1) 4 (C1D8) 3 (C2D1)	4 (C1D1) 4 (C1D8) 4 (C2D1)	6 (C1D1) 4 (C1D8) 4 (C2D1)	5 (C1D1) 3 (C1D8) 5 (C2D1)
Maximum observed plasma concentration (Cmax) of CGM097 following Regimen 1 (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)							
Cycle 1 Day 1 (C1D1)	150.39 (50.66%)	216.85 (35.01%)	622.65 (32.15%)	1684.61 (18.63%)	2007.52 (53.19%)	4772.82 (43.52%)	4618.36 (23.08%)
Cycle 1 Day 8 (C1D8)	133.23 (20.35%)	282.11 (30.56%)	775.49 (0.64%)	1887.81 (39.16%)	2433.83 (65.03%)	6434.36 (52.46%)	6562.79 (23.08%)
Cycle 2 Day 1 (C2D1)	148.84 (19.61%)	389.85 (56.30%)	769.15 (20.04%)	2013.85 (45.92%)	2625.94 (53.67%)	6602.66 (82.83%)	6809.05 (24.97%)

Time to reach maximum plasma concentration (Tmax) of CGM097 following Regimen 1

(Time Frame: pre dose, 0.5, 1, 2, 3, 4, 8 and 24 hours post dose on Cycle 1 Day 1. Samples were taken up to 8 hours post dose on Cycle 1 Day 8 and Cycle 2 Day 1. The duration of each cycle was 4 weeks.)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous
Number of Participants Analyzed [units: participants]	3 (C1D1) 3 (C1D8) 3 (C2D1)	4 (C1D1) 4 (C1D8) 2 (C2D1)	4 (C1D1) 2 (C1D8) 3 (C2D1)	4 (C1D1) 4 (C1D8) 3 (C2D1)	4 (C1D1) 4 (C1D8) 4 (C2D1)	6 (C1D1) 4 (C1D8) 4 (C2D1)	5 (C1D1) 3 (C1D8) 5 (C2D1)
Time to reach maximum plasma concentration (Tmax) of CGM097 following Regimen 1 (units: hours) Median (Full Range)							
Cycle 1 Day 1 (C1D1)	2.00 (1.1 to 3.1)	3.03 (3.0 to 7.9)	1.98 (0.9 to 2.1)	2.50 (2.0 to 3.0)	1.60 (1.1 to 3.0)	2.02 (1.9 to 4.3)	2.95 (2.1 to 3.2)
Cycle 1 Day 8 (C1D8)	2.87 (2.0 to 8.0)	2.02 (2.0 to 2.2)	2.07 (2.04 to 2.1)	3.02 (2.0 to 8.0)	2.03 (2.0 to 2.2)	4.04 (2.0 to 8.0)	2.02 (2.0 to 2.1)
Cycle 2 Day 1 (C2D1)	1.98 (1.3 to 4.0)	3.00 (2.0 to 4.0)	2.33 (1.0 to 8.0)	2.00 (1.1 to 4.0)	3.06 (2.0 to 8.0)	3.29 (2.0 to 5.3)	4.17 (2.1 to 8.1)

Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of CGM097 following Regimen 3

(Time Frame: pre dose, 0.5, 1, 2, 3, 4, 8 and 24 hours post dose on Cycle 1 Day 1. Samples were taken up to 8 hours post dose on Cycle 1 Day 8 and Cycle 2 Day 1, and up to 72 hours post dose on Cycle 1 Day 12. The cycle duration was 3 weeks.)

	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	6 (C1D1) 4 (C1D8) 5 (C1D12) 6 (C2D1)	6 (C1D1) 5 (C1D8) 5 (C1D12) 6 (C2D1)	5 (C1D1) 5 (C1D8) 4 (C1D12) 4 (C2D1)
Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of CGM097 following Regimen 3 (units: h*ng/mL) Geometric Mean (Geometric Coefficient of Variation)			
Cycle 1 Day 1 (C1D1)	43900.31 (15.28%)	69887.58 (52.83%)	77598.31 (11.20%)
Cycle 1 Day 8 (C1D8)	26087.28 (27.57%)	43019.43 (39.67%)	58239.53 (13.95%)
Cycle 1 Day 12 (C1D12)	158955.6 (17.48%)	474841.7 (37.53%)	299676.5 (89.59%)
Cycle 2 Day 1 (C2D1)	14760.09 (31.34%)	25276.49 (43.29%)	34878.85 (27.95%)

Maximum observed plasma concentration (Cmax) of CGM097 following Regimen 3

(Time Frame: pre dose, 0.5, 1, 2, 3, 4, 8 and 24 hours post dose on Cycle 1 Day 1. Samples were taken up to 8 hours post dose on Cycle 1 Day 8 and Cycle 2 Day 1, and up to 72 hours post dose on Cycle 1 Day 12. The cycle duration was 3 weeks.)

	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	6 (C1D1) 5 (C1D8) 5 (C1D12) 6 (C2D1)	6 (C1D1) 6 (C1D8) 5 (C1D12) 6 (C2D1)	6 (C1D1) 5 (C1D8) 4 (C1D12) 4 (C2D1)
Maximum observed plasma concentration (Cmax) of CGM097 following Regimen 3 (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)			
Cycle 1 Day 1 (C1D1)	2962.45 (29.34%)	4299.02 (48.95%)	5757.17 (20.30%)
Cycle 1 Day 8 (C1D8)	3680.02 (39.58%)	7081.83 (44.34%)	9283.41 (18.90%)
Cycle 1 Day 12 (C1D12)	4269.92 (23.09%)	9773.22 (40.66%)	8641.23 (51.92%)
Cycle 2 Day 1 (C2D1)	2769.69 (16.30%)	4501.81 (45.70%)	5829.05 (12.32%)

Time to reach maximum plasma concentration (Tmax) of CGM097 following Regimen 3

(Time Frame: pre dose, 0.5, 1, 2, 3, 4, 8 and 24 hours post dose on Cycle 1 Day 1. Samples were taken up to 8 hours post dose on Cycle 1 Day 8 and Cycle 2 Day 1, and up to 72 hours post dose on Cycle 1 Day 12. The cycle duration was 3 weeks.)

	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	6 (C1D1) 5 (C1D8) 5 (C1D12) 6 (C2D1)	6 (C1D1) 6 (C1D8) 5 (C1D12) 6 (C2D1)	6 (C1D1) 5 (C1D8) 4 (C1D12) 4 (C2D1)
Time to reach maximum plasma concentration (Tmax) of CGM097 following Regimen 3 (units: hours) Median (Full Range)			
Cycle 1 Day 1 (C1D1)	3.00 (2.0 to 7.9)	2.60 (1.2 to 4.1)	2.14 (1.0 to 3.3)
Cycle 1 Day 8 (C1D8)	2.00 (2.0 to 2.2)	2.04 (0.5 to 3.9)	2.23 (2.0 to 4.0)
Cycle 1 Day 12 (C1D12)	2.00 (2.0 to 8.2)	4.17 (2.0 to 8.0)	2.01 (1.3 to 2.1)
Cycle 2 Day 1 (C2D1)	3.13 (2.0 to 8.0)	2.03 (2.0 to 8.2)	2.03 (2.0 to 4.0)

Number of participants with Best Overall Response (BOR) per RECIST 1.1

(Time Frame: From the day of the first dose of CGM097 up to 30 days after the last dose, up to maximum duration of 329 weeks)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	3	4	4	4	4	7	5	8	6	6
Number of participants with Best Overall Response (BOR) per RECIST 1.1 (units: participants) Count of Participants (Not Applicable)										
Complete response (CR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Partial response (PR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (14.29%)	0 (%)	0 (%)	0 (%)	0 (%)
Stable disease (SD)	1 (33.33%)	1 (25%)	1 (25%)	1 (25%)	0 (%)	2 (28.57%)	4 (80%)	5 (62.5%)	3 (50%)	1 (16.67%)
Progressive disease (PD)	2 (66.67%)	2 (50%)	2 (50%)	3 (75%)	3 (75%)	3 (42.86%)	1 (20%)	3 (37.5%)	3 (50%)	3 (50%)
Unknown	0 (%)	1 (25%)	1 (25%)	0 (%)	1 (25%)	1 (14.29%)	0 (%)	0 (%)	0 (%)	2 (33.33%)

Duration of Response (DOR) according to RECIST 1.1

(Time Frame: From the day of the first dose of CGM097 up to 30 days after the last dose, up to maximum duration of 329 weeks)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	0	0	0	0	0	1	0	0	0	0
Duration of Response (DOR) according to RECIST 1.1 (units: days) Median (Full Range)						735 (735 to 735)				

Progression-Free Survival (PFS) rate according to RECIST 1.1

(Time Frame: From the day of the first dose of CGM097 up to 30 days after the last dose, up to maximum duration of 329 weeks)

	All subjects
Arm/Group Description	All subjects
Number of Participants Analyzed [units: participants]	51
Progression-Free Survival (PFS) rate according to RECIST 1.1 (units: percentage of participants) Number (95% Confidence Interval)	
3 months	39.7 (25.6 to 53.4)
6 months	21.9 (10.9 to 35.4)
9 months	13.7 (5.2 to 26.2)
12 months	8.2 (2.2 to 19.6)

Change from baseline of GDF-15 levels in serum

(Time Frame: Cycle 1 Day 1 (baseline), Cycle 1 Day 8 at pre-dose, Cycle 1 Day 8 at 6 hours post-dose. The duration of a cycle is 4 weeks for Regimen 1 and 3 weeks for Regimen 3.)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	2 (C1D8 pre dose) 0 (C1D8 6h post dose)	1 (C1D8 pre dose) 1 (C1D8 6h post dose)	2 (C1D8 pre dose) 1 (C1D8 6h post dose)	0	0	0	0	5 (C1D8 pre dose) 3 (C1D8 6h post dose)	5 (C1D8 pre dose) 5 (C1D8 6h post dose)	4 (C1D8 pre dose) 3 (C1D8 6h post dose)
Change from baseline of GDF-15 levels in serum (units: pg/mL) Median (Full Range)										
Cycle 1 Day 8 – pre dose	-23.9 (-88.2 to 40.5)	128.8 (128.8 to 128.8)	6985.1 (6985.1 to 6985.1)					1013.1 (0.0 to 2165.4)	2387.7 (978.9 to 2458.4)	3488.5 (2599.9 to 8619.6)
Cycle 1 Day 8 – 6 hours post dose		144.9 (144.9 to 144.9)	-4.3 (-4.3 to -4.3)					2678.8 (0.0 to 4585.4)	2890.3 (-116.2 to 4290.5)	4928.8 (3574.7 to 22489.2)

Change from baseline of tumor tissue p21

(Time Frame: Screening (baseline), Cycle 2 Day 8. The duration of a cycle is 4 weeks for Regimen 1 and 3 weeks for Regimen 3.)

	10 mg Reg. 1	20 mg Reg. 1	40 mg Reg. 1	80 mg Reg. 1	150 mg Reg. 1	300 mg Reg. 1	400 mg Reg. 1	300 mg Reg. 3	500 mg Reg. 3	700 mg Reg. 3
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	700 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment
Number of Participants Analyzed [units: participants]	0	2	1	2	1	0	3	3	2	0
Change from baseline of tumor tissue p21 (units: no units) Median (Full Range)										
Cycle 2 Day 8		-16.5 (-23.0 to -10.0)	39.0 (39.0 to 39.0)	-6.0 (-47.0 to 35.0)	30.0 (30.0 to 30.0)		60.0 (10.0 to 80.0)	-10.0 (-14.0 to 30.0)	55.0 (0.0 to 110.0)	

Safety Results

All-Cause Mortality

	10 mg Reg. 1 N = 3	20 mg Reg. 1 N = 4	40 mg Reg. 1 N = 4	80 mg Reg. 1 N = 4	150 mg Reg. 1 N = 4	300 mg Reg. 1 N = 7	400 mg Reg. 1 N = 5	300 mg Reg. 3 N = 8	500 mg Reg. 3 N = 6	700 mg Reg. 3 N = 6	All patients N = 51
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	All patients enrolled in the trial
Total participants affected	1 (33.33%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	2 (40.00%)	2 (25.00%)	1 (16.67%)	0 (0.00%)	8 (15.69%)

Serious Adverse Events by System Organ Class

Time Frame	From the day of the first dose of CGM097 up to 30 days after the last dose, up to maximum duration of 329 weeks.
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment

	10 mg Reg. 1 N = 3	20 mg Reg. 1 N = 4	40 mg Reg. 1 N = 4	80 mg Reg. 1 N = 4	150 mg Reg. 1 N = 4	300 mg Reg. 1 N = 7	400 mg Reg. 1 N = 5	300 mg Reg. 3 N = 8	500 mg Reg. 3 N = 6	700 mg Reg. 3 N = 6	All patients N = 51
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment cycle, continuous	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2 weeks treatment, 1 week off treatment	All patients enrolled in the trial
Total participants affected	1 (33.33 %)	1 (25.00 %)	1 (25.00 %)	2 (50.00 %)	4 (100.00 %)	4 (57.14 %)	2 (40.00 %)	4 (50.00 %)	1 (16.67 %)	4 (66.67 %)	24 (47.06 %)
Blood And Lymphatic System Disorders											
Anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Thrombocytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (33.33 %)	4 (7.84%)
Cardiac Disorders											
Atrial Fibrillation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)

Ear And Labyrinth Disorders											
Vertigo Positional	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Endocrine Disorders											
Hypothyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Gastrointestinal Disorders											
Abdominal Distension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Gastritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Gastrointestinal Haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Intestinal Obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	2 (3.92%)
Lower Gastrointestinal Haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	1 (16.67 %)	0 (0.00%)	2 (3.92%)
Vomiting	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	3 (5.88%)
General Disorders And Administration Site Conditions											
Chills	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)

General Physical Health Deterioration	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Non-Cardiac Chest Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Pyrexia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (16.67 %)	3 (5.88%)
Infections And Infestations											
Device Related Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Lower Respiratory Tract Infection	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Pneumonia	1 (33.33 %)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Respiratory Tract Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)
Sepsis	1 (33.33 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Investigations											
Electrocardiogram Qt Prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)
Neutrophil Count Decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
White Blood Cell Count Decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Musculoskeletal And Connective Tissue Disorders											

Musculoskeletal Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)											
Tumour Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Nervous System Disorders											
Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Loss Of Consciousness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Migraine	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Paresis	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Renal And Urinary Disorders											
Acute Kidney Injury	1 (33.33 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Respiratory, Thoracic And Mediastinal Disorders											
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (25.00%)	1 (14.29 %)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	4 (7.84%)
Pleural Effusion	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)

Vascular Disorders											
Embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Embolism Arterial	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)

Other Adverse Events by System Organ Class

Time Frame	From the day of the first dose of CGM097 up to 30 days after the last dose, up to maximum duration of 329 weeks.
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	10 mg Reg. 1 N = 3	20 mg Reg. 1 N = 4	40 mg Reg. 1 N = 4	80 mg Reg. 1 N = 4	150 mg Reg. 1 N = 4	300 mg Reg. 1 N = 7	400 mg Reg. 1 N = 5	300 mg Reg. 3 N = 8	500 mg Reg. 3 N = 6	700 mg Reg. 3 N = 6	All patients N = 51
Arm/Group Description	10 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment	20 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment	40 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment	80 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment	150 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment	300 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment	400 mg CGM097 Regimen 1: Three times weekly dosing (e.g. Thu, Sat, Mon), 4 weeks treatment	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2	500 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2	300 mg CGM097 Regimen 3: Three times weekly dosing (e.g. Thu, Sat, Mon), 3 weeks cycle: 2	All patients enrolled in the trial

	cycle, continuous	cycle, continuous	cycle, continuous	cycle, continuous	cycle, continuous	cycle, continuous	cycle, continuous	weeks treatment, 1 week off treatment	weeks treatment, 1 week off treatment	weeks treatment, 1 week off treatment	
Total participants affected	3 (100.00 %)	4 (100.00 %)	4 (100.00 %)	4 (100.00 %)	4 (100.00 %)	7 (100.00 %)	5 (100.00 %)	8 (100.00 %)	6 (100.00 %)	6 (100.00 %)	51 (100.00 %)
Blood And Lymphatic System Disorders											
Anaemia	0 (0.00%)	2 (50.00 %)	1 (25.00 %)	2 (50.00 %)	2 (50.00 %)	4 (57.14 %)	3 (60.00 %)	2 (25.00 %)	1 (16.67 %)	2 (33.33 %)	19 (37.25 %)
Granulocytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (42.86 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	4 (7.84%)
Leukocytosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	2 (3.92%)
Leukopenia	1 (33.33 %)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	3 (42.86 %)	5 (100.00 %)	1 (12.50 %)	1 (16.67 %)	3 (50.00 %)	15 (29.41 %)
Lymphopenia	1 (33.33 %)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	2 (50.00 %)	1 (14.29 %)	2 (40.00 %)	3 (37.50 %)	3 (50.00 %)	1 (16.67 %)	15 (29.41 %)
Neutropenia	1 (33.33 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (42.86 %)	4 (80.00 %)	1 (12.50 %)	1 (16.67 %)	3 (50.00 %)	13 (25.49 %)
Thrombocytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	6 (85.71 %)	5 (100.00 %)	2 (25.00 %)	4 (66.67 %)	4 (66.67 %)	22 (43.14 %)
Cardiac Disorders											
Arrhythmia	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Atrial Fibrillation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Cardiac Failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Cardiovascular Disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)

Tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Ear And Labyrinth Disorders											
Tinnitus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Vertigo	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Endocrine Disorders											
Hypothyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Eye Disorders											
Eczema Eyelids	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Visual Impairment	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	1 (16.67 %)	1 (16.67 %)	3 (5.88%)
Gastrointestinal Disorders											
Abdominal Discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Abdominal Distension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	1 (20.00 %)	2 (25.00 %)	0 (0.00%)	0 (0.00%)	4 (7.84%)
Abdominal Pain	1 (33.33 %)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	2 (50.00 %)	0 (0.00%)	2 (40.00 %)	2 (25.00 %)	1 (16.67 %)	0 (0.00%)	9 (17.65%)
Abdominal Pain Upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (42.86 %)	1 (20.00 %)	1 (12.50 %)	2 (33.33 %)	1 (16.67 %)	8 (15.69%)
Ascites	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Constipation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	4 (57.14 %)	3 (60.00 %)	5 (62.50 %)	2 (33.33 %)	1 (16.67 %)	16 (31.37 %)

Diarrhoea	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	2 (28.57 %)	2 (40.00 %)	4 (50.00 %)	1 (16.67 %)	2 (33.33 %)	13 (25.49 %)
Dry Mouth	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Dyspepsia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (25.00 %)	1 (16.67 %)	0 (0.00%)	4 (7.84%)
Dysphagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Eructation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)
Flatulence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Gastric Ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Gastritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Gastrooesophageal Reflux Disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	2 (40.00 %)	0 (0.00%)	2 (33.33 %)	0 (0.00%)	5 (9.80%)
Gingival Bleeding	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)
Inguinal Hernia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Melaena	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	2 (50.00 %)	6 (85.71 %)	3 (60.00 %)	5 (62.50 %)	5 (83.33 %)	4 (66.67 %)	26 (50.98 %)
Reflux Gastritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Salivary Hypersecretion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Toothache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)

Vomiting	0 (0.00%)	2 (50.00 %)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	2 (28.57 %)	4 (80.00 %)	3 (37.50 %)	4 (66.67 %)	3 (50.00 %)	20 (39.22 %)
General Disorders And Administration Site Conditions											
Asthenia	1 (33.33 %)	1 (25.00 %)	0 (0.00%)	1 (25.00 %)	2 (50.00 %)	2 (28.57 %)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	2 (33.33 %)	10 (19.61 %)
Axillary Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Chest Discomfort	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Chest Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)
Chills	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	2 (3.92%)
Effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Fatigue	1 (33.33 %)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	5 (71.43 %)	3 (60.00 %)	4 (50.00 %)	2 (33.33 %)	2 (33.33 %)	18 (35.29 %)
General Physical Health Deterioration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Oedema Peripheral	1 (33.33 %)	1 (25.00 %)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	1 (14.29 %)	1 (20.00 %)	1 (12.50 %)	2 (33.33 %)	0 (0.00%)	9 (17.65%)
Peripheral Swelling	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Pyrexia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	2 (28.57 %)	1 (20.00 %)	1 (12.50 %)	2 (33.33 %)	1 (16.67 %)	8 (15.69%)
Hepatobiliary Disorders											

Hepatic Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (33.33 %)	2 (3.92%)
Hyperbilirubinaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	3 (5.88%)
Immune System Disorders											
Anaphylactic Reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hypersensitivity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Infections And Infestations											
Bacterial Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Cystitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Gastrointestinal Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Influenza	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	3 (37.50 %)	0 (0.00%)	0 (0.00%)	4 (7.84%)
Lower Respiratory Tract Infection	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Nasopharyngitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Oral Candidiasis	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Pertussis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Respiratory Tract Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)

Sepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)
Urinary Tract Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Injury, Poisoning And Procedural Complications											
Contusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Foot Fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Thermal Burn	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Transfusion Reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Upper Limb Fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Investigations											
Alanine Aminotransferase Increased	0 (0.00%)	2 (50.00 %)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	2 (28.57 %)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	8 (15.69%)
Amylase Increased	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	1 (16.67 %)	4 (7.84%)
Aspartate Aminotransferase Increased	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (25.00 %)	2 (50.00 %)	1 (14.29 %)	2 (40.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	8 (15.69%)
Blood Alkaline Phosphatase Increased	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	2 (28.57 %)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	6 (11.76%)
Blood Bilirubin Increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	3 (5.88%)

Blood Calcium Increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Blood Cholesterol Increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Blood Creatine Phosphokinase Increased	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	0 (0.00%)	2 (28.57 %)	0 (0.00%)	2 (25.00 %)	1 (16.67 %)	0 (0.00%)	7 (13.73%)
Blood Creatinine Increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	3 (5.88%)
Blood Triglycerides Increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Body Temperature Increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Electrocardiogra m Qt Prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (5.88%)
Gamma-Glutamyltransfera se Increased	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (14.29 %)	2 (40.00 %)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	6 (11.76%)
Helicobacter Test Positive	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Lipase Increased	0 (0.00%)	0 (0.00%)	1 (25.00 %)	2 (50.00 %)	0 (0.00%)	1 (14.29 %)	1 (20.00 %)	1 (12.50 %)	1 (16.67 %)	1 (16.67 %)	8 (15.69%)
Lymphocyte Count Decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	3 (42.86 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (7.84%)
Neutrophil Count Decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Weight Decreased	1 (33.33 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
White Blood Cell Count Decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (42.86 %)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (7.84%)

White Blood Cell Count Increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Metabolism And Nutrition Disorders											
Cachexia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Decreased Appetite	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	3 (42.86 %)	3 (60.00 %)	3 (37.50 %)	3 (50.00 %)	2 (33.33 %)	16 (31.37 %)
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Gout	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hypercalcaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hypercholesterolaemia	1 (33.33 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (14.29 %)	1 (20.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	5 (9.80%)
Hyperglycaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	3 (5.88%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hyperlipasaemia	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	4 (7.84%)
Hyperlipidaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	2 (3.92%)
Hypertriglyceridaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	2 (28.57 %)	1 (20.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	5 (9.80%)
Hyperuricaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hypoalbuminaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (50.00 %)	1 (14.29 %)	2 (40.00 %)	0 (0.00%)	2 (33.33 %)	1 (16.67 %)	8 (15.69%)

Hypocalcaemia	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	2 (33.33 %)	0 (0.00%)	5 (9.80%)
Hypokalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Hypomagnesaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (14.29 %)	1 (20.00 %)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	4 (7.84%)
Hypophosphataemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	1 (14.29 %)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (7.84%)
Musculoskeletal And Connective Tissue Disorders											
Arthralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	1 (20.00 %)	1 (12.50 %)	1 (16.67 %)	0 (0.00%)	4 (7.84%)
Back Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (50.00 %)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	4 (7.84%)
Bone Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Muscular Weakness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Musculoskeletal Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)
Neck Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Pain In Extremity	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	1 (12.50 %)	0 (0.00%)	1 (16.67 %)	4 (7.84%)
Spinal Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Neoplasms Benign, Malignant And Unspecified											

(Incl Cysts And Polyps)											
Basal Cell Carcinoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Lipoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Melanocytic Naevus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Tumour Pain	0 (0.00%)	2 (50.00 %)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	1 (20.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	5 (9.80%)
Nervous System Disorders											
Dizziness	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	1 (20.00 %)	1 (12.50 %)	2 (33.33 %)	0 (0.00%)	6 (11.76%)
Dysgeusia	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (25.00 %)	2 (33.33 %)	2 (33.33 %)	8 (15.69%)
Headache	1 (33.33 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	1 (20.00 %)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	4 (7.84%)
Hypersomnia	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Hypotonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (25.00 %)	0 (0.00%)	2 (33.33 %)	4 (7.84%)
Neuralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Paraesthesia	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (25.00 %)	0 (0.00%)	0 (0.00%)	3 (5.88%)
Somnolence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (16.67 %)	2 (3.92%)
Syncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Psychiatric Disorders											

Anxiety	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	1 (16.67 %)	3 (5.88%)
Depression	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hallucination	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Insomnia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Sleep Disorder	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Renal And Urinary Disorders											
Acute Kidney Injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Dysuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hydronephrosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Leukocyturia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Pollakiuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Proteinuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Renal Colic	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Renal Failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	1 (12.50 %)	1 (16.67 %)	0 (0.00%)	3 (5.88%)
Reproductive System And Breast Disorders											

Testicular Oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Respiratory, Thoracic And Mediastinal Disorders											
Cough	1 (33.33 %)	1 (25.00 %)	1 (25.00 %)	0 (0.00%)	1 (25.00 %)	1 (14.29 %)	2 (40.00 %)	4 (50.00 %)	0 (0.00%)	2 (33.33 %)	13 (25.49 %)
Dysphonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Dyspnoea	1 (33.33 %)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	1 (25.00 %)	1 (14.29 %)	2 (40.00 %)	1 (12.50 %)	1 (16.67 %)	1 (16.67 %)	10 (19.61 %)
Dyspnoea Exertional	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (25.00 %)	1 (16.67 %)	1 (16.67 %)	4 (7.84%)
Epistaxis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (16.67 %)	2 (3.92%)
Haemoptysis	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hiccups	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hypoxia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Oropharyngeal Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Pleural Effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Rhinorrhoea	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	2 (3.92%)
Skin And Subcutaneous Tissue Disorders											

Actinic Keratosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Decubitus Ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Dermatitis Acneiform	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	1 (1.96%)
Dermatitis Contact	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Dry Skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (1.96%)
Hair Colour Changes	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hirsutism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hyperhidrosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Petechiae	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	2 (3.92%)
Pruritus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	2 (3.92%)
Rash	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	1 (12.50 %)	0 (0.00%)	1 (16.67 %)	6 (11.76%)
Vascular Disorders											
Circulatory Collapse	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Deep Vein Thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Embolism	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)
Haematoma	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.92%)

Hypertension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Orthostatic Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)
Thrombophlebitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.96%)

Conclusion:

- The MTD was not determined in this study, as enrollment was prematurely halted during the dose escalation part. The decision to halt the recruitment was not a consequence of any safety concern.
- No complete response (CR) was observed at any dose. One subject in the 300 mg (Regimen 1) had partial response (PR). Stable disease was observed in 19 subjects (37.3%).
- At the final analysis, overall safety profile of CGM097 remained consistent with the primary clinical study report (CSR) analysis with most frequently reported suspected AEs being gastro-intestinal (nausea, vomiting, diarrhea) and hematological (thrombocytopenia, leukopenia, neutropenia) and fatigue. No new safety signals were reported.

Date of Clinical Trial Report

18-Mar-2021